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Assessing the Readability and Patient Comprehension of Rheumatology Medicine Information Sheets: A Health Literacy Study

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Abstract (word count 295)

Objectives. Patients are often provided with Medicine Information Sheets (MIS). However, up to 60% of patients have low health literacy. The recommended readability level for health-related information is ≤ Grade 8. We sought to assess the readability of MIS given to patients by Rheumatologists in Australia, the United Kingdom (UK) and Canada, and to examine patient comprehension of these documents.

Design. Cross-sectional study.

Setting. Community-based regional Rheumatology practice.

Participants. Random sample of patients attending the Rheumatology practice.

Outcome measures. Readability of MIS was assessed using readability formulae [Flesch Reading Ease formula, Simple Measure of Gobbledygook (SMOG) scale, and the Gunning Fog scale]. Literal comprehension was assessed by asking patients to read various MIS and immediately answer five simple multiple choice questions about the MIS.

Results. The mean grade level for the MIS from Australia, the UK, and Canada was 11.6±0.1, 11.8±0.1 and 9.7±0.1 respectively. The Flesch Reading Ease score for the Australian (50.8±0.6) and UK (48.5±1.5) MIS classified the documents as "fairly difficult" to "difficult". The Canadian MIS (66.1±1.0) were classified as "standard". Overall, 10-79% of patients failed to correctly answer all five simple multiple choice questions assessing MIS comprehension.

Conclusions. The readability of MIS used by Rheumatologists in Australia and the UK exceeds Grade 8 level. This may explain why patient literal comprehension of these documents was poor. Simpler, shorter MIS with pictures and info-graphics may improve

patient comprehension. This may lead to improved medication adherence and better health outcomes.

Study strengths and limitations

- Readability of Medicine Information Sheets (MIS) from three countries (Australia, UK and Canada) was assessed.
- While readability formulae only measure the number/complexity of words/sentences, patient literal comprehension of MIS was also assessed.
- The study population was from a regional community and may not be representative of a more urban population.

Introduction

Health literacy is defined as the "capacity to obtain, process and understand written and oral health information and services needed to make appropriate health decisions".[1] Low health literacy has been associated with poorer health-related knowledge, increased hospitalisations, reduced immunizations, poorer health status and higher mortality.[2] Patients with poor health literacy are less likely to successfully manage chronic disease[3] and have greater difficulty following instructions for prescription medications,[4] Higher health literacy has been associated with increased medication adherence.[5 6]

Although the importance of health literacy and patient-physician communication on health outcomes is well-recognised, many patients have difficulty understanding what their physicians tell them.[7] Immediately after leaving a consultation with their specialist, patients were able to recall less than half the information just provided to them.[8 9] The provision of written health information in addition to verbal information significantly increases patient knowledge and satisfaction.[10] Written information may also lead to increased adherence with treatment. [9] However, designing effective written health information remains challenging due to differences in patient literacy levels.

The recommended level of reading difficulty/readability for health-related written material is up to eighth grade level.[11 12] Yet, written health information provided to patients is often too difficult.[13-15] While there is greater access to health-related information on the internet, this often also exceeds recommended readability levels.[16 17]

Literacy levels in Australia are poor, with up to 60% of the population having low literacy skills.[18 19] The International Adult Literacy Survey (IALS) found 48% of Canadians fall into the lowest two literacy categories and 26% lack skills to effectively participate in society.[20] In the United Kingdom (UK), one in six adults read below the level of an 11-year old.[21] A study

of over 200 rural and urban Australian Rheumatology patients found that 15% of patients had low health literacy and up to one third of patients incorrectly followed dosing instructions for common Rheumatology drugs.[19] Ten percent of patients with rheumatoid arthritis (RA) who attended an urban community-based Australian Rheumatology practice had inadequate/marginal functional health literacy or a reading age at or below the United States (US) high school grade equivalent of 7th-8th grade.[22] Up to 24% of Rheumatology patients at a US medical centre had a reading level of 8th grade or less.[23] One in six Rheumatology patients at a Scottish hospital were illiterate and struggled to understand education materials and prescription labels.[24] These findings are concerning, as Rheumatologists often use medications such as methotrexate or expensive biologic therapies with severe side effects, even death[25], if taken incorrectly.

Given the importance of health literacy and its relationship to health outcomes and medication adherence, we sought to assess: i) the readability of patient Medication Information Sheets (MIS) given to patients by Australian rheumatologists, and ii) patient comprehension of these documents. We also compared the readability of the Australian MIS to similar documents given to Rheumatology patients in the UK and Canada.

Methods

Assessment of readability

Text from the MIS of commonly prescribed Rheumatology medications available on the Australian Rheumatology Association (ARA) website[26] was imported into a Microsoft Word document and readability assessed using Readability Studio™ (Oleander Software, USA).[15 27 28] Non-essential text including logos, headers, footers, hyperlinks and contact information was deleted prior to analysis as these may have adversely affected readability scores.

Readability was assessed using a range of measures such as the Flesch Reading Ease formula, Simple Measure of Gobbledygook (SMOG) scale, and the Gunning Fog scale. The Flesch Reading Ease formula calculates an index score of a document based on sentence length and number of syllables. Scores range between 0-100 with a high score indicating the document was easier to read.[29] The SMOG formula calculates the grade level and reader age based on complex word density and assigns a grade level (4th grade to college level).[28 30] The Gunning Fog formula calculates the grade level and reader age based on number of sentences and complex words.[31]

The readability of 10 corresponding MIS published in the UK by Arthritis Research UK[32] and from Canada published by Rheuminfo[33] was also assessed as above.

Assessment of literal comprehension

Coffs Harbour is a growing regional city of 70 000 people located half-way between the Australian capital cities of Sydney and Brisbane. Its medical specialists provide services to another 50 000 people from the surrounding area. Rheumatology services are provided by two Rheumatologists (PKKW and HB) under the auspices of the Mid-North Coast Arthritis Clinic (MNCAC). The MNCAC has over 16 000 patients on its computerised database. A random sample of patients referred to the MNCAC was asked to read one ARA MIS[26] containing information about one of the following medications which the patient was unfamiliar with (see supplementary material): methotrexate (MTX), non-steroidal anti-inflammatory drugs (NSAIDs), adalimumab (ADA), abatacept (ABA) or prednisone. All patients scheduled for a consulting day were contacted via telephone by an investigator (MO or ET). Patients (n=261) were asked whether they were interested in study participation to determine what they understood after reading information from the doctor. Responses are outlined in Figure 1. Those who expressed interest in study participation were mailed

information about the study and a consent form to be returned in a stamped pre-addressed envelope (n=142). Those who agreed to participate were assessed on the day of the planned consultation (n=95). These was no difference in gender or age between those included compared to those not contactable (data not shown). Comprehension was assessed by asking the patient to answer five multiple choice questions (see supplementary material) about the content of the ARA MIS they had just read. These questions were designed by two Rheumatologists (PKKW, HB), a Rheumatology Nurse (DF) and an education academic with expertise in literacy (JJ). The questions were trialled on small focus groups of patients. A time limit of 15 minutes in a quiet well-lit room was provided. If needed, study participants could refer back to the MIS while answering the questions. Informed consent was obtained from all study participants.

Statistical analyses

Descriptive summary statistics (mean ± sem and median ± interquartile range, as appropriate) were used to analyse parameters. Student's t-test was used to compare means of normally distributed parameters. As some variables were skewed, the Mann-Whitney U test was used to compare medians of groups. For all statistical tests, $p<0.05$ was considered significant. Data analysis was undertaken using GraphPad Prism 6 (GraphPad Software Inc, USA).[34]

Ethics

Approval as a low/negligible risk project was obtained from the New South Wales North Coast Human Research Ethics Committee (NCNSW HREC No LNR 150).

Results

Assessment of readability

The mean grade level for the ARA MIS calculated using Readability Studio™ was 11.6± 0.1 with a mean reading age of 16.6 ± 0.1 years (Table 1). The mean Flesch Reading Ease score of 50.8 ± 0.6 indicated the ARA MIS were either "fairly difficult" or "difficult"[28] (Table 1). Overall, difficult sentences (>22 words) and complex words (≥ 3 syllables) made up 9.0% and 18.4% of the text, respectively (Table 2).

As the validity of the above readability assessment measures has been questioned due to over-reliance on sentence and word length[35 36], we proceeded to assess patient literal comprehension of the ARA MIS.

Assessment of comprehension

A total of 261 patients were contacted, with 95 study participants (Figure 1). Approximately half the patients failed to correctly answer all five questions regarding two commonly prescribed biologics, ADA and ABA, and almost 40% of patients failed to correctly answer all five simple questions assessing literal comprehension of the MTX MIS (Table 3). Questions assessing comprehension of the prednisone MIS were answered correctly by most participants (91%). Of concern, only 21.4% (6/28) of patients correctly answered all questions assessing comprehension of the NSAID MIS. Responses to the five NSAID questions are shown in Figure 2.

Comparison of readability scores for Australian, UK and Canadian MIS

Given our findings, we sought to determine using Readability Studio™ what the readability scores were for MIS used in other countries. The mean grade level for 10 of the commonly

used UK MIS was 11.8 ± 0.1 with a reader age of 16.9 ± 0.1 years (Table 4). The mean Flesch Reading Ease score was 48.5 ± 1.5 - classified as "difficult". Readability of the Canadian MIS was easier with a mean grade level of 9.7 ± 0.1 and mean reader age of 14.8 ± 0.1 years (Table 5). The Flesch Reading Ease score for the Canadian MIS was 66.1 ± 1.0 - classified as "standard".[28]

There was no significant difference in grade levels between the Australian and UK MIS (p=0.10). However, the mean grade level of the Canadian MIS (9.7 ± 0.1) was less than the corresponding Australian MIS (11.7 ± 0.1, p<0.0001).

The Australian MIS were the longest (mean number of words = 1474.1 ± 44.6) (Table 2) compared with the UK (mean number of words = 922.4 ± 109.6) (Table 6a) and Canadian MIS (mean number of words = 297.7 ± 19.2) (Table 6b). The Australian MIS also had the highest percentage of complex words (18%), compared with the UK (16%) and Canadian (14%) MIS.

Discussion

Our results showed that the readability of commonly used Rheumatology MIS given to patients in both Australia and the UK exceeded eighth grade level – the recommended level for a low-literacy population.[11 12 37] The Canadian MIS assessed were easier to read, although remained slightly above eighth grade level. We found that in a population of patients attending a regional private Rheumatology practice where only 20% of participants possessed a university degree, patient comprehension of the Australian MIS was poor, with up to 79% of patients failing to correctly answer all five simple questions assessing literal comprehension of commonly prescribed Rheumatology medications. This, along with high

readability scores, suggested that current ARA MIS may be too difficult for many patients to understand. While comprehension of the Canadian MIS was not performed, this would provide useful information about the effectiveness of these easier-to-read materials.

The Canadian MIS were simpler, more "readable" and included pictures. Many studies have shown that incorporating pictograms into patient information material improves patient comprehension.[38-43] One study of 60 patients showed that pictograms improved comprehension of patient information sheets from 40% to 93%.[39] Another strategy to improve MIS readability is to shorten the document. However, a shorter, simpler MIS may remove important information and be inadequate for patients with high literacy. Yet, studies have shown both low and high literacy groups recalled information best when the text was easy.[44] These findings suggested that written materials designed for patients with low health literacy may also be useful for a general audience.

It is important to consider the primary purpose of providing written health-related information to a patient. Although the provision of information as part of patient education to facilitate informed patient treatment decisions is important, worry over potential medicolegal exposure from a treatment-related adverse event continues to drive complexity of written materials.[45]

Potential limitations of this study include the type of population studied and the measures used to assess readability. All study participants were from Coffs Harbour, a large regional community on the east coast of Australia. Although one may expect literacy levels to be lower in a rural setting, previous work from our centre showed no difference in health literacy between our patients compared to an urban Rheumatology private practice in a capital city.[19]

There has been criticism of readability formulae such as the Flesch Reading Ease formula, SMOG scale and the Gunning Fog scale.[36 46-48] Readability formulae are usually based solely

on word length or syllable number. They may therefore fail to adjust for patient familiarity with vocabulary associated with their illness, therefore over-estimating the difficulty of written information when read by patients familiar with their disease.[46 48] Furthermore, by necessity, health-related written material uses text characterised by polysyllabic technical jargon, which elevates readability formulae scores.[49] For example, exchanging "adalimumab" for "Humira" in the Australian MIS increases the Flesch Reading ease score from 46 to 50 and reduces the Gunning Fog score from 12.7 to 12.5. (The SMOG remains unchanged at 12.8). Readability formulae do not usually consider visual and design factors which may influence MIS readability or patient comprehension.[50 51] While the Flesch Reading Ease formula tends to over-estimate readability of health-related material due to its lower level of expected comprehension criteria[47], the SMOG formula is appropriate for assessing health-related written information as it has been validated against 100% comprehension.[47] One approach to addressing these limitations is the use of a more holistic linguistic framework for assessing written patient information which incorporates structure, factual content, and visual aspects of the material as well as the relationship between writer and reader.[36] This method has been validated using rheumatoid arthritis medication leaflets in an Australian cohort of patients with rheumatoid arthritis. [52] However, the education level of patients in that study exceeded that seen in our cohort, with 17/27 (63%) having completed tertiary studies compared to 19/95 (20%) in ours.

In view of the potential limitations of readability formulae, we were careful to assess patient literal comprehension of various ARA MIS. As suggested by the relatively low readability scores of the ARA MIS, patient literal comprehension of a selection of the ARA MIS was found to be poor. Due to the simplicity of the five questions posed to the patients, we hoped a satisfactory score would be correct answers to all five questions. However, this only occurred in 21% of patients for NSAIDs and 40-60% of patients for the MTX, ADA and ABA MIS.

We hope the results of this study will encourage clinicians from Rheumatology and all other specialities to consider the health literacy of their patients and readability of the written information they provide, particularly given the potential of technology to improve patient education.

Conclusion

Medication information sheets currently used by many Rheumatologists in Australia and the UK exceed eighth grade level – the recommended level for a low-literacy population. This may explain why patient comprehension of the information contained in these materials is limited. Comprehension may be improved using simpler, shorter words and sentences with greater use of pictures and info-graphics. This may lead to greater patient medication adherence, understanding of their condition, and reduced medication-related errors. It is hoped our findings will encourage all health care professionals to consider the appropriateness of written healthcare material provided to patients. The health literacy of patients should always be considered when communicating a management plan.

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Author contributions

MO and ET were responsible for data acquisition. MO was responsible for drafting the manuscript and data analysis under the supervision of PW. PW, JJ, DF and HB conceived and designed the study. All authors contributed to interpretation of data and revision of the manuscript and approve the final manuscript.

Competing interests

The authors declare no competing interests.

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Figure 1: Inclusions and exclusions

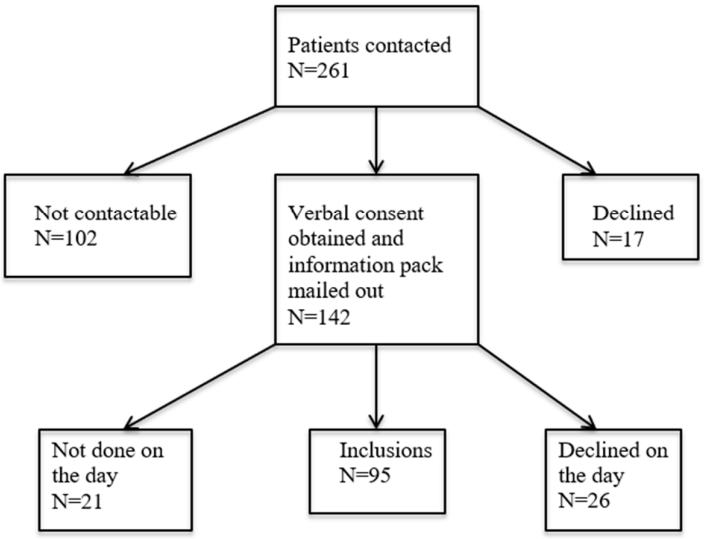

Figure 2: Answers to NSAID questions

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

(note – correct answer ticked)

Non-steroidal anti-inflammatory drugs (NSAIDs) include medications such as Nurofen, Brufen, Voltaren, Naprosyn and Celebrex.

1) Non-steroidal anti-inflammatory drugs (NSAIDs)

✓a) reduce joint pain, swelling and stiffness

b) prevent damage to your joints

c) strengthen your bones

d) will cure your arthritis

No. with correct answer 26/28 (93%)

2) Non-steroidal anti-inflammatory drugs (NSAIDs)

a) can be combined with other NSAIDs

b) can be continued long-term without review

✓c) often cause gut side effects such as nausea, vomiting and bleeding

d) should be continued during surgery

No. with correct answer 17/28 (61%)

3) Non-steroidal anti-inflammatory drugs (NSAIDs)

✓a) may increase the risk of heart attack and stroke

b) prevent attacks of arthritis

c) have no effect on blood pressure

d) are safe in someone with kidney problems

No. with correct answer 24/28 (86%)

4) Non-steroidal anti-inflammatory drugs (NSAIDs) should be used

a) for 4 weeks only

✓b) for the shortest time possible

c) until the script runs out

d) for however long to get rid of the pain

No. with correct answer 12/28 (43%)

5) Bleeding from inside the gut while taking a non-steroidal anti-inflammatory drug (NSAID)

a) can be completely prevented by taking the NSAID with food

b) should stop if you continue taking the NSAID

c) doesn't cause any problems and can be ignored

✓d) can be associated with abdominal pain and indigestion

No. with correct answer 14/28 (50%)

Table 1: Readability scores for Australian Rheumatology Association Medicine Information Sheets

Medicationn	Flesch Reading Ease * (0-100)	FORCAST# grade level	FORCAST# reader age (years)	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level	Mean reader age (years)
Abatacept	49	11.2	16-17	12.3	17-18	12.4	17-18	12.0	17.2
Adalimumab	46	11.2	16-17	12.7	17-18	12.8	17-18	12.2	17.2
Allopurinol	53	10.8	15-16	10.5	15-16	11.5	16-17	10.9	15.8
Apremilast	56	10.6	15-16	11.3	16-17	11.7	16-17	11.2	16.2
Azathioprine	50	10.7	15-16	11.6	16-17	12.2	17-18	11.5	16.5
Bisphosphonates IV	49	11.1	16-17	12.1	17-18	12.2	17-18	11.8	17.2
Bisphosphonates Oral	49	11.2	16-17	12.2	17-18	12.3	17-18	11.9	17.2
Bosentan	59	10.4	15-16	11.0	16-17	11.5	16-17	11.0	16.2
Certolizumab	46	11.1	16-17	12.8	17-18	12.9	17-18	12.3	17.2
Colchicine	53	11.1	16-17	11.7	16-17	11.7	16-17	11.5	16.5
Cyclophosphamide	53	10.7	15-16	10.8	15-16	11.8	16-17	11.1	15.8
Cyclosporin	54	10.7	15-16	11.8	16-17	12.0	17-18	11.5	16.5
Denosumab	50	11.0	16-17	11.9	16-17	12.1	17-18	11.7	16.8
Etanercept	48	11.1	16-17	12.7	17-18	12.8	17-18	12.2	17.2
Febuxostat	54	10.7	15-16	10.8	15-16	11.7	16-17	11.1	15.8
Golimumab	48	11.1	16-17	12.8	17-18	12.8	17-18	12.2	17.2
Hyaluronic Acid	51	11.1	16-17	11.8	16-17	11.9	16-17	11.6	16.5
Hydroxychloroquine	49	10.9	15-16	11.6	16-17	11.7	16-17	11.4	16.2
Infliximab	49	11.1	16-17	12.5	17-18	12.6	17-18	12.1	17.2
Leflunomide	54	10.7	15-16	11.6	16-17	12.2	17-18	11.5	16.5
Methotrexate	52	10.9	15-16	11.4	16-17	12.3	17-18	11.5	16.5
Mycophenolate	50	11.0	16-17	11.6	16-17	12.5	17-18	11.7	16.8
NSAIDs	58	10.6	15-16	11.0	16-17	11.3	16-17	11.0	16.2
Prednisone	51	10.9	15-16	11.2	16-17	11.9	16-17	11.3	16.2
Rituximab	48	11.3	16-17	12.3	17-18	12.5	17-18	12.0	17.2
Sulfasalazine	50	10.9	15-16	11.4	16-17	11.9	16-17	11.4	16.2
Teriparatide	49	10.9	15-16	11.6	16-17	12.1	17-18	11.5	16.5
Tocilizumab	47	11.1	16-17	12.0	17-18	12.5	17-18	11.9	17.2
Tofacitinib	46	11.1	16-17	12.1	17-18	12.2	17-18	11.8	17.2
Ustekinumab	54	10.8	15-16	11.5	16-17	12.0	17-18	11.4	16.5
Mean	**50.8**	**10.9**		**11.8**		**12.1**		**11.6**	**16.6**
SEM	**0.6**	**0.0**		**0.1**		**0.1**		**0.1**	**0.1**

Abbreviations

* Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
[#] FORCAST (named after the authors FORd, CAylor, STicht)
[**] SMOG = Simple Measure Of Gobbledygook

Table 2: Word and sentence statistics for Australian Rheumatology Association Medicine Information Sheets

Medication	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	Total no. of words	No. of complex** words
Abatacept	133	8 (5%)	12.1	1612	314 (19.5%)
Adalimumab	125	11 (8.8%)	12.6	1576	315 (20%)
Allopurinol	124	10 (8.1%)	12.2	1507	252 (16.7%)
Apremilast	92	9 (9.8%)	11.9	1095	184 (16.8%)
Azathioprine	118	9 (7.6%)	13	1539	273 (17.7%)
Bisphosphonates IV	95	11 (11.6%)	12.6	1199	217 (18.1%)
Bisphosphonates Oral	112	11 (9.8%)	13	1456	277 (19%)
Bosentan	107	11 (10.3%)	11.4	1219	214 (17.6%)
Certolizumab	125	12 (9.6%)	13	1624	320(19.7%)
Colchicine	123	8 (6.5%)	11.6	1426	260 (18.2%)
Cyclophosphamide	118	12 (10.2%)	12.4	1469	266 (18.1%)
Cyclosporin	102	8 (7.8%)	12.1	1235	227 (18.4%)
Denosumab	110	10 (9.1%)	12	1317	243 (18.5%)
Etanercept	124	11 (8.9%)	13.1	1621	321 (19.8%)
Febuxostat	120	12 (10%)	12.4	1484	255 (17.2%)
Golimumab	123	12 (9.8%)	12.9	1588	316 (19.9%)
Hyaluronic Acid	81	4 (4.9%)	11.3	919	181 (19.7%)
Hydroxychloroquine	87	9 (10.3)	12	1046	184 (17.6%)
Infliximab	138	13 (9.4%)	13.1	1807	344 (19%)
Leflunomide	111	10 (9%)	12.9	1427	254 (17.8%)
Methotrexate	156	20 (12.8%)	13.4	2097	375 (17.9%)
Mycophenolate	141	15 (10.6%)	12.1	1712	334 (19.5%)
NSAIDs	137	14 (10.2%)	12.8	1750	266 (15.2%)
Prednisone	128	12 (9.4%)	13	1668	292 (17.5%)
Rituximab	132	9 (6.8%)	12.3	1627	318 (19.5%)
Sulfasalazine	124	9 (7.3%)	12.1	1497	276 (18.4%)
Teriparatide	114	13 (11.4%)	11.5	1310	238 (18.2%)
Tocilizumab	130	12 (9.2%)	12.7	1654	311 (18.8%)
Tofacitinib	111	7 (6.3%)	12	1336	249 (18.6%)
Ustekinumab	114	8 (7%)	12.3	1406	259 (18.4%)
Mean	**118.5**	**10.7 (9.0%)**	**12.4**	**1474.1**	**271.2 (18.4%)**
SEM	**3.0**	**0.5**	**0.1**	**44.6**	**9.0**

*Difficult sentence: ≥22 words; **Complex word: ≥3 syllables

Table 3: Assessment of patient literal comprehension (n=95 patients)

age (yrs, mean ± sem)	60.0±13.2
sex (F/M)	71/24
highest level of education	**no. (%)**
≤Yr 10	39 (41)
Yr 10-12	15 (16)
sub-degree, eg TAFE*, apprenticeship	22 (23)
university degree	19 (20)
median total score (max=5)	4
no. with all correct answers (ie, 5/5)	**no. (%)**
adalimumab	9/21 (43)
MTX	7/11 (63.6)
NSAIDs	6/28 (21.4)
prednisone	10/11 (90.9)
abatacept	13/24 (54.2)

Abbreviations
*TAFE= Technical and Further Education

MTX= methotrexate

NSAID=non-steroidal anti-inflammatory drugs

Table 4: Readability scores for Arthritis Research United Kingdom Medicine Information Sheets

Medication	Flesch Reading Ease* (0-100)	FORCAST# grade level	FORCAST# reader age	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level	Mean reader age (years)
Abatacept	46	10.9	15-16	13.1	18-19	13.2	18-19	12.4	17.5
Adalimumab	47	11.1	16-17	12.1	17-18	12.5	17-18	11.9	17.2
Bisphosphonates	53	11.1	16-17	11.9	16-17	12.3	17-18	11.8	16.8
Denosumab	42	11.7	16-17	12	17-18	12.6	17-18	12.1	17.2
Etanercept	49	11	16-17	11.9	16-17	12.4	17-18	11.8	16.8
Hydroxychloroquine	41	11.2	16-17	12.5	17-18	12.5	17-18	12.1	17.2
Leflunomide	53	10.8	15-16	11.9	16-17	12.2	17-18	11.6	16.5
Methotrexate	51	10.8	15-16	12.1	17-18	12.4	17-18	11.8	16.8
Prednisolone	55	11.1	16-17	11.3	16-17	11.6	16-17	11.3	16.5
Sulfasalazine	48	10.8	15-16	11.9	16-17	12.2	17-18	11.6	16.5
Mean	**48.5**	**11.1**		**12.1**		**12.4**		**11.8**	**16.9**
SEM	**1.5**	**0.1**		**0.1**		**0.1**		**0.1**	**0.1**

Abbreviations

*Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
FORCAST (named after the authors FORd, CAylor, STicht)
**SMOG = Simple Measure Of Gobbledygook

Table 5: Readability scores for Canadian Medicine Information Sheets

Medication	Flesch Reading Ease * (0-100)	FORCAST# grade level	FORCAST# reader age (years)	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level	Mean reader age (years)
Abatacept	65	10	15-16	8.5	13-14	10.3	15-16	9.6	14.8
Adalimumab	61	10.1	15-16	9.8	14-15	10.2	15-16	10	15.2
Bisphosphonates	63	10.2	15-16	9.5	14-15	10	15-16	9.9	15.2
Denosumab	66	9.6	14-15	9.6	14-15	10	15-16	9.7	14.8
Etanercept	64	10.1	15-16	9.9	14-15	10.3	15-16	10.1	15.2
Hydroxychloroquine	72	8.8	13-14	8.4	13-14	9.5	14-15	8.9	13.8
Leflunomide	67	9.9	14-15	9.4	14-15	9.9	14-15	9.7	14.5
Methotrexate	66	9.8	14-15	9.5	14-15	10.1	15-16	9.8	14.8
Prednisolone	69	10.2	15-16	9.8	14-15	10.1	15-16	10	15.2
Sulfasalazine	68	9.3	14-15	9.1	14-15	9.7	14-15	9.4	14.5
Mean	**66.1**	**9.8**		**9.4**		**10.0**		**9.7**	**14.8**
SEM	**1.0**	**0.1**		**0.2**		**0.1**		**0.1**	**0.1**

Abbreviations

* Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
# FORCAST (named after the authors FORd, CAylor, STicht)
**SMOG = Simple Measure Of Gobbledygook

Table 6: Word and sentence statistics for a) United Kingdom; and b) Canadian Medicine Information Sheets

a) United Kingdom

Drug	No. of sentences	No. of difficult* sentences	Av. sentence length (no. of words)	No. of words	No. of complex** words
Abatacept	66	18 (27%)	17.1	1130	206 (18%)
Adalimumab	71	10 (14%)	15.3	1086	191 (18%)
Bisphosphonates	36	10 (28%)	15.7	566	92 (16%)
Denosumab	8	2 (25%)	14.4	115	22 (19%)
Etanercept	81	16 (20%)	15.8	1282	214 (17%)
Hydroxychloroquine	60	13 (22%)	15.3	916	159 (17%)
Leflunomide	63	12 (19%)	16.1	1016	157 (15%)
Methotrexate	75	13 (17%)	16.2	1212	193 (16%)
Prednisolone	60	15 (25%)	17	1020	131 (13%)
Sulfasalazine	53	12 (23%)	16.6	881	132 (15%)
Mean	**57.3**	**12.1 (21%)**	**15.95**	**922.4**	**149.7 (16%)**
SEM	**6.7**	**1.4**	**0.3**	**109.6**	**18.7**

b) Canadian

Drug	No. of sentences	No. of difficult* sentences	Av. sentence length (no. of words)	No. of words	No. of complex** words
Abatacept	25	0	11.1	278	38 (14%)
Adalimumab	31	0	11	341	47 (14%)
Bisphosphonates	30	0	10	301	41 (14%)
Denosumab	24	0	10.3	246	34 (14%)
Etanercept	31	0	10.9	339	48 (14%)
Hydroxychloroquine	21	0	9.3	195	23 (12%)
Leflunomide	34	0	10	339	46 (14%)
Methotrexate	32	0	11.2	357	47 (13%)
Prednisolone	36	0	10.1	363	53 (15%)
Sulfasalazine	21	0	10.4	218	27 (12%)
Mean	**28.5**	**0**	**10.43**	**297.7**	**40.4 (14%)**
SEM	**1.7**	**0.0**	**0.2**	**19.2**	**3.1**

*Difficult sentence: ≥22 words; **Complex word: ≥3 syllables

MID NORTH COAST Arthritis Clinic

Please tick (☐) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Methotrexate

1) Methotrexate
a) reduces joint swelling only
b) is a pain killer only
c) will strengthen your bones
d) reduces damage to your joints

2) Methotrexate will
a) work immediately
b) take one year to work
c) take some weeks to work
d) not work unless given as an injection

3) Methotrexate is taken
a) once a day
b) once a week
c) once a month
d) once every 6 months

4) Folic acid is a natural vitamin taken with Methotrexate to
a) reduce pain
b) give you more energy
c) reduce the side effects of Methotrexate
d) stop the arthritis

5) Methotrexate should be taken
a) indefinitely if there are no serious side effects
b) until the script runs out
c) until you feel better
d) for 4 weeks only

(Correct answers based on Patient Information Sheet:
1d, 2c, 3b, 4c, 5a – Not to be included in copy given to patients)

Please tick (□) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Prednisone/Prednisolone/corticosteroids/cortisone all refer to the same drug.

1) Prednisone
a) cures arthritis at high doses
b) reduces joint pain, inflammation and joint swelling
c) makes your muscles bigger
d) makes your bones stronger

2) Prednisone
a) can be stopped suddenly with no problems
b) should be stopped if you get an infection
c) should not be stopped suddenly
d) is a very safe drug and you can change the dose yourself

3) Prednisone works
a) within a few days
b) only in combination with other arthritis medication
c) only if taken long-term
d) by irreversibly suppressing your immune system

4) Prednisone
a) should be stopped in pregnancy
b) can cause thin bones
c) does not affect blood sugar levels
d) helps you lose weight

5) Prednisone
a) should be stopped just before surgery
b) should not be taken with other arthritis medications
c) needs to be taken for the rest of your life
d) is often able to be stopped once the arthritis is controlled

(Correct answers based on Patient Information Sheet:
1b, 2c, 3a, 4b, 5d – Not to be included in copy given to patients)

Please tick (☐) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Adalimumab is also called Humira.

1) Humira
a) is a pain killer
b) reduces damage to your joints
c) will strengthen your bones
d) just reduces joint swelling

2) Humira will
a) work immediately
b) take one year to work
c) take some weeks to work
d) not work unless you take other arthritis medication

3) Humira is taken
a) once a day
b) only when the arthritis flares
c) once every 2 weeks
d) once every 6 months

4) Humira should be continued
a) unless advised by your doctor to stop
b) until the script runs out
c) until you feel better
d) for 4 weeks only

5) If you are taking Humira and get an infection which isn't getting better
a) try some tumeric
b) double the dose of Humira
c) just take some antibiotics
d) stop the Humira

(Correct answers based on Patient Information Sheet:
1b, 2c, 3c, 4a, 5d – Not to be included in copy given to patients)

Please tick (☐) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Non-steroidal anti-inflammatory drugs (NSAIDs) include medications such as Nurofen, Brufen, Voltaren, Naprosyn and Celebrex.

1) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) reduce joint pain, swelling and stiffness
b) prevent damage to your joints
c) strengthen your bones
d) will cure your arthritis

2) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) can be combined with other NSAIDs
b) can be continued long-term without review
c) often cause gut side effects such as nausea, vomiting and bleeding
d) should be continued during surgery

3) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) may increase the risk of heart attack and stroke
b) prevent attacks of arthritis
c) have no effect on blood pressure
d) are safe in someone with kidney problems

4) Non-steroidal anti-inflammatory drugs (NSAIDs) should be used
a) for 4 weeks only
b) for the shortest time possible
c) until the script runs out
d) for however long to get rid of the pain

5) Bleeding from inside the gut while taking a non-steroidal anti-inflammatory drug (NSAID)
a) can be completely prevented by taking the NSAID with food
b) should stop if you continue taking the NSAID
c) doesn't cause any problems and can be ignored
d) can be associated with abdominal pain and indigestion

(Correct answers based on Patient Information Sheet:
1a, 2c, 3a, 4b, 5d – Not to be included in copy given to patients)

Please tick (☐) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Abatacept (Orencia)

1) Abatacept will
a) reduce joint swelling only
b) act as a pain killer only
c) strengthen your bones
d) reduce joint pain, swelling and stiffness in your joints

2) Abatacept will
a) work immediately
b) take one year to work
c) take some weeks to work
d) work only intermittently

3)Abatacept is given via a subcutaneous injection
a) once a day
b) once a week
c) once a month
d) once every 6 months

4) Abatacept works by
a) blocking pain
b) blocking T-cell responses to reduce inflammation
c) making you feel calm
d) making you more alert

5) While on Abatacept you should
a) be monitored regularly
b) take the medication until the script runs out
c) take the medication until you feel better
d) take the medication for 4 weeks only

(Correct answers based on Patient Information Sheet:
1d, 2c, 3b, 4b, 5a – Not to be included in copy given to patients)

Australian Rheumatology Association

Arthritis AUSTRALIA

PATIENT INFORMATION ON

ABATACEPT

(Brand name: Orencia)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition and detect unwanted effects**
- **other precautions you should take while you are taking abatacept**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking abatacept you must see your rheumatologist regularly to ensure the treatment is working and to minimise any possible side effects.
- If you stop abatacept for any reason you must contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.
- If you are worried about any side effects you should contact your rheumatologist as soon as possible.
- If you are injecting abatacept under the skin (subcutaneously) remember to change the injection site each time.
- It is important to tell your doctor if you have had cancer or if you develop cancer.
- If you are taking abatacept and plan to become pregnant you must discuss the timing with your doctor.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website
www.arthritisaustralia.com.au

What is abatacept?

Abatacept (brand name Orencia) belongs to a new class of medicines called **biological disease modifying antirheumatic drugs (biological DMARDs or bDMARDs).**

bDMARDs have now been given to over a million people worldwide since their initial use in the late 1990s.

These medicines block natural substances called cytokines. These are substances found in excessive amounts in the blood and joints of people with rheumatoid arthritis and juvenile arthritis.

The increased levels of cytokines cause inflammation, which results in symptoms of pain, joint swelling and stiffness, and can lead to joint damage.

By blocking T cell (a type of white blood cell) responses, abatacept reduces inflammation, lessens the symptoms and helps stop further joint damage.

What benefit can you expect from your treatment?

Unlike standard antirheumatic drugs (DMARDs), abatacept works relatively quickly. You may notice some relief of joint swelling, pain and stiffness within the first 4-8 weeks of treatment.

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Stopping abatacept

If abatacept treatment is stopped for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop (see *Side effects*).

If you stop abatacept for any reason you **must** contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.

How will your condition be monitored?

In view of the current prescribing restrictions for all bDMARDs:

- Abatacept will only be started if your disease is active and if standard treatments have been unsuccessful.
- It will not be continued unless it helps your condition. This will be assessed at least 12 weeks after the start of treatment.
- Blood tests will be required during your treatment to monitor your condition and to determine the effectiveness of treatment.
- The frequency of blood tests will depend on what other medicines you are taking and what other illnesses you might have. Your rheumatologist will determine the frequency of tests required.

How is abatacept given?

Abatacept is given as a drip (infusion) into the vein, or as an injection under the skin of the abdomen or thigh.

The infusion normally takes thirty minutes. This is followed by a one hour period of observation to make sure you don't have any side effects. Additional doses are usually given at 2 and 4 weeks after the first dose. Subsequent doses are usually given every 4 weeks.

When given as an injection under the skin (subcutaneous injection), doses are given weekly.

The treatment may still begin with a single dose given as an infusion (loading dose).

Abatacept is given in combination with the DMARD methotrexate.

What is the dosage?

For infusions the dose is based on the person's weight, so each person's dose may be different.

The subcutaneous dose is a standard 125mg weekly injection.

Can other medicines be taken with abatacept?

Abatacept may be used with other arthritis medicines including:

- other DMARDs such as methotrexate
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

Abatacept cannot be used with other bDMARDs.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience side effects with your treatment. Contact your doctor if you have any concerns about possible side effects. Many side effects disappear when abatacept treatment is stopped.

Most common possible side effects

- Common possible side effects include:
  - *headaches, runny nose, dizziness or cough*
  - *sore throat, heartburn or nausea*
  - *back, arm or leg pain*
  - *urine infections*

Australian Rheumatology Association

  - *rash.*
- *Stomach and bowel discomfort* may also occur.
- As abatacept affects the immune system, *mild infections*, particularly of the upper respiratory tract (e.g. colds, sinusitis) may occur more frequently than usual. Treatment with abatacept may need to be temporarily stopped so contact your doctor for advice.

Less common or rare possible side effects

- Side effects can occur during the infusion itself. These may include *fever or chills, itch, chest pain, shortness of breath* or *changes in blood pressure*. These effects are more likely to occur during the first or second infusion.
- Mild pain, swelling, bruising or itching may occur at the injection site (for subcutaneous doses). It is therefore important to rotate the injection site.
- *Serious infections* such as tuberculosis (TB) are seen rarely, and screening for TB is needed before treatment begins (see *Precautions*).
- Rarely abatacept may cause an *allergic reaction* with itchy, red skin or a rash.
- It is still unclear from research if there is an increased risk of cancer due to abatacept treatment (see *Precautions*).

What precautions are necessary?

Infections

- If you have an active infection of any kind, treatment with abatacept will not be given until the infection is treated successfully.
- Abatacept will not be given if you have active untreated tuberculosis (TB) or HIV (AIDS) infection as it is likely to make these conditions worse.
- If you have latent (inactive) TB preventative anti-TB treatment will be started at least 4 weeks before abatacept. The anti-TB treatment will usually need to be taken for 9 months.
- Hepatitis B or C infection may not necessarily exclude treatment.
- Because of the risks associated with infection the following tests may be conducted before commencing treatment with abatacept:
  - blood tests for hepatitis B and C
  - chest x-ray and two step Tuberculin Skin Test (Mantoux) or QuantiFERON blood test for tuberculosis (TB)
  - HIV tests are required for those who are at risk of this infection.

Precautions with other diseases

- People with chronic lung disease (COPD) are not usually given abatacept but each case will be assessed individually.

Use with other medicines

- Abatacept can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals.
- Abatacept does not increase the risk of side effects from low dose aspirin (taken for prevention of heart attack and strokes).
- The simple pain reliever paracetamol and combined pain medicines such as Panadeine and Panadeine Forte can be used while you are receiving abatacept treatment provided you take them as directed.

Vaccines

- If you are on abatacept it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio virus), BCG (Bacillus Calmette Guerin) or yellow fever. Talk with your rheumatologist before receiving any vaccines.
- Pneumovax and the combined yearly seasonal flu/swine flu vaccinations are

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safe and recommended to reduce your risk of those infections.

Surgery

- If you require surgery for any reason, treatment with abatacept will be stopped before surgery.

  It will be restarted again after the operation at a time determined by your surgeon and rheumatologist. Treatment will be restarted once the wound is healed and if there is no infection present.

Use with alcohol

- You may drink alcohol while taking abatacept. However, if you are also taking methotrexate you should be particularly cautious about your alcohol intake.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Cancer risk

- Lymphoma, a cancer of lymph glands, is found more commonly in patients with severe active rheumatoid arthritis than in the general population. Studies are in progress to see if treatment with abatacept changes this. To date there is no evidence to suggest that this medicine increases lymphoma.

  If cancer has been previously treated and cured it is unclear whether abatacept can be used safely. An interval of 5 years is normally recommended between cure of a cancer and starting TNF-bDMARDs.
- For general cancer prevention, stopping smoking and taking skin cancer prevention measures are recommended. It is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.
- Talk to your doctor if you have any concerns about issues relating to cancer risk.

Use in pregnancy and when breastfeeding

- Not enough is known regarding the possible side effects of abatacept. If you plan to become pregnant, it is important to discuss this with your doctor, as each case is different.
- You should not breastfeed when taking abatacept.

How to store abatacept

- Keep the medicine refrigerated, even when travelling.
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking abatacept you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

PATIENT INFORMATION ON

ADALIMUMAB

(Brand name: Humira)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition**
- **other precautions you should take while you are taking adalimumab.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking adalimumab you must see your rheumatologist regularly to ensure the treatment is working and minimise any possible side effects.
- If you stop adalimumab for any reason you must contact your doctor. Failure to do so may mean that your continued treatment will no longer be subsidised.
- Remember to change the injection site each time adalimumab is injected.
- If you are worried about any side effects you should contact your rheumatologist as soon as possible.
- It is important to tell your doctor if you have had cancer or if you develop cancer.
- If you are taking adalimumab and plan to become pregnant you must discuss the timing with your doctor.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html.

What is adalimumab?

Adalimumab (brand name Humira) belongs to a new class of medicines called **biological disease modifying antirheumatic drugs (biological DMARDs or bDMARDs).**

bDMARDs have now been given to over a million people worldwide since their initial use in the late 1990s.

These medicines block natural substances, called cytokines. These are substances found in excessive amounts in the blood and joints of people with rheumatoid arthritis, psoriatic arthritis, juvenile arthritis and ankylosing spondylitis.

The increased levels of cytokines cause inflammation, which results in symptoms of pain, joint swelling and stiffness, and can lead to joint damage.

By blocking the cytokine called Tumour Necrosis Factor (TNF), adalimumab reduces inflammation, lessens the symptoms and helps stop further joint damage.

What benefit can you expect from your treatment?

Unlike standard antirheumatic drugs (DMARDs), adalimumab works relatively quickly. You may notice some relief of joint swelling, pain and stiffness within the first 4 weeks of treatment.

Stopping adalimumab

If adalimumab treatment is stopped for more than a few weeks there is a risk that your condition will get worse again. Continue with your treatment unless advised by your doctor or unless side effects develop (see *Side effects*).

If you stop adalimumab for any reason you **must** contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.

How will your condition be monitored?

Due to the current prescribing restrictions for all bDMARDs:

- Adalimumab will only be started if your disease is active and if standard treatments have been unsuccessful.
- It will not be continued unless it helps your condition. This will be assessed at least 12 weeks after the start of treatment.
- Blood tests will be required during your treatment to monitor your condition and to determine the effectiveness of treatment.
- The frequency of blood tests will depend on what other medicines you are taking and what other illnesses you might have. Your rheumatologist will determine the frequency of tests required.

How is adalimumab taken?

Adalimumab is injected under the skin of the abdomen or thigh.

It can be injected by your doctor, nurse, carer or by you. If injecting yourself, be sure to follow the detailed instructions carefully to ensure the best response. It is particularly important to change the injection site each time.

What is the dosage?

The usual dose for adults with rheumatoid arthritis is 40mg once every two weeks.

Can other medicines be taken with adalimumab?

Adalimumab may be used with other arthritis medicines including:

- other DMARDs such as methotrexate
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

Adalimumab cannot be used with other bDMARDs.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience side effects with your treatment. Contact your doctor if you have any concerns about possible side effects. Many side effects disappear when adalimumab treatment is stopped.

Most common possible side effects

- *Mild pain, swelling or itching* at the site of the injection are very common (up to 20% of patients) but can be reduced by applying ice and antihistamine/steroid creams to the injection site.
- *Headaches, cough and stomach and bowel discomfort* may also occur.
- As adalimumab affects the immune system, *mild infections,* particularly of the upper respiratory tract (e.g. colds, sinusitis) may occur more frequently than usual. Treatment with adalimumab may need to be temporarily stopped so contact your doctor for advice.

Less common or rare possible side effects

- *Serious infection*s such as Tuberculosis (TB) are seen rarely, and screening for TB is needed before treatment begins (see *Precautions*).
- Rarely adalimumab may cause an *allergic reaction* with itchy, red skin or a rash or a feeling of tightness in the chest and difficulty breathing.

- Side effects involving the nerves, such as *inflammation of the nerve to the eye*, may also occur rarely, causing changes in vision or sensation.
- Very rarely *'drug-induced lupus'* has occurred with symptoms of rash, fever and increased joint pain.
- It is still unclear from research if there is an increased risk of cancer due to adalimumab treatment (see *Precautions*).

What precautions are necessary?

Infections

- If you have an active infection of any kind treatment with adalimumab will not be given until the infection is treated successfully.
- Adalimumab will not be given if you have active untreated tuberculosis (TB) or HIV (AIDS) infection as it is likely to make these conditions worse.
- If you have latent (inactive) TB preventative anti-TB treatment will be started at least 4 weeks before adalimumab. The anti-TB treatment will usually need to be taken for 9 months.
- Hepatitis B or C infection may not necessarily exclude treatment.
- Because of the risks associated with infection the following tests may be conducted before commencing treatment with adalimumab:
  - blood tests for hepatitis B and C
  - chest x-ray and two step Tuberculin Skin Test (Mantoux) or QuantiFERON blood test for tuberculosis (TB)
  - HIV tests are required for those who are at risk of this infection.

Precautions with other diseases

- People with multiple sclerosis should not be treated with adalimumab due to the possible effects on the nerves.
- People with moderate to severe heart failure may not be treated with adalimumab as the medicine can make heart failure worse.
- People with systemic lupus erythematosus (lupus/SLE) are not usually given adalimumab but each case will be assessed individually.

Use with other medicines

- Adalimumab can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals.
- Adalimumab does not increase the risk of side effects from low dose aspirin (taken for prevention of heart attack and strokes).
- The simple pain reliever paracetamol and combined pain medicines such as Panadeine and Panadeine Forte can be used while you are receiving adalimumab treatment provided you take them as directed.

Vaccines

- If you are on adalimumab it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio virus), BCG (Bacillus Calmette Guerin) or yellow fever. Talk with your rheumatologist before receiving any vaccines.
- Pneumovax and the combined yearly seasonal flu /swine flu vaccinations are safe and recommended to reduce your risk of those infections.

Surgery

- If you require surgery for any reason, treatment with adalimumab will be stopped before surgery. It will be restarted again after the operation, at a time determined by your surgeon and rheumatologist. Treatment will be restarted once the wound is healed and if there is no infection present.

Cancer risk

- Lymphoma, a cancer of lymph glands, is found more commonly in patients with severe active rheumatoid arthritis than in the general population. Studies are in progress to see if treatment with adalimumab changes this. To date there is no evidence to suggest that this medicine increases lymphoma.

- If cancer has been previously treated and cured it is unclear whether a TNF-bDMARD such as adalimumab can be used safely. An interval of 5 years is normally recommended between cure of a cancer and starting TNF-bDMARDs.
- For general cancer prevention, stopping smoking and taking skin cancer prevention measures are recommended. It is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.
- Talk to your doctor, if you have any concerns about issues relating to cancer risk.

Use with alcohol

- You may drink alcohol while taking adalimumab. However, if you are also taking methotrexate you should be particularly cautious about your alcohol intake.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Use in pregnancy and when breastfeeding

- Not enough is known regarding the possible side effects of adalimumab on the unborn baby. If you plan to become pregnant, it is important to discuss this with your doctor as each case is different.

How to store adalimumab

- Keep the medicine refrigerated, even when travelling.
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking adalimumab you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

How to help us help you

Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!

Contact us in any of the following ways:

Email: ARAD@monash.edu
Telephone: Sydney 02 9463 1889
or Melbourne 03 9508 3424
Fax: 1-800-022-730

Visit our website:
www.ARAD.org.au

PATIENT INFORMATION ON

METHOTREXATE

(Brand names: Methoblastin)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **what are the possible side effects**
- **what tests you must have to monitor your condition and to detect unwanted effects**
- **other precautions you should take when you are taking methotrexate.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking methotrexate you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.
- You should have regular blood tests as directed by your rheumatologist.
- If you are concerned about any side effects you should contact your rheumatologist as soon as possible.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html

What is methotrexate?

Methotrexate (brand name Methoblastin) is a medicine used to treat rheumatoid arthritis as well as other rheumatic conditions such as juvenile arthritis, lupus (also known as SLE), psoriatic arthritis and polymyositis (muscle inflammation).

Methotrexate is an immunosuppressive medicine. It works by reducing the activity of several enzymes involved in the immune system. By blocking an enzyme called dihydrofolate reductase, it reduces production of a form of folic acid.

It is not entirely clear how methotrexate decreases the severity of arthritis, but it reduces inflammation in the joints and associated pain and swelling.

Because methotrexate reduces the damage to the joints, rather than just relieving the pain, it belongs to the group of medicines called **disease modifying antirheumatic drugs (DMARDS)**.

Methotrexate has been used to treat rheumatoid arthritis for more than 25 years. It is also used at very high doses (1000mg-5000mg a day) to treat some cancers.

What benefit can you expect from your treatment?

Methotrexate is one of the most effective treatments for rheumatoid arthritis. Most, but not all, patients will benefit from this medicine. Some achieve remission, where the arthritis virtually disappears.

Methotrexate does not work straight away. Reduced pain, stiffness and swelling may be noticed after 4 weeks. The effects to delay or prevent joint damage will take several months.

Other medicines may be given to improve your symptoms while waiting for methotrexate to work.

How is methotrexate taken?

Methotrexate may be taken by mouth as a tablet or given by injection either into the muscle or under the skin.

Injections may be used instead of tablets if the medicine is not being absorbed well, or if you feel sick (nausea) or vomit when you take the tablets, or if your condition is not improving with tablets.

Care should be taken when disposing of the needles and syringes.

When should it be taken?

Methotrexate is taken just **once a week,** on the same day each week. If you are taking the tablets, it is a good idea to specify and diarise the day of the week that you will take your tablets to avoid making mistakes.

Methotrexate tablets are best absorbed when taken on an empty stomach. However if nausea is a problem, taking them at mealtime can help to reduce this side effect and does not reduce the benefits too much.

What is the dosage?

Tablets come in 2.5mg or 10mg strengths. Treatment may start with a very low dose of 5mg or 10mg a week, increasing to an average dose of 20mg a week. The dose is adjusted depending on the response, up to about 30mg once a week.

The dose is usually taken all at once on a single day. It may be divided into separate doses taken during that day if necessary.

Can other medicines be taken with methotrexate?

In order to reduce side effects, it is recommended that you also take folic acid or folinic acid. Your doctor will explain how much of the folic/folinic acid to take and when to take it.

Methotrexate is often taken in combination with other arthritis medicines, including:

- other DMARDs
- biological DMARDs (a newer type of DMARD, which act on natural substances in the body that contribute to inflammation and joint damage)
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen/Nurofen)
- simple pain medicines such as paracetamol.

There are separate information sheets for the medicines mentioned above.

How long is the treatment continued?

Treatment with methotrexate is continued indefinitely as long as it is effective and as long as no serious side effects occur.

If you stop methotrexate treatment for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop.

If you have an illness that makes you unwell enough to change plans for the day (e.g. gastroenteritis or fever), it is reasonable to miss the weekly dose until you have recovered.

Are there any side effects?

You might experience side effects with your treatment. Tell your doctor if you are concerned about possible side effects.

A reduction in dose may minimise side effects so that you can continue to take the treatment. Your doctor will advise on any dose changes that are necessary.

Most common possible side effects

- The most common side effects are *nausea, vomiting* and *diarrhoea*. These can be reduced if methotrexate is taken with food or in the evening. Antinausea tablets can be used if needed.
- *Mouth ulcers* can occur, but the use of folic acid or folinic acid supplements makes this less likely.
- *Skin dryness, a variety of skin rashes* and *increased sensitivity to the sun* may also occur. You should wear sunscreen and a hat when out in the sun.
- Some people report mild *tiredness, headache* and *mental clouding*. Some also experience a temporary increase in muscle and joint pain after taking the weekly dose.

Less common or rare possible side effects

There are some rare but potentially serious side effects with methotrexate.

- *Blood counts*: Methotrexate can rarely cause a drop in the number of white blood cells, which are needed to fight infection. It can also cause a drop in the number of platelets, which help to stop bleeding.

  Regular blood tests aim to pick these problems up early if they occur.

  However, if you develop a sore mouth, mouth ulcers, easy bruising, nosebleeds, bleeding gums, breathlessness, infection or fever tell your doctor straight away.

- *Liver*: Methotrexate can inflame the liver causing a type of hepatitis. Regular blood tests aim to pick this up early if it occurs. The dose of methotrexate may need to be reduced or stopped if problems occur. Liver problems may be increased when methotrexate is combined with the medicines azathioprine (Azamun, Azapin, Imuran, Thioprine) or leflunomide (Arabloc, Arava) or with heavy alcohol use (see *Alcohol* overleaf).
- *Lungs*: Methotrexate can cause inflammation of the lungs. This may be more likely if leflunomide is being taken at the same time. The problem may develop quickly, so if you have a sudden onset of breathing difficulties seek medical attention as soon as possible. It may also develop slowly with symptoms such as a dry cough.
- *Hair thinning*: This may occur rarely. It is not permanent and hair will grow back when the medicine is stopped.
- *Nodule formations*: Some people with rheumatoid arthritis develop nodules on their elbows or other pressure points. In some cases methotrexate may increase this.
- *Cancer:* see below.

Long term side effects

Methotrexate may be taken for long periods (more than 25 years) to manage rheumatoid arthritis. In addition to the possible effects mentioned above, the following are rare but possible long-term side effects, or long-term issues that may concern patients:

- *Liver:* Very rare cases of increased fibrous tissue in the liver have been reported after long-term treatment. Regular monitoring can minimise the risk of this occurring.
- *Cancer:* People who have rheumatoid arthritis have an increased risk of lymphoma (a lymph node cancer). It is not clear whether methotrexate increases this risk further but any additional risk is likely to be very small. Methotrexate may reduce the risk of these cancers by controlling the rheumatoid arthritis, but this is unproven. For general cancer prevention, stopping smoking is recommended. An annual skin check to detect any early skin cancer is also recommended.
- *Fertility:* Methotrexate does not affect a person's ability to have children in the long term. See also *Precautions*.

More information about possible side effects

Information that comes with your methotrexate medicine will also describe in detail the potential serious side effects that may occur with methotrexate. Many of those side effects relate to **high dose** methotrexate used for the treatment of cancer. These may not be applicable to the much lower doses that are prescribed for the treatment of rheumatoid arthritis. Talk to your doctor if you have concerns about any possible side effects.

What precautions are necessary?

Blood tests

- As methotrexate may affect the liver and blood cells, you **must** have regular blood tests during your treatment. This is very important, as you may not get symptoms with some of these problems.
- Blood tests are particularly important during the first few months of treatment and when methotrexate is taken with leflunomide.
- As well as monitoring for side effects, blood tests help to monitor your condition to determine if the treatment is effective.
- You will need to have full blood counts and liver function tests every 2 to 4 weeks for the first few months of treatment and then every 1 to 3 months after that.
- If there are no problems seen after 3 months of treatment at a specific dose of methotrexate, the blood tests may be done less frequently.
- Your general practitioner (GP) will be informed about the monitoring schedule. It is important to see your GP if you have been asked to do so as they play an important role in monitoring your condition.

Risk of infections

- Because your immune system may be depressed, there is an increased risk of developing some infections, especially herpes zoster (chicken pox and shingles). You should try to avoid contact with people who have these infections. If you have an infection or persistent fever, tell your doctor straight away.

Use with other medicines

- Methotrexate can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes

over the counter or herbal/naturopathic medicines. You should also mention your treatment when you see other health professionals.

- Antibiotics containing **trimethoprim (e.g. Bactrim, Septrim or Triprim)** can cause problems when taken with methotrexate. If you are prescribed any of these medications you **must** tell the doctor you are taking methotrexate.
- Aspirin can be used safely in the low doses taken for prevention of heart attack and stroke.
- Methotrexate can be taken safely with anti-inflammatory drugs (NSAIDs), as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte, can be used while taking methotrexate provided you take them as directed.
- Most vaccines can be given safely but live vaccines, such as MMR (measles, mumps and rubella), OPV (oral polio vaccine) or yellow fever, may need special consideration.
- Pneumovax and yearly flu vaccinations are safe and recommended to reduce your risk of those infections. Talk with your rheumatologist before receiving any vaccines.

Use with alcohol

- Alcohol increases the risk of liver damage while taking methotrexate. Methotrexate usage in heavy drinkers has been associated with cirrhosis of the liver.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Surgery

- If low dose once weekly methotrexate is continued during surgery there seems to be no change in wound healing or increased infection.

Use in pregnancy and breastfeeding

- Methotrexate should not be taken during pregnancy as it can cause miscarriage or foetal deformity. It should also not be taken when breastfeeding.
- Women of child-bearing age should use effective contraception while taking methotrexate.
- Women planning to become pregnant should stop taking methotrexate 3 months before attempting to conceive.
- The best time for a male partner to stop taking methotrexate before trying to conceive is not known.
- Methotrexate does not affect a person's ability to have children in the long term.

How to store methotrexate

- Store methotrexate in a cool, dry place, away from direct heat and light (e.g. not in the bathrom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

You should see your rheumatologist regularly to make sure the treatment is working and to minimise any potential side effects.

How to help us help you
Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!

Contact us in any of the following ways:
Email: ARAD@monash.edu
Telephone: Sydney 02 9463 1889
or Melbourne 03 9508 3424
Fax: 1-800-022-730
Visit our website: www.ARAD.org.au

Australian Rheumatology Association

PATIENT INFORMATION ON

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

(Examples of brand names: Brufen, Celebrex, Mobic, Naprosyn, Nurofen, Orudis, Voltaren)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you may need to have to detect unwanted effects**
- **other precautions you should take while you are taking these medicines.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking NSAID you should see your doctor regularly to make sure the treatment is working and to minimise any possible side effects.
- If you develop severe stomach pains, pass blood or black stools, or vomit blood, stop taking the medicine immediately. You should see your doctor as soon as possible or go to the nearest emergency department.
- If you are worried about any side effects you should contact your doctor as soon as possible.

For more information about arthritis see the Arthritis Australia website www.empowered.org.au.

What are NSAIDs?

Non-steroidal anti-inflammatory drugs, or NSAIDs, are common medicines used to treat the symptoms of arthritis. The name means they reduce pain and stiffness due to inflammation of the joints, without using steroids. You can find out about steroids from the separate ARA information sheet on corticosteroids.

There are many different NSAIDs. Some can be bought over the counter (OTC) e.g. ibuprofen (Nurofen). Others such as ketoprofen (Orudis) are only available with a prescription. The brand name of your NSAID will have the generic name next to it on the packet or bottle. See the table at the end of this information sheet for further examples.

In recent years a newer type of NSAID, the selective NSAIDs (also called cox-2 inhibitors or coxibs) have been developed. These are less likely to cause stomach irritation and ulcers compared to traditional NSAIDs.

How do they work?

NSAIDs stop cells making prostaglandins. Prostaglandins are chemicals released by injured cells. They cause inflammation and swelling and they sensitise nerve endings, which can lead to pain. If you make less prostaglandin, you have less inflammation and less pain. By stopping cells making prostaglandins, NSAIDs relieve the symptoms of arthritis. They do not stop the inflammation occurring in the future or prevent the disease progressing to joint damage.

What benefit can you expect from your treatment?

NSAIDs provide relief from pain and stiffness. They work quickly, usually within a few hours. The maximum benefit can take 2 to 4 weeks or sometimes longer. You may need to try two or three different NSAIDs to find one that suits you best. You **must** only take one type of NSAID at a time.

Australian Rheumatology Association

How are NSAIDs taken?

NSAIDs are usually taken by mouth in tablet or capsule form. They are also available as liquids, injections, creams, sprays and suppositories.

Side effects may still occur with any method of administration, even when NSAIDs are applied to the skin (see *Side effects*).

When should they be taken?

NSAIDS can be taken when needed to treat short term symptoms. They can also be taken regularly to manage persistent pain and stiffness.

While NSAIDs may be more effective if taken regularly, the possible side effects are less if they are only taken when needed, for example before exercise.

How often you take a NSAID also depends on the one you are prescribed. Ask your doctor or pharmacist if you are uncertain about how often to take your medicine.

Tablets and capsules should be taken with food to reduce possible side effects.

What is the dosage?

NSAIDs usually come in different strengths. Treatment usually starts with a low dose. This can be adjusted depending on your response.

The dose will depend on the type of NSAID and the condition for which it is being used.

To minimise side effects, the lowest dose that controls symptoms is usually recommended.

Always follow the instructions provided in the packaging unless otherwise directed by your doctor.

Can other medicines be taken with NSAIDs?

To minimise side effects, sometimes a medicine to protect the stomach may be given (see page 3).

NSAIDs may be used with other arthritis medicines including:

- DMARDs (anti rheumatoid arthritis drugs) such as methotrexate
- simple pain medicines such as paracetamol.

Corticosteroids are not generally used with NSAIDs as the risk of side effects such as ulcer is increased.
There are separate information sheets for the medicines mentioned above.

How long is the treatment continued?

Treatment with NSAIDs can be for a short period or long term. A NSAID should not be continued indefinitely without regular review by your doctor to confirm the NSAID still works and no serious side effects are occurring.

Are there any side effects?

You might experience side effects with your treatment. Tell your doctor if you are concerned about possible side effects. A reduction in dose or change to another NSAID may decrease the side effects so that you can continue to take the treatment.

Alternatively, your doctor may recommend a different pain relieving medicine with fewer potential side effects, such as paracetamol. This may allow you take the NSAID less often or stop it altogether.

Most common possible side effects:

- The most common side effects are *gastrointestinal* and may include decreased appetite, nausea (feeling sick), vomiting, diarrhoea, constipation, heartburn and stomach pain or cramps.
- *Heart disease and stroke*: All NSAIDs, including the newer selective types (cox-2 inhibitors/coxibs), may slightly increase the risk of heart attacks and strokes. This risk seems higher in those already at high risk of heart attack or stroke.
- NSAIDs can increase *blood pressure* (see *Precautions*, page 3).
- NSAIDs can make *heart failure or kidney failure* worse. Fluid retention can lead to weight gain or swelling of ankles or legs. Kidney failure is more likely if you are also taking fluid tablets and certain blood pressure tablets (see *Precautions*, page 3).
- *Dizziness, lightheadedness, tiredness, ringing in the ears (tinnitus)* and *headache* can occur.
- *Bleeding* more easily than usual is often noticed.

Less common or rare possible side effect:

There are some rare but potentially serious side effects with NSAIDs.

- *Stomach or duodenal ulcers:* NSAIDs can cause ulcers in the stomach or duodenum (upper bowel).

  If you develop severe stomach pains, pass blood or black stools, or vomit blood, stop taking the medicine immediately. You should see your doctor as soon as possible or go to the nearest emergency department.

  The risk of ulcers is higher if:

  - you are older than 65 years
  - you have had a previous stomach or duodenal ulcer
  - you are also taking warfarin, corticosteroid tablets or low-dose aspirin (used by many people to help prevent a heart attack or stroke).

  If you have an infection (helicobacter bacteria) in your stomach this should be treated before you start NSAIDs. Your doctor may advise that you take an anti-ulcer medicine to help reduce the risk of getting a stomach or duodenal ulcer.

  The selective NSAIDs e.g. celecoxib (brand name Celebrex), may be less likely to cause stomach ulcers and irritation than traditional NSAIDs. They have been used to treat arthritis in people who have suffered stomach upset or ulcers while taking a traditional NSAID or who were thought to be at risk for ulcers.
- *Allergy* to NSAIDs can occur resulting in skin rashes.
- *Shortness of breath* may occur in some people with asthma. Seek medical help if your asthma suddenly becomes worse after taking NSAIDs.
- *Liver inflammation* (hepatitis) is another uncommon side effect.

There are also a number of other uncommon side effects. Read the leaflet that comes with the medicine, which lists all the precautions and possible side effects.

What precautions are necessary?

Blood pressure

- Because NSAIDs can affect your blood pressure it is a good idea to have your blood pressure monitored monthly for the first two months. This is more important if you already have high blood pressure or you are on treatment for high blood pressure. If your blood pressure is stable, it should be checked every 3 to 6 months while you continue to take the NSAIDs.

Blood tests

- Usually blood tests are not required for people taking NSAIDs.
- They may be needed in certain situations. For example, your kidney function may need to be monitored if you have other risk factors for reduced kidney function, such as being over 65 years old and taking blood pressure medicines or fluid tablets. In this case your doctor may recommend you have a blood test in the first few weeks after starting a NSAID.

Use with other medicines

- NSAIDs can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking, including herbal and naturopathic medicines. This includes over the counter (OTC) medicines as some contain NSAIDs. You should also mention your treatment when you see other health professionals.
- NSAIDs are generally used for joint and muscle pain. However sometimes they can be used for other reasons, for example mefanamic acid (Ponstan) may be used for period pain.
- Despite the possible increased risk of ulcer, low doses of aspirin used to prevent heart attack and stroke can probably be used safely with NSAIDs if the risk for ulcer is low in the first place.
- Methotrexate for rheumatoid arthritis or other arthritis treatment can be taken safely with NSAIDs as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte can be used while taking NSAIDs provided you take them as directed.
- If you are taking anticoagulants such as warfarin you should tell your doctor as combination with NSAIDs can increase the risk of bleeding.

Use with alcohol

- NSAIDs can increase the risk of a stomach or duodenal ulcer. Heavy alcohol use (more than

Australian Rheumatology Association

4 standard drinks in one session) should be avoided while taking these medicines.

Use in pregnancy and breastfeeding

- NSAIDs are not recommended during pregnancy or during breastfeeding unless specifically advised by your doctor. If you are planning a family or you become pregnant you should discuss this with your doctor as soon as possible.
- Some studies suggest that if NSAIDs are taken around the time of conception there may be an increased risk of miscarriage.
- If NSAIDs are taken in later stages of pregnancy they may have an effect on the blood vessels near the baby's heart. Paracetamol does not have these effects.

How to store NSAIDs

- Store NSAIDs in a cool, dry place, away from direct heat and light.
- Keep all medicines out of reach of children.

Non-selective NSAIDS (cox-1 and cox-2 inhibitors)	
Generic/chemical name	**Brand names**
Diclofenac	Chemists' Own, Clonac, Diclohexal, Fenac, Imflac, Viclofen, Voltaren, Voltaren Rapid, Voltfast
Ibuprofen	Advil, Brufen, Bugesic, Chemists' Own, Dimotapp, Gold Cross, Herron Blue, iProfen, Nurofen, Panafen, ProVen, Rafen, Tri-Profen
Indomethacin	Arthrexin, Indocid
Ketoprofen	Orudis, Oruvail
Ketorolac	Ketoral, Toradol
Mefenamic acid	Ponstan
Naproxen	Aleve, Anaprox, Chemists' Own, Crysanal, Eazydayz, Inza, Naprosyn, Naprofem, Naprogesic, Proxen
Piroxicam	Feldene, Feldene-D, Mobilis, Mobilis D,
Sulindac	Aclin
Selective NSAIDS (cox-2 inhibitors)	
Celecoxib	Celebrex
Etoricoxib	Arcoxia
Meloxicam	Meloxibell, Mobic, Movalis, Moxicam
Paracoxib	Dynastat

Source: Australian Medicines Handbook, 2013.
Note: This may not be a comprehensive list – ask your pharmacist or doctor for more information.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details:~

When taking NSAIDs should see your doctor regularly to make sure the treatment is working and to minimise any potential side effects.

How to help us help you

Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!
Contact us in any of the following ways:
Email: ARAD@monash.edu
Telephone: **Sydney 02 9463 1889**
or **Melbourne 03 9508 3424**
Fax: **1-800-022-730**

Visit our website: www.ARAD.org.au

Australian Rheumatology Association

Arthritis AUSTRALIA

PATIENT INFORMATION ON

PREDNISOLONE & PREDNISONE

(Also known as corticosteroids / cortisone / steroids)

(Examples of brand names: Panafcort, Panafcortelone, Predsone, Predsolone, Solone, Sone)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **what are the possible side effects**
- **what tests you should have to monitor your condition and to detect unwanted effects**
- **other precautions you should take when you are taking prednisolone or prednisone.**

Please read it carefully and discuss it with your doctor.

Important things to remember:

- While taking prednisolone you should see your treating doctor regularly to make sure the treatment is working as it should and to minimise any possible side effects.
- You should not stop your treatment unless your doctor tells you to.
- You should not increase or reduce the dose of prednisolone unless your doctor tells you to.

For more information about RHEUMATOID ARTHRITIS see Arthritis Australia's Empowered website:
www.empowered.org.au

What is prednisolone?

Corticosteroids are hormones that are produced naturally in the body. They are necessary for normal working of the body.

Prednisolone and prednisone are man-made corticosteroids (also called steroids for short). Man-made corticosteroids are used to treat inflammatory diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE/lupus) and other inflammatory disease. They have a strong anti-inflammatory effect and reduce the swelling and pain in joints and other organs. They do not cure the disease.

They should not be confused with male or female steroid hormones, which are known for their misuse among athletes.

Prednisolone is the most common type of corticosteroid prescribed. Although prednisone is slightly different the information contained in this document also applies to that medication.

What benefit can you expect from your treatment?

Prednisolone works very quickly. Within a few days you may notice your pain and stiffness is much better and/or your joints are less swollen.

How is prednisolone taken?

Prednisolone can be swallowed as tablets or liquid. It is usually taken once or twice a day. Sometimes it is taken every second day. It is usually taken in the morning, with or immediately after food.

Other corticosteroids can be given by injection into joints, soft tissues or muscles. An injection into a vein (intravenous) may also be given if required.

What is the dosage?

There are three different strengths of prednisolone tablets: 1mg, 5mg and 25mg. This means the dosage can be adjusted to suit your needs without you having to take large numbers of tablets. It is important to check the strength of the tablets as they look very similar.

The dose depends on the severity of the disease. A high dose may be used initially and then reduced by your doctor as symptoms improve. To minimise the risk of side effects the smallest dose possible will be used.

Sometimes your doctor may increase the dose temporarily when your body is under stress, for example during a surgical procedure or if you have a severe illness such as an infection.

After you have stopped prednisolone your doctor may prescribe it again for a short period in certain situations as described above.

Can other medicines be taken with prednisolone?

Prednisolone may be used with other arthritis medicines including:

- antirheumatoid arthritis medicine (also called disease modifying antirheumatic drugs or DMARDs) such as methotrexate
- biological DMARDs (a newer type of DMARD, which acts on natural substances in the body that contribute to inflammation and joint damage)
- simple pain relieving medicines such as paracetamol.

Prednisolone and other corticosteroids should be taken with caution with nonsteroidal anti-inflammatory drugs (NSAIDs) as the risk of side effects such as stomach ulcer is increased.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

Low dose prednisolone, taken for a few days or even a few weeks, does not normally cause any unwanted side effects.

If prednisolone is taken in high doses or for a long time certain predictable side effects can occur. Some of these improve after prednisolone is stopped. Many can be minimised by giving the lowest effective dose over the shortest possible period of time.

The effects may also be minimised by giving the medicine by injection into the joints or into a muscle.

Most common possible side effects

- *Weight gain*: The most common side effects are rounding of the face and weight gain around the stomach. These are due to altered metabolism, increased appetite and salt retention.
- *Osteoporosis (thinning of the bones):* While very low doses of prednisolone (less than 5 mg/day) are not very likely to cause thinning of the bones, moderate and high doses taken for long periods usually cause this problem.

  Your doctor will tell you if you need a *bone density (BMD)* test to check your risk of osteoporosis.

  To reduce the risk it is recommended that you:
  - have 1000mg of calcium each day (e.g. 3 serves of dairy or calcium tablets)
  - take 30 minutes of weight bearing exercise each day (e.g. walking)
  - avoid smoking and avoid drinking more than 2 standard drinks of alcohol a day
  - get some sunlight exposure each day to maintain vitamin D levels. You should wear sunscreen as usual to protect your skin from sun damage. As well as sun exposure, a vitamin D supplement may be recommended if vitamin D levels are low.
- *Skin:* The skin, especially on the arms and legs, can become thin, easily bruised and slow to heal. This occurs particularly after long term use, on higher doses and in older people with skin problems related to aging. In younger people acne may be a problem.

- *Diabetes:* Prednisolone can cause a rise in blood sugar in people with diabetes. This may require a change in their diabetes medicine. You should consult your general practitioner if you experience an increase in blood sugar levels.

  Prednisolone can also cause the onset of diabetic symptoms in people who are at risk of diabetes.
- *Blood pressure:* Prednisolone may cause an increase in blood pressure or make it more difficult to control. This can be monitored and changes can be made to your blood pressure medicine if required. Your doctor will advise about frequency of monitoring.
- *Cholesterol:* Prednisolone can cause a rise in blood cholesterol. This can be monitored and changes can be made to your treatment if required.
- *Psychological effects:* Prednisolone can cause euphoria (feeling high) and/or other mood or personality changes such as irritability, agitation or depression. While some psychological effects are quite common, they rarely cause significant problems.
- *Trouble sleeping* may also occur but can be minimised by taking prednisolone in the morning.
- *Infections:* There may be an increased risk of some infections, including mouth infections (such as thrush), shingles and lung infections. Pre-existing infections such as tuberculosis (TB) may become active again. **It is important to tell your doctor if you have a chronic infection or you have been exposed to TB earlier in your life.**
- *Indigestion* or heartburn can occur. Taking prednisolone with food can reduce this.
- *Ulcers:* If taken with nonsteroidal anti-inflammatory medicines (NSAIDs) prednisolone can further increase the risk of stomach or duodenal ulcers. Your doctor will advise you about how to reduce this risk and about what symptoms to look out for.

Less common or rare possible side effects

- *Eyes:* With long term high dose treatment prednisolone may increase development of cataracts.
- *Other:* Facial flushes, constipation and avascular necrosis (a painful bone condition usually seen in the hip or knee) can occur very rarely.

Many of the above side effects can be managed or prevented by close medical supervision and by following your doctor's recommendations (see also *Precautions*, below).

What precautions are necessary?

Tests

- Blood sugar and cholesterol levels can be increased by prednisolone, so you will need to have *blood tests* to check these levels. Your doctor will tell you when the blood tests are required.
- Your general practitioner will be told about the tests you need to have. It is important to see your general practitioner if you have been asked to do so as they have an important role to play in monitoring your condition.

Use in pregnancy and breastfeeding

- Prednisolone may be used safely in pregnancy and breastfeeding. It is important to tell your doctor if you are, or intend to become pregnant or if you are breastfeeding.

Use with other medicines

- Prednisolone can affect how other medicines work. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals, even if you have stopped taking corticosteroids within the last 12 months.
- Most vaccines can be given safely with prednisolone. Talk with your rheumatologist before receiving any vaccines.
- Yearly flu vaccines and Pneumovax are safe and recommended.

Surgery

- If you are going to have an operation it is important to tell the anaesthetist that you are taking or have been taking prednisolone or other corticosteroids in the last year.

- Your doctor may tell you that you need some additional prednisolone at the time of surgery.

Never stop taking prednisolone suddenly

- You should not stop taking prednisolone suddenly or increase or reduce the dose you have been prescribed unless your doctor tells you to.
- Your adrenal glands, which are just above the kidneys, normally make corticosteroids in small amounts. These are important for many normal body functions.
- If prescribed corticosteroids are taken, the body begins to make less than usual or even stops making corticosteroids completely.
- If the medicine is then *suddenly* stopped there may be a problem as the adrenal glands won't have had time to make the corticosteroids needed. This problem is called *adrenal insufficiency*.
- Signs of adrenal insufficiency include weakness, fatigue, fever, weight loss, vomiting, diarrhoea and abdominal pain. If you experience any of these problems, seek medical help.

How to store prednisolone

- Store prednisolone tablets at room temperature, away from heat, moisture and light (e.g. not in the bathroom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking prednisolone or other corticosteroids you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7-8, figure 1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	NA
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	6-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7-8

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1, 4
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 3
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	Table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Table 1,2,4,5,6
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Assessing the Readability and Patient Comprehension of Rheumatology Medicine Information Sheets: A Cross-Sectional Health Literacy Study

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Assessing the Readability and Patient Comprehension of Rheumatology Medicine Information Sheets: A Cross-Sectional Health Literacy Study

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Abstract (word count 278)

Objectives. Patients are often provided with Medicine Information Sheets (MIS). However, up to 60% of patients have low health literacy. The recommended readability level for health-related information is ≤ Grade 8. We sought to assess the readability of MIS given to patients by Rheumatologists in Australia, the United Kingdom (UK) and Canada, and to examine **Australian** patient comprehension of these documents.

Design. Cross-sectional study.

Setting. Community-based regional Rheumatology practice.

Participants. Random sample of patients attending the Rheumatology practice.

Outcome measures. Readability of MIS was assessed using readability formulae [Flesch Reading Ease formula, Simple Measure of Gobbledygook (SMOG) scale, FORCAST (named after the authors FORd, CAylor, STicht) and the Gunning Fog scale]. Literal comprehension was assessed by asking patients to read various Australian MIS and immediately answer five simple multiple choice questions about the MIS.

Results. The mean (±SD) grade level for the MIS from Australia, the UK, and Canada was 11.6±0.1, 11.8±0.1 and 9.7±0.1 respectively. The Flesch Reading Ease score for the Australian (50.8±0.6) and UK (48.5±1.5) MIS classified the documents as "fairly difficult" to "difficult". The Canadian MIS (66.1±1.0) were classified as "standard". The five questions assessing comprehension were correctly answered by 9/21 patients for the adalimumab MIS, 7/11 for the methotrexate MIS, 6/28 for the non-steroidal anti-inflammatory MIS, 10/11 for the prednisone MIS and 13/24 for the abatacept MIS.

Conclusions. The readability of MIS used by Rheumatologists in Australia, the UK and Canada exceeds Grade 8 level. This may explain why patient literal comprehension of these documents may be poor. Simpler, shorter MIS with pictures and info-graphics may improve

patient comprehension. This may lead to improved medication adherence and better health outcomes.

Study strengths and limitations

- Readability of Medicine Information Sheets (MIS) from three countries (Australia, UK and Canada) was assessed.
- While readability formulae only measure the number/complexity of words/sentences, Australian patient literal comprehension of MIS was also assessed.
- The study population was from a regional community and may not be representative of a more urban population.

Introduction

Health literacy is defined as the "capacity to obtain, process and understand written and oral health information and services needed to make appropriate health decisions".[1] Low health literacy has been associated with poorer health-related knowledge, increased hospitalisations, reduced immunizations, poorer health status and higher mortality.[2] Patients with poor health literacy are less likely to successfully manage chronic disease[3] and have greater difficulty following instructions for prescription medications.[4] Higher health literacy has been associated with increased medication adherence.[5 6]

Although the importance of health literacy and patient-physician communication on health outcomes is well-recognised, many patients have difficulty understanding what their physicians tell them.[7] Immediately after leaving a consultation with their specialist, patients were able to recall less than half the information just provided to them.[8 9] The provision of written health information in addition to verbal information significantly increases patient knowledge and satisfaction.[10] Written information may also lead to increased adherence with treatment. [9] However, designing effective written health information remains challenging due to differences in patient literacy levels.

The recommended level of reading difficulty for health-related written material in inconsistent. Some agencies have recommended up to eighth grade level [11] - the average reading level of an adult in the United States [12 13], whereas others have suggested levels as low as fifth grade to be more inclusive of those with limited literacy.[14] No national guidelines exist in Australia, although the South Australian government has recommended up to eighth grade level. [15] Despite these inconsistencies, many studies have found written health information provided to patients often exceeds these levels.[16-19] While there is greater access

to health-related information on the internet, this often also exceeds recommended readability levels.[20 21]

Literacy levels in Australia are poor, with up to 60% of the population having low literacy skills[22 23] - defined as the "minimum required for individuals to meet the complex demands of everyday life".[24] The International Adult Literacy Survey found 57% of Canadians fall into the lowest two literacy categories.[25] In the United Kingdom (UK), just under one in six adults has the literacy of an 11-year old. [26] A study of over 200 rural and urban Australian Rheumatology patients found that 15% of patients had low health literacy and up to one third of patients incorrectly followed dosing instructions for common Rheumatology drugs.[23] Ten percent of patients with rheumatoid arthritis (RA) who attended an urban community-based Australian Rheumatology practice had inadequate/marginal functional health literacy or a reading age at or below the United States (US) high school grade equivalent of 7th-8th grade.[27] Up to 24% of Rheumatology patients at a US medical centre had a reading level of 8th grade or less.[28] In 2002, one in six Rheumatology patients at a Scottish hospital were illiterate and struggled to understand education materials and prescription labels.[29] These findings are concerning, as Rheumatologists often use medications such as methotrexate or expensive biologic therapies with severe side effects, even death[30], if taken incorrectly.

Given the importance of health literacy and its relationship to health outcomes and medication adherence, we sought to assess:

i) the readability of patient Medication Information Sheets (MIS) given to patients by Australian Rheumatologists, and

ii) patient comprehension of these documents.

We also compared the readability of the Australian MIS to similar documents given to Rheumatology patients in the UK and Canada.

Methods

Assessment of readability

Text from the MIS of commonly prescribed Rheumatology medications available on the Australian Rheumatology Association (ARA) website[31] was imported into a Microsoft Word document and readability assessed using Readability Studio™ (Oleander Software, USA).[18 32 33 34 35]

Non-essential text including logos, headers, footers, hyperlinks and contact information was deleted prior to analysis as these may have adversely affected readability scores. Readability was assessed using a range of measures such as the Flesch Reading Ease formula, Simple Measure of Gobbledygook (SMOG) scale, FORCAST (named after the authors FORd, CAylor, STicht) and the Gunning Fog scale. The Flesch Reading Ease formula calculates an index score of a document based on sentence length and number of syllables. It is often used for school textbooks and technical manuals. The standard score is between 0-100, with a high score indicating the document is easier to read.[36] (However, it is possible to also gain minus scores and scores over 100). The SMOG formula calculates grade level and reader age based on complex word density and assigns a grade level (4th grade to college level).[33 37] It is particularly useful for secondary age readers and attempts to predict 100% comprehension, whereas most other formulae predict 50-75% comprehension. Consequently, SMOG may produce grade level scores one to two grades higher than other formulae. [33 37] The Gunning Fog formula calculates grade level and reader age based on number of sentences, their mean length and number of complex words (three or more syllables).[38] The FORCAST readability formula was initially used for assessing technical documents by calculating the grade level of

text based on number of monosyllabic words. It is the only test not designed for running narrative, for example multiple-choice quizzes and applications. As sentence length is not considered, there may be some variability in grade level compared to other readability formulae. [33]

It was felt the above four formulae allowed comprehensive assessment of an MIS by focussing on various aspects: Flesch Reading Ease - sentence length and syllable number, SMOG - complex word density, Gunning Fog - sentence number/length and complex words and FORCAST - number of monosyllabic words and non-dependence on running narrative.

The readability of 10 corresponding MIS of a sample of commonly prescribed Rheumatology medications published in the UK by Arthritis Research UK[39] and from Canada published by Rheuminfo[40] was also assessed as above. These 10 MIS were representative of the MIS available on both these websites.

Assessment of literal comprehension

Coffs Harbour is a growing regional city of 70 000 people located half-way between the Australian capital cities of Sydney and Brisbane. Its medical specialists provide services to another 50 000 people from the surrounding area. Rheumatology services are provided by two Rheumatologists (PKKW and HB) under the auspices of the Mid-North Coast Arthritis Clinic (MNCAC). The MNCAC has over 16 000 patients on its computerised database.

A random sample of patients referred to the MNCAC was asked to read one ARA MIS[31] containing information about one of the following medications which the patient was unfamiliar with (see supplementary material): methotrexate (MTX), non-steroidal anti-inflammatory drugs (NSAIDs), adalimumab (ADA), abatacept (ABA) or prednisone. All consecutive patients scheduled for a randomly selected consulting day were contacted via telephone by an investigator (MO or ET). Patients (n=261) were asked whether they were interested in study participation to determine what they understood after reading information from the doctor. Responses are outlined in Figure 1. Those who expressed interest in study participation were mailed information about the study and a consent form to be returned in a stamped pre-addressed envelope (n=142). Those who agreed to participate were assessed on the day of the planned consultation (n=95). These was no difference in gender or age between those included compared to those not contactable (data not shown). Comprehension was assessed by asking the patient to answer five multiple choice questions (see supplementary material) about the content of the one ARA MIS they had just read. These questions were designed by two Rheumatologists (PKKW, HB), a Rheumatology Nurse (DF) and an education academic with expertise in literacy (JJ). The questions were trialled on small focus groups of patients. A time limit of 15 minutes in a quiet well-lit room was provided. If needed, study participants could refer back to the MIS while answering the questions. Informed consent was obtained from all study participants.

Patient and Public Involvement

Previous work by us found that up to 15% of patients had low health literacy and up to one third of patients incorrectly followed dosing instructions for common Rheumatology drugs. [23]

These findings prompted us to conduct this study which examined the readability of MIS routinely used in our clinical practice. Furthermore, some of our patients had previously commented that the ARA MIS were difficult to understand. A summary of study results will be disseminated to all study participants. Patients were not involved in the recruitment to, and conduct of the study. However, many study participants indicated they hoped their study involvement would lead to the development of better written material for future patients.

Statistical analyses

Descriptive summary statistics (mean ± SD and median ± interquartile range, as appropriate) were used to analyse parameters. Student's t-test was used to compare means of normally distributed parameters. The Mann-Whitney U test was used to compare medians of groups. For all statistical tests, $p<0.05$ was considered significant. Data analysis was undertaken using GraphPad Prism 6 (GraphPad Software Inc, USA).[41] The correlation (r-value) between comprehension score and various parameters (age, gender, postcode, highest level of education) was performed using STATA (Stata 11.1, StataCorp, TX, USA).

Ethics

Approval as a low/negligible risk project was obtained from the New South Wales North Coast Human Research Ethics Committee (NCNSW HREC No LNR 150).

Results

Assessment of readability

The mean (± SD) grade level for the ARA MIS calculated using Readability Studio™ was 11.6± 0.1 with a mean reading age of 16.6 ± 0.1 years (Table 1). (These were obtained by

calculating the mean of the FORCAST, Gunning Fog and SMOG mean grade level and reading age). The mean (± SD) Flesch Reading Ease score of 50.8 ± 0.6 indicated the ARA MIS were either "fairly difficult" or "difficult"[33] (Table 1). Overall, difficult sentences (>22 words) and complex words (≥ 3 syllables) made up 9.0% and 18.4% of the text, respectively (Table 2).

As the validity of the above readability assessment measures has been questioned due to over-reliance on sentence and word length[42 43], we proceeded to assess patient literal comprehension of the ARA MIS.

Assessment of comprehension

A total of 261 patients were contacted, with 95 study participants (Figure 1). Mean (± SD) age of study participants was 60 ± 13.2 years, with 71/95 (75%) females and 24/95 (25%) males (Table 3). Nineteen of the 95 (20%) patients had a university degree (Table 3). Only 9/21 (43%) and 13/24 (54.2%) patients correctly answered all five questions for adalimumab and abatacept, respectively (Table 3). Only 7/11 (63.6%) of patients correctly answered all five simple questions assessing literal comprehension of the MTX MIS (Table 3). Questions assessing comprehension of the prednisone MIS were correctly answered by most participants (10/11; 90.9%). Of concern, only 21.4% (6/28) of patients correctly answered all questions assessing comprehension of the NSAID MIS. Responses to the five NSAID questions are shown in Figure 2.

Highest level of education achieved (r=0.33, p =0.001) and age (r= -0.3, p=0.0002) correlated moderately strongly with a higher comprehension score.

Comparison of readability scores for Australian, UK and Canadian MIS

Given our findings, we sought to determine using Readability Studio™ what the readability scores were for MIS used in other countries. The mean (± SD) grade level for 10 of the commonly used UK MIS was 11.8 ± 0.1 with a reader age of 16.9 ± 0.1 years (Table 4). The mean Flesch Reading Ease score was 48.5 ± 1.5 - classified as "difficult". Readability of the Canadian MIS was easier with a mean (± SD) grade level of 9.7 ± 0.1 and mean (± SD) reader age of 14.8 ± 0.1 years (Table 5). The mean (± SD) Flesch Reading Ease score for the Canadian MIS was 66.1 ± 1.0 - classified as "standard".[33]

There was no significant difference in mean grade levels between the Australian and UK MIS ($p=0.10$). However, the mean grade level of the Canadian MIS (9.7 ± 0.1) was less than that of the corresponding Australian MIS (11.7 ± 0.1, $p<0.0001$).

The Australian MIS were the longest (mean ± SD, number of words = 1474.1 ± 44.6) (Table 2) compared with the UK (mean ± SD, number of words = 922.4 ± 109.6) (Table 6a) and Canadian MIS (mean ± SD, number of words = 297.7 ± 19.2) (Table 6b). The Australian MIS also had the highest percentage of complex words (three or more syllables, 18%), compared with the UK (16%) and Canadian (14%) MIS.

Discussion

We showed that the readability of commonly used Rheumatology MIS given to patients in Australia, the UK and Canada exceeded eighth grade level – the recommended level for a low-literacy population. [11 15] The Canadian MIS assessed were easier to read, although

remained slightly above eighth grade level. We found that in a population of patients attending a regional private Rheumatology practice where only 20% of participants possessed a university degree, patient comprehension of the Australian MIS was poor, with up to 79% of patients failing to correctly answer all five simple questions assessing literal comprehension of commonly prescribed Rheumatology medications. As expected, a higher level of education achieved was associated with better comprehension ($r = 0.33$, $p = 0.001$). This, along with high readability scores, suggested that current ARA MIS may be too difficult for many patients to understand. While comprehension of the Canadian MIS was not performed, this would provide useful information about the effectiveness of these easier-to-read materials.

The Canadian MIS were simpler, more "readable" and included pictures. Many studies have shown that incorporating pictograms into patient information material improves patient comprehension.[44-49] One study of 60 patients showed that pictograms improved comprehension of patient information sheets from 40% to 93%.[45] Another strategy to improve MIS readability is to shorten the document. However, a shorter, simpler MIS may remove important information and be inadequate for patients with high literacy. Yet, studies have shown both low and high literacy groups recalled information best when the text was easy.[50] These findings suggest that written materials designed for patients with low health literacy may also be useful for a general audience.

It is important to consider the primary purpose of providing written health-related information to a patient. Although the provision of information as part of patient education to facilitate informed patient treatment decisions is important, worry over potential medicolegal exposure from a treatment-related adverse event continues to drive complexity of written materials.[51]

Potential limitations of this study include the type of population studied and the measures used to assess readability. All study participants were from Coffs Harbour, a large regional community on the east coast of Australia. Although one may expect literacy levels to be lower in a rural setting, previous work from our centre showed no difference in health literacy between our patients compared to an urban Rheumatology private practice in a capital city.[23]

There has been criticism of readability formulae such as the Flesch Reading Ease formula, SMOG scale and the Gunning Fog scale.[43 52-54] Readability formulae are usually based solely on word length or syllable number. They may therefore fail to adjust for patient familiarity with vocabulary associated with their illness, therefore over-estimating the difficulty of written information when read by patients familiar with their disease.[52 54] By necessity, health-related written material uses text characterised by polysyllabic technical jargon, which elevates readability formulae scores.[55] For example, exchanging "adalimumab" for "Humira" in the Australian MIS increases the Flesch Reading ease score from 46 to 50 and reduces the Gunning Fog score from 12.7 to 12.5. (The SMOG remains unchanged at 12.8). Readability formulae fail to account for the stylistic properties of text as well as grammatical errors which influence readability of written text. Textual coherence, that is, the relationship and connection between sentences within a document and the relationship between the reader and practitioner are also unaccounted for. Lastly, readability formulae do not usually consider visual and design factors which may influence MIS readability or patient comprehension.[56 57] While the Flesch Reading Ease formula tends to over-estimate readability of health-related material due to its lower level of expected comprehension criteria[53], the SMOG formula is appropriate for assessing health-related written information as it has been validated against 100% comprehension.[53] One approach to addressing these limitations is the use of a more holistic linguistic framework for assessing written patient information which incorporates structure, factual content, and visual aspects of the material as well as the relationship

between writer and reader.[43] This method has been validated using RA medication leaflets in an Australian cohort of RA patients. [58] However, the education level of patients in that study exceeded that seen in our cohort, with 17/27 (63%) having completed tertiary studies compared to 19/95 (20%) in ours.

In view of the potential limitations of readability formulae, we were careful to assess patient literal comprehension of various ARA MIS. As suggested by the relatively low readability scores of the ARA MIS, patient literal comprehension of a selection of the ARA MIS was poor. Due to the simplicity of the five questions posed to the patients, we hoped a satisfactory score would be correct answers to all five questions. However, this only occurred in 21% of patients for NSAIDs and 40-60% of patients for the MTX, ADA and ABA MIS.

Despite the confines and limitations of readability formulae, we believe they remain an important guide when developing written patient information or revising original drafts. This has been validated by several studies that used these formulae to simplify existing written patient information - resulting in enhanced patient comprehension. [59 60] We hope the results of this study will encourage clinicians from Rheumatology and all other specialities to consider the health literacy of their patients and readability of the written information they provide, particularly given the potential of technology to improve patient education.

Conclusion

Medication information sheets currently used by many Rheumatologists in Australia, the UK and Canada exceed eighth grade level – the recommended level for a low-literacy population. This may explain why patient comprehension of the information contained in these materials is limited. Comprehension may be improved using simpler, shorter words and sentences with greater use of pictures and info-graphics. This may lead to greater patient medication

adherence, understanding of their condition, and reduced medication-related errors. It is hoped our findings will encourage all healthcare professionals to consider the appropriateness of written healthcare material provided to patients. The health literacy of patients should always be considered when communicating a management plan.

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Author contributions

MO and ET were responsible for data acquisition. MO was responsible for drafting the manuscript and data analysis under the supervision of PW. PW, JJ, DF and HB conceived and designed the study. All authors contributed to interpretation of data and revision of the manuscript and approve the final manuscript.

Competing interests

The authors declare no competing interests.

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Data sharing statement

No additional data available.

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Figure Legends

Figure 1: Inclusions and exclusions

Figure 2: Answers to NSAID questions

Table 1: Readability scores for Australian Rheumatology Association Medicine Information Sheets

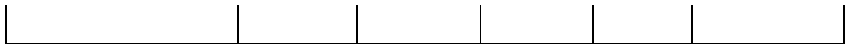
Medicationn	Flesch Reading Ease * (0-100)	FORCAST# grade level	FORCAST# reader age (years)	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level@	Mean reader age@ (years)
Abatacept	49	11.2	16-17	12.3	17-18	12.4	17-18	12.0	17.2
Adalimumab	46	11.2	16-17	12.7	17-18	12.8	17-18	12.2	17.2
Allopurinol	53	10.8	15-16	10.5	15-16	11.5	16-17	10.9	15.8
Apremilast	56	10.6	15-16	11.3	16-17	11.7	16-17	11.2	16.2
Azathioprine	50	10.7	15-16	11.6	16-17	12.2	17-18	11.5	16.5
Bisphosphonates IV	49	11.1	16-17	12.1	17-18	12.2	17-18	11.8	17.2
Bisphosphonates Oral	49	11.2	16-17	12.2	17-18	12.3	17-18	11.9	17.2
Bosentan	59	10.4	15-16	11.0	16-17	11.5	16-17	11.0	16.2
Certolizumab	46	11.1	16-17	12.8	17-18	12.9	17-18	12.3	17.2
Colchicine	53	11.1	16-17	11.7	16-17	11.7	16-17	11.5	16.5
Cyclophosphamide	53	10.7	15-16	10.8	15-16	11.8	16-17	11.1	15.8
Cyclosporin	54	10.7	15-16	11.8	16-17	12.0	17-18	11.5	16.5
Denosumab	50	11.0	16-17	11.9	16-17	12.1	17-18	11.7	16.8
Etanercept	48	11.1	16-17	12.7	17-18	12.8	17-18	12.2	17.2
Febuxostat	54	10.7	15-16	10.8	15-16	11.7	16-17	11.1	15.8
Golimumab	48	11.1	16-17	12.8	17-18	12.8	17-18	12.2	17.2
Hyaluronic Acid	51	11.1	16-17	11.8	16-17	11.9	16-17	11.6	16.5
Hydroxychloroquine	49	10.9	15-16	11.6	16-17	11.7	16-17	11.4	16.2
Infliximab	49	11.1	16-17	12.5	17-18	12.6	17-18	12.1	17.2
Leflunomide	54	10.7	15-16	11.6	16-17	12.2	17-18	11.5	16.5
Methotrexate	52	10.9	15-16	11.4	16-17	12.3	17-18	11.5	16.5
Mycophenolate	50	11.0	16-17	11.6	16-17	12.5	17-18	11.7	16.8
NSAIDs	58	10.6	15-16	11.0	16-17	11.3	16-17	11.0	16.2
Prednisone	51	10.9	15-16	11.2	16-17	11.9	16-17	11.3	16.2
Rituximab	48	11.3	16-17	12.3	17-18	12.5	17-18	12.0	17.2
Sulfasalazine	50	10.9	15-16	11.4	16-17	11.9	16-17	11.4	16.2
Teriparatide	49	10.9	15-16	11.6	16-17	12.1	17-18	11.5	16.5
Tocilizumab	47	11.1	16-17	12.0	17-18	12.5	17-18	11.9	17.2
Tofacitinib	46	11.1	16-17	12.1	17-18	12.2	17-18	11.8	17.2
Ustekinumab	54	10.8	15-16	11.5	16-17	12.0	17-18	11.4	16.5
Mean	**50.8**	**10.9**		**11.8**		**12.1**		**11.6**	**16.6**
SD	**0.6**	**0.0**		**0.1**		**0.1**		**0.1**	**0.1**

Abbreviations

* Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
[#] FORCAST (named after the authors FORd, CAylor, STicht)
[**] SMOG = Simple Measure Of Gobbledygook
@ Mean of FORCAST, Gunning Fog and SMOG scores

Table 2: Word and sentence statistics for Australian Rheumatology Association Medicine Information Sheets

Medication	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	Total no. of words	No. of complex** words
Abatacept	133	8 (5%)	12.1	1612	314 (19.5%)
Adalimumab	125	11 (8.8%)	12.6	1576	315 (20%)
Allopurinol	124	10 (8.1%)	12.2	1507	252 (16.7%)
Apremilast	92	9 (9.8%)	11.9	1095	184 (16.8%)
Azathioprine	118	9 (7.6%)	13	1539	273 (17.7%)
Bisphosphonates IV	95	11 (11.6%)	12.6	1199	217 (18.1%)
Bisphosphonates Oral	112	11 (9.8%)	13	1456	277 (19%)
Bosentan	107	11 (10.3%)	11.4	1219	214 (17.6%)
Certolizumab	125	12 (9.6%)	13	1624	320(19.7%)
Colchicine	123	8 (6.5%)	11.6	1426	260 (18.2%)
Cyclophosphamide	118	12 (10.2%)	12.4	1469	266 (18.1%)
Cyclosporin	102	8 (7.8%)	12.1	1235	227 (18.4%)
Denosumab	110	10 (9.1%)	12	1317	243 (18.5%)
Etanercept	124	11 (8.9%)	13.1	1621	321 (19.8%)
Febuxostat	120	12 (10%)	12.4	1484	255 (17.2%)
Golimumab	123	12 (9.8%)	12.9	1588	316 (19.9%)
Hyaluronic Acid	81	4 (4.9%)	11.3	919	181 (19.7%)
Hydroxychloroquine	87	9 (10.3)	12	1046	184 (17.6%)
Infliximab	138	13 (9.4%)	13.1	1807	344 (19%)
Leflunomide	111	10 (9%)	12.9	1427	254 (17.8%)
Methotrexate	156	20 (12.8%)	13.4	2097	375 (17.9%)
Mycophenolate	141	15 (10.6%)	12.1	1712	334 (19.5%)
NSAIDs	137	14 (10.2%)	12.8	1750	266 (15.2%)
Prednisone	128	12 (9.4%)	13	1668	292 (17.5%)
Rituximab	132	9 (6.8%)	12.3	1627	318 (19.5%)
Sulfasalazine	124	9 (7.3%)	12.1	1497	276 (18.4%)
Teriparatide	114	13 (11.4%)	11.5	1310	238 (18.2%)
Tocilizumab	130	12 (9.2%)	12.7	1654	311 (18.8%)
Tofacitinib	111	7 (6.3%)	12	1336	249 (18.6%)
Ustekinumab	114	8 (7%)	12.3	1406	259 (18.4%)
Mean	**118.5**	**10.7 (9.0%)**	**12.4**	**1474.1**	**271.2 (18.4%)**
SD	**3.0**	**0.5**	**0.1**	**44.6**	**9.0**



*Difficult sentence: ≥22 words; **Complex word: ≥3 syllables

Table 3: Assessment of patient literal comprehension (n=95 patients)

age (yrs, mean ± SD)	60.0±13.2
sex (F/M)	71/24
highest level of education	**no. (%)**
≤Yr 10	39 (41)
Yr 10-12	15 (16)
sub-degree, eg TAFE*, apprenticeship	22 (23)
university degree	19 (20)
median total score (max=5)	4
no. with all correct answers (ie, 5/5)	**no. (%)**
adalimumab	9/21 (43)
MTX	7/11 (63.6)
NSAIDs	6/28 (21.4)
prednisone	10/11 (90.9)
abatacept	13/24 (54.2)

Abbreviations
*TAFE= Technical and Further Education

MTX= methotrexate

NSAID=non-steroidal anti-inflammatory drugs

Table 4: Readability scores for Arthritis Research United Kingdom Medicine Information Sheets

Medication	Flesch Reading Ease* (0-100)	FORCAST# grade level	FORCAST# reader age	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level @	Mean reader age@ (years)
Abatacept	46	10.9	15-16	13.1	18-19	13.2	18-19	12.4	17.5
Adalimumab	47	11.1	16-17	12.1	17-18	12.5	17-18	11.9	17.2
Bisphosphonates	53	11.1	16-17	11.9	16-17	12.3	17-18	11.8	16.8
Denosumab	42	11.7	16-17	12	17-18	12.6	17-18	12.1	17.2
Etanercept	49	11	16-17	11.9	16-17	12.4	17-18	11.8	16.8
Hydroxychloroquine	41	11.2	16-17	12.5	17-18	12.5	17-18	12.1	17.2
Leflunomide	53	10.8	15-16	11.9	16-17	12.2	17-18	11.6	16.5
Methotrexate	51	10.8	15-16	12.1	17-18	12.4	17-18	11.8	16.8
Prednisolone	55	11.1	16-17	11.3	16-17	11.6	16-17	11.3	16.5
Sulfasalazine	48	10.8	15-16	11.9	16-17	12.2	17-18	11.6	16.5
Mean	**48.5**	**11.1**		**12.1**		**12.4**		**11.8**	**16.9**
SD	**1.5**	**0.1**		**0.1**		**0.1**		**0.1**	**0.1**

Abbreviations

*Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
FORCAST (named after the authors FORd, CAylor, STicht)
**SMOG = Simple Measure Of Gobbledygook
@ Mean of FORCAST, Gunning Fog and SMOG scores

Table 5: Readability scores for Canadian Medicine Information Sheets

Medication	Flesch Reading Ease * (0-100)	FORCAST# grade level	FORCAST# reader age (years)	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level@	Mean reader age@ (years)
Abatacept	65	10	15-16	8.5	13-14	10.3	15-16	9.6	14.8
Adalimumab	61	10.1	15-16	9.8	14-15	10.2	15-16	10	15.2
Bisphosphonates	63	10.2	15-16	9.5	14-15	10	15-16	9.9	15.2
Denosumab	66	9.6	14-15	9.6	14-15	10	15-16	9.7	14.8
Etanercept	64	10.1	15-16	9.9	14-15	10.3	15-16	10.1	15.2
Hydroxychloroquine	72	8.8	13-14	8.4	13-14	9.5	14-15	8.9	13.8
Leflunomide	67	9.9	14-15	9.4	14-15	9.9	14-15	9.7	14.5
Methotrexate	66	9.8	14-15	9.5	14-15	10.1	15-16	9.8	14.8
Prednisolone	69	10.2	15-16	9.8	14-15	10.1	15-16	10	15.2
Sulfasalazine	68	9.3	14-15	9.1	14-15	9.7	14-15	9.4	14.5
Mean	**66.1**	**9.8**		**9.4**		**10.0**		**9.7**	**14.8**
SD	**1.0**	**0.1**		**0.2**		**0.1**		**0.1**	**0.1**

Abbreviations

* Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
# FORCAST (named after the authors FORd, CAylor, STicht)
**SMOG = Simple Measure Of Gobbledygook
@ Mean of FORCAST, Gunning Fog and SMOG scores

Table 6: Word and sentence statistics for a) United Kingdom; and b) Canadian Medicine Information Sheets

a) United Kingdom

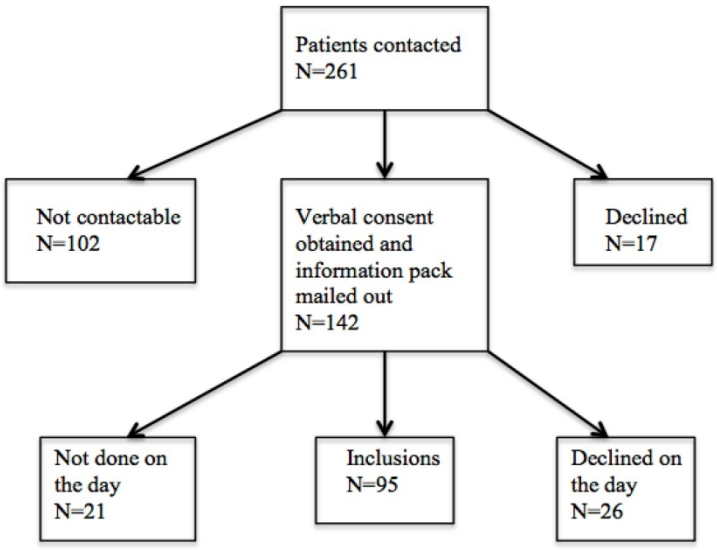
Drug	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	No. of words	No. of complex** words
Abatacept	66	18 (27%)	17.1	1130	206 (18%)
Adalimumab	71	10 (14%)	15.3	1086	191 (18%)
Bisphosphonates	36	10 (28%)	15.7	566	92 (16%)
Denosumab	8	2 (25%)	14.4	115	22 (19%)
Etanercept	81	16 (20%)	15.8	1282	214 (17%)
Hydroxychloroquine	60	13 (22%)	15.3	916	159 (17%)
Leflunomide	63	12 (19%)	16.1	1016	157 (15%)
Methotrexate	75	13 (17%)	16.2	1212	193 (16%)
Prednisolone	60	15 (25%)	17	1020	131 (13%)
Sulfasalazine	53	12 (23%)	16.6	881	132 (15%)
Mean	**57.3**	**12.1 (21%)**	**15.95**	**922.4**	**149.7 (16%)**
SD	**6.7**	**1.4**	**0.3**	**109.6**	**18.7**

b) Canadian

Drug	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	No. of words	No. of complex** words
Abatacept	25	0	11.1	278	38 (14%)
Adalimumab	31	0	11	341	47 (14%)
Bisphosphonates	30	0	10	301	41 (14%)
Denosumab	24	0	10.3	246	34 (14%)
Etanercept	31	0	10.9	339	48 (14%)
Hydroxychloroquine	21	0	9.3	195	23 (12%)
Leflunomide	34	0	10	339	46 (14%)
Methotrexate	32	0	11.2	357	47 (13%)
Prednisolone	36	0	10.1	363	53 (15%)
Sulfasalazine	21	0	10.4	218	27 (12%)
Mean	**28.5**	**0**	**10.43**	**297.7**	**40.4 (14%)**
SD	**1.7**	**0.0**	**0.2**	**19.2**	**3.1**

*Difficult sentence: ≥22 words; **Complex word: ≥3 syllables

Figure 1: Inclusions and exclusions



Inclusions and exclusions

276x197mm (144 x 144 DPI)

Figure 2: Answers to NSAID questions

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions: (note – correct answer ticked)

Non-steroidal anti-inflammatory drugs (NSAIDs) include medications such as Nurofen, Brufen, Voltaren, Naprosyn and Celebrex.

1) Non-steroidal anti-inflammatory drugs (NSAIDs)
✓a) reduce joint pain, swelling and stiffness
b) prevent damage to your joints
c) strengthen your bones
d) will cure your arthritis

No. with correct answer 26/28 (93%)

2) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) can be combined with other NSAIDs
b) can be continued long-term without review
✓c) often cause gut side effects such as nausea, vomiting and bleeding
d) should be continued during surgery

No. with correct answer 17/28 (61%)

3) Non-steroidal anti-inflammatory drugs (NSAIDs)
✓a) may increase the risk of heart attack and stroke
b) prevent attacks of arthritis
c) have no effect on blood pressure
d) are safe in someone with kidney problems

No. with correct answer 24/28 (86%)

4) Non-steroidal anti-inflammatory drugs (NSAIDs) should be used
a) for 4 weeks only
✓b) for the shortest time possible
c) until the script runs out
d) for however long to get rid of the pain

No. with correct answer 12/28 (43%)

5) Bleeding from inside the gut while taking a non-steroidal anti-inflammatory drug (NSAID)
a) can be completely prevented by taking the NSAID with food
b) should stop if you continue taking the NSAID
c) doesn't cause any problems and can be ignored
✓d) can be associated with abdominal pain and indigestion

No. with correct answer 14/28 (50%)

Answers to NSAID questions

170x210mm (144 x 144 DPI)

Please tick (✓) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Methotrexate

1) Methotrexate
a) reduces joint swelling only
b) is a pain killer only
c) will strengthen your bones
d) reduces damage to your joints

2) Methotrexate will
a) work immediately
b) take one year to work
c) take some weeks to work
d) not work unless given as an injection

3) Methotrexate is taken
a) once a day
b) once a week
c) once a month
d) once every 6 months

4) Folic acid is a natural vitamin taken with Methotrexate to
a) reduce pain
b) give you more energy
c) reduce the side effects of Methotrexate
d) stop the arthritis

5) Methotrexate should be taken
a) indefinitely if there are no serious side effects
b) until the script runs out
c) until you feel better
d) for 4 weeks only

(Correct answers based on Patient Information Sheet:
1d, 2c, 3b, 4c, 5a – Not to be included in copy given to patients)

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

Prednisone/Prednisolone/corticosteroids/cortisone all refer to the same drug.

1) Prednisone
a) cures arthritis at high doses
b) reduces joint pain, inflammation and joint swelling
c) makes your muscles bigger
d) makes your bones stronger

2) Prednisone
a) can be stopped suddenly with no problems
b) should be stopped if you get an infection
c) should not be stopped suddenly
d) is a very safe drug and you can change the dose yourself

3) Prednisone works
a) within a few days
b) only in combination with other arthritis medication
c) only if taken long-term
d) by irreversibly suppressing your immune system

4) Prednisone
a) should be stopped in pregnancy
b) can cause thin bones
c) does not affect blood sugar levels
d) helps you lose weight

5) Prednisone
a) should be stopped just before surgery
b) should not be taken with other arthritis medications
c) needs to be taken for the rest of your life
d) is often able to be stopped once the arthritis is controlled

(Correct answers based on Patient Information Sheet:
1b, 2c, 3a, 4b, 5d – Not to be included in copy given to patients)

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

Adalimumab is also called Humira.

1) Humira
a) is a pain killer
b) reduces damage to your joints
c) will strengthen your bones
d) just reduces joint swelling

2) Humira will
a) work immediately
b) take one year to work
c) take some weeks to work
d) not work unless you take other arthritis medication

3) Humira is taken
a) once a day
b) only when the arthritis flares
c) once every 2 weeks
d) once every 6 months

4) Humira should be continued
a) unless advised by your doctor to stop
b) until the script runs out
c) until you feel better
d) for 4 weeks only

5) If you are taking Humira and get an infection which isn't getting better
a) try some tumeric
b) double the dose of Humira
c) just take some antibiotics
d) stop the Humira

(Correct answers based on Patient Information Sheet:
1b, 2c, 3c, 4a, 5d – Not to be included in copy given to patients)

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

Non-steroidal anti-inflammatory drugs (NSAIDs) include medications such as Nurofen, Brufen, Voltaren, Naprosyn and Celebrex.

1) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) reduce joint pain, swelling and stiffness
b) prevent damage to your joints
c) strengthen your bones
d) will cure your arthritis

2) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) can be combined with other NSAIDs
b) can be continued long-term without review
c) often cause gut side effects such as nausea, vomiting and bleeding
d) should be continued during surgery

3) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) may increase the risk of heart attack and stroke
b) prevent attacks of arthritis
c) have no effect on blood pressure
d) are safe in someone with kidney problems

4) Non-steroidal anti-inflammatory drugs (NSAIDs) should be used
a) for 4 weeks only
b) for the shortest time possible
c) until the script runs out
d) for however long to get rid of the pain

5) Bleeding from inside the gut while taking a non-steroidal anti-inflammatory drug (NSAID)
a) can be completely prevented by taking the NSAID with food
b) should stop if you continue taking the NSAID
c) doesn't cause any problems and can be ignored
d) can be associated with abdominal pain and indigestion

(Correct answers based on Patient Information Sheet:
1a, 2c, 3a, 4b, 5d – Not to be included in copy given to patients)

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

Abatacept (Orencia)

1) Abatacept will
a) reduce joint swelling only
b) act as a pain killer only
c) strengthen your bones
d) reduce joint pain, swelling and stiffness in your joints

2) Abatacept will
a) work immediately
b) take one year to work
c) take some weeks to work
d) work only intermittently

3)Abatacept is given via a subcutaneous injection
a) once a day
b) once a week
c) once a month
d) once every 6 months

4) Abatacept works by
a) blocking pain
b) blocking T-cell responses to reduce inflammation
c) making you feel calm
d) making you more alert

5) While on Abatacept you should
a) be monitored regularly
b) take the medication until the script runs out
c) take the medication until you feel better
d) take the medication for 4 weeks only

(Correct answers based on Patient Information Sheet:
1d, 2c, 3b, 4b, 5a – Not to be included in copy given to patients)

Australian Rheumatology Association

Arthritis AUSTRALIA

PATIENT INFORMATION ON

ABATACEPT

(Brand name: Orencia)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition and detect unwanted effects**
- **other precautions you should take while you are taking abatacept**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking abatacept you must see your rheumatologist regularly to ensure the treatment is working and to minimise any possible side effects.
- If you stop abatacept for any reason you must contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.
- If you are worried about any side effects you should contact your rheumatologist as soon as possible.
- If you are injecting abatacept under the skin (subcutaneously) remember to change the injection site each time.
- It is important to tell your doctor if you have had cancer or if you develop cancer.
- If you are taking abatacept and plan to become pregnant you must discuss the timing with your doctor.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website
www.arthritisaustralia.com.au

What is abatacept?

Abatacept (brand name Orencia) belongs to a new class of medicines called **biological disease modifying antirheumatic drugs (biological DMARDs or bDMARDs).**

bDMARDs have now been given to over a million people worldwide since their initial use in the late 1990s.

These medicines block natural substances called cytokines. These are substances found in excessive amounts in the blood and joints of people with rheumatoid arthritis and juvenile arthritis.

The increased levels of cytokines cause inflammation, which results in symptoms of pain, joint swelling and stiffness, and can lead to joint damage.

By blocking T cell (a type of white blood cell) responses, abatacept reduces inflammation, lessens the symptoms and helps stop further joint damage.

What benefit can you expect from your treatment?

Unlike standard antirheumatic drugs (DMARDs), abatacept works relatively quickly. You may notice some relief of joint swelling, pain and stiffness within the first 4-8 weeks of treatment.

Australian Rheumatology Association

Stopping abatacept

If abatacept treatment is stopped for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop (see *Side effects*).

If you stop abatacept for any reason you **must** contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.

How will your condition be monitored?

In view of the current prescribing restrictions for all bDMARDs:

- Abatacept will only be started if your disease is active and if standard treatments have been unsuccessful.
- It will not be continued unless it helps your condition. This will be assessed at least 12 weeks after the start of treatment.
- Blood tests will be required during your treatment to monitor your condition and to determine the effectiveness of treatment.
- The frequency of blood tests will depend on what other medicines you are taking and what other illnesses you might have. Your rheumatologist will determine the frequency of tests required.

How is abatacept given?

Abatacept is given as a drip (infusion) into the vein, or as an injection under the skin of the abdomen or thigh.

The infusion normally takes thirty minutes. This is followed by a one hour period of observation to make sure you don't have any side effects. Additional doses are usually given at 2 and 4 weeks after the first dose. Subsequent doses are usually given every 4 weeks.

When given as an injection under the skin (subcutaneous injection), doses are given weekly.

The treatment may still begin with a single dose given as an infusion (loading dose).

Abatacept is given in combination with the DMARD methotrexate.

What is the dosage?

For infusions the dose is based on the person's weight, so each person's dose may be different.

The subcutaneous dose is a standard 125mg weekly injection.

Can other medicines be taken with abatacept?

Abatacept may be used with other arthritis medicines including:

- other DMARDs such as methotrexate
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

Abatacept cannot be used with other bDMARDs.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience side effects with your treatment. Contact your doctor if you have any concerns about possible side effects. Many side effects disappear when abatacept treatment is stopped.

Most common possible side effects

- Common possible side effects include:
  - *headaches, runny nose, dizziness or cough*
  - *sore throat, heartburn or nausea*
  - *back, arm or leg pain*
  - *urine infections*

Australian Rheumatology Association

  - *rash.*
- *Stomach and bowel discomfort* may also occur.
- As abatacept affects the immune system, *mild infections*, particularly of the upper respiratory tract (e.g. colds, sinusitis) may occur more frequently than usual. Treatment with abatacept may need to be temporarily stopped so contact your doctor for advice.

Less common or rare possible side effects

- Side effects can occur during the infusion itself. These may include *fever or chills, itch, chest pain, shortness of breath* or *changes in blood pressure*. These effects are more likely to occur during the first or second infusion.
- Mild pain, swelling, bruising or itching may occur at the injection site (for subcutaneous doses). It is therefore important to rotate the injection site.
- *Serious infections* such as tuberculosis (TB) are seen rarely, and screening for TB is needed before treatment begins (see *Precautions*).
- Rarely abatacept may cause an *allergic reaction* with itchy, red skin or a rash.
- It is still unclear from research if there is an increased risk of cancer due to abatacept treatment (see *Precautions*).

What precautions are necessary?

Infections

- If you have an active infection of any kind, treatment with abatacept will not be given until the infection is treated successfully.
- Abatacept will not be given if you have active untreated tuberculosis (TB) or HIV (AIDS) infection as it is likely to make these conditions worse.
- If you have latent (inactive) TB preventative anti-TB treatment will be started at least 4 weeks before abatacept. The anti-TB treatment will usually need to be taken for 9 months.
- Hepatitis B or C infection may not necessarily exclude treatment.
- Because of the risks associated with infection the following tests may be conducted before commencing treatment with abatacept:
  - blood tests for hepatitis B and C
  - chest x-ray and two step Tuberculin Skin Test (Mantoux) or QuantiFERON blood test for tuberculosis (TB)
  - HIV tests are required for those who are at risk of this infection.

Precautions with other diseases

- People with chronic lung disease (COPD) are not usually given abatacept but each case will be assessed individually.

Use with other medicines

- Abatacept can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals.
- Abatacept does not increase the risk of side effects from low dose aspirin (taken for prevention of heart attack and strokes).
- The simple pain reliever paracetamol and combined pain medicines such as Panadeine and Panadeine Forte can be used while you are receiving abatacept treatment provided you take them as directed.

Vaccines

- If you are on abatacept it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio virus), BCG (Bacillus Calmette Guerin) or yellow fever. Talk with your rheumatologist before receiving any vaccines.
- Pneumovax and the combined yearly seasonal flu/swine flu vaccinations are

Australian Rheumatology Association

safe and recommended to reduce your risk of those infections.

Surgery

- If you require surgery for any reason, treatment with abatacept will be stopped before surgery.

  It will be restarted again after the operation at a time determined by your surgeon and rheumatologist. Treatment will be restarted once the wound is healed and if there is no infection present.

Use with alcohol

- You may drink alcohol while taking abatacept. However, if you are also taking methotrexate you should be particularly cautious about your alcohol intake.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Cancer risk

- Lymphoma, a cancer of lymph glands, is found more commonly in patients with severe active rheumatoid arthritis than in the general population. Studies are in progress to see if treatment with abatacept changes this. To date there is no evidence to suggest that this medicine increases lymphoma.

  If cancer has been previously treated and cured it is unclear whether abatacept can be used safely. An interval of 5 years is normally recommended between cure of a cancer and starting TNF-bDMARDs.
- For general cancer prevention, stopping smoking and taking skin cancer prevention measures are recommended. It is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.
- Talk to your doctor if you have any concerns about issues relating to cancer risk.

Use in pregnancy and when breastfeeding

- Not enough is known regarding the possible side effects of abatacept. If you plan to become pregnant, it is important to discuss this with your doctor, as each case is different.
- You should not breastfeed when taking abatacept.

How to store abatacept

- Keep the medicine refrigerated, even when travelling.
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking abatacept you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

PATIENT INFORMATION ON

ADALIMUMAB

(Brand name: Humira)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition**
- **other precautions you should take while you are taking adalimumab.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking adalimumab you must see your rheumatologist regularly to ensure the treatment is working and minimise any possible side effects.
- If you stop adalimumab for any reason you must contact your doctor. Failure to do so may mean that your continued treatment will no longer be subsidised.
- Remember to change the injection site each time adalimumab is injected.
- If you are worried about any side effects you should contact your rheumatologist as soon as possible.
- It is important to tell your doctor if you have had cancer or if you develop cancer.
- If you are taking adalimumab and plan to become pregnant you must discuss the timing with your doctor.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html.

What is adalimumab?

Adalimumab (brand name Humira) belongs to a new class of medicines called **biological disease modifying antirheumatic drugs (biological DMARDs or bDMARDs).**

bDMARDs have now been given to over a million people worldwide since their initial use in the late 1990s.

These medicines block natural substances, called cytokines. These are substances found in excessive amounts in the blood and joints of people with rheumatoid arthritis, psoriatic arthritis, juvenile arthritis and ankylosing spondylitis.

The increased levels of cytokines cause inflammation, which results in symptoms of pain, joint swelling and stiffness, and can lead to joint damage.

By blocking the cytokine called Tumour Necrosis Factor (TNF), adalimumab reduces inflammation, lessens the symptoms and helps stop further joint damage.

What benefit can you expect from your treatment?

Unlike standard antirheumatic drugs (DMARDs), adalimumab works relatively quickly. You may notice some relief of joint swelling, pain and stiffness within the first 4 weeks of treatment.

Stopping adalimumab

If adalimumab treatment is stopped for more than a few weeks there is a risk that your condition will get worse again. Continue with your treatment unless advised by your doctor or unless side effects develop (see *Side effects*).

If you stop adalimumab for any reason you **must** contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.

How will your condition be monitored?

Due to the current prescribing restrictions for all bDMARDs:

- Adalimumab will only be started if your disease is active and if standard treatments have been unsuccessful.
- It will not be continued unless it helps your condition. This will be assessed at least 12 weeks after the start of treatment.
- Blood tests will be required during your treatment to monitor your condition and to determine the effectiveness of treatment.
- The frequency of blood tests will depend on what other medicines you are taking and what other illnesses you might have. Your rheumatologist will determine the frequency of tests required.

How is adalimumab taken?

Adalimumab is injected under the skin of the abdomen or thigh.

It can be injected by your doctor, nurse, carer or by you. If injecting yourself, be sure to follow the detailed instructions carefully to ensure the best response. It is particularly important to change the injection site each time.

What is the dosage?

The usual dose for adults with rheumatoid arthritis is 40mg once every two weeks.

Can other medicines be taken with adalimumab?

Adalimumab may be used with other arthritis medicines including:

- other DMARDs such as methotrexate
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

Adalimumab cannot be used with other bDMARDs.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience side effects with your treatment. Contact your doctor if you have any concerns about possible side effects. Many side effects disappear when adalimumab treatment is stopped.

Most common possible side effects

- *Mild pain, swelling or itching* at the site of the injection are very common (up to 20% of patients) but can be reduced by applying ice and antihistamine/steroid creams to the injection site.
- *Headaches, cough and stomach and bowel discomfort* may also occur.
- As adalimumab affects the immune system, *mild infections,* particularly of the upper respiratory tract (e.g. colds, sinusitis) may occur more frequently than usual. Treatment with adalimumab may need to be temporarily stopped so contact your doctor for advice.

Less common or rare possible side effects

- *Serious infection*s such as Tuberculosis (TB) are seen rarely, and screening for TB is needed before treatment begins (see *Precautions*).
- Rarely adalimumab may cause an *allergic reaction* with itchy, red skin or a rash or a feeling of tightness in the chest and difficulty breathing.

- Side effects involving the nerves, such as *inflammation of the nerve to the eye*, may also occur rarely, causing changes in vision or sensation.
- Very rarely *'drug-induced lupus'* has occurred with symptoms of rash, fever and increased joint pain.
- It is still unclear from research if there is an increased risk of cancer due to adalimumab treatment (see *Precautions*).

What precautions are necessary?

Infections

- If you have an active infection of any kind treatment with adalimumab will not be given until the infection is treated successfully.
- Adalimumab will not be given if you have active untreated tuberculosis (TB) or HIV (AIDS) infection as it is likely to make these conditions worse.
- If you have latent (inactive) TB preventative anti-TB treatment will be started at least 4 weeks before adalimumab. The anti-TB treatment will usually need to be taken for 9 months.
- Hepatitis B or C infection may not necessarily exclude treatment.
- Because of the risks associated with infection the following tests may be conducted before commencing treatment with adalimumab:
  - blood tests for hepatitis B and C
  - chest x-ray and two step Tuberculin Skin Test (Mantoux) or QuantiFERON blood test for tuberculosis (TB)
  - HIV tests are required for those who are at risk of this infection.

Precautions with other diseases

- People with multiple sclerosis should not be treated with adalimumab due to the possible effects on the nerves.
- People with moderate to severe heart failure may not be treated with adalimumab as the medicine can make heart failure worse.
- People with systemic lupus erythematosus (lupus/SLE) are not usually given adalimumab but each case will be assessed individually.

Use with other medicines

- Adalimumab can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals.
- Adalimumab does not increase the risk of side effects from low dose aspirin (taken for prevention of heart attack and strokes).
- The simple pain reliever paracetamol and combined pain medicines such as Panadeine and Panadeine Forte can be used while you are receiving adalimumab treatment provided you take them as directed.

Vaccines

- If you are on adalimumab it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio virus), BCG (Bacillus Calmette Guerin) or yellow fever. Talk with your rheumatologist before receiving any vaccines.
- Pneumovax and the combined yearly seasonal flu /swine flu vaccinations are safe and recommended to reduce your risk of those infections.

Surgery

- If you require surgery for any reason, treatment with adalimumab will be stopped before surgery. It will be restarted again after the operation, at a time determined by your surgeon and rheumatologist. Treatment will be restarted once the wound is healed and if there is no infection present.

Cancer risk

- Lymphoma, a cancer of lymph glands, is found more commonly in patients with severe active rheumatoid arthritis than in the general population. Studies are in progress to see if treatment with adalimumab changes this. To date there is no evidence to suggest that this medicine increases lymphoma.

- If cancer has been previously treated and cured it is unclear whether a TNF-bDMARD such as adalimumab can be used safely. An interval of 5 years is normally recommended between cure of a cancer and starting TNF-bDMARDs.
- For general cancer prevention, stopping smoking and taking skin cancer prevention measures are recommended. It is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.
- Talk to your doctor, if you have any concerns about issues relating to cancer risk.

Use with alcohol

- You may drink alcohol while taking adalimumab. However, if you are also taking methotrexate you should be particularly cautious about your alcohol intake.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Use in pregnancy and when breastfeeding

- Not enough is known regarding the possible side effects of adalimumab on the unborn baby. If you plan to become pregnant, it is important to discuss this with your doctor as each case is different.

How to store adalimumab

- Keep the medicine refrigerated, even when travelling.
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking adalimumab you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

How to help us help you

Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!

Contact us in any of the following ways:

Email: ARAD@monash.edu
Telephone: Sydney 02 9463 1889
or Melbourne 03 9508 3424
Fax: 1-800-022-730

Visit our website:
www.ARAD.org.au

PATIENT INFORMATION ON

METHOTREXATE

(Brand names: Methoblastin)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **what are the possible side effects**
- **what tests you must have to monitor your condition and to detect unwanted effects**
- **other precautions you should take when you are taking methotrexate.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking methotrexate you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.
- You should have regular blood tests as directed by your rheumatologist.
- If you are concerned about any side effects you should contact your rheumatologist as soon as possible.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html

What is methotrexate?

Methotrexate (brand name Methoblastin) is a medicine used to treat rheumatoid arthritis as well as other rheumatic conditions such as juvenile arthritis, lupus (also known as SLE), psoriatic arthritis and polymyositis (muscle inflammation).

Methotrexate is an immunosuppressive medicine. It works by reducing the activity of several enzymes involved in the immune system. By blocking an enzyme called dihydrofolate reductase, it reduces production of a form of folic acid.

It is not entirely clear how methotrexate decreases the severity of arthritis, but it reduces inflammation in the joints and associated pain and swelling.

Because methotrexate reduces the damage to the joints, rather than just relieving the pain, it belongs to the group of medicines called **disease modifying antirheumatic drugs (DMARDS)**.

Methotrexate has been used to treat rheumatoid arthritis for more than 25 years. It is also used at very high doses (1000mg-5000mg a day) to treat some cancers.

What benefit can you expect from your treatment?

Methotrexate is one of the most effective treatments for rheumatoid arthritis. Most, but not all, patients will benefit from this medicine. Some achieve remission, where the arthritis virtually disappears.

Methotrexate does not work straight away. Reduced pain, stiffness and swelling may be noticed after 4 weeks. The effects to delay or prevent joint damage will take several months.

Other medicines may be given to improve your symptoms while waiting for methotrexate to work.

How is methotrexate taken?

Methotrexate may be taken by mouth as a tablet or given by injection either into the muscle or under the skin.

Injections may be used instead of tablets if the medicine is not being absorbed well, or if you feel sick (nausea) or vomit when you take the tablets, or if your condition is not improving with tablets.

Care should be taken when disposing of the needles and syringes.

When should it be taken?

Methotrexate is taken just **once a week,** on the same day each week. If you are taking the tablets, it is a good idea to specify and diarise the day of the week that you will take your tablets to avoid making mistakes.

Methotrexate tablets are best absorbed when taken on an empty stomach. However if nausea is a problem, taking them at mealtime can help to reduce this side effect and does not reduce the benefits too much.

What is the dosage?

Tablets come in 2.5mg or 10mg strengths. Treatment may start with a very low dose of 5mg or 10mg a week, increasing to an average dose of 20mg a week. The dose is adjusted depending on the response, up to about 30mg once a week.

The dose is usually taken all at once on a single day. It may be divided into separate doses taken during that day if necessary.

Can other medicines be taken with methotrexate?

In order to reduce side effects, it is recommended that you also take folic acid or folinic acid. Your doctor will explain how much of the folic/folinic acid to take and when to take it.

Methotrexate is often taken in combination with other arthritis medicines, including:

- other DMARDs
- biological DMARDs (a newer type of DMARD, which act on natural substances in the body that contribute to inflammation and joint damage)
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen/Nurofen)
- simple pain medicines such as paracetamol.

There are separate information sheets for the medicines mentioned above.

How long is the treatment continued?

Treatment with methotrexate is continued indefinitely as long as it is effective and as long as no serious side effects occur.

If you stop methotrexate treatment for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop.

If you have an illness that makes you unwell enough to change plans for the day (e.g. gastroenteritis or fever), it is reasonable to miss the weekly dose until you have recovered.

Are there any side effects?

You might experience side effects with your treatment. Tell your doctor if you are concerned about possible side effects.

A reduction in dose may minimise side effects so that you can continue to take the treatment. Your doctor will advise on any dose changes that are necessary.

Most common possible side effects

- The most common side effects are *nausea, vomiting* and *diarrhoea*. These can be reduced if methotrexate is taken with food or in the evening. Antinausea tablets can be used if needed.
- *Mouth ulcers* can occur, but the use of folic acid or folinic acid supplements makes this less likely.
- *Skin dryness, a variety of skin rashes* and *increased sensitivity to the sun* may also occur. You should wear sunscreen and a hat when out in the sun.
- Some people report mild *tiredness, headache* and *mental clouding*. Some also experience a temporary increase in muscle and joint pain after taking the weekly dose.

Less common or rare possible side effects

There are some rare but potentially serious side effects with methotrexate.

- *Blood counts*: Methotrexate can rarely cause a drop in the number of white blood cells, which are needed to fight infection. It can also cause a drop in the number of platelets, which help to stop bleeding.

  Regular blood tests aim to pick these problems up early if they occur.

  However, if you develop a sore mouth, mouth ulcers, easy bruising, nosebleeds, bleeding gums, breathlessness, infection or fever tell your doctor straight away.

- *Liver*: Methotrexate can inflame the liver causing a type of hepatitis. Regular blood tests aim to pick this up early if it occurs. The dose of methotrexate may need to be reduced or stopped if problems occur. Liver problems may be increased when methotrexate is combined with the medicines azathioprine (Azamun, Azapin, Imuran, Thioprine) or leflunomide (Arabloc, Arava) or with heavy alcohol use (see *Alcohol* overleaf).
- *Lungs*: Methotrexate can cause inflammation of the lungs. This may be more likely if leflunomide is being taken at the same time. The problem may develop quickly, so if you have a sudden onset of breathing difficulties seek medical attention as soon as possible. It may also develop slowly with symptoms such as a dry cough.
- *Hair thinning*: This may occur rarely. It is not permanent and hair will grow back when the medicine is stopped.
- *Nodule formations*: Some people with rheumatoid arthritis develop nodules on their elbows or other pressure points. In some cases methotrexate may increase this.
- *Cancer:* see below.

Long term side effects

Methotrexate may be taken for long periods (more than 25 years) to manage rheumatoid arthritis. In addition to the possible effects mentioned above, the following are rare but possible long-term side effects, or long-term issues that may concern patients:

- *Liver:* Very rare cases of increased fibrous tissue in the liver have been reported after long-term treatment. Regular monitoring can minimise the risk of this occurring.
- *Cancer:* People who have rheumatoid arthritis have an increased risk of lymphoma (a lymph node cancer). It is not clear whether methotrexate increases this risk further but any additional risk is likely to be very small. Methotrexate may reduce the risk of these cancers by controlling the rheumatoid arthritis, but this is unproven. For general cancer prevention, stopping smoking is recommended. An annual skin check to detect any early skin cancer is also recommended.
- *Fertility:* Methotrexate does not affect a person's ability to have children in the long term. See also *Precautions*.

More information about possible side effects

Information that comes with your methotrexate medicine will also describe in detail the potential serious side effects that may occur with methotrexate. Many of those side effects relate to **high dose** methotrexate used for the treatment of cancer. These may not be applicable to the much lower doses that are prescribed for the treatment of rheumatoid arthritis. Talk to your doctor if you have concerns about any possible side effects.

What precautions are necessary?

Blood tests

- As methotrexate may affect the liver and blood cells, you **must** have regular blood tests during your treatment. This is very important, as you may not get symptoms with some of these problems.
- Blood tests are particularly important during the first few months of treatment and when methotrexate is taken with leflunomide.
- As well as monitoring for side effects, blood tests help to monitor your condition to determine if the treatment is effective.
- You will need to have full blood counts and liver function tests every 2 to 4 weeks for the first few months of treatment and then every 1 to 3 months after that.
- If there are no problems seen after 3 months of treatment at a specific dose of methotrexate, the blood tests may be done less frequently.
- Your general practitioner (GP) will be informed about the monitoring schedule. It is important to see your GP if you have been asked to do so as they play an important role in monitoring your condition.

Risk of infections

- Because your immune system may be depressed, there is an increased risk of developing some infections, especially herpes zoster (chicken pox and shingles). You should try to avoid contact with people who have these infections. If you have an infection or persistent fever, tell your doctor straight away.

Use with other medicines

- Methotrexate can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes

over the counter or herbal/naturopathic medicines. You should also mention your treatment when you see other health professionals.

- Antibiotics containing **trimethoprim (e.g. Bactrim, Septrim or Triprim)** can cause problems when taken with methotrexate. If you are prescribed any of these medications you **must** tell the doctor you are taking methotrexate.
- Aspirin can be used safely in the low doses taken for prevention of heart attack and stroke.
- Methotrexate can be taken safely with anti-inflammatory drugs (NSAIDs), as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte, can be used while taking methotrexate provided you take them as directed.
- Most vaccines can be given safely but live vaccines, such as MMR (measles, mumps and rubella), OPV (oral polio vaccine) or yellow fever, may need special consideration.
- Pneumovax and yearly flu vaccinations are safe and recommended to reduce your risk of those infections. Talk with your rheumatologist before receiving any vaccines.

Use with alcohol

- Alcohol increases the risk of liver damage while taking methotrexate. Methotrexate usage in heavy drinkers has been associated with cirrhosis of the liver.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Surgery

- If low dose once weekly methotrexate is continued during surgery there seems to be no change in wound healing or increased infection.

Use in pregnancy and breastfeeding

- Methotrexate should not be taken during pregnancy as it can cause miscarriage or foetal deformity. It should also not be taken when breastfeeding.
- Women of child-bearing age should use effective contraception while taking methotrexate.
- Women planning to become pregnant should stop taking methotrexate 3 months before attempting to conceive.
- The best time for a male partner to stop taking methotrexate before trying to conceive is not known.
- Methotrexate does not affect a person's ability to have children in the long term.

How to store methotrexate

- Store methotrexate in a cool, dry place, away from direct heat and light (e.g. not in the bathrom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

You should see your rheumatologist regularly to make sure the treatment is working and to minimise any potential side effects.

How to help us help you
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Australian Rheumatology Association

PATIENT INFORMATION ON

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

(Examples of brand names: Brufen, Celebrex, Mobic, Naprosyn, Nurofen, Orudis, Voltaren)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you may need to have to detect unwanted effects**
- **other precautions you should take while you are taking these medicines.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking NSAID you should see your doctor regularly to make sure the treatment is working and to minimise any possible side effects.
- If you develop severe stomach pains, pass blood or black stools, or vomit blood, stop taking the medicine immediately. You should see your doctor as soon as possible or go to the nearest emergency department.
- If you are worried about any side effects you should contact your doctor as soon as possible.

For more information about arthritis see the Arthritis Australia website www.empowered.org.au.

What are NSAIDs?

Non-steroidal anti-inflammatory drugs, or NSAIDs, are common medicines used to treat the symptoms of arthritis. The name means they reduce pain and stiffness due to inflammation of the joints, without using steroids. You can find out about steroids from the separate ARA information sheet on corticosteroids.

There are many different NSAIDs. Some can be bought over the counter (OTC) e.g. ibuprofen (Nurofen). Others such as ketoprofen (Orudis) are only available with a prescription. The brand name of your NSAID will have the generic name next to it on the packet or bottle. See the table at the end of this information sheet for further examples.

In recent years a newer type of NSAID, the selective NSAIDs (also called cox-2 inhibitors or coxibs) have been developed. These are less likely to cause stomach irritation and ulcers compared to traditional NSAIDs.

How do they work?

NSAIDs stop cells making prostaglandins. Prostaglandins are chemicals released by injured cells. They cause inflammation and swelling and they sensitise nerve endings, which can lead to pain. If you make less prostaglandin, you have less inflammation and less pain. By stopping cells making prostaglandins, NSAIDs relieve the symptoms of arthritis. They do not stop the inflammation occurring in the future or prevent the disease progressing to joint damage.

What benefit can you expect from your treatment?

NSAIDs provide relief from pain and stiffness. They work quickly, usually within a few hours. The maximum benefit can take 2 to 4 weeks or sometimes longer. You may need to try two or three different NSAIDs to find one that suits you best. You **must** only take one type of NSAID at a time.

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How are NSAIDs taken?

NSAIDs are usually taken by mouth in tablet or capsule form. They are also available as liquids, injections, creams, sprays and suppositories.

Side effects may still occur with any method of administration, even when NSAIDs are applied to the skin (see *Side effects*).

When should they be taken?

NSAIDS can be taken when needed to treat short term symptoms. They can also be taken regularly to manage persistent pain and stiffness.

While NSAIDs may be more effective if taken regularly, the possible side effects are less if they are only taken when needed, for example before exercise.

How often you take a NSAID also depends on the one you are prescribed. Ask your doctor or pharmacist if you are uncertain about how often to take your medicine.

Tablets and capsules should be taken with food to reduce possible side effects.

What is the dosage?

NSAIDs usually come in different strengths. Treatment usually starts with a low dose. This can be adjusted depending on your response.

The dose will depend on the type of NSAID and the condition for which it is being used.

To minimise side effects, the lowest dose that controls symptoms is usually recommended.

Always follow the instructions provided in the packaging unless otherwise directed by your doctor.

Can other medicines be taken with NSAIDs?

To minimise side effects, sometimes a medicine to protect the stomach may be given (see page 3).

NSAIDs may be used with other arthritis medicines including:

- DMARDs (anti rheumatoid arthritis drugs) such as methotrexate
- simple pain medicines such as paracetamol.

Corticosteroids are not generally used with NSAIDs as the risk of side effects such as ulcer is increased.
There are separate information sheets for the medicines mentioned above.

How long is the treatment continued?

Treatment with NSAIDs can be for a short period or long term. A NSAID should not be continued indefinitely without regular review by your doctor to confirm the NSAID still works and no serious side effects are occurring.

Are there any side effects?

You might experience side effects with your treatment. Tell your doctor if you are concerned about possible side effects. A reduction in dose or change to another NSAID may decrease the side effects so that you can continue to take the treatment.

Alternatively, your doctor may recommend a different pain relieving medicine with fewer potential side effects, such as paracetamol. This may allow you take the NSAID less often or stop it altogether.

Most common possible side effects:

- The most common side effects are *gastrointestinal* and may include decreased appetite, nausea (feeling sick), vomiting, diarrhoea, constipation, heartburn and stomach pain or cramps.
- *Heart disease and stroke*: All NSAIDs, including the newer selective types (cox-2 inhibitors/coxibs), may slightly increase the risk of heart attacks and strokes. This risk seems higher in those already at high risk of heart attack or stroke.
- NSAIDs can increase *blood pressure* (see *Precautions*, page 3).
- NSAIDs can make *heart failure or kidney failure* worse. Fluid retention can lead to weight gain or swelling of ankles or legs. Kidney failure is more likely if you are also taking fluid tablets and certain blood pressure tablets (see *Precautions*, page 3).
- *Dizziness, lightheadedness, tiredness, ringing in the ears (tinnitus)* and *headache* can occur.
- *Bleeding* more easily than usual is often noticed.

Less common or rare possible side effect:

There are some rare but potentially serious side effects with NSAIDs.

- *Stomach or duodenal ulcers:* NSAIDs can cause ulcers in the stomach or duodenum (upper bowel).

  If you develop severe stomach pains, pass blood or black stools, or vomit blood, stop taking the medicine immediately. You should see your doctor as soon as possible or go to the nearest emergency department.

  The risk of ulcers is higher if:

  - you are older than 65 years
  - you have had a previous stomach or duodenal ulcer
  - you are also taking warfarin, corticosteroid tablets or low-dose aspirin (used by many people to help prevent a heart attack or stroke).

  If you have an infection (helicobacter bacteria) in your stomach this should be treated before you start NSAIDs. Your doctor may advise that you take an anti-ulcer medicine to help reduce the risk of getting a stomach or duodenal ulcer.

  The selective NSAIDs e.g. celecoxib (brand name Celebrex), may be less likely to cause stomach ulcers and irritation than traditional NSAIDs. They have been used to treat arthritis in people who have suffered stomach upset or ulcers while taking a traditional NSAID or who were thought to be at risk for ulcers.
- *Allergy* to NSAIDs can occur resulting in skin rashes.
- *Shortness of breath* may occur in some people with asthma. Seek medical help if your asthma suddenly becomes worse after taking NSAIDs.
- *Liver inflammation* (hepatitis) is another uncommon side effect.

There are also a number of other uncommon side effects. Read the leaflet that comes with the medicine, which lists all the precautions and possible side effects.

What precautions are necessary?

Blood pressure

- Because NSAIDs can affect your blood pressure it is a good idea to have your blood pressure monitored monthly for the first two months. This is more important if you already have high blood pressure or you are on treatment for high blood pressure. If your blood pressure is stable, it should be checked every 3 to 6 months while you continue to take the NSAIDs.

Blood tests

- Usually blood tests are not required for people taking NSAIDs.
- They may be needed in certain situations. For example, your kidney function may need to be monitored if you have other risk factors for reduced kidney function, such as being over 65 years old and taking blood pressure medicines or fluid tablets. In this case your doctor may recommend you have a blood test in the first few weeks after starting a NSAID.

Use with other medicines

- NSAIDs can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking, including herbal and naturopathic medicines. This includes over the counter (OTC) medicines as some contain NSAIDs. You should also mention your treatment when you see other health professionals.
- NSAIDs are generally used for joint and muscle pain. However sometimes they can be used for other reasons, for example mefanamic acid (Ponstan) may be used for period pain.
- Despite the possible increased risk of ulcer, low doses of aspirin used to prevent heart attack and stroke can probably be used safely with NSAIDs if the risk for ulcer is low in the first place.
- Methotrexate for rheumatoid arthritis or other arthritis treatment can be taken safely with NSAIDs as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte can be used while taking NSAIDs provided you take them as directed.
- If you are taking anticoagulants such as warfarin you should tell your doctor as combination with NSAIDs can increase the risk of bleeding.

Use with alcohol

- NSAIDs can increase the risk of a stomach or duodenal ulcer. Heavy alcohol use (more than

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4 standard drinks in one session) should be avoided while taking these medicines.

Use in pregnancy and breastfeeding

- NSAIDs are not recommended during pregnancy or during breastfeeding unless specifically advised by your doctor. If you are planning a family or you become pregnant you should discuss this with your doctor as soon as possible.
- Some studies suggest that if NSAIDs are taken around the time of conception there may be an increased risk of miscarriage.
- If NSAIDs are taken in later stages of pregnancy they may have an effect on the blood vessels near the baby's heart. Paracetamol does not have these effects.

How to store NSAIDs

- Store NSAIDs in a cool, dry place, away from direct heat and light.
- Keep all medicines out of reach of children.

Non-selective NSAIDS (cox-1 and cox-2 inhibitors)	
Generic/chemical name	**Brand names**
Diclofenac	Chemists' Own, Clonac, Diclohexal, Fenac, Imflac, Viclofen, Voltaren, Voltaren Rapid, Voltfast
Ibuprofen	Advil, Brufen, Bugesic, Chemists' Own, Dimotapp, Gold Cross, Herron Blue, iProfen, Nurofen, Panafen, ProVen, Rafen, Tri-Profen
Indomethacin	Arthrexin, Indocid
Ketoprofen	Orudis, Oruvail
Ketorolac	Ketoral, Toradol
Mefenamic acid	Ponstan
Naproxen	Aleve, Anaprox, Chemists' Own, Crysanal, Eazydayz, Inza, Naprosyn, Naprofem, Naprogesic, Proxen
Piroxicam	Feldene, Feldene-D, Mobilis, Mobilis D,
Sulindac	Aclin
Selective NSAIDS (cox-2 inhibitors)	
Celecoxib	Celebrex
Etoricoxib	Arcoxia
Meloxicam	Meloxibell, Mobic, Movalis, Moxicam
Paracoxib	Dynastat

Source: Australian Medicines Handbook, 2013.
Note: This may not be a comprehensive list – ask your pharmacist or doctor for more information.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details:~

When taking NSAIDs should see your doctor regularly to make sure the treatment is working and to minimise any potential side effects.

How to help us help you

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or **Melbourne 03 9508 3424**
Fax: **1-800-022-730**

Visit our website: www.ARAD.org.au

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Arthritis AUSTRALIA

PATIENT INFORMATION ON

PREDNISOLONE & PREDNISONE

(Also known as corticosteroids / cortisone / steroids)

(Examples of brand names: Panafcort, Panafcortelone, Predsone, Predsolone, Solone, Sone)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **what are the possible side effects**
- **what tests you should have to monitor your condition and to detect unwanted effects**
- **other precautions you should take when you are taking prednisolone or prednisone.**

Please read it carefully and discuss it with your doctor.

Important things to remember:

- While taking prednisolone you should see your treating doctor regularly to make sure the treatment is working as it should and to minimise any possible side effects.
- You should not stop your treatment unless your doctor tells you to.
- You should not increase or reduce the dose of prednisolone unless your doctor tells you to.

For more information about RHEUMATOID ARTHRITIS see Arthritis Australia's Empowered website:
www.empowered.org.au

What is prednisolone?

Corticosteroids are hormones that are produced naturally in the body. They are necessary for normal working of the body.

Prednisolone and prednisone are man-made corticosteroids (also called steroids for short). Man-made corticosteroids are used to treat inflammatory diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE/lupus) and other inflammatory disease. They have a strong anti-inflammatory effect and reduce the swelling and pain in joints and other organs. They do not cure the disease.

They should not be confused with male or female steroid hormones, which are known for their misuse among athletes.

Prednisolone is the most common type of corticosteroid prescribed. Although prednisone is slightly different the information contained in this document also applies to that medication.

What benefit can you expect from your treatment?

Prednisolone works very quickly. Within a few days you may notice your pain and stiffness is much better and/or your joints are less swollen.

How is prednisolone taken?

Prednisolone can be swallowed as tablets or liquid. It is usually taken once or twice a day. Sometimes it is taken every second day. It is usually taken in the morning, with or immediately after food.

Other corticosteroids can be given by injection into joints, soft tissues or muscles. An injection into a vein (intravenous) may also be given if required.

What is the dosage?

There are three different strengths of prednisolone tablets: 1mg, 5mg and 25mg. This means the dosage can be adjusted to suit your needs without you having to take large numbers of tablets. It is important to check the strength of the tablets as they look very similar.

The dose depends on the severity of the disease. A high dose may be used initially and then reduced by your doctor as symptoms improve. To minimise the risk of side effects the smallest dose possible will be used.

Sometimes your doctor may increase the dose temporarily when your body is under stress, for example during a surgical procedure or if you have a severe illness such as an infection.

After you have stopped prednisolone your doctor may prescribe it again for a short period in certain situations as described above.

Can other medicines be taken with prednisolone?

Prednisolone may be used with other arthritis medicines including:

- antirheumatoid arthritis medicine (also called disease modifying antirheumatic drugs or DMARDs) such as methotrexate
- biological DMARDs (a newer type of DMARD, which acts on natural substances in the body that contribute to inflammation and joint damage)
- simple pain relieving medicines such as paracetamol.

Prednisolone and other corticosteroids should be taken with caution with nonsteroidal anti-inflammatory drugs (NSAIDs) as the risk of side effects such as stomach ulcer is increased.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

Low dose prednisolone, taken for a few days or even a few weeks, does not normally cause any unwanted side effects.

If prednisolone is taken in high doses or for a long time certain predictable side effects can occur. Some of these improve after prednisolone is stopped. Many can be minimised by giving the lowest effective dose over the shortest possible period of time.

The effects may also be minimised by giving the medicine by injection into the joints or into a muscle.

Most common possible side effects

- *Weight gain*: The most common side effects are rounding of the face and weight gain around the stomach. These are due to altered metabolism, increased appetite and salt retention.
- *Osteoporosis (thinning of the bones):* While very low doses of prednisolone (less than 5 mg/day) are not very likely to cause thinning of the bones, moderate and high doses taken for long periods usually cause this problem.

  Your doctor will tell you if you need a *bone density (BMD)* test to check your risk of osteoporosis.

  To reduce the risk it is recommended that you:
  - have 1000mg of calcium each day (e.g. 3 serves of dairy or calcium tablets)
  - take 30 minutes of weight bearing exercise each day (e.g. walking)
  - avoid smoking and avoid drinking more than 2 standard drinks of alcohol a day
  - get some sunlight exposure each day to maintain vitamin D levels. You should wear sunscreen as usual to protect your skin from sun damage. As well as sun exposure, a vitamin D supplement may be recommended if vitamin D levels are low.
- *Skin:* The skin, especially on the arms and legs, can become thin, easily bruised and slow to heal. This occurs particularly after long term use, on higher doses and in older people with skin problems related to aging. In younger people acne may be a problem.

- *Diabetes:* Prednisolone can cause a rise in blood sugar in people with diabetes. This may require a change in their diabetes medicine. You should consult your general practitioner if you experience an increase in blood sugar levels.

  Prednisolone can also cause the onset of diabetic symptoms in people who are at risk of diabetes.
- *Blood pressure:* Prednisolone may cause an increase in blood pressure or make it more difficult to control. This can be monitored and changes can be made to your blood pressure medicine if required. Your doctor will advise about frequency of monitoring.
- *Cholesterol:* Prednisolone can cause a rise in blood cholesterol. This can be monitored and changes can be made to your treatment if required.
- *Psychological effects:* Prednisolone can cause euphoria (feeling high) and/or other mood or personality changes such as irritability, agitation or depression. While some psychological effects are quite common, they rarely cause significant problems.
- *Trouble sleeping* may also occur but can be minimised by taking prednisolone in the morning.
- *Infections:* There may be an increased risk of some infections, including mouth infections (such as thrush), shingles and lung infections. Pre-existing infections such as tuberculosis (TB) may become active again. **It is important to tell your doctor if you have a chronic infection or you have been exposed to TB earlier in your life.**
- *Indigestion* or heartburn can occur. Taking prednisolone with food can reduce this.
- *Ulcers:* If taken with nonsteroidal anti-inflammatory medicines (NSAIDs) prednisolone can further increase the risk of stomach or duodenal ulcers. Your doctor will advise you about how to reduce this risk and about what symptoms to look out for.

Less common or rare possible side effects

- *Eyes:* With long term high dose treatment prednisolone may increase development of cataracts.
- *Other:* Facial flushes, constipation and avascular necrosis (a painful bone condition usually seen in the hip or knee) can occur very rarely.

Many of the above side effects can be managed or prevented by close medical supervision and by following your doctor's recommendations (see also *Precautions*, below).

What precautions are necessary?

Tests

- Blood sugar and cholesterol levels can be increased by prednisolone, so you will need to have *blood tests* to check these levels. Your doctor will tell you when the blood tests are required.
- Your general practitioner will be told about the tests you need to have. It is important to see your general practitioner if you have been asked to do so as they have an important role to play in monitoring your condition.

Use in pregnancy and breastfeeding

- Prednisolone may be used safely in pregnancy and breastfeeding. It is important to tell your doctor if you are, or intend to become pregnant or if you are breastfeeding.

Use with other medicines

- Prednisolone can affect how other medicines work. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals, even if you have stopped taking corticosteroids within the last 12 months.
- Most vaccines can be given safely with prednisolone. Talk with your rheumatologist before receiving any vaccines.
- Yearly flu vaccines and Pneumovax are safe and recommended.

Surgery

- If you are going to have an operation it is important to tell the anaesthetist that you are taking or have been taking prednisolone or other corticosteroids in the last year.

- Your doctor may tell you that you need some additional prednisolone at the time of surgery.

Never stop taking prednisolone suddenly

- You should not stop taking prednisolone suddenly or increase or reduce the dose you have been prescribed unless your doctor tells you to.
- Your adrenal glands, which are just above the kidneys, normally make corticosteroids in small amounts. These are important for many normal body functions.
- If prescribed corticosteroids are taken, the body begins to make less than usual or even stops making corticosteroids completely.
- If the medicine is then *suddenly* stopped there may be a problem as the adrenal glands won't have had time to make the corticosteroids needed. This problem is called *adrenal insufficiency*.
- Signs of adrenal insufficiency include weakness, fatigue, fever, weight loss, vomiting, diarrhoea and abdominal pain. If you experience any of these problems, seek medical help.

How to store prednisolone

- Store prednisolone tablets at room temperature, away from heat, moisture and light (e.g. not in the bathroom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking prednisolone or other corticosteroids you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7-8, figure 1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	NA
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	6-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7-8

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1, 4
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 3
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	Table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Table 1,2,4,5,6
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Assessing the Readability and Patient Comprehension of Rheumatology Medicine Information Sheets: A Cross-Sectional Health Literacy Study

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Assessing the Readability and Patient Comprehension of Rheumatology Medicine Information Sheets: A Cross-Sectional Health Literacy Study

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Objectives. Patients are often provided with Medicine Information Sheets (MIS). However, up to 60% of patients have low health literacy. The recommended readability level for health-related information is ≤ Grade 8. We sought to assess the readability of MIS given to patients by Rheumatologists in Australia, the United Kingdom (UK) and Canada, and to examine Australian patient comprehension of these documents.

Design. Cross-sectional study.

Setting. Community-based regional Rheumatology practice.

Participants. Random sample of patients attending the Rheumatology practice.

Outcome measures. Readability of MIS was assessed using readability formulae [Flesch Reading Ease formula, Simple Measure of Gobbledygook (SMOG) scale, FORCAST (named after the authors FORd, CAylor, STicht) and the Gunning Fog scale]. Literal comprehension was assessed by asking patients to read various Australian MIS and immediately answer five simple multiple choice questions about the MIS.

Results. The mean (±SD) grade level for the MIS from Australia, the UK, and Canada was 11.6±0.1, 11.8±0.1 and 9.7±0.1 respectively. The Flesch Reading Ease score for the Australian (50.8±0.6) and UK (48.5±1.5) MIS classified the documents as "fairly difficult" to "difficult". The Canadian MIS (66.1±1.0) were classified as "standard". The five questions assessing comprehension were correctly answered by 9/21 patients for the adalimumab MIS, 7/11 for the methotrexate MIS, 6/28 for the non-steroidal anti-inflammatory MIS, 10/11 for the prednisone MIS and 13/24 for the abatacept MIS.

Conclusions. The readability of MIS used by Rheumatologists in Australia, the UK and Canada exceeds Grade 8 level. This may explain why patient literal comprehension of these documents may be poor. Simpler, shorter MIS with pictures and info-graphics may improve

patient comprehension. This may lead to improved medication adherence and better health outcomes.

Study strengths and limitations

- Readability of Medicine Information Sheets (MIS) from three countries (Australia, UK and Canada) was assessed.
- While readability formulae only measure the number/complexity of words/sentences, Australian patient literal comprehension of MIS was also assessed.
- The study population was from a regional community and may not be representative of a more urban population.

Introduction

Health literacy is defined as the "capacity to obtain, process and understand written and oral health information and services needed to make appropriate health decisions".[1] Low health literacy has been associated with poorer health-related knowledge, increased hospitalisations, reduced immunizations, poorer health status and higher mortality.[2] Patients with poor health literacy are less likely to successfully manage chronic disease[3] and have greater difficulty following instructions for prescription medications.[4] Higher health literacy has been associated with increased medication adherence.[5 6]

Although the importance of health literacy and patient-physician communication on health outcomes is well-recognised, many patients have difficulty understanding what their physicians tell them.[7] Immediately after leaving a consultation with their specialist, patients were able to recall less than half the information just provided to them.[8 9] The provision of written health information in addition to verbal information significantly increases patient knowledge and satisfaction.[10] Written information may also lead to increased adherence with treatment. [9] However, designing effective written health information remains challenging due to differences in patient literacy levels.

The recommended level of reading difficulty for health-related written material in inconsistent. Some agencies have recommended up to eighth grade level [11] - the average reading level of an adult in the United States [12 13], whereas others have suggested levels as low as fifth grade to be more inclusive of those with limited literacy.[14] No national guidelines exist in Australia, although the South Australian government has recommended up to eighth grade level. [15] Despite these inconsistencies, many studies have found written health information provided to patients often exceeds these levels.[16-19] While there is greater access

to health-related information on the internet, this often also exceeds recommended readability levels.[20 21]

Literacy levels in Australia are poor, with up to 60% of the population having low literacy skills[22 23] - defined as the "minimum required for individuals to meet the complex demands of everyday life".[24] The International Adult Literacy Survey found 57% of Canadians fall into the lowest two literacy categories.[25] In the United Kingdom (UK), just under one in six adults has the literacy of an 11-year old. [26] A study of over 200 rural and urban Australian Rheumatology patients found that 15% of patients had low health literacy and up to one third of patients incorrectly followed dosing instructions for common Rheumatology drugs.[23] Ten percent of patients with rheumatoid arthritis (RA) who attended an urban community-based Australian Rheumatology practice had inadequate/marginal functional health literacy or a reading age at or below the United States (US) high school grade equivalent of 7th-8th grade.[27] Up to 24% of Rheumatology patients at a US medical centre had a reading level of 8th grade or less.[28] In 2002, one in six Rheumatology patients at a Scottish hospital were illiterate and struggled to understand education materials and prescription labels.[29] These findings are concerning, as Rheumatologists often use medications such as methotrexate or expensive biologic therapies with severe side effects, even death[30], if taken incorrectly.

Given the importance of health literacy and its relationship to health outcomes and medication adherence, we sought to assess:

i) the readability of patient Medication Information Sheets (MIS) given to patients by Australian Rheumatologists, and

ii) patient comprehension of these documents.

We also compared the readability of the Australian MIS to similar documents given to Rheumatology patients in the UK and Canada.

Methods

Assessment of readability

Text from the MIS of commonly prescribed Rheumatology medications available on the Australian Rheumatology Association (ARA) website[31] was imported into a Microsoft Word document and readability assessed using Readability Studio™ (Oleander Software, USA).[18] [32] [33] [34] [35]

Non-essential text including logos, headers, footers, hyperlinks and contact information was deleted prior to analysis as these may have adversely affected readability scores. Readability was assessed using a range of measures such as the Flesch Reading Ease formula, Simple Measure of Gobbledygook (SMOG) scale, FORCAST (named after the authors FORd, CAylor, STicht) and the Gunning Fog scale. The Flesch Reading Ease formula calculates an index score of a document based on sentence length and number of syllables. It is often used for school textbooks and technical manuals. The standard score is between 0-100, with a high score indicating the document is easier to read.[36] (However, it is possible to also gain minus scores and scores over 100). The SMOG formula calculates grade level and reader age based on complex word density and assigns a grade level (4th grade to college level).[33] [37] It is particularly useful for secondary age readers and attempts to predict 100% comprehension, whereas most other formulae predict 50-75% comprehension. Consequently, SMOG may produce grade level scores one to two grades higher than other formulae. [33] [37] The Gunning Fog formula calculates grade level and reader age based on number of sentences, their mean length and number of complex words (three or more syllables).[38] The FORCAST readability formula was initially used for assessing technical documents by calculating the grade level of

text based on number of monosyllabic words. It is the only test not designed for running narrative, for example multiple-choice quizzes and applications. As sentence length is not considered, there may be some variability in grade level compared to other readability formulae. [33]

It was felt the above four formulae allowed comprehensive assessment of an MIS by focussing on various aspects: Flesch Reading Ease - sentence length and syllable number, SMOG - complex word density, Gunning Fog - sentence number/length and complex words and FORCAST - number of monosyllabic words and non-dependence on running narrative.

The readability of 10 corresponding MIS of a sample of commonly prescribed Rheumatology medications published in the UK by Arthritis Research UK[39] and from Canada published by Rheuminfo[40] was also assessed as above. These 10 MIS were representative of the MIS available on both these websites.

Assessment of literal comprehension

Coffs Harbour is a growing regional city of 70 000 people located half-way between the Australian capital cities of Sydney and Brisbane. Its medical specialists provide services to another 50 000 people from the surrounding area. Rheumatology services are provided by two Rheumatologists (PKKW and HB) under the auspices of the Mid-North Coast Arthritis Clinic (MNCAC). The MNCAC has over 16 000 patients on its computerised database.

A random sample of patients referred to the MNCAC was asked to read one ARA MIS[31] containing information about one of the following medications which the patient was unfamiliar with: Supplementary Material 1 methotrexate (MTX)[41], Supplementary Material 2 non-steroidal anti-inflammatory drugs (NSAIDs)[42], Supplementary Material 3 adalimumab (ADA)[43], Supplementary Material 4 abatacept (ABA)[44] or Supplementary Material 5 prednisone.[45] All consecutive patients scheduled for a randomly selected consulting day were contacted via telephone by an investigator (MO or ET). Patients (n=261) were asked whether they were interested in study participation to determine what they understood after reading information from the doctor. Responses are outlined in Figure 1. Those who expressed interest in study participation were mailed information about the study and a consent form to be returned in a stamped pre-addressed envelope (n=142). Those who agreed to participate were assessed on the day of the planned consultation (n=95). These was no difference in gender or age between those included compared to those not contactable (data not shown). Comprehension was assessed by asking the patient to answer five multiple choice questions (see Supplementary Material 6) about the content of the one ARA MIS they had just read. These questions were designed by two Rheumatologists (PKKW, HB), a Rheumatology Nurse (DF) and an education academic with expertise in literacy (JJ). The questions were trialled on small focus groups of patients. A time limit of 15 minutes in a quiet well-lit room was provided. If needed, study participants could refer back to the MIS while answering the questions. Informed consent was obtained from all study participants.

Patient and public involvement

Previous work by us found that up to 15% of patients had low health literacy and up to one

third of patients incorrectly followed dosing instructions for common rheumatology drugs. [23] These findings prompted us to conduct this study which examined the readability of MIS routinely used in our clinical practice. Furthermore, some of our patients had previously commented that the ARA MIS were difficult to understand. A summary of study results will be disseminated to all study participants. Patients were not involved in the recruitment to, and conduct of the study. However, many study participants indicated they hoped their study involvement would lead to the development of better written material for future patients.

Statistical analyses

Descriptive summary statistics (mean ± SD and median ± interquartile range, as appropriate) were used to analyse parameters. Student's t-test (unpaired) was used to compare means of normally distributed parameters. The Mann-Whitney U test was used to compare medians of groups. For all statistical tests, $p<0.05$ was considered significant. Data analysis was undertaken using GraphPad Prism 6 (GraphPad Software Inc, USA).[46] The correlation (r-value) between comprehension score and various parameters (age, gender, postcode, highest level of education) was performed using STATA (Stata 11.1, StataCorp, TX, USA).

Ethics

Approval as a low/negligible risk project was obtained from the New South Wales North Coast Human Research Ethics Committee (NCNSW HREC No LNR 150).

Results

Assessment of readability

The mean (± SD) grade level for the ARA MIS calculated using Readability Studio™ was 11.6± 0.1 with a mean reading age of 16.6 ± 0.1 years (Table 1). (These were obtained by calculating the mean of the FORCAST, Gunning Fog and SMOG mean grade level and reading age. Due to the heterogeneity of these instruments, the mean of each of these measures is available in the relevant Table). The mean (± SD) Flesch Reading Ease score of 50.8 ± 0.6 indicated the ARA MIS were either "fairly difficult" or "difficult"[33] (Table 1). Overall, difficult sentences (>22 words) and complex words (≥ 3 syllables) made up 9.0% and 18.4% of the text, respectively (Table 2).

As the validity of the above readability assessment measures has been questioned due to over-reliance on sentence and word length[47 48], we proceeded to assess patient literal comprehension of the ARA MIS.

Assessment of comprehension

A total of 261 patients were contacted, with 95 study participants (Figure 1). Mean (± SD) age of study participants was 60 ± 13.2 years, with 71/95 (75%) females and 24/95 (25%) males (Table 3). Nineteen of the 95 (20%) patients had a university degree (Table 3). Only 9/21 (43%) and 13/24 (54.2%) patients correctly answered all five questions for adalimumab and abatacept, respectively (Table 3). Only 7/11 (63.6%) of patients correctly answered all five simple questions assessing literal comprehension of the MTX MIS (Table 3). Questions assessing comprehension of the prednisone MIS were correctly answered by most participants (10/11; 90.9%). Of concern, only 21.4% (6/28) of patients correctly answered all questions assessing comprehension of the NSAID MIS. Responses to the five NSAID questions are shown in Figure 2.

Highest level of education achieved (r=0.33, p =0.001) and age (r= -0.3, p=0.0002) correlated moderately strongly with a higher comprehension score.

Comparison of readability scores for Australian, UK and Canadian MIS

Given our findings, we sought to determine using Readability Studio™ what the readability scores were for MIS used in other countries. The mean (± SD) grade level for 10 of the commonly used UK MIS was 11.8 ± 0.1 with a reader age of 16.9 ± 0.1 years (Table 4). The mean Flesch Reading Ease score was 48.5 ± 1.5 - classified as "difficult". Readability of the Canadian MIS was easier with a mean (± SD) grade level of 9.7 ± 0.1 and mean (± SD) reader age of 14.8 ± 0.1 years (Table 5). The mean (± SD) Flesch Reading Ease score for the Canadian MIS was 66.1 ± 1.0 - classified as "standard".[33]

There was no significant difference in mean grade levels between the Australian and UK MIS (p=0.10). However, the mean grade level of the Canadian MIS (9.7 ± 0.1) was less than that of the corresponding Australian MIS (11.7 ± 0.1, p<0.0001).

The Australian MIS were the longest (mean ± SD, number of words = 1474.1 ± 44.6) (Table 2) compared with the UK (mean ± SD, number of words = 922.4 ± 109.6) (Table 6a) and Canadian MIS (mean ± SD, number of words = 297.7 ± 19.2) (Table 6b). The Australian MIS also had the highest percentage of complex words (three or more syllables, 18%), compared with the UK (16%) and Canadian (14%) MIS.

Discussion

We showed that the readability of commonly used Rheumatology MIS given to patients in Australia, the UK and Canada exceeded eighth grade level – the recommended level for a low-literacy population. [11 15] The Canadian MIS assessed were easier to read, although remained slightly above eighth grade level. We found that in a population of patients attending a regional private Rheumatology practice where only 20% of participants possessed a university degree, patient comprehension of the Australian MIS was poor, with up to 79% of patients failing to correctly answer all five simple questions assessing literal comprehension of commonly prescribed Rheumatology medications. As expected, a higher level of education achieved was associated with better comprehension ($r = 0.33$, $p = 0.001$). This, along with high readability scores, suggested that current ARA MIS may be too difficult for many patients to understand. While comprehension of the Canadian MIS was not performed, this would provide useful information about the effectiveness of these easier-to-read materials.

The Canadian MIS were simpler, more "readable" and included pictures. Many studies have shown that incorporating pictograms into patient information material improves patient comprehension.[49-54] One study of 60 patients showed that pictograms improved comprehension of patient information sheets from 40% to 93%.[50] Another strategy to improve MIS readability is to shorten the document. However, a shorter, simpler MIS may remove important information and be inadequate for patients with high literacy. Yet, studies have shown both low and high literacy groups recalled information best when the text was easy.[55] These findings suggest that written materials designed for patients with low health literacy may also be useful for a general audience.

It is important to consider the primary purpose of providing written health-related information to a patient. Although the provision of information as part of patient education to facilitate informed patient treatment decisions is important, worry over potential medicolegal

exposure from a treatment-related adverse event continues to drive complexity of written materials.[56]

Potential limitations of this study include the type of population studied and the measures used to assess readability. All study participants were from Coffs Harbour, a large regional community on the east coast of Australia. Although one may expect literacy levels to be lower in a rural setting, previous work from our centre showed no difference in health literacy between our patients compared to an urban Rheumatology private practice in a capital city.[23]

There has been criticism of readability formulae such as the Flesch Reading Ease formula, SMOG scale and the Gunning Fog scale.[48 57-59] Readability formulae are usually based solely on word length or syllable number. They may therefore fail to adjust for patient familiarity with vocabulary associated with their illness, therefore over-estimating the difficulty of written information when read by patients familiar with their disease.[57 59] By necessity, health-related written material uses text characterised by polysyllabic technical jargon, which elevates readability formulae scores.[60] For example, exchanging "adalimumab" for "Humira" in the Australian MIS increases the Flesch Reading ease score from 46 to 50 and reduces the Gunning Fog score from 12.7 to 12.5. (The SMOG remains unchanged at 12.8). Readability formulae fail to account for the stylistic properties of text as well as grammatical errors, which influences the readability of written text. Textual coherence, that is, the relationship and connection between sentences within a document and the relationship between the reader and practitioner are also unaccounted for. Lastly, readability formulae do not usually consider visual and design factors which may influence MIS readability or patient comprehension.[61 62] While the Flesch Reading Ease formula tends to over-estimate readability of health-related material due to its lower level of expected comprehension criteria[58], the SMOG formula is appropriate for assessing health-related written information as it has been validated against 100% comprehension.[58] One approach to addressing these

limitations is the use of a more holistic linguistic framework for assessing written patient information which incorporates structure, factual content, and visual aspects of the material as well as the relationship between writer and reader.[48] This method has been validated using RA medication leaflets in an Australian cohort of RA patients. [63] However, the education level of patients in that study exceeded that seen in our cohort, with 17/27 (63%) having completed tertiary studies compared to 19/95 (20%) in ours.

In view of the potential limitations of readability formulae, we were careful to assess patient literal comprehension of various ARA MIS. As suggested by the relatively low readability scores of the ARA MIS, patient literal comprehension of a selection of the ARA MIS was poor. Due to the simplicity of the five questions posed to the patients, we hoped a satisfactory score would be correct answers to all five questions. However, this only occurred in 21% of patients for NSAIDs and 40-60% of patients for the MTX, ADA and ABA MIS.

Despite the confines and limitations of readability formulae, we believe they remain an important guide when developing written patient information or revising original drafts. This has been validated by several studies that used these formulae to simplify existing written patient information - resulting in enhanced patient comprehension. [64 65] We hope the results of this study will encourage clinicians from Rheumatology and all other specialities to consider the health literacy of their patients and readability of the written information they provide, particularly given the potential of technology to improve patient education.

Conclusion

Medication information sheets currently used by many Rheumatologists in Australia, the UK and Canada exceed eighth grade level – the recommended level for a low-literacy population. This may explain why patient comprehension of the information contained in these materials

is limited. Comprehension may be improved using simpler, shorter words and sentences with greater use of pictures and info-graphics. This may lead to greater patient medication adherence, understanding of their condition, and reduced medication-related errors. It is hoped our findings will encourage all healthcare professionals to consider the appropriateness of written healthcare material provided to patients. The health literacy of patients should always be considered when communicating a management plan.

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Author contributions

MO and ET were responsible for data acquisition. MO was responsible for drafting the manuscript and data analysis under the supervision of PW. PW, JJ, DF and HB conceived and designed the study. All authors contributed to interpretation of data and revision of the manuscript and approve the final manuscript.

Competing interests

The authors declare no competing interests.

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Data sharing statement

No additional data available.

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Figure Legends

Figure 1: Inclusions and exclusions

Figure 2: Answers to NSAID questions

Table 1: Readability scores for Australian Rheumatology Association Medicine Information Sheets

Medicationn	Flesch Reading Ease * (0-100)	FORCAST# grade level	FORCAST# reader age (years)	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level@	Mean reader age@ (years)
Abatacept	49	11.2	16-17	12.3	17-18	12.4	17-18	12.0	17.2
Adalimumab	46	11.2	16-17	12.7	17-18	12.8	17-18	12.2	17.2
Allopurinol	53	10.8	15-16	10.5	15-16	11.5	16-17	10.9	15.8
Apremilast	56	10.6	15-16	11.3	16-17	11.7	16-17	11.2	16.2
Azathioprine	50	10.7	15-16	11.6	16-17	12.2	17-18	11.5	16.5
Bisphosphonates IV	49	11.1	16-17	12.1	17-18	12.2	17-18	11.8	17.2
Bisphosphonates Oral	49	11.2	16-17	12.2	17-18	12.3	17-18	11.9	17.2
Bosentan	59	10.4	15-16	11.0	16-17	11.5	16-17	11.0	16.2
Certolizumab	46	11.1	16-17	12.8	17-18	12.9	17-18	12.3	17.2
Colchicine	53	11.1	16-17	11.7	16-17	11.7	16-17	11.5	16.5
Cyclophosphamide	53	10.7	15-16	10.8	15-16	11.8	16-17	11.1	15.8
Cyclosporin	54	10.7	15-16	11.8	16-17	12.0	17-18	11.5	16.5
Denosumab	50	11.0	16-17	11.9	16-17	12.1	17-18	11.7	16.8
Etanercept	48	11.1	16-17	12.7	17-18	12.8	17-18	12.2	17.2
Febuxostat	54	10.7	15-16	10.8	15-16	11.7	16-17	11.1	15.8
Golimumab	48	11.1	16-17	12.8	17-18	12.8	17-18	12.2	17.2
Hyaluronic Acid	51	11.1	16-17	11.8	16-17	11.9	16-17	11.6	16.5
Hydroxychloroquine	49	10.9	15-16	11.6	16-17	11.7	16-17	11.4	16.2
Infliximab	49	11.1	16-17	12.5	17-18	12.6	17-18	12.1	17.2
Leflunomide	54	10.7	15-16	11.6	16-17	12.2	17-18	11.5	16.5
Methotrexate	52	10.9	15-16	11.4	16-17	12.3	17-18	11.5	16.5
Mycophenolate	50	11.0	16-17	11.6	16-17	12.5	17-18	11.7	16.8
NSAIDs	58	10.6	15-16	11.0	16-17	11.3	16-17	11.0	16.2
Prednisone	51	10.9	15-16	11.2	16-17	11.9	16-17	11.3	16.2
Rituximab	48	11.3	16-17	12.3	17-18	12.5	17-18	12.0	17.2
Sulfasalazine	50	10.9	15-16	11.4	16-17	11.9	16-17	11.4	16.2
Teriparatide	49	10.9	15-16	11.6	16-17	12.1	17-18	11.5	16.5
Tocilizumab	47	11.1	16-17	12.0	17-18	12.5	17-18	11.9	17.2
Tofacitinib	46	11.1	16-17	12.1	17-18	12.2	17-18	11.8	17.2
Ustekinumab	54	10.8	15-16	11.5	16-17	12.0	17-18	11.4	16.5
Mean	**50.8**	**10.9**		**11.8**		**12.1**		**11.6**	**16.6**
SD	**0.6**	**0.0**		**0.1**		**0.1**		**0.1**	**0.1**

Abbreviations

* Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
# FORCAST (named after the authors FORd, CAylor, STicht)
** SMOG = Simple Measure Of Gobbledygook
@ Mean of FORCAST, Gunning Fog and SMOG scores

Table 2: Word and sentence statistics for Australian Rheumatology Association Medicine Information Sheets

Medication	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	Total no. of words	No. of complex** words
Abatacept	133	8 (5%)	12.1	1612	314 (19.5%)
Adalimumab	125	11 (8.8%)	12.6	1576	315 (20%)
Allopurinol	124	10 (8.1%)	12.2	1507	252 (16.7%)
Apremilast	92	9 (9.8%)	11.9	1095	184 (16.8%)
Azathioprine	118	9 (7.6%)	13	1539	273 (17.7%)
Bisphosphonates IV	95	11 (11.6%)	12.6	1199	217 (18.1%)
Bisphosphonates Oral	112	11 (9.8%)	13	1456	277 (19%)
Bosentan	107	11 (10.3%)	11.4	1219	214 (17.6%)
Certolizumab	125	12 (9.6%)	13	1624	320(19.7%)
Colchicine	123	8 (6.5%)	11.6	1426	260 (18.2%)
Cyclophosphamide	118	12 (10.2%)	12.4	1469	266 (18.1%)
Cyclosporin	102	8 (7.8%)	12.1	1235	227 (18.4%)
Denosumab	110	10 (9.1%)	12	1317	243 (18.5%)
Etanercept	124	11 (8.9%)	13.1	1621	321 (19.8%)
Febuxostat	120	12 (10%)	12.4	1484	255 (17.2%)
Golimumab	123	12 (9.8%)	12.9	1588	316 (19.9%)
Hyaluronic Acid	81	4 (4.9%)	11.3	919	181 (19.7%)
Hydroxychloroquine	87	9 (10.3)	12	1046	184 (17.6%)
Infliximab	138	13 (9.4%)	13.1	1807	344 (19%)
Leflunomide	111	10 (9%)	12.9	1427	254 (17.8%)
Methotrexate	156	20 (12.8%)	13.4	2097	375 (17.9%)
Mycophenolate	141	15 (10.6%)	12.1	1712	334 (19.5%)
NSAIDs	137	14 (10.2%)	12.8	1750	266 (15.2%)
Prednisone	128	12 (9.4%)	13	1668	292 (17.5%)
Rituximab	132	9 (6.8%)	12.3	1627	318 (19.5%)
Sulfasalazine	124	9 (7.3%)	12.1	1497	276 (18.4%)
Teriparatide	114	13 (11.4%)	11.5	1310	238 (18.2%)
Tocilizumab	130	12 (9.2%)	12.7	1654	311 (18.8%)

Tofacitinib	111	7 (6.3%)	12	1336	249 (18.6%)
Ustekinumab	114	8 (7%)	12.3	1406	259 (18.4%)
Mean	**118.5**	**10.7 (9.0%)**	**12.4**	**1474.1**	**271.2 (18.4%)**
SD	**3.0**	**0.5**	**0.1**	**44.6**	**9.0**

*Difficult sentence: ≥22 words; **Complex word: ≥3 syllables

Table 3: Assessment of patient literal comprehension (n=95 patients)

age (yrs, mean ± SD)	60.0±13.2
sex (F/M)	71/24
highest level of education	**no. (%)**
≤Yr 10	39 (41)
Yr 10-12	15 (16)
sub-degree, eg TAFE*, apprenticeship	22 (23)
university degree	19 (20)
median total score (max=5)	4
no. with all correct answers (ie, 5/5)	**no. (%)**
adalimumab	9/21 (43)
MTX	7/11 (63.6)
NSAIDs	6/28 (21.4)
prednisone	10/11 (90.9)
abatacept	13/24 (54.2)

Abbreviations
*TAFE= Technical and Further Education

MTX= methotrexate

NSAID=non-steroidal anti-inflammatory drugs

Table 4: Readability scores for Arthritis Research United Kingdom Medicine Information Sheets

Medication	Flesch Reading Ease* (0-100)	FORCAST# grade level	FORCAST# reader age	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level @	Mean reader age@ (years)
Abatacept	46	10.9	15-16	13.1	18-19	13.2	18-19	12.4	17.5
Adalimumab	47	11.1	16-17	12.1	17-18	12.5	17-18	11.9	17.2
Bisphosphonates	53	11.1	16-17	11.9	16-17	12.3	17-18	11.8	16.8
Denosumab	42	11.7	16-17	12	17-18	12.6	17-18	12.1	17.2
Etanercept	49	11	16-17	11.9	16-17	12.4	17-18	11.8	16.8
Hydroxychloroquine	41	11.2	16-17	12.5	17-18	12.5	17-18	12.1	17.2
Leflunomide	53	10.8	15-16	11.9	16-17	12.2	17-18	11.6	16.5
Methotrexate	51	10.8	15-16	12.1	17-18	12.4	17-18	11.8	16.8
Prednisolone	55	11.1	16-17	11.3	16-17	11.6	16-17	11.3	16.5
Sulfasalazine	48	10.8	15-16	11.9	16-17	12.2	17-18	11.6	16.5
Mean	**48.5**	**11.1**		**12.1**		**12.4**		**11.8**	**16.9**
SD	**1.5**	**0.1**		**0.1**		**0.1**		**0.1**	**0.1**

Abbreviations

*Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
FORCAST (named after the authors FORd, CAylor, STicht)
**SMOG = Simple Measure Of Gobbledygook
@ Mean of FORCAST, Gunning Fog and SMOG scores

Table 5: Readability scores for Canadian Medicine Information Sheets

Medication	Flesch Reading Ease * (0-100)	FORCAST# grade level	FORCAST# reader age (years)	Gunning Fog grade level	Gunning Fog reader age (years)	SMOG** grade level	SMOG** reader age (years)	Mean grade level@	Mean reader age@ (years)
Abatacept	65	10	15-16	8.5	13-14	10.3	15-16	9.6	14.8
Adalimumab	61	10.1	15-16	9.8	14-15	10.2	15-16	10	15.2
Bisphosphonates	63	10.2	15-16	9.5	14-15	10	15-16	9.9	15.2
Denosumab	66	9.6	14-15	9.6	14-15	10	15-16	9.7	14.8
Etanercept	64	10.1	15-16	9.9	14-15	10.3	15-16	10.1	15.2
Hydroxychloroquine	72	8.8	13-14	8.4	13-14	9.5	14-15	8.9	13.8
Leflunomide	67	9.9	14-15	9.4	14-15	9.9	14-15	9.7	14.5
Methotrexate	66	9.8	14-15	9.5	14-15	10.1	15-16	9.8	14.8
Prednisolone	69	10.2	15-16	9.8	14-15	10.1	15-16	10	15.2
Sulfasalazine	68	9.3	14-15	9.1	14-15	9.7	14-15	9.4	14.5
Mean	**66.1**	**9.8**		**9.4**		**10.0**		**9.7**	**14.8**
SD	**1.0**	**0.1**		**0.2**		**0.1**		**0.1**	**0.1**

Abbreviations

* Flesch Scale Value: very easy (90-100), easy (80-89), fairly easy (70-79), standard (60-69), fairly difficult (50-59), difficult (30-49), very confusing (0-29)
# FORCAST (named after the authors FORd, CAylor, STicht)
**SMOG = Simple Measure Of Gobbledygook
@ Mean of FORCAST, Gunning Fog and SMOG scores

Table 6: Word and sentence statistics for a) United Kingdom; and b) Canadian Medicine Information Sheets

a) United Kingdom

Drug	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	No. of words	No. of complex** words
Abatacept	66	18 (27%)	17.1	1130	206 (18%)
Adalimumab	71	10 (14%)	15.3	1086	191 (18%)
Bisphosphonates	36	10 (28%)	15.7	566	92 (16%)
Denosumab	8	2 (25%)	14.4	115	22 (19%)
Etanercept	81	16 (20%)	15.8	1282	214 (17%)
Hydroxychloroquine	60	13 (22%)	15.3	916	159 (17%)
Leflunomide	63	12 (19%)	16.1	1016	157 (15%)
Methotrexate	75	13 (17%)	16.2	1212	193 (16%)
Prednisolone	60	15 (25%)	17	1020	131 (13%)
Sulfasalazine	53	12 (23%)	16.6	881	132 (15%)
Mean	**57.3**	**12.1 (21%)**	**15.95**	**922.4**	**149.7 (16%)**
SD	**6.7**	**1.4**	**0.3**	**109.6**	**18.7**

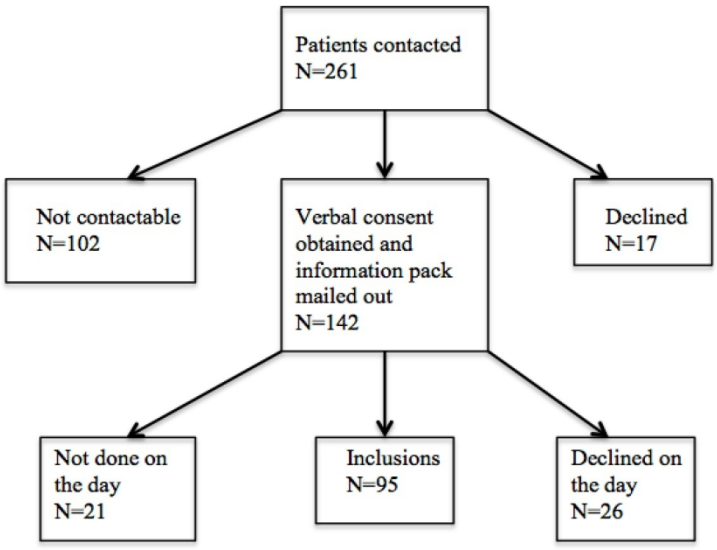
b) Canadian

Drug	No. of sentences	No. of difficult* sentences	Mean sentence length (no. of words)	No. of words	No. of complex** words
Abatacept	25	0	11.1	278	38 (14%)
Adalimumab	31	0	11	341	47 (14%)
Bisphosphonates	30	0	10	301	41 (14%)
Denosumab	24	0	10.3	246	34 (14%)
Etanercept	31	0	10.9	339	48 (14%)
Hydroxychloroquine	21	0	9.3	195	23 (12%)
Leflunomide	34	0	10	339	46 (14%)
Methotrexate	32	0	11.2	357	47 (13%)
Prednisolone	36	0	10.1	363	53 (15%)
Sulfasalazine	21	0	10.4	218	27 (12%)
Mean	**28.5**	**0**	**10.43**	**297.7**	**40.4 (14%)**

SD	**1.7**	**0.0**	**0.2**	**19.2**	**3.1**

*Difficult sentence: ≥22 words; **Complex word: ≥3 syllables

Figure 1: Inclusions and exclusions



Inclusions and exclusions

276x197mm (144 x 144 DPI)

Figure 2: Answers to NSAID questions

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions: (note – correct answer ticked)

Non-steroidal anti-inflammatory drugs (NSAIDs) include medications such as Nurofen, Brufen, Voltaren, Naprosyn and Celebrex.

1) Non-steroidal anti-inflammatory drugs (NSAIDs)
✓a) reduce joint pain, swelling and stiffness
b) prevent damage to your joints
c) strengthen your bones
d) will cure your arthritis

No. with correct answer 26/28 (93%)

2) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) can be combined with other NSAIDs
b) can be continued long-term without review
✓c) often cause gut side effects such as nausea, vomiting and bleeding
d) should be continued during surgery

No. with correct answer 17/28 (61%)

3) Non-steroidal anti-inflammatory drugs (NSAIDs)
✓a) may increase the risk of heart attack and stroke
b) prevent attacks of arthritis
c) have no effect on blood pressure
d) are safe in someone with kidney problems

No. with correct answer 24/28 (86%)

4) Non-steroidal anti-inflammatory drugs (NSAIDs) should be used
a) for 4 weeks only
✓b) for the shortest time possible
c) until the script runs out
d) for however long to get rid of the pain

No. with correct answer 12/28 (43%)

5) Bleeding from inside the gut while taking a non-steroidal anti-inflammatory drug (NSAID)
a) can be completely prevented by taking the NSAID with food
b) should stop if you continue taking the NSAID
c) doesn't cause any problems and can be ignored
✓d) can be associated with abdominal pain and indigestion

No. with correct answer 14/28 (50%)

Answers to NSAID questions

170x210mm (144 x 144 DPI)

PATIENT INFORMATION ON

METHOTREXATE

(Brand names: Methoblastin)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **what are the possible side effects**
- **what tests you must have to monitor your condition and to detect unwanted effects**
- **other precautions you should take when you are taking methotrexate.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking methotrexate you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.
- You should have regular blood tests as directed by your rheumatologist.
- If you are concerned about any side effects you should contact your rheumatologist as soon as possible.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html

What is methotrexate?

Methotrexate (brand name Methoblastin) is a medicine used to treat rheumatoid arthritis as well as other rheumatic conditions such as juvenile arthritis, lupus (also known as SLE), psoriatic arthritis and polymyositis (muscle inflammation).

Methotrexate is an immunosuppressive medicine. It works by reducing the activity of several enzymes involved in the immune system. By blocking an enzyme called dihydrofolate reductase, it reduces production of a form of folic acid.

It is not entirely clear how methotrexate decreases the severity of arthritis, but it reduces inflammation in the joints and associated pain and swelling.

Because methotrexate reduces the damage to the joints, rather than just relieving the pain, it belongs to the group of medicines called **disease modifying antirheumatic drugs (DMARDS)**.

Methotrexate has been used to treat rheumatoid arthritis for more than 25 years. It is also used at very high doses (1000mg-5000mg a day) to treat some cancers.

What benefit can you expect from your treatment?

Methotrexate is one of the most effective treatments for rheumatoid arthritis. Most, but not all, patients will benefit from this medicine. Some achieve remission, where the arthritis virtually disappears.

Methotrexate does not work straight away. Reduced pain, stiffness and swelling may be noticed after 4 weeks. The effects to delay or prevent joint damage will take several months.

Other medicines may be given to improve your symptoms while waiting for methotrexate to work.

How is methotrexate taken?

Methotrexate may be taken by mouth as a tablet or given by injection either into the muscle or under the skin.

Injections may be used instead of tablets if the medicine is not being absorbed well, or if you feel sick (nausea) or vomit when you take the tablets, or if your condition is not improving with tablets.

Care should be taken when disposing of the needles and syringes.

When should it be taken?

Methotrexate is taken just **once a week,** on the same day each week. If you are taking the tablets, it is a good idea to specify and diarise the day of the week that you will take your tablets to avoid making mistakes.

Methotrexate tablets are best absorbed when taken on an empty stomach. However if nausea is a problem, taking them at mealtime can help to reduce this side effect and does not reduce the benefits too much.

What is the dosage?

Tablets come in 2.5mg or 10mg strengths. Treatment may start with a very low dose of 5mg or 10mg a week, increasing to an average dose of 20mg a week. The dose is adjusted depending on the response, up to about 30mg once a week.

The dose is usually taken all at once on a single day. It may be divided into separate doses taken during that day if necessary.

Can other medicines be taken with methotrexate?

In order to reduce side effects, it is recommended that you also take folic acid or folinic acid. Your doctor will explain how much of the folic/folinic acid to take and when to take it.

Methotrexate is often taken in combination with other arthritis medicines, including:

- other DMARDs
- biological DMARDs (a newer type of DMARD, which act on natural substances in the body that contribute to inflammation and joint damage)
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen/Nurofen)
- simple pain medicines such as paracetamol.

There are separate information sheets for the medicines mentioned above.

How long is the treatment continued?

Treatment with methotrexate is continued indefinitely as long as it is effective and as long as no serious side effects occur.

If you stop methotrexate treatment for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop.

If you have an illness that makes you unwell enough to change plans for the day (e.g. gastroenteritis or fever), it is reasonable to miss the weekly dose until you have recovered.

Are there any side effects?

You might experience side effects with your treatment. Tell your doctor if you are concerned about possible side effects.

A reduction in dose may minimise side effects so that you can continue to take the treatment. Your doctor will advise on any dose changes that are necessary.

Most common possible side effects

- The most common side effects are *nausea, vomiting* and *diarrhoea*. These can be reduced if methotrexate is taken with food or in the evening. Antinausea tablets can be used if needed.
- *Mouth ulcers* can occur, but the use of folic acid or folinic acid supplements makes this less likely.
- *Skin dryness, a variety of skin rashes* and *increased sensitivity to the sun* may also occur. You should wear sunscreen and a hat when out in the sun.
- Some people report mild *tiredness, headache* and *mental clouding*. Some also experience a temporary increase in muscle and joint pain after taking the weekly dose.

Less common or rare possible side effects

There are some rare but potentially serious side effects with methotrexate.

- *Blood counts*: Methotrexate can rarely cause a drop in the number of white blood cells, which are needed to fight infection. It can also cause a drop in the number of platelets, which help to stop bleeding.

  Regular blood tests aim to pick these problems up early if they occur.

  However, if you develop a sore mouth, mouth ulcers, easy bruising, nosebleeds, bleeding gums, breathlessness, infection or fever tell your doctor straight away.

- *Liver*: Methotrexate can inflame the liver causing a type of hepatitis. Regular blood tests aim to pick this up early if it occurs. The dose of methotrexate may need to be reduced or stopped if problems occur. Liver problems may be increased when methotrexate is combined with the medicines azathioprine (Azamun, Azapin, Imuran, Thioprine) or leflunomide (Arabloc, Arava) or with heavy alcohol use (see *Alcohol* overleaf).
- *Lungs*: Methotrexate can cause inflammation of the lungs. This may be more likely if leflunomide is being taken at the same time. The problem may develop quickly, so if you have a sudden onset of breathing difficulties seek medical attention as soon as possible. It may also develop slowly with symptoms such as a dry cough.
- *Hair thinning*: This may occur rarely. It is not permanent and hair will grow back when the medicine is stopped.
- *Nodule formations*: Some people with rheumatoid arthritis develop nodules on their elbows or other pressure points. In some cases methotrexate may increase this.
- *Cancer:* see below.

Long term side effects

Methotrexate may be taken for long periods (more than 25 years) to manage rheumatoid arthritis. In addition to the possible effects mentioned above, the following are rare but possible long-term side effects, or long-term issues that may concern patients:

- *Liver:* Very rare cases of increased fibrous tissue in the liver have been reported after long-term treatment. Regular monitoring can minimise the risk of this occurring.
- *Cancer:* People who have rheumatoid arthritis have an increased risk of lymphoma (a lymph node cancer). It is not clear whether methotrexate increases this risk further but any additional risk is likely to be very small. Methotrexate may reduce the risk of these cancers by controlling the rheumatoid arthritis, but this is unproven. For general cancer prevention, stopping smoking is recommended. An annual skin check to detect any early skin cancer is also recommended.
- *Fertility:* Methotrexate does not affect a person's ability to have children in the long term. See also *Precautions*.

More information about possible side effects

Information that comes with your methotrexate medicine will also describe in detail the potential serious side effects that may occur with methotrexate. Many of those side effects relate to **high dose** methotrexate used for the treatment of cancer. These may not be applicable to the much lower doses that are prescribed for the treatment of rheumatoid arthritis. Talk to your doctor if you have concerns about any possible side effects.

What precautions are necessary?

Blood tests

- As methotrexate may affect the liver and blood cells, you **must** have regular blood tests during your treatment. This is very important, as you may not get symptoms with some of these problems.
- Blood tests are particularly important during the first few months of treatment and when methotrexate is taken with leflunomide.
- As well as monitoring for side effects, blood tests help to monitor your condition to determine if the treatment is effective.
- You will need to have full blood counts and liver function tests every 2 to 4 weeks for the first few months of treatment and then every 1 to 3 months after that.
- If there are no problems seen after 3 months of treatment at a specific dose of methotrexate, the blood tests may be done less frequently.
- Your general practitioner (GP) will be informed about the monitoring schedule. It is important to see your GP if you have been asked to do so as they play an important role in monitoring your condition.

Risk of infections

- Because your immune system may be depressed, there is an increased risk of developing some infections, especially herpes zoster (chicken pox and shingles). You should try to avoid contact with people who have these infections. If you have an infection or persistent fever, tell your doctor straight away.

Use with other medicines

- Methotrexate can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes

over the counter or herbal/naturopathic medicines. You should also mention your treatment when you see other health professionals.

- Antibiotics containing **trimethoprim (e.g. Bactrim, Septrim or Triprim)** can cause problems when taken with methotrexate. If you are prescribed any of these medications you **must** tell the doctor you are taking methotrexate.
- Aspirin can be used safely in the low doses taken for prevention of heart attack and stroke.
- Methotrexate can be taken safely with anti-inflammatory drugs (NSAIDs), as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte, can be used while taking methotrexate provided you take them as directed.
- Most vaccines can be given safely but live vaccines, such as MMR (measles, mumps and rubella), OPV (oral polio vaccine) or yellow fever, may need special consideration.
- Pneumovax and yearly flu vaccinations are safe and recommended to reduce your risk of those infections. Talk with your rheumatologist before receiving any vaccines.

Use with alcohol

- Alcohol increases the risk of liver damage while taking methotrexate. Methotrexate usage in heavy drinkers has been associated with cirrhosis of the liver.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Surgery

- If low dose once weekly methotrexate is continued during surgery there seems to be no change in wound healing or increased infection.

Use in pregnancy and breastfeeding

- Methotrexate should not be taken during pregnancy as it can cause miscarriage or foetal deformity. It should also not be taken when breastfeeding.
- Women of child-bearing age should use effective contraception while taking methotrexate.
- Women planning to become pregnant should stop taking methotrexate 3 months before attempting to conceive.
- The best time for a male partner to stop taking methotrexate before trying to conceive is not known.
- Methotrexate does not affect a person's ability to have children in the long term.

How to store methotrexate

- Store methotrexate in a cool, dry place, away from direct heat and light (e.g. not in the bathrom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

You should see your rheumatologist regularly to make sure the treatment is working and to minimise any potential side effects.

How to help us help you
Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!

Contact us in any of the following ways:
Email: ARAD@monash.edu
Telephone: Sydney 02 9463 1889
or Melbourne 03 9508 3424
Fax: 1-800-022-730
Visit our website: www.ARAD.org.au

Australian Rheumatology Association

PATIENT INFORMATION ON

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

(Examples of brand names: Brufen, Celebrex, Mobic, Naprosyn, Nurofen, Orudis, Voltaren)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you may need to have to detect unwanted effects**
- **other precautions you should take while you are taking these medicines.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking NSAID you should see your doctor regularly to make sure the treatment is working and to minimise any possible side effects.
- If you develop severe stomach pains, pass blood or black stools, or vomit blood, stop taking the medicine immediately. You should see your doctor as soon as possible or go to the nearest emergency department.
- If you are worried about any side effects you should contact your doctor as soon as possible.

For more information about arthritis see the Arthritis Australia website www.empowered.org.au.

What are NSAIDs?

Non-steroidal anti-inflammatory drugs, or NSAIDs, are common medicines used to treat the symptoms of arthritis. The name means they reduce pain and stiffness due to inflammation of the joints, without using steroids. You can find out about steroids from the separate ARA information sheet on corticosteroids.

There are many different NSAIDs. Some can be bought over the counter (OTC) e.g. ibuprofen (Nurofen). Others such as ketoprofen (Orudis) are only available with a prescription. The brand name of your NSAID will have the generic name next to it on the packet or bottle. See the table at the end of this information sheet for further examples.

In recent years a newer type of NSAID, the selective NSAIDs (also called cox-2 inhibitors or coxibs) have been developed. These are less likely to cause stomach irritation and ulcers compared to traditional NSAIDs.

How do they work?

NSAIDs stop cells making prostaglandins. Prostaglandins are chemicals released by injured cells. They cause inflammation and swelling and they sensitise nerve endings, which can lead to pain. If you make less prostaglandin, you have less inflammation and less pain. By stopping cells making prostaglandins, NSAIDs relieve the symptoms of arthritis. They do not stop the inflammation occurring in the future or prevent the disease progressing to joint damage.

What benefit can you expect from your treatment?

NSAIDs provide relief from pain and stiffness. They work quickly, usually within a few hours. The maximum benefit can take 2 to 4 weeks or sometimes longer. You may need to try two or three different NSAIDs to find one that suits you best. You **must** only take one type of NSAID at a time.

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How are NSAIDs taken?

NSAIDs are usually taken by mouth in tablet or capsule form. They are also available as liquids, injections, creams, sprays and suppositories.

Side effects may still occur with any method of administration, even when NSAIDs are applied to the skin (see *Side effects*).

When should they be taken?

NSAIDS can be taken when needed to treat short term symptoms. They can also be taken regularly to manage persistent pain and stiffness.

While NSAIDs may be more effective if taken regularly, the possible side effects are less if they are only taken when needed, for example before exercise.

How often you take a NSAID also depends on the one you are prescribed. Ask your doctor or pharmacist if you are uncertain about how often to take your medicine.

Tablets and capsules should be taken with food to reduce possible side effects.

What is the dosage?

NSAIDs usually come in different strengths. Treatment usually starts with a low dose. This can be adjusted depending on your response.

The dose will depend on the type of NSAID and the condition for which it is being used.

To minimise side effects, the lowest dose that controls symptoms is usually recommended.

Always follow the instructions provided in the packaging unless otherwise directed by your doctor.

Can other medicines be taken with NSAIDs?

To minimise side effects, sometimes a medicine to protect the stomach may be given (see page 3).

NSAIDs may be used with other arthritis medicines including:

- DMARDs (anti rheumatoid arthritis drugs) such as methotrexate
- simple pain medicines such as paracetamol.

Corticosteroids are not generally used with NSAIDs as the risk of side effects such as ulcer is increased.
There are separate information sheets for the medicines mentioned above.

How long is the treatment continued?

Treatment with NSAIDs can be for a short period or long term. A NSAID should not be continued indefinitely without regular review by your doctor to confirm the NSAID still works and no serious side effects are occurring.

Are there any side effects?

You might experience side effects with your treatment. Tell your doctor if you are concerned about possible side effects. A reduction in dose or change to another NSAID may decrease the side effects so that you can continue to take the treatment.

Alternatively, your doctor may recommend a different pain relieving medicine with fewer potential side effects, such as paracetamol. This may allow you take the NSAID less often or stop it altogether.

Most common possible side effects:

- The most common side effects are *gastrointestinal* and may include decreased appetite, nausea (feeling sick), vomiting, diarrhoea, constipation, heartburn and stomach pain or cramps.
- *Heart disease and stroke*: All NSAIDs, including the newer selective types (cox-2 inhibitors/coxibs), may slightly increase the risk of heart attacks and strokes. This risk seems higher in those already at high risk of heart attack or stroke.
- NSAIDs can increase *blood pressure* (see *Precautions*, page 3).
- NSAIDs can make *heart failure or kidney failure* worse. Fluid retention can lead to weight gain or swelling of ankles or legs. Kidney failure is more likely if you are also taking fluid tablets and certain blood pressure tablets (see *Precautions*, page 3).
- *Dizziness, lightheadedness, tiredness, ringing in the ears (tinnitus)* and *headache* can occur.
- *Bleeding* more easily than usual is often noticed.

Less common or rare possible side effect:

There are some rare but potentially serious side effects with NSAIDs.

- *Stomach or duodenal ulcers:* NSAIDs can cause ulcers in the stomach or duodenum (upper bowel).

  If you develop severe stomach pains, pass blood or black stools, or vomit blood, stop taking the medicine immediately. You should see your doctor as soon as possible or go to the nearest emergency department.

  The risk of ulcers is higher if:

  - you are older than 65 years
  - you have had a previous stomach or duodenal ulcer
  - you are also taking warfarin, corticosteroid tablets or low-dose aspirin (used by many people to help prevent a heart attack or stroke).

  If you have an infection (helicobacter bacteria) in your stomach this should be treated before you start NSAIDs. Your doctor may advise that you take an anti-ulcer medicine to help reduce the risk of getting a stomach or duodenal ulcer.

  The selective NSAIDs e.g. celecoxib (brand name Celebrex), may be less likely to cause stomach ulcers and irritation than traditional NSAIDs. They have been used to treat arthritis in people who have suffered stomach upset or ulcers while taking a traditional NSAID or who were thought to be at risk for ulcers.
- *Allergy* to NSAIDs can occur resulting in skin rashes.
- *Shortness of breath* may occur in some people with asthma. Seek medical help if your asthma suddenly becomes worse after taking NSAIDs.
- *Liver inflammation* (hepatitis) is another uncommon side effect.

There are also a number of other uncommon side effects. Read the leaflet that comes with the medicine, which lists all the precautions and possible side effects.

What precautions are necessary?

Blood pressure

- Because NSAIDs can affect your blood pressure it is a good idea to have your blood pressure monitored monthly for the first two months. This is more important if you already have high blood pressure or you are on treatment for high blood pressure. If your blood pressure is stable, it should be checked every 3 to 6 months while you continue to take the NSAIDs.

Blood tests

- Usually blood tests are not required for people taking NSAIDs.
- They may be needed in certain situations. For example, your kidney function may need to be monitored if you have other risk factors for reduced kidney function, such as being over 65 years old and taking blood pressure medicines or fluid tablets. In this case your doctor may recommend you have a blood test in the first few weeks after starting a NSAID.

Use with other medicines

- NSAIDs can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking, including herbal and naturopathic medicines. This includes over the counter (OTC) medicines as some contain NSAIDs. You should also mention your treatment when you see other health professionals.
- NSAIDs are generally used for joint and muscle pain. However sometimes they can be used for other reasons, for example mefanamic acid (Ponstan) may be used for period pain.
- Despite the possible increased risk of ulcer, low doses of aspirin used to prevent heart attack and stroke can probably be used safely with NSAIDs if the risk for ulcer is low in the first place.
- Methotrexate for rheumatoid arthritis or other arthritis treatment can be taken safely with NSAIDs as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte can be used while taking NSAIDs provided you take them as directed.
- If you are taking anticoagulants such as warfarin you should tell your doctor as combination with NSAIDs can increase the risk of bleeding.

Use with alcohol

- NSAIDs can increase the risk of a stomach or duodenal ulcer. Heavy alcohol use (more than

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4 standard drinks in one session) should be avoided while taking these medicines.

Use in pregnancy and breastfeeding

- NSAIDs are not recommended during pregnancy or during breastfeeding unless specifically advised by your doctor. If you are planning a family or you become pregnant you should discuss this with your doctor as soon as possible.
- Some studies suggest that if NSAIDs are taken around the time of conception there may be an increased risk of miscarriage.
- If NSAIDs are taken in later stages of pregnancy they may have an effect on the blood vessels near the baby's heart. Paracetamol does not have these effects.

How to store NSAIDs

- Store NSAIDs in a cool, dry place, away from direct heat and light.
- Keep all medicines out of reach of children.

Non-selective NSAIDS (cox-1 and cox-2 inhibitors)	
Generic/chemical name	**Brand names**
Diclofenac	Chemists' Own, Clonac, Diclohexal, Fenac, Imflac, Viclofen, Voltaren, Voltaren Rapid, Voltfast
Ibuprofen	Advil, Brufen, Bugesic, Chemists' Own, Dimotapp, Gold Cross, Herron Blue, iProfen, Nurofen, Panafen, ProVen, Rafen, Tri-Profen
Indomethacin	Arthrexin, Indocid
Ketoprofen	Orudis, Oruvail
Ketorolac	Ketoral, Toradol
Mefenamic acid	Ponstan
Naproxen	Aleve, Anaprox, Chemists' Own, Crysanal, Eazydayz, Inza, Naprosyn, Naprofem, Naprogesic, Proxen
Piroxicam	Feldene, Feldene-D, Mobilis, Mobilis D,
Sulindac	Aclin
Selective NSAIDS (cox-2 inhibitors)	
Celecoxib	Celebrex
Etoricoxib	Arcoxia
Meloxicam	Meloxibell, Mobic, Movalis, Moxicam
Paracoxib	Dynastat

Source: Australian Medicines Handbook, 2013.
Note: This may not be a comprehensive list – ask your pharmacist or doctor for more information.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details:~

When taking NSAIDs should see your doctor regularly to make sure the treatment is working and to minimise any potential side effects.

How to help us help you

Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!
Contact us in any of the following ways:
Email: ARAD@monash.edu
Telephone: **Sydney 02 9463 1889**
or **Melbourne 03 9508 3424**
Fax: **1-800-022-730**

Visit our website: www.ARAD.org.au

PATIENT INFORMATION ON

ADALIMUMAB

(Brand name: Humira)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition**
- **other precautions you should take while you are taking adalimumab.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking adalimumab you must see your rheumatologist regularly to ensure the treatment is working and minimise any possible side effects.
- If you stop adalimumab for any reason you must contact your doctor. Failure to do so may mean that your continued treatment will no longer be subsidised.
- Remember to change the injection site each time adalimumab is injected.
- If you are worried about any side effects you should contact your rheumatologist as soon as possible.
- It is important to tell your doctor if you have had cancer or if you develop cancer.
- If you are taking adalimumab and plan to become pregnant you must discuss the timing with your doctor.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html.

What is adalimumab?

Adalimumab (brand name Humira) belongs to a new class of medicines called **biological disease modifying antirheumatic drugs (biological DMARDs or bDMARDs).**

bDMARDs have now been given to over a million people worldwide since their initial use in the late 1990s.

These medicines block natural substances, called cytokines. These are substances found in excessive amounts in the blood and joints of people with rheumatoid arthritis, psoriatic arthritis, juvenile arthritis and ankylosing spondylitis.

The increased levels of cytokines cause inflammation, which results in symptoms of pain, joint swelling and stiffness, and can lead to joint damage.

By blocking the cytokine called Tumour Necrosis Factor (TNF), adalimumab reduces inflammation, lessens the symptoms and helps stop further joint damage.

What benefit can you expect from your treatment?

Unlike standard antirheumatic drugs (DMARDs), adalimumab works relatively quickly. You may notice some relief of joint swelling, pain and stiffness within the first 4 weeks of treatment.

Stopping adalimumab

If adalimumab treatment is stopped for more than a few weeks there is a risk that your condition will get worse again. Continue with your treatment unless advised by your doctor or unless side effects develop (see *Side effects*).

If you stop adalimumab for any reason you **must** contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.

How will your condition be monitored?

Due to the current prescribing restrictions for all bDMARDs:

- Adalimumab will only be started if your disease is active and if standard treatments have been unsuccessful.
- It will not be continued unless it helps your condition. This will be assessed at least 12 weeks after the start of treatment.
- Blood tests will be required during your treatment to monitor your condition and to determine the effectiveness of treatment.
- The frequency of blood tests will depend on what other medicines you are taking and what other illnesses you might have. Your rheumatologist will determine the frequency of tests required.

How is adalimumab taken?

Adalimumab is injected under the skin of the abdomen or thigh.

It can be injected by your doctor, nurse, carer or by you. If injecting yourself, be sure to follow the detailed instructions carefully to ensure the best response. It is particularly important to change the injection site each time.

What is the dosage?

The usual dose for adults with rheumatoid arthritis is 40mg once every two weeks.

Can other medicines be taken with adalimumab?

Adalimumab may be used with other arthritis medicines including:

- other DMARDs such as methotrexate
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

Adalimumab cannot be used with other bDMARDs.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience side effects with your treatment. Contact your doctor if you have any concerns about possible side effects. Many side effects disappear when adalimumab treatment is stopped.

Most common possible side effects

- *Mild pain, swelling or itching* at the site of the injection are very common (up to 20% of patients) but can be reduced by applying ice and antihistamine/steroid creams to the injection site.
- *Headaches, cough and stomach and bowel discomfort* may also occur.
- As adalimumab affects the immune system, *mild infections,* particularly of the upper respiratory tract (e.g. colds, sinusitis) may occur more frequently than usual. Treatment with adalimumab may need to be temporarily stopped so contact your doctor for advice.

Less common or rare possible side effects

- *Serious infection*s such as Tuberculosis (TB) are seen rarely, and screening for TB is needed before treatment begins (see *Precautions*).
- Rarely adalimumab may cause an *allergic reaction* with itchy, red skin or a rash or a feeling of tightness in the chest and difficulty breathing.

- Side effects involving the nerves, such as *inflammation of the nerve to the eye*, may also occur rarely, causing changes in vision or sensation.
- Very rarely *'drug-induced lupus'* has occurred with symptoms of rash, fever and increased joint pain.
- It is still unclear from research if there is an increased risk of cancer due to adalimumab treatment (see *Precautions*).

What precautions are necessary?

Infections

- If you have an active infection of any kind treatment with adalimumab will not be given until the infection is treated successfully.
- Adalimumab will not be given if you have active untreated tuberculosis (TB) or HIV (AIDS) infection as it is likely to make these conditions worse.
- If you have latent (inactive) TB preventative anti-TB treatment will be started at least 4 weeks before adalimumab. The anti-TB treatment will usually need to be taken for 9 months.
- Hepatitis B or C infection may not necessarily exclude treatment.
- Because of the risks associated with infection the following tests may be conducted before commencing treatment with adalimumab:
  - blood tests for hepatitis B and C
  - chest x-ray and two step Tuberculin Skin Test (Mantoux) or QuantiFERON blood test for tuberculosis (TB)
  - HIV tests are required for those who are at risk of this infection.

Precautions with other diseases

- People with multiple sclerosis should not be treated with adalimumab due to the possible effects on the nerves.
- People with moderate to severe heart failure may not be treated with adalimumab as the medicine can make heart failure worse.
- People with systemic lupus erythematosus (lupus/SLE) are not usually given adalimumab but each case will be assessed individually.

Use with other medicines

- Adalimumab can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals.
- Adalimumab does not increase the risk of side effects from low dose aspirin (taken for prevention of heart attack and strokes).
- The simple pain reliever paracetamol and combined pain medicines such as Panadeine and Panadeine Forte can be used while you are receiving adalimumab treatment provided you take them as directed.

Vaccines

- If you are on adalimumab it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio virus), BCG (Bacillus Calmette Guerin) or yellow fever. Talk with your rheumatologist before receiving any vaccines.
- Pneumovax and the combined yearly seasonal flu /swine flu vaccinations are safe and recommended to reduce your risk of those infections.

Surgery

- If you require surgery for any reason, treatment with adalimumab will be stopped before surgery. It will be restarted again after the operation, at a time determined by your surgeon and rheumatologist. Treatment will be restarted once the wound is healed and if there is no infection present.

Cancer risk

- Lymphoma, a cancer of lymph glands, is found more commonly in patients with severe active rheumatoid arthritis than in the general population. Studies are in progress to see if treatment with adalimumab changes this. To date there is no evidence to suggest that this medicine increases lymphoma.

- If cancer has been previously treated and cured it is unclear whether a TNF-bDMARD such as adalimumab can be used safely. An interval of 5 years is normally recommended between cure of a cancer and starting TNF-bDMARDs.
- For general cancer prevention, stopping smoking and taking skin cancer prevention measures are recommended. It is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.
- Talk to your doctor, if you have any concerns about issues relating to cancer risk.

Use with alcohol

- You may drink alcohol while taking adalimumab. However, if you are also taking methotrexate you should be particularly cautious about your alcohol intake.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Use in pregnancy and when breastfeeding

- Not enough is known regarding the possible side effects of adalimumab on the unborn baby. If you plan to become pregnant, it is important to discuss this with your doctor as each case is different.

How to store adalimumab

- Keep the medicine refrigerated, even when travelling.
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking adalimumab you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

How to help us help you

Sign up to the ARAD project now!

The Australian Rheumatology Association collects information on how well these drugs work and how often they cause problems.

The best way to get this information is from you!

Contact us in any of the following ways:

Email: ARAD@monash.edu
Telephone: Sydney 02 9463 1889
or Melbourne 03 9508 3424
Fax: 1-800-022-730

Visit our website:
www.ARAD.org.au

Australian Rheumatology Association

Arthritis AUSTRALIA

PATIENT INFORMATION ON

ABATACEPT

(Brand name: Orencia)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition and detect unwanted effects**
- **other precautions you should take while you are taking abatacept**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking abatacept you must see your rheumatologist regularly to ensure the treatment is working and to minimise any possible side effects.
- If you stop abatacept for any reason you must contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.
- If you are worried about any side effects you should contact your rheumatologist as soon as possible.
- If you are injecting abatacept under the skin (subcutaneously) remember to change the injection site each time.
- It is important to tell your doctor if you have had cancer or if you develop cancer.
- If you are taking abatacept and plan to become pregnant you must discuss the timing with your doctor.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website
www.arthritisaustralia.com.au

What is abatacept?

Abatacept (brand name Orencia) belongs to a new class of medicines called **biological disease modifying antirheumatic drugs (biological DMARDs or bDMARDs).**

bDMARDs have now been given to over a million people worldwide since their initial use in the late 1990s.

These medicines block natural substances called cytokines. These are substances found in excessive amounts in the blood and joints of people with rheumatoid arthritis and juvenile arthritis.

The increased levels of cytokines cause inflammation, which results in symptoms of pain, joint swelling and stiffness, and can lead to joint damage.

By blocking T cell (a type of white blood cell) responses, abatacept reduces inflammation, lessens the symptoms and helps stop further joint damage.

What benefit can you expect from your treatment?

Unlike standard antirheumatic drugs (DMARDs), abatacept works relatively quickly. You may notice some relief of joint swelling, pain and stiffness within the first 4-8 weeks of treatment.

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Stopping abatacept

If abatacept treatment is stopped for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop (see *Side effects*).

If you stop abatacept for any reason you **must** contact your doctor. Failure to do so may mean that your continued treatment may no longer be subsidised.

How will your condition be monitored?

In view of the current prescribing restrictions for all bDMARDs:

- Abatacept will only be started if your disease is active and if standard treatments have been unsuccessful.
- It will not be continued unless it helps your condition. This will be assessed at least 12 weeks after the start of treatment.
- Blood tests will be required during your treatment to monitor your condition and to determine the effectiveness of treatment.
- The frequency of blood tests will depend on what other medicines you are taking and what other illnesses you might have. Your rheumatologist will determine the frequency of tests required.

How is abatacept given?

Abatacept is given as a drip (infusion) into the vein, or as an injection under the skin of the abdomen or thigh.

The infusion normally takes thirty minutes. This is followed by a one hour period of observation to make sure you don't have any side effects. Additional doses are usually given at 2 and 4 weeks after the first dose. Subsequent doses are usually given every 4 weeks.

When given as an injection under the skin (subcutaneous injection), doses are given weekly.

The treatment may still begin with a single dose given as an infusion (loading dose).

Abatacept is given in combination with the DMARD methotrexate.

What is the dosage?

For infusions the dose is based on the person's weight, so each person's dose may be different.

The subcutaneous dose is a standard 125mg weekly injection.

Can other medicines be taken with abatacept?

Abatacept may be used with other arthritis medicines including:

- other DMARDs such as methotrexate
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

Abatacept cannot be used with other bDMARDs.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience side effects with your treatment. Contact your doctor if you have any concerns about possible side effects. Many side effects disappear when abatacept treatment is stopped.

Most common possible side effects

- Common possible side effects include:
  - *headaches, runny nose, dizziness or cough*
  - *sore throat, heartburn or nausea*
  - *back, arm or leg pain*
  - *urine infections*

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  - *rash.*
- *Stomach and bowel discomfort* may also occur.
- As abatacept affects the immune system, *mild infections*, particularly of the upper respiratory tract (e.g. colds, sinusitis) may occur more frequently than usual. Treatment with abatacept may need to be temporarily stopped so contact your doctor for advice.

Less common or rare possible side effects

- Side effects can occur during the infusion itself. These may include *fever or chills, itch, chest pain, shortness of breath* or *changes in blood pressure*. These effects are more likely to occur during the first or second infusion.
- Mild pain, swelling, bruising or itching may occur at the injection site (for subcutaneous doses). It is therefore important to rotate the injection site.
- *Serious infections* such as tuberculosis (TB) are seen rarely, and screening for TB is needed before treatment begins (see *Precautions*).
- Rarely abatacept may cause an *allergic reaction* with itchy, red skin or a rash.
- It is still unclear from research if there is an increased risk of cancer due to abatacept treatment (see *Precautions*).

What precautions are necessary?

Infections

- If you have an active infection of any kind, treatment with abatacept will not be given until the infection is treated successfully.
- Abatacept will not be given if you have active untreated tuberculosis (TB) or HIV (AIDS) infection as it is likely to make these conditions worse.
- If you have latent (inactive) TB preventative anti-TB treatment will be started at least 4 weeks before abatacept. The anti-TB treatment will usually need to be taken for 9 months.
- Hepatitis B or C infection may not necessarily exclude treatment.
- Because of the risks associated with infection the following tests may be conducted before commencing treatment with abatacept:
  - blood tests for hepatitis B and C
  - chest x-ray and two step Tuberculin Skin Test (Mantoux) or QuantiFERON blood test for tuberculosis (TB)
  - HIV tests are required for those who are at risk of this infection.

Precautions with other diseases

- People with chronic lung disease (COPD) are not usually given abatacept but each case will be assessed individually.

Use with other medicines

- Abatacept can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals.
- Abatacept does not increase the risk of side effects from low dose aspirin (taken for prevention of heart attack and strokes).
- The simple pain reliever paracetamol and combined pain medicines such as Panadeine and Panadeine Forte can be used while you are receiving abatacept treatment provided you take them as directed.

Vaccines

- If you are on abatacept it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio virus), BCG (Bacillus Calmette Guerin) or yellow fever. Talk with your rheumatologist before receiving any vaccines.
- Pneumovax and the combined yearly seasonal flu/swine flu vaccinations are

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safe and recommended to reduce your risk of those infections.

Surgery

- If you require surgery for any reason, treatment with abatacept will be stopped before surgery.

  It will be restarted again after the operation at a time determined by your surgeon and rheumatologist. Treatment will be restarted once the wound is healed and if there is no infection present.

Use with alcohol

- You may drink alcohol while taking abatacept. However, if you are also taking methotrexate you should be particularly cautious about your alcohol intake.
- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Cancer risk

- Lymphoma, a cancer of lymph glands, is found more commonly in patients with severe active rheumatoid arthritis than in the general population. Studies are in progress to see if treatment with abatacept changes this. To date there is no evidence to suggest that this medicine increases lymphoma.

  If cancer has been previously treated and cured it is unclear whether abatacept can be used safely. An interval of 5 years is normally recommended between cure of a cancer and starting TNF-bDMARDs.
- For general cancer prevention, stopping smoking and taking skin cancer prevention measures are recommended. It is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.
- Talk to your doctor if you have any concerns about issues relating to cancer risk.

Use in pregnancy and when breastfeeding

- Not enough is known regarding the possible side effects of abatacept. If you plan to become pregnant, it is important to discuss this with your doctor, as each case is different.
- You should not breastfeed when taking abatacept.

How to store abatacept

- Keep the medicine refrigerated, even when travelling.
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking abatacept you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

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PATIENT INFORMATION ON

PREDNISOLONE & PREDNISONE

(Also known as corticosteroids / cortisone / steroids)

(Examples of brand names: Panafcort, Panafcortelone, Predsone, Predsolone, Solone, Sone)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **what are the possible side effects**
- **what tests you should have to monitor your condition and to detect unwanted effects**
- **other precautions you should take when you are taking prednisolone or prednisone.**

Please read it carefully and discuss it with your doctor.

Important things to remember:

- While taking prednisolone you should see your treating doctor regularly to make sure the treatment is working as it should and to minimise any possible side effects.
- You should not stop your treatment unless your doctor tells you to.
- You should not increase or reduce the dose of prednisolone unless your doctor tells you to.

For more information about RHEUMATOID ARTHRITIS see Arthritis Australia's Empowered website:
www.empowered.org.au

What is prednisolone?

Corticosteroids are hormones that are produced naturally in the body. They are necessary for normal working of the body.

Prednisolone and prednisone are man-made corticosteroids (also called steroids for short). Man-made corticosteroids are used to treat inflammatory diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE/lupus) and other inflammatory disease. They have a strong anti-inflammatory effect and reduce the swelling and pain in joints and other organs. They do not cure the disease.

They should not be confused with male or female steroid hormones, which are known for their misuse among athletes.

Prednisolone is the most common type of corticosteroid prescribed. Although prednisone is slightly different the information contained in this document also applies to that medication.

What benefit can you expect from your treatment?

Prednisolone works very quickly. Within a few days you may notice your pain and stiffness is much better and/or your joints are less swollen.

How is prednisolone taken?

Prednisolone can be swallowed as tablets or liquid. It is usually taken once or twice a day. Sometimes it is taken every second day. It is usually taken in the morning, with or immediately after food.

Other corticosteroids can be given by injection into joints, soft tissues or muscles. An injection into a vein (intravenous) may also be given if required.

What is the dosage?

There are three different strengths of prednisolone tablets: 1mg, 5mg and 25mg. This means the dosage can be adjusted to suit your needs without you having to take large numbers of tablets. It is important to check the strength of the tablets as they look very similar.

The dose depends on the severity of the disease. A high dose may be used initially and then reduced by your doctor as symptoms improve. To minimise the risk of side effects the smallest dose possible will be used.

Sometimes your doctor may increase the dose temporarily when your body is under stress, for example during a surgical procedure or if you have a severe illness such as an infection.

After you have stopped prednisolone your doctor may prescribe it again for a short period in certain situations as described above.

Can other medicines be taken with prednisolone?

Prednisolone may be used with other arthritis medicines including:

- antirheumatoid arthritis medicine (also called disease modifying antirheumatic drugs or DMARDs) such as methotrexate
- biological DMARDs (a newer type of DMARD, which acts on natural substances in the body that contribute to inflammation and joint damage)
- simple pain relieving medicines such as paracetamol.

Prednisolone and other corticosteroids should be taken with caution with nonsteroidal anti-inflammatory drugs (NSAIDs) as the risk of side effects such as stomach ulcer is increased.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

Low dose prednisolone, taken for a few days or even a few weeks, does not normally cause any unwanted side effects.

If prednisolone is taken in high doses or for a long time certain predictable side effects can occur. Some of these improve after prednisolone is stopped. Many can be minimised by giving the lowest effective dose over the shortest possible period of time.

The effects may also be minimised by giving the medicine by injection into the joints or into a muscle.

Most common possible side effects

- *Weight gain*: The most common side effects are rounding of the face and weight gain around the stomach. These are due to altered metabolism, increased appetite and salt retention.
- *Osteoporosis (thinning of the bones):* While very low doses of prednisolone (less than 5 mg/day) are not very likely to cause thinning of the bones, moderate and high doses taken for long periods usually cause this problem.

  Your doctor will tell you if you need a *bone density (BMD)* test to check your risk of osteoporosis.

  To reduce the risk it is recommended that you:
  - have 1000mg of calcium each day (e.g. 3 serves of dairy or calcium tablets)
  - take 30 minutes of weight bearing exercise each day (e.g. walking)
  - avoid smoking and avoid drinking more than 2 standard drinks of alcohol a day
  - get some sunlight exposure each day to maintain vitamin D levels. You should wear sunscreen as usual to protect your skin from sun damage. As well as sun exposure, a vitamin D supplement may be recommended if vitamin D levels are low.
- *Skin:* The skin, especially on the arms and legs, can become thin, easily bruised and slow to heal. This occurs particularly after long term use, on higher doses and in older people with skin problems related to aging. In younger people acne may be a problem.

- *Diabetes:* Prednisolone can cause a rise in blood sugar in people with diabetes. This may require a change in their diabetes medicine. You should consult your general practitioner if you experience an increase in blood sugar levels.

  Prednisolone can also cause the onset of diabetic symptoms in people who are at risk of diabetes.
- *Blood pressure:* Prednisolone may cause an increase in blood pressure or make it more difficult to control. This can be monitored and changes can be made to your blood pressure medicine if required. Your doctor will advise about frequency of monitoring.
- *Cholesterol:* Prednisolone can cause a rise in blood cholesterol. This can be monitored and changes can be made to your treatment if required.
- *Psychological effects:* Prednisolone can cause euphoria (feeling high) and/or other mood or personality changes such as irritability, agitation or depression. While some psychological effects are quite common, they rarely cause significant problems.
- *Trouble sleeping* may also occur but can be minimised by taking prednisolone in the morning.
- *Infections:* There may be an increased risk of some infections, including mouth infections (such as thrush), shingles and lung infections. Pre-existing infections such as tuberculosis (TB) may become active again. **It is important to tell your doctor if you have a chronic infection or you have been exposed to TB earlier in your life.**
- *Indigestion* or heartburn can occur. Taking prednisolone with food can reduce this.
- *Ulcers:* If taken with nonsteroidal anti-inflammatory medicines (NSAIDs) prednisolone can further increase the risk of stomach or duodenal ulcers. Your doctor will advise you about how to reduce this risk and about what symptoms to look out for.

Less common or rare possible side effects

- *Eyes:* With long term high dose treatment prednisolone may increase development of cataracts.
- *Other:* Facial flushes, constipation and avascular necrosis (a painful bone condition usually seen in the hip or knee) can occur very rarely.

Many of the above side effects can be managed or prevented by close medical supervision and by following your doctor's recommendations (see also *Precautions*, below).

What precautions are necessary?

Tests

- Blood sugar and cholesterol levels can be increased by prednisolone, so you will need to have *blood tests* to check these levels. Your doctor will tell you when the blood tests are required.
- Your general practitioner will be told about the tests you need to have. It is important to see your general practitioner if you have been asked to do so as they have an important role to play in monitoring your condition.

Use in pregnancy and breastfeeding

- Prednisolone may be used safely in pregnancy and breastfeeding. It is important to tell your doctor if you are, or intend to become pregnant or if you are breastfeeding.

Use with other medicines

- Prednisolone can affect how other medicines work. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- You should also mention your treatment when you see other health professionals, even if you have stopped taking corticosteroids within the last 12 months.
- Most vaccines can be given safely with prednisolone. Talk with your rheumatologist before receiving any vaccines.
- Yearly flu vaccines and Pneumovax are safe and recommended.

Surgery

- If you are going to have an operation it is important to tell the anaesthetist that you are taking or have been taking prednisolone or other corticosteroids in the last year.

- Your doctor may tell you that you need some additional prednisolone at the time of surgery.

Never stop taking prednisolone suddenly

- You should not stop taking prednisolone suddenly or increase or reduce the dose you have been prescribed unless your doctor tells you to.
- Your adrenal glands, which are just above the kidneys, normally make corticosteroids in small amounts. These are important for many normal body functions.
- If prescribed corticosteroids are taken, the body begins to make less than usual or even stops making corticosteroids completely.
- If the medicine is then *suddenly* stopped there may be a problem as the adrenal glands won't have had time to make the corticosteroids needed. This problem is called *adrenal insufficiency*.
- Signs of adrenal insufficiency include weakness, fatigue, fever, weight loss, vomiting, diarrhoea and abdominal pain. If you experience any of these problems, seek medical help.

How to store prednisolone

- Store prednisolone tablets at room temperature, away from heat, moisture and light (e.g. not in the bathroom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking prednisolone or other corticosteroids you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.

Please tick (✓) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Methotrexate

1) Methotrexate
a) reduces joint swelling only
b) is a pain killer only
c) will strengthen your bones
d) reduces damage to your joints

2) Methotrexate will
a) work immediately
b) take one year to work
c) take some weeks to work
d) not work unless given as an injection

3) Methotrexate is taken
a) once a day
b) once a week
c) once a month
d) once every 6 months

4) Folic acid is a natural vitamin taken with Methotrexate to
a) reduce pain
b) give you more energy
c) reduce the side effects of Methotrexate
d) stop the arthritis

5) Methotrexate should be taken
a) indefinitely if there are no serious side effects
b) until the script runs out
c) until you feel better
d) for 4 weeks only

(Correct answers based on Patient Information Sheet:
1d, 2c, 3b, 4c, 5a – Not to be included in copy given to patients)

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

Prednisone/Prednisolone/corticosteroids/cortisone all refer to the same drug.

1) Prednisone
a) cures arthritis at high doses
b) reduces joint pain, inflammation and joint swelling
c) makes your muscles bigger
d) makes your bones stronger

2) Prednisone
a) can be stopped suddenly with no problems
b) should be stopped if you get an infection
c) should not be stopped suddenly
d) is a very safe drug and you can change the dose yourself

3) Prednisone works
a) within a few days
b) only in combination with other arthritis medication
c) only if taken long-term
d) by irreversibly suppressing your immune system

4) Prednisone
a) should be stopped in pregnancy
b) can cause thin bones
c) does not affect blood sugar levels
d) helps you lose weight

5) Prednisone
a) should be stopped just before surgery
b) should not be taken with other arthritis medications
c) needs to be taken for the rest of your life
d) is often able to be stopped once the arthritis is controlled

(Correct answers based on Patient Information Sheet:
1b, 2c, 3a, 4b, 5d – Not to be included in copy given to patients)

Please tick (✓) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Adalimumab is also called Humira.

1) Humira
a) is a pain killer
b) reduces damage to your joints
c) will strengthen your bones
d) just reduces joint swelling

2) Humira will
a) work immediately
b) take one year to work
c) take some weeks to work
d) not work unless you take other arthritis medication

3) Humira is taken
a) once a day
b) only when the arthritis flares
c) once every 2 weeks
d) once every 6 months

4) Humira should be continued
a) unless advised by your doctor to stop
b) until the script runs out
c) until you feel better
d) for 4 weeks only

5) If you are taking Humira and get an infection which isn't getting better
a) try some tumeric
b) double the dose of Humira
c) just take some antibiotics
d) stop the Humira

(Correct answers based on Patient Information Sheet:
1b, 2c, 3c, 4a, 5d – Not to be included in copy given to patients)

Please tick (✓) the ONE BEST answer (a-d) to each of the following questions:

Non-steroidal anti-inflammatory drugs (NSAIDs) include medications such as Nurofen, Brufen, Voltaren, Naprosyn and Celebrex.

1) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) reduce joint pain, swelling and stiffness
b) prevent damage to your joints
c) strengthen your bones
d) will cure your arthritis

2) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) can be combined with other NSAIDs
b) can be continued long-term without review
c) often cause gut side effects such as nausea, vomiting and bleeding
d) should be continued during surgery

3) Non-steroidal anti-inflammatory drugs (NSAIDs)
a) may increase the risk of heart attack and stroke
b) prevent attacks of arthritis
c) have no effect on blood pressure
d) are safe in someone with kidney problems

4) Non-steroidal anti-inflammatory drugs **(**NSAIDs) should be used
a) for 4 weeks only
b) for the shortest time possible
c) until the script runs out
d) for however long to get rid of the pain

5) Bleeding from inside the gut while taking a non-steroidal anti-inflammatory drug (NSAID)
a) can be completely prevented by taking the NSAID with food
b) should stop if you continue taking the NSAID
c) doesn't cause any problems and can be ignored
d) can be associated with abdominal pain and indigestion

(Correct answers based on Patient Information Sheet:
1a, 2c, 3a, 4b, 5d – Not to be included in copy given to patients)

Please tick (✓) the <u>ONE BEST</u> answer (a-d) to each of the following questions:

Abatacept (Orencia)

1) Abatacept will
a) reduce joint swelling only
b) act as a pain killer only
c) strengthen your bones
d) reduce joint pain, swelling and stiffness in your joints

2) Abatacept will
a) work immediately
b) take one year to work
c) take some weeks to work
d) work only intermittently

3)Abatacept is given via a subcutaneous injection
a) once a day
b) once a week
c) once a month
d) once every 6 months

4) Abatacept works by
a) blocking pain
b) blocking T-cell responses to reduce inflammation
c) making you feel calm
d) making you more alert

5) While on Abatacept you should
a) be monitored regularly
b) take the medication until the script runs out
c) take the medication until you feel better
d) take the medication for 4 weeks only

(Correct answers based on Patient Information Sheet:
1d, 2c, 3b, 4b, 5a – Not to be included in copy given to patients)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7-8, figure 1
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	NA
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	6-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	7-8

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1, 4
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 3
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	NA
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	NA
		Cross-sectional study—Report numbers of outcome events or summary measures	Table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Table 1,2,4,5,6
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.