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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain



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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

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## ABSTRACT

**Objective:** Biologic disease-modifying antirheumatic drugs (bDMARDs) are a major cost driver in the management of psoriatic arthritis (PsA). Currently there are no published cost-effectiveness analyses (CEAs) comparing the interleukin-17A antagonists ixekizumab and secukinumab in Spain. We conducted a CEA from the perspective of the Spanish National Health System comparing ixekizumab versus secukinumab in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

**Design:** A Markov model with a lifetime horizon and monthly cycles was developed based on the widely accepted York model. Four health states were included: a 12- or 16-week bDMARD induction period, maintenance therapy, best supportive care (BSC) and death. Treatment response was assessed based on both Psoriatic Arthritis Response Criteria (PsARC) and ≥90% improvement in the Psoriasis Area Severity Index (PASI90). At the end of the induction period, responders transitioned to maintenance therapy. Non-responders and patients who discontinued maintenance therapy transitioned to BSC. Clinical efficacy data were derived from a network meta-analysis. Health utilities were generated by applying a regression analysis to PASI and Health Assessment Questionnaire – Disability Index scores collected in the ixekizumab SPIRIT studies. Results were subject to extensive sensitivity and scenario analysis.

**Results:** Ixekizumab was less costly and provided more quality-adjusted life-years (QALYs) than secukinumab. Although ixekizumab performed favourably over secukinumab in the base-case analysis, cost savings and QALY gains were modest. Total costs were €153,901 compared with €156,559 for secukinumab (difference −€2,658). Total QALYs were 9.175 versus 9.082 (difference 0.093). Base-case results were most sensitive to the annual bDMARD discontinuation rate and the modification of PsARC and PASI90 response to ixekizumab or secukinumab.

**Conclusions:** Ixekizumab provided more QALYs at a lower cost than secukinumab in bDMARD-naïve patients in Spain. However, total costs and QALYs differences were modest. Sensitivity analysis showed that base-case results were generally robust to changes in most input parameters.

## ARTICLE SUMMARY

### Strengths and limitations of this study

- A cost-effectiveness analysis was performed from the perspective of the Spanish National Health System comparing two interleukin-17A antagonists, ixekizumab and secukinumab
- The framework of this model is closely aligned with the York model; the 'gold standard' model for the economic evaluation of biologic treatments in PsA
- The current model uses a combined response criterion of PsARC and PASI to capture both joint and skin manifestations of PsA
- This analysis was limited by a lack of data available for related to constituents, costs and efficacy of supportive care given to PsA patients in Spain
- Due to uncertainty regarding the annual all-cause discontinuation rate, this model used assumptions consistent with previous models

## INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease characterised by pain, swelling and erosion of the joints.[1] PsA affects approximately 0.25% of the population worldwide [1] and 0.6% of the adult population in Spain.[2] PsA commonly co-exists with psoriasis, developing in up to 30% of psoriatic patients, and over 90% of patients with PsA will have concomitant psoriasis.[3,4] As a lifelong condition, PsA has a detrimental impact on quality of life due to pain and/or physical functional limitations associated with the disease.[1,3] It is also associated with substantial use of healthcare resources and high socioeconomic costs.[5,6]

A number of biologic disease-modifying antirheumatic drugs (bDMARDs), which inhibit key inflammatory cytokines, are approved for treating patients with PsA. Interleukin (IL)-17 has been identified as an effective target for the treatment of inflammatory diseases including PsA.[1,3] Ixekizumab, a high-affinity monoclonal antibody, is the most recently approved bDMARD targeting IL-17A for PsA, joining secukinumab, which uses the same target and similar mode of action.[7,8]

bDMARDs are considered major drivers of healthcare costs,[5] and the cost-effectiveness of these therapies often comes under scrutiny. Cost-effectiveness analyses (CEAs) comparing bDMARDs have been conducted using the York model,[9] an established economic framework, which, together with its subsequent versions, is considered the `gold standard' for conducting CEAs in PsA.[10,11]

As inhibition of IL-17A is a relatively new mechanism of action, drugs in this class have not been the focus of CEAs.[12] To date, there are no published CEAs comparing ixekizumab with secukinumab (another IL-17A inhibitor) in Spain.

We conducted a CEA assessing the cost effectiveness, in terms of the incremental cost per quality-adjusted life-year (QALY) gained, of ixekizumab versus secukinumab in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis from the

perspective of the Spanish National Health System (NHS). Secukinumab was selected as a comparator for this CEA as both drugs belong to the same class, and this may be of interest to decision makers assessing these IL-17A inhibitors. In addition, both drugs are approved for the treatment of PsA and plaque psoriasis, and have demonstrated high efficacy, particularly on skin symptoms.[7,8] This CEA focused on bDMARD-naïve patients, as this patient population may receive greater clinical benefit from earlier (i.e. first-line) treatment.[13]

## METHODS

### Model overview

A Markov model was developed to assess the cost effectiveness of ixekizumab versus secukinumab in a hypothetical cohort of bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis in Spain. The Markov model framework accommodates different health states and is based on the assumption that future events depend on the current health state of the patient. The model was programmed in Visual Basics for Applications with a user interface in Microsoft® Excel.

The model is based on the most recent version of the York model [11] with monthly cycles and a lifetime horizon, which was considered appropriate to reflect the chronic nature of PsA as well as the treatment aim of delaying disease progression.[14] The model incorporated age- and gender-dependent mortality data for the normal Spanish population. Mean age and gender distribution was taken from the patient population in the SPIRIT-P1 and -P2 trials of ixekizumab in PsA.[15,16] Increased PsA-specific mortality risks from two different sources [17,18] were implemented in scenario analyses.

The model includes four health states: 1) a 12- or 16-week bDMARD induction period; 2) maintenance bDMARD therapy; 3) best supportive care (BSC); and 4) death (Figure 1). A combination of Psoriatic Arthritis Response Criteria (PsARC) and Psoriasis Area Severity Index (PASI) was used to measure joint and skin response at the end of the induction period (Figure 2). The induction period was set to 12 weeks and 16 weeks for ixekizumab and

secukinumab, respectively. The induction period was chosen to reflect the time at which treatment efficacy is usually followed-up in clinical practice (approximately 3 months in Spain).[19,20] The PsARC response to treatment was defined as an improvement from baseline in two of four criteria without worsening in any measure: tender/swollen joints; and physician/patient global assessment of disease activity (one of which must be a joint count). In a consensus from the Spanish Psoriasis Group, a panel of dermatologists agreed that a complete or nearly complete PASI response is the most relevant measure of effectiveness in clinical practice.[21] With this in mind, ≥90% improvement in PASI (PASI90) was chosen in the base-case analysis as part of the response criteria and the treatment effect measures in this model.

**Treatment sequences**

At the end of the induction period, responders transitioned to maintenance therapy, while non-responders and discontinuers transitioned to BSC (Figure 1) in which patients were assumed to receive standard treatment depending on their Health Assessment Questionnaire – Disability Index (HAQ-DI) and PASI status.[22] Dosage regimens for ixekizumab and secukinumab were as per the European Union label.[7,8] During maintenance therapy, patients were assumed to face a constant risk of all-cause treatment discontinuation, which was reflected by an annual discontinuation rate of 16.5% in line with previously applied methods.[10,11]

In the base-case analysis, baseline cohort characteristics were reflective of the demographic data from the ixekizumab SPIRIT-P1 and -P2 clinical trials [15,16] (Table 1).

**Treatment effect**

While PsARC and PASI90 were used as the combined response criterion (i.e. treatment continuation rule), the treatment effect was modelled as a change in baseline of the HAQ-DI and PASI scores,[23] reflecting the joint and skin components of PsA, respectively. Baseline HAQ-DI and PASI scores were derived from the SPIRIT-P1 and -P2 trials [15,16] (Table 1).

Treatment effect, represented by improvement (i.e. reductions) in HAQ-DI and PASI scores, was assumed to be instantaneous; as such, the response was also applied during the induction period. Absolute change in HAQ-DI and PASI scores is based on data from a network meta-analysis (NMA).[23]

For patients who met the combined response of PsARC and PASI90 at the end of the induction period, the initial improvements in HAQ-DI and PASI continued during maintenance therapy until they transitioned into BSC. For patients entering BSC following discontinuation, it was assumed that some benefit was maintained from the initial bDMARD treatment. In the base case, for patients progressing to BSC, the HAQ-DI score was assumed to revert to the baseline HAQ-DI level prior to discontinuation ("rebound equal to initial gain"). The rebound effect was assumed to be immediate and patients were modelled to progress at the same rate as natural history progression (an increase of 0.018 per 3-month period) (Figure 3). For PASI score, it was assumed that for non-responders not meeting PASI90, there would still be some gain in PASI – albeit lower – while they were treated with a bDMARD in the induction period. Once in the BSC state, due to the progressive nature of PsA, it was assumed that patients would deteriorate at a rate of natural progression.

**Health utilities**

Health utilities were based on HAQ-DI and PASI scores from the SPIRIT-P1 and -P2 clinical trials[15,16] with Spanish tariffs applied. Calculation of utilities followed the established methodology of mapping three-level version of EuroQol-5 Dimensions (EQ-5D-3L) utilities on HAQ and PASI scores using a parsimonious linear regression model without further covariates or interaction terms. [9–11] Alternative coefficients based on a similar algorithm using different data were applied in a sensitivity analysis. Utilities were calculated in each model cycle by multiplying HAQ and PASI levels with the estimated regression coefficients.

**Resource use and costs**

As the CEA was conducted from the perspective of the Spanish NHS, only direct medical costs were considered in the model, and included medication, injection training, physician visits and therapy monitoring. Drug acquisition costs were derived from the Botplus database in Spain,[24] and costs for the administration and monitoring of treatments were obtained from various sources in Spain [25] (Table 2). Drug costs were based on the list prices as of Q4 2018. Monitoring costs were based on the costing schedule published in 2017, which was still valid in 2018. Due to a lack of healthcare resource utilisation data by drug or class, healthcare costs and resource utilisation related to the administration and monitoring of bDMARDs was determined by an expert panel of four Spanish physicians (two rheumatologists and two dermatologists).

The severity of arthritis and psoriasis also may have an impact on healthcare costs.[10,11] To reflect this, costs related to HAQ-DI and PASI were also included per cycle in the model.[22;10] These costs were derived using algorithms that provided estimates of costs based on absolute HAQ-DI and PASI in the modelled cohort.

Aside from costs related to HAQ-DI and PASI, no additional costs were applied for patients in BSC. The costs of serious adverse events (i.e. requiring hospitalisation) associated with bDMARD treatment were not included in the base-case analysis, but they were included in a sensitivity analysis. The rates of adverse events were derived from the summary of product characteristics of ixekizumab and secukinumab.[7,8]

**Sensitivity analyses**

To explore the uncertainty inherent in the model, one-way (deterministic) sensitivity analysis, probabilistic sensitivity analysis and scenario analyses were undertaken. In the one-way sensitivity analysis, one variable at a time was altered to examine the effect on the results. Most input parameters varied by ±20% of the mean value, as 95% confidence interval (CI) values were not available. Exceptions to this included ranges of values used for the annual discontinuation rate (95% CI); discount rates for costs and health utilities (0%; 5%); treatment

efficacy (±10% of the mean value); HAQ-DI improvement conditional on response (NMA results); physician and monitoring costs (±1 visit); and utility equations for PASI and HAQ-DI coefficients.

A probabilistic sensitivity analysis was conducted by assigning distributions to input parameters and sampling from these distributions in 1000 iterations. For efficacy inputs, the convergence diagnostics and output analysis of the Bayesian NMA was used instead of applying parametric distributions. The input parameters included PsARC and PASI response rates, changes in HAQ-DI based on response criterion, costs based on HAQ-DI and PASI, discontinuation rates, various healthcare-related costs and the use of resources.

A scenario analysis was conducted using a 10-year time horizon and alternative inputs for discount rates, increased PsA mortality, the definition of responders, the HAQ-DI rebound method, the utility equation, health state costs and placebo efficacy in BSC.

**RESULTS**

Results of the base-case analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis are summarised in Table 3. Ixekizumab was associated with total cost savings of €2,658 compared with secukinumab (total costs €153,901 vs €156,559). Total QALYs were higher for ixekizumab (9.175 vs 9.082, difference 0.093). Although ixekizumab performed favourably over secukinumab in the base-case analysis, cost savings and QALY gains were modest.

The deterministic sensitivity analysis showed that base-case results were generally robust to changes in most input parameters, but were most sensitive to the annual discontinuation rate for bDMARD therapy and modifications in PsARC and PASI90 response to ixekizumab or secukinumab (Figure 4).

The probabilistic sensitivity analysis showed that approximately 49.5% of observations were in the south-east quadrant, indicating that ixekizumab was still less costly and provided more

QALYs than secukinumab (Figure 5). Across the cost-effectiveness plane, 99% of replications were located south-east of the line defined by a willingness to pay threshold of €30,000 per QALY gained.

Overall, the scenario analyses showed that most of the parameters tested had relatively little impact on the base-case results (Figure 6). In most scenarios, ixekizumab provided more QALYs at a lower cost than secukinumab. While there was some variability regarding incremental cost and QALYs between ixekizumab versus secukinumab, in all scenarios the mean results still indicated the dominance of ixekizumab over secukinumab.

## DISCUSSION

In this CEA, the cost effectiveness of ixekizumab compared to secukinumab was evaluated in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis from the perspective of the Spanish NHS. In general, ixekizumab performed favourably over secukinumab in the base-case analysis; however, differences in cost savings and QALY gains were modest. The total difference in cost between ixekizumab and secukinumab was −€2,658, while the total difference in QALYs was 0.093. In the deterministic sensitivity analysis, the most influential variables were the annual discontinuation rate and the PsARC and PASI90 response for ixekizumab and secukinumab. Drug costs are usually a major driver; however, according to this model, other parameters related to disease were shown to have an impact.

The framework of this model is closely aligned with the most recently revised version of the York model,[11] which is considered a `benchmark' model for the economic evaluation of biologic treatments in PsA. The original York model has subsequently been revised to accommodate the analysis of patient subgroups. The model used in this analysis includes this amendment as a key feature. The current model also allows for combining PsARC and PASI as a response criterion, therefore capturing both joint and skin response. A combined response criterion presents a more realistic representation of this multifaceted disease and

may be especially useful when evaluating clinical benefits of bDMARDs, such as IL-17A antagonists, which are known for their proven efficacy on skin response.[26,27]

A limitation of this analysis was a lack of available data for health state cost estimates and constituents and the efficacy of BSC. There is also uncertainty regarding the annual all-cause discontinuation rate; therefore, our model used input data that were consistent with previously applied methods.[10,11] In addition, the actual acquisition costs of bDMARDs in clinical practice tend to differ from list prices because any confidential discounts are unknown and therefore cannot be reflected in the analyses.

## CONCLUSION

In this CEA of ixekizumab versus secukinumab in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis in Spain, ixekizumab provided more QALYs at a lower cost than secukinumab. However, differences in total costs and QALYs were modest; therefore, other factors, such as patient preferences, may also be considered during clinical decision making. Base-case results were generally robust to modifications in most input parameters, but were most sensitive to the annual bDMARD discontinuation rate and variations in PsARC and PASI90 response to ixekizumab or secukinumab.

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## CONFLICTS OF INTEREST

**BS** and **CM** are full-time employees of ICON who were commissioned by Eli Lilly and Company to conduct the analysis for this work. **MN**, **TD**, **CS** and **SH** are full-time employees of Eli Lilly and Company; they receive a salary and own company stock.

## AUTHOR CONTRIBUTIONS

**BS** and **CM** were involved with the conception and design of the work, and the interpretation of the data. **MN** and **CS** were involved with the acquisition and interpretation of the data. **TD** was involved with the conception of the work and interpretation of the data. **SH** was involved with the interpretation of the data. All named have provided critical revision of the manuscript for important intellectual content and have given their approval for this version to be published. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.

## DATA SHARING STATEMENT

No additional data are available.

## PATIENT AND PUBLIC INVOLVEMENT

Patients or the public were not involved in this work.

## REFERENCES


1. McArdle A, Pennington S, FitzGerald O. Clinical features of psoriatic arthritis: a comprehensive review of unmet clinical needs. *Clin Rev Allergy Immunol* 2018;55:271–94.
2. Seoane-Mato D, Sánchez-Piedra C, Díaz-González F, et al. THU0684 Prevalence of rheumatic diseases in adult population in Spain. Episer 2016 study. *Ann Rheum Dis* 2018;77:535–36.
3. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med* 2017;376:957–70.
4. Ciocon DH, Kimball AB. Psoriasis and psoriatic arthritis: separate or one and the same? *Br J Dermatol* 2007;157(5):850-60.
5. D'Angiolella LS, Cortesi PA, Lafranconi A, et al. Cost and cost effectiveness of treatments for psoriatic arthritis: a systematic literature review. *Pharmacoeconomics* 2018;36:567–89.
6. Kawalec P, Malinowski KP. The indirect costs of psoriatic arthritis: systematic review and meta-analysis. *Expert Rev Pharmacoecon Outcomes Res* 2015;15:125–32.
7. European Medicines Agency. Ixekizumab (Taltz): Summary of product characteristics 2016. www.ema.europa.eu/documents/product-information/taltz-epar-product-information_en.pdf (accessed 22 Mar 2019).
8. European Medicines Agency. Secukinumab (Cosentyx): Summary of product characteristics 2015. www.ema.europa.eu/documents/product-information/cosentyx-epar-product-information_en.pdf (accessed 22 Mar 2019).
9. Woolacott N, Bravo Vergel Y, Hawkins N, et al. Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess* 2006;10:iii–iv, xiii–xvi,1–239.

10. Rodgers M, Epstein D, Bojke L, et al. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess* 2011;15:i–xxi, 1–329.
11. Corbett M, Chehadah F, Biswas M, et al. Certolizumab pegol and secukinumab for treating active psoriatic arthritis following inadequate response to disease-modifying antirheumatic drugs: a systematic review and economic evaluation. *Health Technol Assess* 2017;21:1–326.
12. Wasilewska A, Winiarska M, Olszewska M, et al. Interleukin-17 inhibitors. A new era in treatment of psoriasis and other skin diseases. *Postepy Dermatol Alergol* 2016;33:247–52.
13. Raychaudhuri SP, Wilken R, Sukhov AC, et al. Management of psoriatic arthritis: Early diagnosis, monitoring of disease severity and cutting edge therapies. *J Autoimmun* 2017;76:21–37.
14. Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. *Drugs* 2014;74:423–41.
15. Mease PJ, van der Heijde D, Ritchlin CT, et al. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naïve patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Ann Rheum Dis* 2017;76:79–87.
16. Nash P, Kirkham B, Okada M, et al. Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *Lancet* 2017;389:2317–27.
17. Ali Y, Tom BD, Schentag CT, et al. Improved survival in psoriatic arthritis with calendar time. *Arthritis Rheum* 2007;56:2708–14.

18. Wong K, Gladman DD, Husted J, et al. Mortality studies in psoriatic arthritis: results from a single outpatient clinic. I. Causes and risk of death. *Arthritis Rheum* 1997;40:1868–72.
19. Torre Alonso JC, Díaz Del Campo Fontecha P, Almodóvar R, et al. Recommendations of the Spanish Society of Rheumatology on treatment and use of systemic biological and non-biological therapies in psoriatic arthritis. *Reumatol Clin* 2018;14:254–68.
20. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Galán-Gutierrez M, et al. Eficacia del secukinumab en psoriasis y artritis psoriásica: estudio multicéntrico retrospectivo. *Med Clin* (Barc) 2019; pii:S0025-7753(19)30006-5 doi.org/10.1016/j.medcli.2018.12.009
21. Carretero G, Puig L, Carrascosa JM, et al. Redefining the therapeutic objective in psoriatic patient candidates for biological therapy. *J Dermatolog Treat* 2018;29:334–46.
22. Kobelt G, Jönsson L, Lindgren P, et al. Modeling the progression of rheumatoid arthritis: a two-country model to estimate costs and consequences of rheumatoid arthritis. *Arthritis Rheum* 2002;46:2310–19.
23. Ruyssen-Witrand A, Sapin C, Hartz S, et al. THU0290 Effects of biologic dmards on physical function in patients with active psoriatic arthritis: results of network meta-analyses. *Ann Rheum Dis* 2018;77:363–4.
24. Consejo General de Colegios Oficiales de Farmacéuticos. Botplus database 2018. https://botplusweb.portalfarma.com/botplus.aspx (accessed 22 Mar 2019).
25. Oblikue Consulting. Base de datos de costes sanitarios españoles: eSalud 2007. http://www.oblikue.com/bddcostes/ (accessed 22 Mar 2019).
26. Betteridge N, Boehncke WH, Bundy C, et al. Promoting patient-centred care in psoriatic arthritis: a multidisciplinary European perspective on improving the patient experience. *J Eur Acad Dermatol Venereol* 2016;30:576–85.

27. Gottlieb AB, Strand V, Kishimoto M, et al. Ixekizumab improves patient-reported outcomes up to 52 weeks in bDMARD-naïve patients with active psoriatic arthritis (SPIRIT-P1). *Rheumatology* (Oxford). 2018;57:1777–88.
28. Mease PJ, Antoni CE, Gladman DD, et al. Psoriatic arthritis assessment tools in clinical trials. *Ann Rheum Dis* 2005;64:ii49–54.
29. Fransen J, Antoni C, Mease PJ, et al. Performance of response criteria for assessing peripheral arthritis in patients with psoriatic arthritis: analysis of data from randomised controlled trials of two tumour necrosis factor inhibitors. *Ann Rheum Dis* 2006;65:1373–8.

**Table 1.** Characteristics of the target population of bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis based on pooled data from the intent-to-treat trial populations of SPIRIT-P1 and -P2 with ixekizumab [15,16]

| Parameter | Mean value |
|---|---|
| Age | 51.0 years |
| Proportion male | 51.8% |
| Proportion female | 48.2% |
| Body weight | 87.0 kg |
| Baseline HAQ-DI score | 1.19 |
| Baseline PASI score | 20.4 |

bDMARD, biologic disease-modifying anti-rheumatic drug; HAQ-DI, Health Assessment Questionnaire — Disability Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis.

**Table 2.** Costs for administration and monitoring of treatment in Spain [24,25]

| Resource | Cost[a] | Source |
|---|---|---|
| *Drug acquisition costs (list prices)* | | |
| Ixekizumab 80 mg Q4W pre-filled pen | €934.25 per dose | Botplus database [24] minus rebate of 7.5% according to Spanish regulation RDL 8/2010 |
| Secukinumab 300 mg pre-filled pen | €1,057.38 per dose | Botplus database [24] minus rebate of 7.5% according to Spanish regulation RDL 8/2010 |
| *Visits* | | |
| Rheumatologist | €220.62 | Base de datos de costes sanitarios españoles [25] |
| Dermatologist | €100.58 | Base de datos de costes sanitarios españoles [25] |
| GP | €33.86 | Base de datos de costes sanitarios españoles [25] |
| *Monitoring* | | |
| Full blood count | €67.98 | Base de datos de costes sanitarios españoles [25] |
| Erythrocyte sedimentation rate | €1.03 | Base de datos de costes sanitarios españoles [25] |
| Chest X-ray | €42.23 | Base de datos de costes sanitarios españoles [25] |
| Tuberculosis test | €8.95 | Base de datos de costes sanitarios españoles [25] |
| C-reactive protein test | €8.95 | Base de datos de costes sanitarios españoles [25] |

GP, general practitioner; Q4W, every four weeks.

**Table 3.** Results of the base-case analysis comparing ixekizumab and secukinumab in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis

| Parameter | Ixekizumab | Secukinumab | Difference |
|---|---|---|---|
| *Costs (year 2018 values)* | | | |
| Total costs | €153,901 | €156,559 | −€2,658 |
| Treatment costs | €26,424 | €27,729 | −€1,305 |
| Administration costs | €26 | €24 | €2 |
| Physician visit costs | €4,141 | €4,202 | −€61 |
| Monitoring costs | €797 | €706 | €92 |
| On treatment HAQ-DI/PASI-related costs | €4,608 | €4,115 | €494 |
| BSC costs | €117,904 | €119,784 | −€1,880 |
| *QALYs* | | | |
| Total QALYs | 9.175 | 9.082 | 0.093 |

BSC, best supportive care; HAQ-DI, Health Assessment Questionnaire – Disability Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; QALYs, quality-adjusted life-years.

## Figure Legends

**Figure 1.** Schematic representation of the model structure in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis. Dosage regimens were according to European Union labelling. Although not shown in the figure, patients could transition to death from any state.

BSC, best supportive care; bDMARD, biologic disease-modifying anti-rheumatic drug; PsA, psoriatic arthritis; Q4W, every 4 weeks.

**Figure 2.** Psoriatic Arthritis Response Criteria (PsARC) and Psoriasis Area Severity Index (PASI) criteria used for the treatment continuation rule for ixekizumab and secukinumab.[28,29] A combination of PsARC response and ≥90% improvement in PASI (PASI90) was used to capture both joint and skin response at the end of the induction period.

**Figure 3.** Scenarios for HAQ-DI rebound after the discontinuation of treatment.

HAQ-DI, Health Assessment Questionnaire – Disability Index.

**Figure 4.** Results of the one-way sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

bDMARD, biologic disease-modifying anti-rheumatic drug; CI, confidence interval; FBC, full blood count; HAQ-DI, Health Assessment Questionnaire-Disability Index; ICER, incremental cost-effectiveness ratio; Ixe, ixekizumab; p.a., per annum; PASI90, ≥90% reduction from baseline Psoriasis Area Severity Index score; PsA, psoriatic arthritis; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life-year; Q4W, every 4 weeks; SE, standard error; Sec, secukinumab; Trt, treatment.

**Figure 5.** Results of the probabilistic sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis. Approximately 49.5% of observations were in the south-east quadrant, 28.6% were in the south-west quadrant and 21.9% were in the north-east quadrant of the cost-effectiveness plane.

bDMARD, biologic disease-modifying anti-rheumatic drug; Ixe, ixekizumab; PsA, psoriatic arthritis; QALY, quality-adjusted life-year; Q4W, every 4 weeks; Sec, secukinumab; WTP, willingness to pay.

**Figure 6.** Results of scenario analyses in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

bDMARD, biologic disease-modifying anti-rheumatic drug; PASI75, ≥75% reduction in Psoriasis Area Severity Index score; PASI100, 100% reduction in PASI score; PsA, psoriatic arthritis; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life-year; Resp, response; yrs, years.

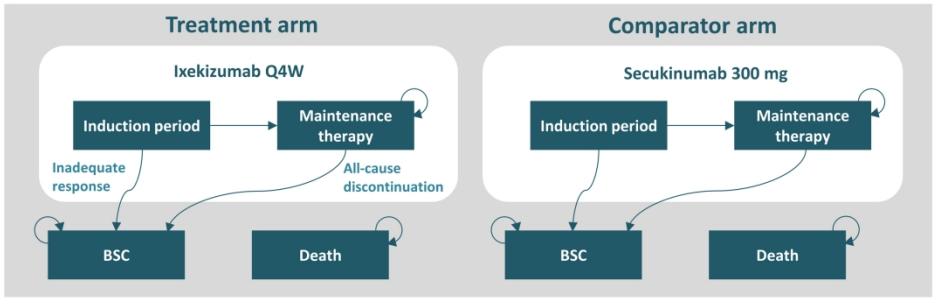


Figure 1. Schematic representation of the model structure in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis. Dosage regimens were according to European Union labelling. Although not shown in the figure, patients could transition to death from any state.

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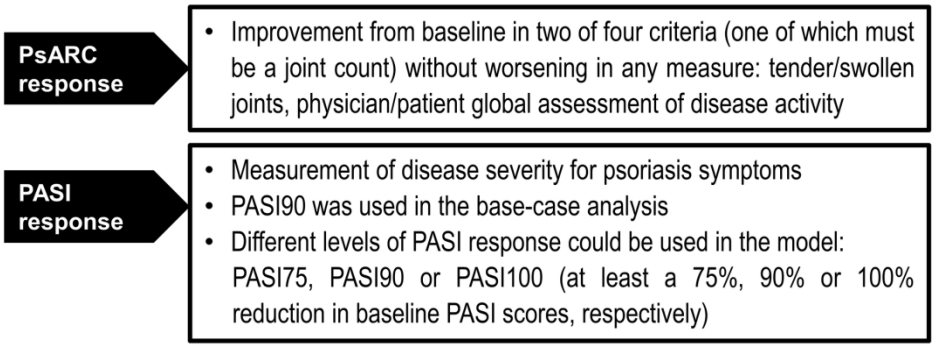


Figure 2. Psoriatic Arthritis Response Criteria (PsARC) and Psoriasis Area Severity Index (PASI) criteria used for the treatment continuation rule for ixekizumab and secukinumab.[28,29] A combination of PsARC response and ≥90% improvement in PASI (PASI90) was used to capture both joint and skin response at the end of the induction period.

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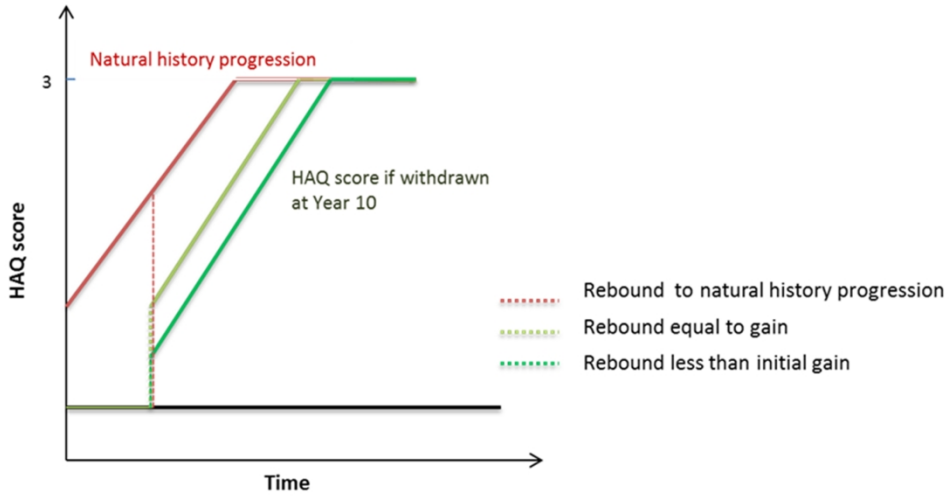


Figure 3. Scenarios for HAQ-DI rebound after the discontinuation of treatment.

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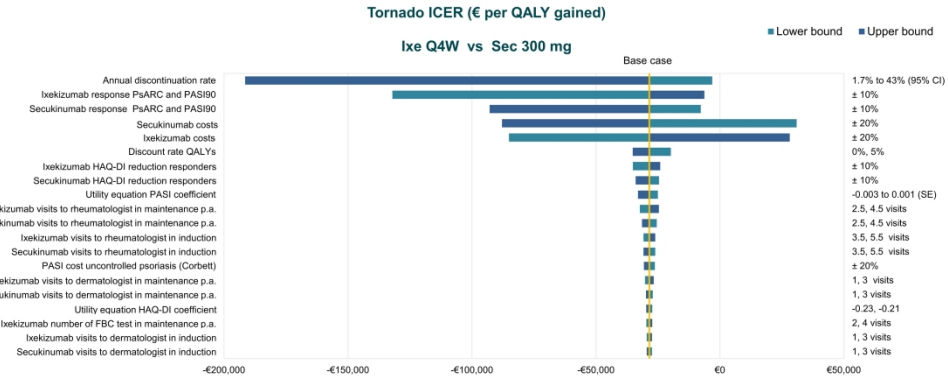


Figure 4. Results of the one-way sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

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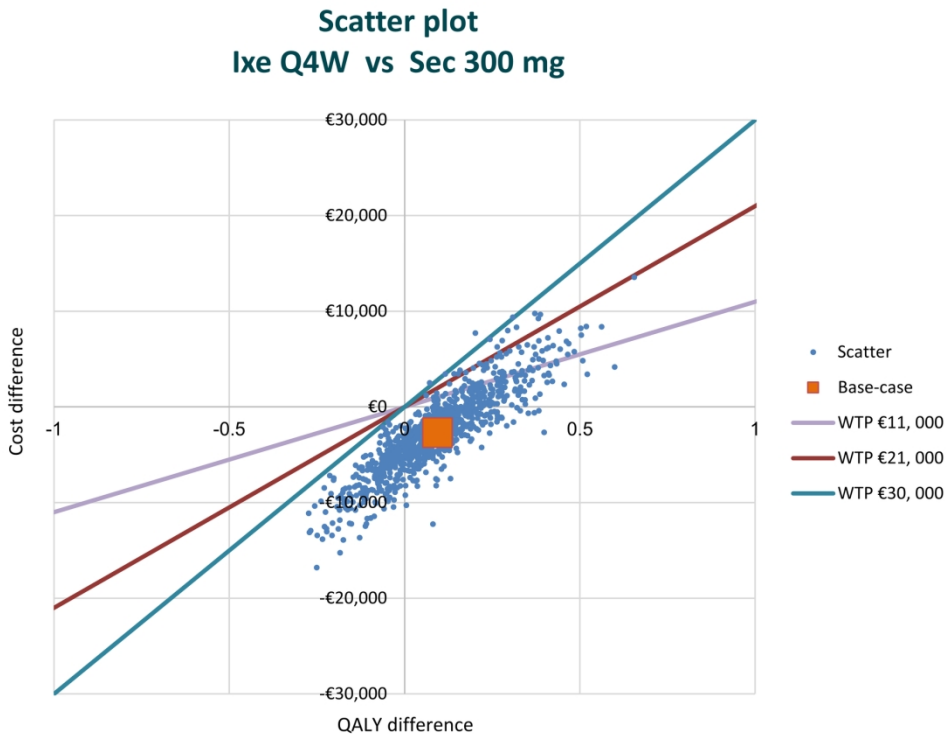


Figure 5. Results of the probabilistic sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis. Approximately 49.5% of observations were in the south-east quadrant, 28.6% were in the south-west quadrant and 21.9% were in the north-east quadrant of the cost-effectiveness plane.

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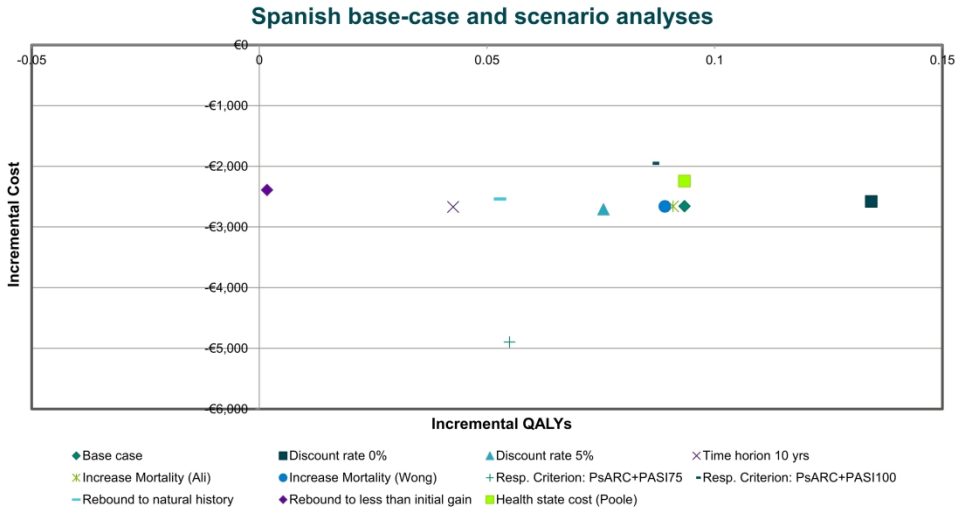


Figure 6. Results of scenario analyses in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

273x145mm (300 x 300 DPI)

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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

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## ABSTRACT

**Objective:** To conduct a cost-effectiveness analyses (CEA) from the perspective of the Spanish National Health System comparing ixekizumab versus secukinumab.

**Design:** A Markov model with a lifetime horizon and monthly cycles was developed based on the York model. Four health states were included: a 12- or 16-week biologic disease-modifying antirheumatic drugs (bDMARD) induction period, maintenance therapy, best supportive care (BSC) and death. Treatment response was assessed based on both Psoriatic Arthritis Response Criteria (PsARC) and ≥90% improvement in the Psoriasis Area Severity Index (PASI90). At the end of the induction period, responders transitioned to maintenance therapy. Non-responders and patients who discontinued maintenance therapy transitioned to BSC. Clinical efficacy data were derived from a network meta-analysis. Health utilities were generated by applying a regression analysis to PASI and Health Assessment Questionnaire – Disability Index (HAQ-DI) scores collected in the ixekizumab SPIRIT studies. Results were subject to extensive sensitivity and scenario analysis.

**Setting:** Spanish National Health System.

**Participants:** A hypothetical cohort of bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis was modelled.

**Interventions:** Ixekizumab and secukinumab.

**Results:** Ixekizumab performed favourably over secukinumab in the base-case analysis, although cost savings and quality-adjusted life-years (QALY) gains were modest. Total costs were €153,901 compared with €156,559 for secukinumab (difference −€2,658). Total QALYs were 9.175 versus 9.082 (difference 0.093). Base-case results were most sensitive to the annual bDMARD discontinuation rate and the modification of PsARC and PASI90 response to ixekizumab or secukinumab.

**Conclusions:** Ixekizumab provided more QALYs at a lower cost than secukinumab, with differences being on a relatively small scale. Sensitivity analysis showed that base-case results were generally robust to changes in most input parameters.

## ARTICLE SUMMARY

### Strengths and limitations of this study

- A CEA was performed from the perspective of the Spanish National Health System comparing two interleukin-17A antagonists, ixekizumab and secukinumab
- The framework of this model is aligned with the York model; the 'gold standard' model for the economic evaluation of biologic treatments in PsA
- The current model uses a combined response criterion of PsARC and PASI to capture both joint and skin manifestations of PsA
- This analysis was limited by a lack of data available for costs and efficacy of supportive care given to PsA patients in Spain
- Due to uncertainty regarding the annual all-cause discontinuation rate, this model used assumptions consistent with previous models

## INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease characterised by pain, swelling and erosion of the joints.[1] PsA affects approximately 0.25% of the population worldwide [1] and 0.6% of the adult population in Spain.[2] PsA commonly co-exists with psoriasis, developing in up to 30% of psoriatic patients, and over 90% of patients with PsA will have concomitant psoriasis.[3,4] As a lifelong condition, PsA has a detrimental impact on quality of life due to pain and/or physical functional limitations associated with the disease.[1,3] It is also associated with substantial use of healthcare resources and high socioeconomic costs.[5,6]

A number of biologic disease-modifying antirheumatic drugs (bDMARDs), which inhibit key inflammatory cytokines, are approved for treating patients with PsA. Interleukin (IL)-17 has been identified as an effective target for the treatment of inflammatory diseases including PsA.[1,3] Ixekizumab, a high-affinity monoclonal antibody, is the most recently approved bDMARD targeting IL-17A for PsA, joining secukinumab, which uses the same target and similar mode of action.[7,8]

bDMARDs are considered major drivers of healthcare costs,[5] and the cost-effectiveness of these therapies often comes under scrutiny. Cost-effectiveness analyses (CEAs) comparing bDMARDs have been conducted using the York model,[9] an established economic framework, which, together with its subsequent versions, is considered the `gold standard' for conducting CEAs in PsA.[10,11]

As inhibition of IL-17A is a relatively new mechanism of action, drugs in this class have not been the focus of CEAs.[12] To date, there are no published CEAs comparing ixekizumab with secukinumab (another IL-17A inhibitor) in Spain.

We conducted a CEA assessing the cost effectiveness, in terms of the incremental cost per quality-adjusted life-year (QALY) gained, of ixekizumab versus secukinumab in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis from the

perspective of the Spanish National Health System (NHS). Secukinumab was selected as a comparator for this CEA as both drugs belong to the same class, and this may be of interest to decision makers assessing these IL-17A inhibitors. In addition, both drugs are approved for the treatment of PsA and plaque psoriasis, and have demonstrated high efficacy, particularly on skin symptoms.[7,8] This CEA focused on bDMARD-naïve patients, as this patient population may receive greater clinical benefit from earlier (i.e. first-line) treatment.[13]

## METHODS

### Model overview

A Markov model was developed to assess the cost effectiveness of ixekizumab versus secukinumab in a hypothetical cohort of bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis in Spain. The Markov model framework accommodates different health states and is based on the assumption that future events depend on the current health state of the patient. The model was programmed in Visual Basics for Applications with a user interface in Microsoft® Excel.

The model is based on the most recent version of the York model [11] with monthly cycles and a lifetime horizon, which was considered appropriate to reflect the chronic nature of PsA as well as the treatment aim of delaying disease progression.[14] The model incorporated age- and gender-dependent mortality data for the normal Spanish population. Mean age and gender distribution was taken from the patient population in the SPIRIT-P1 and -P2 trials of ixekizumab in PsA.[15,16] Increased PsA-specific mortality risks from two different sources [17,18] were implemented in scenario analyses.

The model includes four health states: 1) a 12- or 16-week bDMARD induction period; 2) maintenance bDMARD therapy; 3) best supportive care (BSC); and 4) death (Figure 1). A combination of Psoriatic Arthritis Response Criteria (PsARC) and Psoriasis Area Severity Index (PASI) was used to measure joint and skin response at the end of the induction period and to determine treatment continuation of ixekizumab and secukinumab (Figure 2).[19,20]

The induction period was set to 12 weeks and 16 weeks for ixekizumab and secukinumab, respectively. The induction period was chosen to reflect the time at which treatment efficacy is usually followed-up in clinical practice (approximately 3 months in Spain).[21,22] The difference in the length of induction period between the two drugs also acknowledges a degree of difference in the availability of clinical trial data for ixekizumab and secukinumab (i.e., across the included studies, more week 16 than week 12 data is available for secukinumab). The PsARC response to treatment was defined as an improvement from baseline in two of four criteria without worsening in any measure: tender/swollen joints; and physician/patient global assessment of disease activity (one of which must be a joint count). In a consensus from the Spanish Psoriasis Group, a panel of dermatologists agreed that a complete or nearly complete PASI response is the most relevant measure of effectiveness in clinical practice.[23] With this in mind, ≥90% improvement in PASI (PASI90) was chosen in the base-case analysis as part of the response criteria and the treatment effect measures in this model.

**Treatment sequences**

At the end of the induction period, responders transitioned to maintenance therapy, while non-responders and discontinuers transitioned to BSC (Figure 1) in which patients were assumed to receive standard treatment depending on their Health Assessment Questionnaire – Disability Index (HAQ-DI) and PASI status.[24] Dosage regimens for ixekizumab and secukinumab were aligned with the European market authorisation.[7,8] During maintenance therapy, patients were assumed to face a constant risk of all-cause treatment discontinuation, which was reflected by an annual discontinuation rate of 16.5% in line with previously applied methods.[10,11]

In the base-case analysis, baseline cohort characteristics were reflective of the demographic data from the ixekizumab SPIRIT-P1 and -P2 clinical trials [15,16] (Table 1).

**Treatment effect**

While PsARC and PASI90 were used as the combined response criterion (i.e. treatment continuation rule), the treatment effect was modelled as a change in baseline of the HAQ-DI and PASI scores,[25] reflecting the joint and skin components of PsA, respectively. Baseline HAQ-DI and PASI scores were derived from the SPIRIT-P1 and -P2 trials [15,16] (Table 1). Treatment effect, represented by improvement (i.e. reductions) in HAQ-DI and PASI scores, was assumed to be instantaneous; as such, the response was also applied during the induction period. Absolute change in HAQ-DI and PASI scores is based on data from a network meta-analysis (NMA).[25, 26] Key efficacy input data, derived from the NMA [25, 26] are provided in Supplementary Table 1.

For patients who met the combined response of PsARC and PASI90 at the end of the induction period, the initial improvements in HAQ-DI and PASI continued during maintenance therapy until they transitioned into BSC. For patients entering BSC following discontinuation, it was assumed that some benefit was maintained from the initial bDMARD treatment. In the base case, for patients progressing to BSC, the HAQ-DI score was assumed to revert to the baseline HAQ-DI level prior to discontinuation ("rebound equal to initial gain"). The rebound effect was assumed to be immediate and patients were modelled to progress at the same rate as natural history progression (an increase of 0.018 per 3-month period) (Figure 3). For PASI score, it was assumed that for non-responders not meeting PASI90, there would still be some gain in PASI – albeit lower – while they were treated with a bDMARD in the induction period. Once in the BSC state, due to the progressive nature of PsA, it was assumed that patients would deteriorate at a rate of natural progression.

**Health utilities**

Health utilities were based on HAQ-DI and PASI scores from the SPIRIT-P1 and -P2 clinical trials [15,16] with Spanish tariffs applied. Calculation of utilities followed the established methodology of mapping three-level version of EuroQol-5 Dimensions (EQ-5D-3L) utilities on HAQ and PASI scores using a parsimonious linear regression model without further covariates or interaction terms. [9–11] Alternative coefficients based on a similar algorithm using different

data were applied in a sensitivity analysis. Utilities were calculated in each model cycle by multiplying HAQ and PASI levels with the estimated regression coefficients.

**Resource use and costs**

As the CEA was conducted from the perspective of the Spanish NHS, only direct medical costs were considered in the model, and included medication, injection training, physician visits and therapy monitoring. Drug acquisition costs were derived from the Botplus database in Spain,[27] and costs for the administration and monitoring of treatments were obtained from various sources in Spain [28] (Table 2). Drug costs were based on the list prices as of Q4 2018. Monitoring costs were based on the costing schedule published in 2017, which was still valid in 2018. Due to a lack of healthcare resource utilisation data by drug or class, healthcare costs and resource utilisation related to the administration and monitoring of bDMARDs was determined by an expert panel of four Spanish physicians (two rheumatologists and two dermatologists).

The severity of arthritis and psoriasis also may have an impact on healthcare costs.[10,11] To reflect this, costs related to HAQ-DI and PASI were also included per cycle in the model.[10,24] These costs were derived by converting and inflating results of established algorithms, which relate cost to absolute HAQ-DI and PASI values.

Aside from costs related to HAQ-DI and PASI, no additional costs were applied for patients in BSC. The costs of serious adverse events (i.e. requiring hospitalisation) associated with bDMARD treatment were not included in the base-case analysis, but they were included in a sensitivity analysis. The rates of adverse events were derived from the summary of product characteristics of ixekizumab and secukinumab.[7,8]

**Sensitivity analyses**

To explore the uncertainty inherent in the model, one-way (deterministic) sensitivity analysis, probabilistic sensitivity analysis and scenario analyses were undertaken. In the one-way

sensitivity analysis, one variable at a time was altered to examine the effect on the results. Most input parameters varied by ±20% of the mean value, as 95% confidence interval (CI) values were not available. Exceptions to this included ranges of values used for the annual discontinuation rate (95% CI); discount rates for costs and health utilities (0%; 5%); treatment efficacy (±10% of the mean value); HAQ-DI improvement conditional on response (NMA results); physician and monitoring costs (±1 visit); and utility equations for PASI and HAQ-DI coefficients.

A probabilistic sensitivity analysis was conducted by assigning distributions to input parameters (Supplementary Table 2) and sampling from these distributions in 1000 iterations. For efficacy inputs, the convergence diagnostics and output analysis (CODA) of the Bayesian NMA was used instead of applying parametric distributions, in line with internationally recognised technical guidance.[29] The input parameters included PsARC and PASI response rates, changes in HAQ-DI based on response criterion, costs based on HAQ-DI and PASI, discontinuation rates, various healthcare-related costs and the use of resources.

A scenario analysis was conducted using a 10-year time horizon and alternative inputs for discount rates, increased PsA mortality, the definition of responders, the HAQ-DI rebound method, the utility equation, health state costs and placebo efficacy in BSC.

**Patient and public involvement**

Patients or the public were not involved in the design, planning or execution of this work.

**RESULTS**

Results of the base-case analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis are summarised in Table 3. Ixekizumab was associated with total cost savings of €2,658 compared with secukinumab (total costs €153,901 vs €156,559). Total QALYs were higher for ixekizumab (9.175 vs 9.082, difference 0.093). Although

ixekizumab performed favourably over secukinumab in the base-case analysis, cost savings and QALY gains were modest.

The deterministic sensitivity analysis showed that base-case results were generally robust to changes in most input parameters, but were most sensitive to the annual discontinuation rate for bDMARD therapy and modifications in PsARC and PASI90 response to ixekizumab or secukinumab (Figure 4).

The probabilistic sensitivity analysis showed that approximately 49.5% of observations were in the south-east quadrant, indicating that ixekizumab was still less costly and provided more QALYs than secukinumab (Figure 5). Across the cost-effectiveness plane, 99% of replications were located south-east of the line defined by a willingness to pay threshold of €30,000 per QALY gained.

Overall, the scenario analyses showed that most of the parameters tested had relatively little impact on the base-case results (Figure 6). In most scenarios, ixekizumab provided more QALYs at a lower cost than secukinumab. While there was some variability regarding incremental cost and QALYs between ixekizumab versus secukinumab, in all scenarios the mean results still indicated the dominance of ixekizumab over secukinumab.

## DISCUSSION

In this CEA, the cost effectiveness of ixekizumab compared to secukinumab was evaluated in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis from the perspective of the Spanish NHS. In general, ixekizumab performed favourably compared to secukinumab in the base-case analysis, with differences in cost savings and QALY gains being modest. The total difference in cost between ixekizumab and secukinumab was −€2,658, with a small total difference in QALYs of 0.093. In the deterministic sensitivity analysis, the most influential variables were the annual discontinuation rate and the PsARC and PASI90 response for ixekizumab and secukinumab.

The framework of this model is closely aligned with the most recently revised version of the York model,[11] which is considered a `benchmark' model for the economic evaluation of biologic treatments in PsA. The original York model has subsequently been revised to accommodate the analysis of patient subgroups. The model used in this analysis includes this amendment as a key feature. The current model also allows for combining PsARC and PASI as a response criterion, therefore capturing both joint and skin response. A combined response criterion presents a more realistic representation of this multifaceted disease and may be especially useful when evaluating clinical benefits of bDMARDs, such as IL-17A antagonists, which are known for their proven efficacy on skin response.[30,31]

A limitation of this analysis was a lack of current data for health state cost estimates and the efficacy of BSC. There is also uncertainty regarding the annual all-cause discontinuation rate; therefore, our model used input data consistent with previously applied methods.[10,11] Given the sensitivity of the results to this parameter, correction or confirmation of the current assumptions based on mature real-world drug survival data is a clear research need for the future.

In addition, the actual acquisition costs of bDMARDs in clinical practice tend to differ from list prices because any confidential discounts are unknown and therefore cannot be reflected in the analyses. Therefore, the respective differences in drug prices in clinical practice would also affect the true cost differences between treatment arms in the analysis.

## CONCLUSION

In this CEA of ixekizumab versus secukinumab in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis in Spain, ixekizumab provided more QALYs at a lower cost, with differences being on a relatively small scale. As differences in total costs and QALYs were modest, other factors, such as patient preferences, may also be considered during clinical decision making. Base-case results were generally robust to modifications in most input parameters, but were most sensitive to the annual bDMARD discontinuation rate and variations in PsARC and PASI90 response to ixekizumab or secukinumab.

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## FUNDING

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## CONFLICTS OF INTEREST

**BS** and **CM** are full-time employees of ICON who were commissioned by Eli Lilly and Company to conduct the analysis for this work. **MN**, **TD**, **CS** and **SH** are full-time employees of Eli Lilly and Company; they receive a salary and own company stock.

## AUTHOR CONTRIBUTIONS

**BS** and **CM** were involved with the conception and design of the work, and the interpretation of the data. **MN** and **CS** were involved with the acquisition and interpretation of the data. **TD** was involved with the conception of the work and interpretation of the data. **SH** was involved with the interpretation of the data. All named have provided critical revision of the manuscript for important intellectual content and have given their approval for this version to be published. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.

## DATA SHARING STATEMENT

All data relevant to the study are included in the article or uploaded as supplementary information.

## REFERENCES

1. McArdle A, Pennington S, FitzGerald O. Clinical features of psoriatic arthritis: a comprehensive review of unmet clinical needs. *Clin Rev Allergy Immunol* 2018;55:271–94.
2. Seoane-Mato D, Sánchez-Piedra C, Díaz-González F, et al. THU0684 Prevalence of rheumatic diseases in adult population in Spain. Episer 2016 study. *Ann Rheum Dis* 2018;77:535–36.
3. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med* 2017;376:957–70.
4. Ciocon DH, Kimball AB. Psoriasis and psoriatic arthritis: separate or one and the same? *Br J Dermatol* 2007;157(5):850-60.
5. D'Angiolella LS, Cortesi PA, Lafranconi A, et al. Cost and cost effectiveness of treatments for psoriatic arthritis: a systematic literature review. *Pharmacoeconomics* 2018;36:567–89.
6. Kawalec P, Malinowski KP. The indirect costs of psoriatic arthritis: systematic review and meta-analysis. *Expert Rev Pharmacoecon Outcomes Res* 2015;15:125–32.
7. European Medicines Agency. Ixekizumab (Taltz): Summary of product characteristics 2016. www.ema.europa.eu/documents/product-information/taltz-epar-product-information_en.pdf (accessed 22 Mar 2019).
8. European Medicines Agency. Secukinumab (Cosentyx): Summary of product characteristics 2015. www.ema.europa.eu/documents/product-information/cosentyx-epar-product-information_en.pdf (accessed 22 Mar 2019).
9. Woolacott N, Bravo Vergel Y, Hawkins N, et al. Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess* 2006;10:iii–iv, xiii–xvi,1–239.

10. Rodgers M, Epstein D, Bojke L, et al. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess* 2011;15:i–xxi, 1–329.
11. Corbett M, Chehadah F, Biswas M, et al. Certolizumab pegol and secukinumab for treating active psoriatic arthritis following inadequate response to disease-modifying antirheumatic drugs: a systematic review and economic evaluation. *Health Technol Assess* 2017;21:1–326.
12. Wasilewska A, Winiarska M, Olszewska M, et al. Interleukin-17 inhibitors. A new era in treatment of psoriasis and other skin diseases. *Postepy Dermatol Alergol* 2016;33:247–52.
13. Raychaudhuri SP, Wilken R, Sukhov AC, et al. Management of psoriatic arthritis: Early diagnosis, monitoring of disease severity and cutting edge therapies. *J Autoimmun* 2017;76:21–37.
14. Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. *Drugs* 2014;74:423–41.
15. Mease PJ, van der Heijde D, Ritchlin CT, et al. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naïve patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Ann Rheum Dis* 2017;76:79–87.
16. Nash P, Kirkham B, Okada M, et al. Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *Lancet* 2017;389:2317–27.
17. Ali Y, Tom BD, Schentag CT, et al. Improved survival in psoriatic arthritis with calendar time. *Arthritis Rheum* 2007;56:2708–14.

18. Wong K, Gladman DD, Husted J, et al. Mortality studies in psoriatic arthritis: results from a single outpatient clinic. I. Causes and risk of death. *Arthritis Rheum* 1997;40:1868–72.

19. Mease PJ, Antoni CE, Gladman DD, et al. Psoriatic arthritis assessment tools in clinical trials. *Ann Rheum Dis* 2005;64:ii49–54.

20. Fransen J, Antoni C, Mease PJ, et al. Performance of response criteria for assessing peripheral arthritis in patients with psoriatic arthritis: analysis of data from randomised controlled trials of two tumour necrosis factor inhibitors. *Ann Rheum Dis* 2006;65:1373–8.

21. Torre Alonso JC, Díaz Del Campo Fontecha P, Almodóvar R, et al. Recommendations of the Spanish Society of Rheumatology on treatment and use of systemic biological and non-biological therapies in psoriatic arthritis. *Reumatol Clin* 2018;14:254–68.

22. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Galán-Gutierrez M, et al. Eficacia del secukinumab en psoriasis y artritis psoriásica: estudio multicéntrico retrospectivo. *Med Clin* (Barc) 2019; pii:S0025-7753(19)30006-5 doi.org/10.1016/j.medcli.2018.12.009

23. Carretero G, Puig L, Carrascosa JM, et al. Redefining the therapeutic objective in psoriatic patient candidates for biological therapy. *J Dermatolog Treat* 2018;29:334–46.

24. Kobelt G, Jönsson L, Lindgren P, et al. Modeling the progression of rheumatoid arthritis: a two-country model to estimate costs and consequences of rheumatoid arthritis. *Arthritis Rheum* 2002;46:2310–19.

25. Ruyssen-Witrand A, Perry R, Watkins C, et al. Efficacy and safety of biologics in psoriatic arthritis: a systematic literature review and network meta-analysis. *RMD Open 2020*;6:e001117.

26. Ruyssen-Witrand A, Sapin C, Hartz S, et al. THU0290 Effects of biologic dmards on physical function in patients with active psoriatic arthritis: results of network meta-analyses. *Ann Rheum Dis* 2018;77:363–4.

27. Consejo General de Colegios Oficiales de Farmacéuticos. Botplus database 2018. https://botplusweb.portalfarma.com/botplus.aspx (accessed 22 Mar 2019).
28. Oblikue Consulting. Base de datos de costes sanitarios españoles: eSalud 2007. http://www.oblikue.com/bddcostes/ (accessed 22 Mar 2019).
29. Dias S, Sutton AJ, Welton NJ, et al. Evidence synthesis for decision making 6: embedding evidence synthesis in probabilistic cost-effectiveness analysis. *Med Decis Making* 2013;33:671–8.
30. Betteridge N, Boehncke WH, Bundy C, et al. Promoting patient-centred care in psoriatic arthritis: a multidisciplinary European perspective on improving the patient experience. *J Eur Acad Dermatol Venereol* 2016;30:576–85.
31. Gottlieb AB, Strand V, Kishimoto M, et al. Ixekizumab improves patient-reported outcomes up to 52 weeks in bDMARD-naïve patients with active psoriatic arthritis (SPIRIT-P1). *Rheumatology* (Oxford) 2018;57:1777–88.

**Table 1.** Characteristics of the target population of bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis based on the ixekizumab SPIRIT-P1 and -P2 clinical trials.

| Parameter | Mean value |
|---|---|
| Age | 51.0 years |
| Proportion male | 51.8% |
| Proportion female | 48.2% |
| Body weight | 87.0 kg |
| Baseline HAQ-DI score | 1.19 |
| Baseline PASI score | 20.4 |

Patient characteristics based on pooled data from the intent-to-treat trial populations of SPIRIT-P1 and -P2 with ixekizumab. [15,16]

bDMARD, biologic disease-modifying anti-rheumatic drug; HAQ-DI, Health Assessment Questionnaire — Disability Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis.

**Table 2.** Costs for administration and monitoring of treatment in Spain.

| Resource | Cost | Source |
|---|---|---|
| *Drug acquisition costs (list prices)* | | |
| Ixekizumab 80 mg Q4W pre-filled pen | €934.25 per dose | Botplus database [27] minus rebate of 7.5% according to Spanish regulation RDL 8/2010 |
| Secukinumab 300 mg pre-filled pen | €1,057.38 per dose | Botplus database [27] minus rebate of 7.5% according to Spanish regulation RDL 8/2010 |
| *Visits* | | |
| Rheumatologist | €220.62 | Base de datos de costes sanitarios españoles [28] |
| Dermatologist | €100.58 | Base de datos de costes sanitarios españoles [28] |
| GP | €33.86 | Base de datos de costes sanitarios españoles [28] |
| *Monitoring* | | |
| Full blood count | €67.98 | Base de datos de costes sanitarios españoles [28] |
| Erythrocyte sedimentation rate | €1.03 | Base de datos de costes sanitarios españoles [28] |
| Chest X-ray | €42.23 | Base de datos de costes sanitarios españoles [28] |
| Tuberculosis test | €8.95 | Base de datos de costes sanitarios españoles [28] |
| C-reactive protein test | €8.95 | Base de datos de costes sanitarios españoles [28] |

GP, general practitioner; Q4W, every four weeks.

**Table 3.** Results of the base-case analysis comparing ixekizumab and secukinumab in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis.

| Parameter | Ixekizumab | Secukinumab | Difference |
|---|---|---|---|
| *Costs (year 2018 values)* | | | |
| Total costs | €153,901 | €156,559 | −€2,658 |
| Treatment costs | €26,424 | €27,729 | −€1,305 |
| Administration costs | €26 | €24 | €2 |
| Physician visit costs | €4,141 | €4,202 | −€61 |
| Monitoring costs | €797 | €706 | €92 |
| On treatment HAQ-DI/PASI-related costs | €4,608 | €4,115 | €494 |
| BSC costs | €117,904 | €119,784 | −€1,880 |
| *QALYs* | | | |
| Total QALYs | 9.175 | 9.082 | 0.093 |

BSC, best supportive care; HAQ-DI, Health Assessment Questionnaire – Disability Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; QALYs, quality-adjusted life-years.

## Figure Legends and abbreviations

**Figure 1.** Schematic representation of the model structure in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis. Dosage regimens were aligned with the European market authorisation. Although not shown in the figure, patients could transition to death from any state.

BSC, best supportive care; bDMARD, biologic disease-modifying anti-rheumatic drug; PsA, psoriatic arthritis; Q4W, every 4 weeks.

**Figure 2.** A combination of PsARC response and ≥90% improvement in PASI (PASI90) was used to capture both joint and skin response at the end of the induction period.

**Figure 3.** Scenarios for HAQ-DI rebound after the discontinuation of treatment.

HAQ-DI, Health Assessment Questionnaire – Disability Index.

**Figure 4.** Results of the one-way sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

bDMARD, biologic disease-modifying anti-rheumatic drug; CI, confidence interval; FBC, full blood count; HAQ-DI, Health Assessment Questionnaire-Disability Index; ICER, incremental cost-effectiveness ratio; Ixe, ixekizumab; p.a., per annum; PASI90, ≥90% reduction from baseline Psoriasis Area Severity Index score; PsA, psoriatic arthritis; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life-year; Q4W, every 4 weeks; SE, standard error; Sec, secukinumab; Trt, treatment.

**Figure 5.** Results of the probabilistic sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis. Approximately 49.5% of observations were in the south-east quadrant, 28.6% were in the south-west quadrant and 21.9% were in the north-east quadrant of the cost-effectiveness plane.

bDMARD, biologic disease-modifying anti-rheumatic drug; Ixe, ixekizumab; PsA, psoriatic arthritis; QALY, quality-adjusted life-year; Q4W, every 4 weeks; Sec, secukinumab; WTP, willingness to pay.

**Figure 6.** Results of scenario analyses in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

bDMARD, biologic disease-modifying anti-rheumatic drug; PASI75, ≥75% reduction in Psoriasis Area Severity Index score; PASI100, 100% reduction in PASI score; PsA, psoriatic arthritis; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life-year; Resp, response; yrs, years.

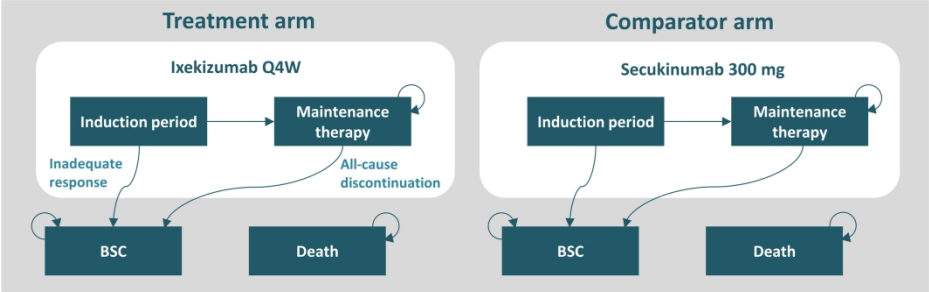


Figure 1. Schematic representation of the model structure in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis. Dosage regimens were aligned with the European market authorisation. Although not shown in the figure, patients could transition to death from any state.

228x75mm (300 x 300 DPI)

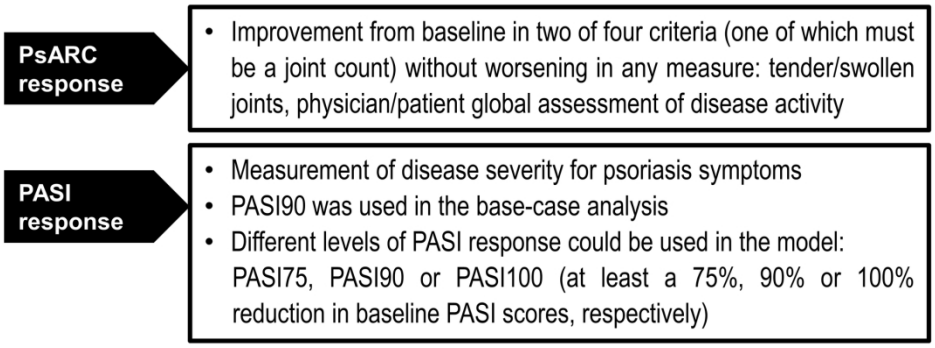


Figure 2. A combination of PsARC response and ≥90% improvement in PASI (PASI90) was used to capture both joint and skin response at the end of the induction period.

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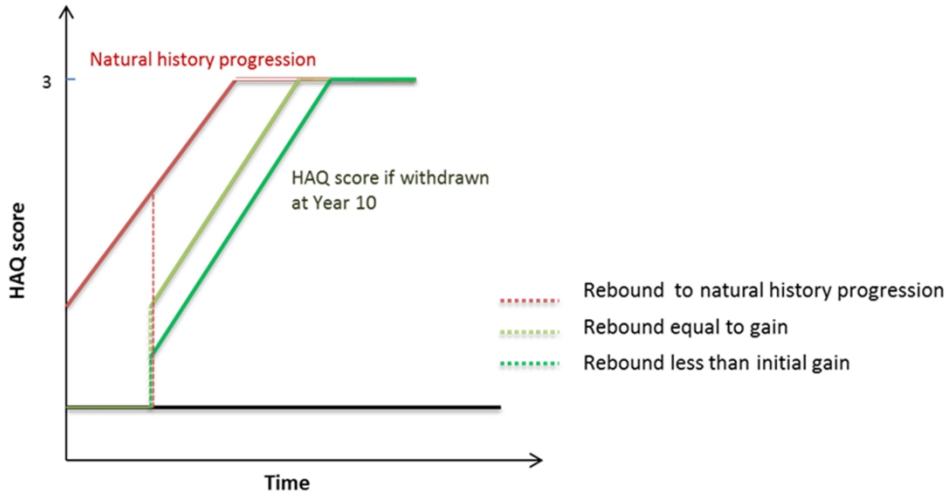


Figure 3. Scenarios for HAQ-DI rebound after the discontinuation of treatment.

228x120mm (600 x 600 DPI)

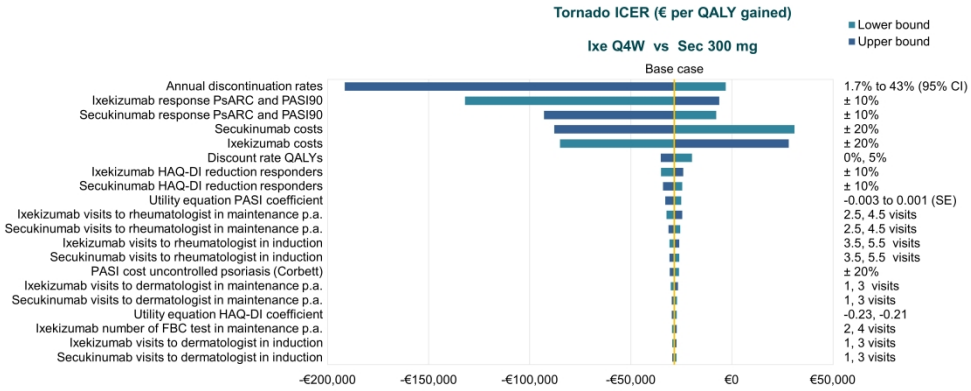


Figure 4. Results of the one-way sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

338x140mm (300 x 300 DPI)

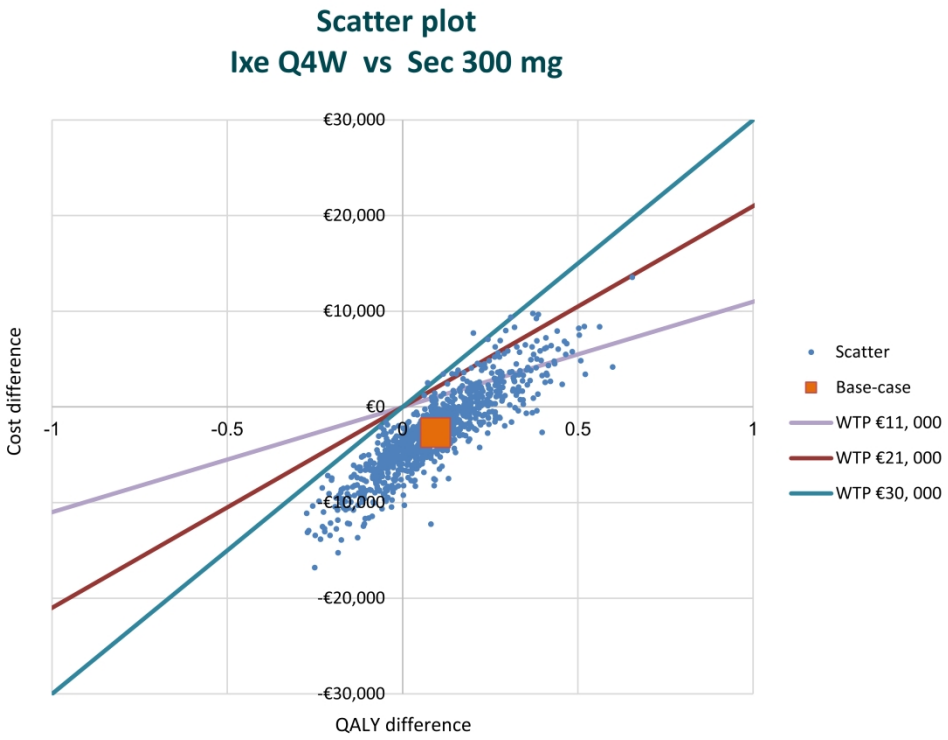


Figure 5. Results of the probabilistic sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis. Approximately 49.5% of observations were in the south-east quadrant, 28.6% were in the south-west quadrant and 21.9% were in the north-east quadrant of the cost-effectiveness plane.

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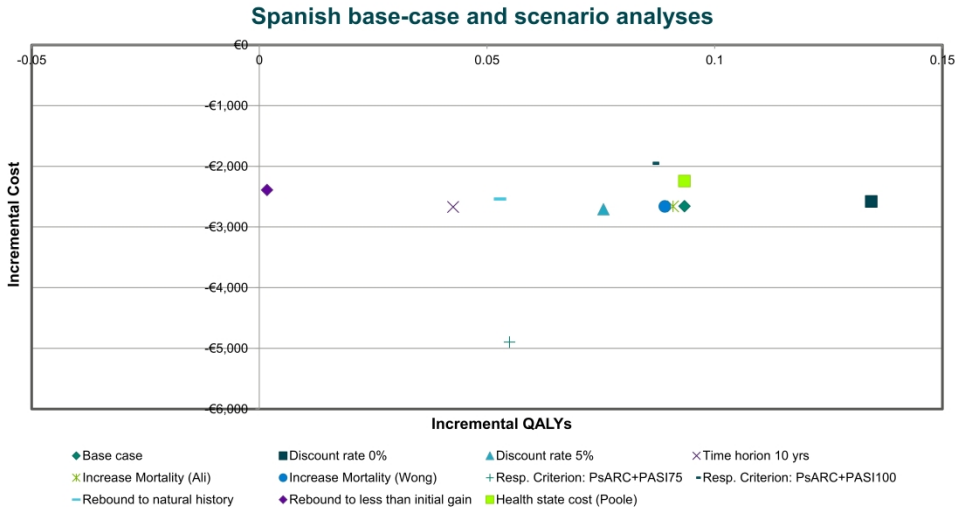


Figure 6. Results of scenario analyses in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

273x145mm (600 x 600 DPI)

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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

Bernd Schweikert, Chiara Malmberg, Mercedes Nuñez, Tatiana Dilla, Christophe Sapin, Susanne Hartz

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**Supplementary Table 1.** Efficacy input data used in the base-case analysis based on data from a related network meta-analysis. [23, 24]

| Treatment | Probability of response for chosen criterion | | HAQ reduction | | PASI response | | | PASI reduction | |
|---|---|---|---|---|---|---|---|---|---|
| | PsARC | PsARC and PASI90 | Responders | Non-responders | PASI75 | PASI90 | PASI100 | Responders | Non-responders |
| Ixe 80 mg Q4W | 53.0% | 34.4% | 0.51 | 0.05 | 70.9% | 52.0% | 35.4% | 18.36 | 9.49 |
| Sec 300 mg | 54.1%[a] | 26.5%[a] | 0.56 | 0.14 | 56.6%[a] | 36.8%[a] | 22.4%[a] | 18.36 | 8.13 |

[a]Data derived from a mixed population of bDMARD-naïve and -experienced patients (due to lack of data reported specifically for bDMARD-naïve patients).
DMARD, biologic disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; Ixe, ixekizumab, PASI, Psoriasis Area and Severity Index; PASI75, 90, 100, ≥75%, ≥90% or 100% reduction from baseline PASI; PsARC, Psoriatic Arthritis Response Criteria; Q4W, every 4 weeks; Sec, secukinumab.

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**Supplementary Table 2.** Parameters used in the probabilistic sensitivity analysis

| Parameter | Mean (SE) | Distribution type | CI/assumptions |
|---|---|---|---|
| *Utility regression calculation* | | | |
| Intercept | 0.903 (0.009) | BETA | |
| HAQ | -0.219 (0.010) | NORMAL | |
| PASI | -0.001 (0.002) | NORMAL | |
| Annual HAQ progression | 0.072 (0.018) | GAMMA | Assumption SE=mean/4 |
| Annual discontinuation rate | 0.165 (0.041) | BETA | Assumption SE=mean/4 |
| Mean weight | 87.02 (0.454) | NORMAL | Based on SPIRIT trials |
| Additional annual cost of BSC | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *Monitoring Costs* | | | |
| Cost of full blood count | 67.98 (17.0) | GAMMA | Assumption SE=mean/4 |
| Cost of liver function test | 5.9566 (1.5) | GAMMA | Assumption SE=mean/4 |
| Cost of ESR | 1.03 (0.3) | GAMMA | Assumption SE=mean/4 |
| Cost of urea and electrolytes test | 75.8183 (19.0) | GAMMA | Assumption SE=mean/4 |
| Cost of X-Ray | 42.23 (10.6) | GAMMA | Assumption SE=mean/4 |
| Cost of TB test | 8.95 (2.2) | GAMMA | Assumption SE=mean/4 |
| Cost of ANA test | 8.9507 (2.2) | GAMMA | Assumption SE=mean/4 |
| Cost of dsDNA test | 0 (0.0) | GAMMA | Assumption SE=mean/4 |
| *Admin costs* | | | |
| Cost of subcutaneous injection | 1.11 (0.3) | GAMMA | Assumption SE=mean/4 |
| Cost of intravenous infusion | 81.82 (20.5) | GAMMA | Assumption SE=mean/4 |
| *Physician costs* | | | |
| Cost of rheumatologist visit | 220.62 (55.2) | GAMMA | Assumption SE=mean/4 |
| Cost of dermatologist visit | 100.58 (25.1) | GAMMA | Assumption SE=mean/4 |
| Cost of GP visit | 33.86 (8.5) | GAMMA | Assumption SE=mean/4 |
| *AEs hospital costs* | | | |
| NMSC | 3858.07 (964.5) | GAMMA | Assumption SE=mean/4 |
| Lymphoma | 10345.71 (2586.4) | GAMMA | Assumption SE=mean/4 |
| Melanoma | 3966.44 (991.6) | GAMMA | Assumption SE=mean/4 |
| Sepsis | 7769.76 (1942.4) | GAMMA | Assumption SE=mean/4 |

| | | | |
|---|---|---|---|
| TB | 7110.13 (1777.5) | GAMMA | Assumption SE=mean/4 |
| Pneumonia | 4558.02 (1139.5) | GAMMA | Assumption SE=mean/4 |
| Skin and soft tissue infection | 4171.03 (1042.8) | GAMMA | Assumption SE=mean/4 |
| one and joint infection | 7245.83 (1811.5) | GAMMA | Assumption SE=mean/4 |
| Urinary tract infection | 3347.43 (836.9) | GAMMA | Assumption SE=mean/4 |
| *Health state costs* | | | |
| Kobelt HAQ regression constant | 636.56 (410.7) | NORMAL | Kobelt |
| Kobelt HAQ regression intercept | 2101.70 (739.7) | NORMAL | Kobelt |
| Corbett PASI cost uncontrolled psoriasis | 2871.95 (718.0) | GAMMA | Assumption SE=mean/4 |
| Corbett PASI cost controlled psoriasis | 81.03 (2.03) | GAMMA | Assumption SE=mean/4 |
| Kobelt cost adjustment factor | 0.85 (0.2) | BETA | Assumption SE=mean/4 |
| *Efficacy of BSC* | | | |
| PsARC | 30.60% | CODA | |
| PsARC and PASI75 | 5.04% | CODA | |
| PsARC and PASI90 | 1.77% | CODA | |
| PsARC and PASI100 | 0.61% | CODA | |
| HAQ reduction responders | 0.257 | CODA | |
| HAQ reduction non-responders | -0.009 | CODA | |
| PASI50 response | 17.40% | CODA | |
| PASI75 response | 6.40% | CODA | |
| PASI90 response | 2.20% | CODA | |
| PASI100 response | 0.70% | CODA | |
| *Treatment specific costs - Ixekizumab Q4W* | | | |
| PsARC | 53.00% | CODA | |
| PsARC and PASI75 | 46.65% | CODA | |
| PsARC and PASI90 | 34.40% | CODA | |
| PsARC and PASI 100 | 23.01% | CODA | |
| HAQ reduction responders | 0.506 | CODA | |
| HAQ reduction non-responders | 0.052 | CODA | |
| PASI50 response | 87.20% | CODA | |
| PASI75 response | 70.90% | CODA | |
| PASI90 response | 52.00% | CODA | |
| PASI100 response | 35.40% | CODA | |
| *Physician Visits - Induction period* | | | |
| Rheumatologist | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Dermatologist | 6.00 (1.50) | GAMMA | Assumption SE=mean/4 |
| GP | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Physician Visits - Maintenance therapy* | | | |
| Rheumatologist (annually) | 3.50 (0.875) | GAMMA | Assumption SE=mean/4 |
| Dermatologist (annually) | 2.00 (0.50) | GAMMA | Assumption SE=mean/4 |
| GP (annually) | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Induction period* | | | |
| Number of FBC | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of ESR | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |

| | | | |
|---|---|---|---|
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of dsDNA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Maintenance therapy* | | | |
| Number of FBC | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of ESR | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of dsANA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *AEs* | | | |
| Rate NMSC/patient year | 0.00 (0.000) | BETA | Assumption SE=mean/4 |
| Rate of malignancies/patient year | 0.00 (0.000) | BETA | Assumption SE=mean/4 |
| Rate of severe infections/patient year | 0.02 (0.004) | BETA | Assumption SE=mean/4 |
| *Treatment specific costs - Secukinumab 300 mg* | | | |
| PsARC | 54.10% | CODA | |
| PsARC and PASI75 | 40.50% | CODA | |
| PsARC and PASI90 | 26.50% | CODA | |
| PsARC and PASI 100 | 15.82% | CODA | |
| HAQ reduction responders | 0.561 | CODA | |
| HAQ reduction non-responders | 0.139 | CODA | |
| PASI50 response | 77.30% | CODA | |
| PASI75 response | 56.60% | CODA | |
| PASI90 response | 36.80% | CODA | |
| PASI100 response | 22.40% | CODA | |
| *Physician Visits - Induction period* | | | |
| Rheumatologist | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Dermatologist | 6.00 (1.50) | GAMMA | Assumption SE=mean/4 |
| GP | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Physician Visits - Maintenance therapy* | | | |
| Rheumatologist | 3.50 (0.875) | GAMMA | Assumption SE=mean/4 |
| Dermatologist (annually) | 6.50 (1.625) | GAMMA | Assumption SE=mean/4 |
| GP (annually) | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Induction period* | | | |
| Number of FBC | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of ESR | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of dsANA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Maintenance therapy* | | | |
| Number of FBC | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |

| | | | |
|---|---|---|---|
| Number of ESR | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of dsANA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *AEs* | | | |
| Rate NMSC/patient year | 0.00 (0.000) | BETA | Assumption SE=mean/4 |
| Rate of malignancies/patient year | 0.01 (0.001) | BETA | Assumption SE=mean/4 |
| Rate of severe infections/patient year | 0.02 (0.005) | BETA | Assumption SE=mean/4 |

AEs, adverse events; ANA, antinuclear antibody; BSC, best supportive care; CODA, convergence diagnostics and output analysis; dsDNA, double-stranded deoxyribonucleic acid; ESR, erythrocyte sedimentation rate; FBC, full blood count; HAQ, Health Assessment Questionnaire; LFT, liver function test; MD, medical doctor; NMSC, nonmelanoma skin cancers; PASI, Psoriasis Area and Severity Index; PASI50, 75, 90, 100, ≥50%, ≥75%, ≥90% or 100% reduction from baseline PASI; PsARC, Psoriatic Arthritis Response Criteria; Q4W, every 4 weeks; SE, standard error; TB, tuberculosis; U&E, urea and electrolyte.

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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

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# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

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## ABSTRACT

**Objective:** To conduct a cost-effectiveness analyses (CEA) from the perspective of the Spanish National Health System comparing ixekizumab versus secukinumab.

**Design:** A Markov model with a lifetime horizon and monthly cycles was developed based on the York model. Four health states were included: a 12- or 16-week biologic disease-modifying antirheumatic drugs (bDMARD) induction period, maintenance therapy, best supportive care (BSC) and death. Treatment response was assessed based on both Psoriatic Arthritis Response Criteria (PsARC) and ≥90% improvement in the Psoriasis Area Severity Index (PASI90). At the end of the induction period, responders transitioned to maintenance therapy. Non-responders and patients who discontinued maintenance therapy transitioned to BSC. Clinical efficacy data were derived from a network meta-analysis. Health utilities were generated by applying a regression analysis to PASI and Health Assessment Questionnaire – Disability Index (HAQ-DI) scores collected in the ixekizumab SPIRIT studies. Results were subject to extensive sensitivity and scenario analysis.

**Setting:** Spanish National Health System.

**Participants:** A hypothetical cohort of bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis was modelled.

**Interventions:** Ixekizumab and secukinumab.

**Results:** Ixekizumab performed favourably over secukinumab in the base-case analysis, although cost savings and quality-adjusted life-years (QALY) gains were modest. Total costs were €153,901 compared with €156,559 for secukinumab (difference −€2,658). Total QALYs were 9.175 versus 9.082 (difference 0.093). Base-case results were most sensitive to the annual bDMARD discontinuation rate and the modification of PsARC and PASI90 response to ixekizumab or secukinumab.

**Conclusions:** Ixekizumab provided more QALYs at a lower cost than secukinumab, with differences being on a relatively small scale. Sensitivity analysis showed that base-case results were generally robust to changes in most input parameters.

## ARTICLE SUMMARY

### Strengths and limitations of this study

- A CEA was performed from the perspective of the Spanish National Health System comparing two interleukin-17A antagonists, ixekizumab and secukinumab
- The framework of this model is aligned with the York model; the 'gold standard' model for the economic evaluation of biologic treatments in PsA
- The current model uses a combined response criterion of PsARC and PASI to capture both joint and skin manifestations of PsA
- This analysis was limited by a lack of data available for costs and efficacy of supportive care given to PsA patients in Spain
- Due to uncertainty regarding the annual all-cause discontinuation rate, this model used assumptions consistent with previous models

## INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease characterised by pain, swelling and erosion of the joints.[1] PsA affects approximately 0.25% of the population worldwide [1] and 0.6% of the adult population in Spain.[2] PsA commonly co-exists with psoriasis, developing in up to 30% of psoriatic patients, and over 90% of patients with PsA will have concomitant psoriasis.[3,4] As a lifelong condition, PsA has a detrimental impact on quality of life due to pain and/or physical functional limitations associated with the disease.[1,3] It is also associated with substantial use of healthcare resources and high socioeconomic costs.[5,6]

A number of biologic disease-modifying antirheumatic drugs (bDMARDs), which inhibit key inflammatory cytokines, are approved for treating patients with PsA. Interleukin (IL)-17 has been identified as an effective target for the treatment of inflammatory diseases including PsA.[1,3] Ixekizumab, a high-affinity monoclonal antibody, is the most recently approved bDMARD targeting IL-17A for PsA, joining secukinumab, which uses the same target and similar mode of action.[7,8]

bDMARDs are considered major drivers of healthcare costs,[5] and the cost-effectiveness of these therapies often comes under scrutiny. Cost-effectiveness analyses (CEAs) comparing bDMARDs have been conducted using the York model,[9] an established economic framework, which, together with its subsequent versions, is considered the `gold standard' for conducting CEAs in PsA.[10,11]

As inhibition of IL-17A is a relatively new mechanism of action, drugs in this class have not been the focus of CEAs.[12] To date, there are no published CEAs comparing ixekizumab with secukinumab (another IL-17A inhibitor) in Spain.

We conducted a CEA assessing the cost effectiveness, in terms of the incremental cost per quality-adjusted life-year (QALY) gained, of ixekizumab versus secukinumab in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis from the

perspective of the Spanish National Health System (NHS). Secukinumab was selected as a comparator for this CEA as both drugs belong to the same class, and this may be of interest to decision makers assessing these IL-17A inhibitors. In addition, both drugs are approved for the treatment of PsA and plaque psoriasis, and have demonstrated high efficacy, particularly on skin symptoms.[7,8] This CEA focused on bDMARD-naïve patients, as this patient population may receive greater clinical benefit from earlier (i.e. first-line) treatment.[13]

## METHODS

### Model overview

A Markov model was developed to assess the cost effectiveness of ixekizumab versus secukinumab in a hypothetical cohort of bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis in Spain. The Markov model framework accommodates different health states and is based on the assumption that future events depend on the current health state of the patient. The model was programmed in Visual Basics for Applications with a user interface in Microsoft® Excel.

The model is based on the most recent version of the York model [11] with monthly cycles and a lifetime horizon, which was considered appropriate to reflect the chronic nature of PsA as well as the treatment aim of delaying disease progression.[14] The model incorporated age- and gender-dependent mortality data for the normal Spanish population. Mean age and gender distribution was taken from the patient population in the SPIRIT-P1 and -P2 trials of ixekizumab in PsA.[15,16] Increased PsA-specific mortality risks from two different sources [17,18] were implemented in scenario analyses.

The model includes four health states: 1) a 12- or 16-week bDMARD induction period; 2) maintenance bDMARD therapy; 3) best supportive care (BSC); and 4) death (Figure 1). A combination of Psoriatic Arthritis Response Criteria (PsARC) and Psoriasis Area Severity Index (PASI) was used to measure joint and skin response at the end of the induction period and to determine treatment continuation of ixekizumab and secukinumab (Figure 2).[19,20]

The induction period was set to 12 weeks and 16 weeks for ixekizumab and secukinumab, respectively. The induction period was chosen to reflect the time at which treatment efficacy is usually followed-up in clinical practice (approximately 3 months in Spain).[21,22] The difference in the length of induction period between the two drugs also acknowledges a degree of difference in the availability of clinical trial data for ixekizumab and secukinumab (i.e., across the included studies, more week 16 than week 12 data is available for secukinumab). The PsARC response to treatment was defined as an improvement from baseline in two of four criteria without worsening in any measure: tender/swollen joints; and physician/patient global assessment of disease activity (one of which must be a joint count). In a consensus from the Spanish Psoriasis Group, a panel of dermatologists agreed that a complete or nearly complete PASI response is the most relevant measure of effectiveness in clinical practice.[23] With this in mind, ≥90% improvement in PASI (PASI90) was chosen in the base-case analysis as part of the response criteria and the treatment effect measures in this model.

**Treatment sequences**

At the end of the induction period, responders transitioned to maintenance therapy, while non-responders and discontinuers transitioned to BSC (Figure 1) in which patients were assumed to receive standard treatment depending on their Health Assessment Questionnaire – Disability Index (HAQ-DI) and PASI status.[24] Dosage regimens for ixekizumab and secukinumab were aligned with the European market authorisation.[7,8] During maintenance therapy, patients were assumed to face a constant risk of all-cause treatment discontinuation, which was reflected by an annual discontinuation rate of 16.5% in line with previously applied methods.[10,11]

In the base-case analysis, baseline cohort characteristics were reflective of the demographic data from the ixekizumab SPIRIT-P1 and -P2 clinical trials [15,16] (Table 1).

**Treatment effect**

While PsARC and PASI90 were used as the combined response criterion (i.e. treatment continuation rule), the treatment effect was modelled as a change in baseline of the HAQ-DI and PASI scores,[25] reflecting the joint and skin components of PsA, respectively. Baseline HAQ-DI and PASI scores were derived from the SPIRIT-P1 and -P2 trials [15,16] (Table 1). Treatment effect, represented by improvement (i.e. reductions) in HAQ-DI and PASI scores, was assumed to be instantaneous; as such, the response was also applied during the induction period. Absolute change in HAQ-DI and PASI scores is based on data from a network meta-analysis (NMA).[25, 26] Key efficacy input data, derived from the NMA [25, 26] are provided in Supplementary Table 1.

For patients who met the combined response of PsARC and PASI90 at the end of the induction period, the initial improvements in HAQ-DI and PASI continued during maintenance therapy until they transitioned into BSC. For patients entering BSC following discontinuation, it was assumed that some benefit was maintained from the initial bDMARD treatment. In the base case, for patients progressing to BSC, the HAQ-DI score was assumed to revert to the baseline HAQ-DI level prior to discontinuation ("rebound equal to initial gain"). The rebound effect was assumed to be immediate and patients were modelled to progress at the same rate as natural history progression (an increase of 0.018 per 3-month period) (Figure 3). For PASI score, it was assumed that for non-responders not meeting PASI90, there would still be some gain in PASI – albeit lower – while they were treated with a bDMARD in the induction period. Once in the BSC state, due to the progressive nature of PsA, it was assumed that patients would deteriorate at a rate of natural progression.

**Health utilities**

Health utilities were based on HAQ-DI and PASI scores from the SPIRIT-P1 and -P2 clinical trials [15,16] with Spanish tariffs applied. Calculation of utilities followed the established methodology of mapping three-level version of EuroQol-5 Dimensions (EQ-5D-3L) utilities on HAQ and PASI scores using a parsimonious linear regression model without further covariates or interaction terms. [9–11] Alternative coefficients based on a similar algorithm using different

data were applied in a sensitivity analysis. Utilities were calculated in each model cycle by multiplying HAQ and PASI levels with the estimated regression coefficients.

**Resource use and costs**

As the CEA was conducted from the perspective of the Spanish NHS, only direct medical costs were considered in the model, and included medication, injection training, physician visits and therapy monitoring. Drug acquisition costs were derived from the Botplus database in Spain,[27] and costs for the administration and monitoring of treatments were obtained from various sources in Spain [28] (Table 2). Drug costs were based on the list prices as of Q4 2018. Monitoring costs were based on the costing schedule published in 2017, which was still valid in 2018. Due to a lack of healthcare resource utilisation data by drug or class, healthcare costs and resource utilisation related to the administration and monitoring of bDMARDs was determined by an expert panel of four Spanish physicians (two rheumatologists and two dermatologists).

The severity of arthritis and psoriasis also may have an impact on healthcare costs.[10,11] To reflect this, costs related to HAQ-DI and PASI were also included per cycle in the model.[10,24] These costs were derived by converting and inflating results of established algorithms, which relate cost to absolute HAQ-DI and PASI values.

Aside from costs related to HAQ-DI and PASI, no additional costs were applied for patients in BSC. The costs of serious adverse events (i.e. requiring hospitalisation) associated with bDMARD treatment were not included in the base-case analysis, but they were included in a sensitivity analysis. The rates of adverse events were derived from the summary of product characteristics of ixekizumab and secukinumab.[7,8] Both costs and health utilities were discounted by 3% in the base case.

**Sensitivity analyses**

To explore the uncertainty inherent in the model, one-way (deterministic) sensitivity analysis, probabilistic sensitivity analysis and scenario analyses were undertaken. In the one-way sensitivity analysis, one variable at a time was altered to examine the effect on the results. Most input parameters varied by ±20% of the mean value, as 95% confidence interval (CI) values were not available. Exceptions to this included ranges of values used for the annual discontinuation rate (95% CI); discount rates for costs and health utilities (0%; 5%); treatment efficacy (±10% of the mean value); HAQ-DI improvement conditional on response (NMA results); physician and monitoring costs (±1 visit); and utility equations for PASI and HAQ-DI coefficients.

A probabilistic sensitivity analysis was conducted by assigning distributions to input parameters (Supplementary Table 2) and sampling from these distributions in 1000 iterations. For efficacy inputs, the convergence diagnostics and output analysis (CODA) of the Bayesian NMA was used instead of applying parametric distributions, in line with internationally recognised technical guidance.[29] The input parameters included PsARC and PASI response rates, changes in HAQ-DI based on response criterion, costs based on HAQ-DI and PASI, discontinuation rates, various healthcare-related costs and the use of resources.

A scenario analysis was conducted using a 10-year time horizon and alternative inputs for discount rates, increased PsA mortality, the definition of responders, the HAQ-DI rebound method, the utility equation, health state costs and placebo efficacy in BSC.

**Patient and public involvement**

Patients or the public were not involved in the design, planning or execution of this work.

**RESULTS**

Results of the base-case analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis are summarised in Table 3. Ixekizumab was associated with total cost savings of €2,658 compared with secukinumab (total costs €153,901 vs €156,559).

Total QALYs were higher for ixekizumab (9.175 vs 9.082, difference 0.093). Although ixekizumab performed favourably over secukinumab in the base-case analysis, cost savings and QALY gains were modest.

The deterministic sensitivity analysis showed that base-case results were generally robust to changes in most input parameters, but were most sensitive to the annual discontinuation rate for bDMARD therapy and modifications in PsARC and PASI90 response to ixekizumab or secukinumab (Figure 4).

The probabilistic sensitivity analysis showed that approximately 49.5% of observations were in the south-east quadrant, indicating that ixekizumab was still less costly and provided more QALYs than secukinumab (Figure 5). Across the cost-effectiveness plane, 99% of replications were located south-east of the line defined by a willingness to pay threshold of €30,000 per QALY gained.

Overall, the scenario analyses showed that most of the parameters tested had relatively little impact on the base-case results (Figure 6). In most scenarios, ixekizumab provided more QALYs at a lower cost than secukinumab. While there was some variability regarding incremental cost and QALYs between ixekizumab versus secukinumab, in all scenarios the mean results still indicated the dominance of ixekizumab over secukinumab.

## DISCUSSION

In this CEA, the cost effectiveness of ixekizumab compared to secukinumab was evaluated in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis from the perspective of the Spanish NHS. In general, ixekizumab performed favourably compared to secukinumab in the base-case analysis, with differences in cost savings and QALY gains being modest. The total difference in cost between ixekizumab and secukinumab was −€2,658, with a small total difference in QALYs of 0.093. In the deterministic sensitivity analysis, the most influential variables were the annual discontinuation rate and the PsARC and PASI90 response for ixekizumab and secukinumab.

The framework of this model is closely aligned with the most recently revised version of the York model,[11] which is considered a `benchmark' model for the economic evaluation of biologic treatments in PsA. The original York model has subsequently been revised to accommodate the analysis of patient subgroups. The model used in this analysis includes this amendment as a key feature. The current model also allows for combining PsARC and PASI as a response criterion, therefore capturing both joint and skin response. A combined response criterion presents a more realistic representation of this multifaceted disease and may be especially useful when evaluating clinical benefits of bDMARDs, such as IL-17A antagonists, which are known for their proven efficacy on skin response.[30,31]

A limitation of this analysis was a lack of current data for health state cost estimates and the efficacy of BSC. There is also uncertainty regarding the annual all-cause discontinuation rate; therefore, our model used input data consistent with previously applied methods.[10,11] Given the sensitivity of the results to this parameter, correction or confirmation of the current assumptions based on mature real-world drug survival data is a clear research need for the future.

In addition, the actual acquisition costs of bDMARDs in clinical practice tend to differ from list prices because any confidential discounts are unknown and therefore cannot be reflected in the analyses. Therefore, the respective differences in drug prices in clinical practice would also affect the true cost differences between treatment arms in the analysis.

It should also be noted that the NMA [25, 26], which provided key efficacy data for this analysis, may not include some very recently published studies. However, at the time the NMA was performed all relevant evidence available for approved drugs was included and any studies published after are unlikely to have a substantial impact on the NMA findings, and by extension the results of this analysis.

## CONCLUSION

In this CEA of ixekizumab versus secukinumab in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis in Spain, ixekizumab provided more QALYs at a lower cost, with differences being on a relatively small scale. As differences in total costs and QALYs were modest, other factors, such as patient preferences, may also be considered during clinical decision making. Base-case results were generally robust to modifications in most input parameters, but were most sensitive to the annual bDMARD discontinuation rate and variations in PsARC and PASI90 response to ixekizumab or secukinumab.

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## CONFLICTS OF INTEREST

**BS** and **CM** are full-time employees of ICON who were commissioned by Eli Lilly and Company to conduct the analysis for this work. **MN**, **TD**, **CS** and **SH** are full-time employees of Eli Lilly and Company; they receive a salary and own company stock.

## AUTHOR CONTRIBUTIONS

**BS** and **CM** were involved with the conception and design of the work, and the interpretation of the data. **MN** and **CS** were involved with the acquisition and interpretation of the data. **TD** was involved with the conception of the work and interpretation of the data. **SH** was involved with the interpretation of the data. All named have provided critical revision of the manuscript for important intellectual content and have given their approval for this version to be published. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.

## DATA SHARING STATEMENT

All data relevant to the study are included in the article or uploaded as supplementary information.

## REFERENCES

1. McArdle A, Pennington S, FitzGerald O. Clinical features of psoriatic arthritis: a comprehensive review of unmet clinical needs. *Clin Rev Allergy Immunol* 2018;55:271–94.
2. Seoane-Mato D, Sánchez-Piedra C, Díaz-González F, et al. THU0684 Prevalence of rheumatic diseases in adult population in Spain. Episer 2016 study. *Ann Rheum Dis* 2018;77:535–36.
3. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med* 2017;376:957–70.
4. Ciocon DH, Kimball AB. Psoriasis and psoriatic arthritis: separate or one and the same? *Br J Dermatol* 2007;157(5):850-60.
5. D'Angiolella LS, Cortesi PA, Lafranconi A, et al. Cost and cost effectiveness of treatments for psoriatic arthritis: a systematic literature review. *Pharmacoeconomics* 2018;36:567–89.
6. Kawalec P, Malinowski KP. The indirect costs of psoriatic arthritis: systematic review and meta-analysis. *Expert Rev Pharmacoecon Outcomes Res* 2015;15:125–32.
7. European Medicines Agency. Ixekizumab (Taltz): Summary of product characteristics 2016. www.ema.europa.eu/documents/product-information/taltz-epar-product-information_en.pdf (accessed 22 Mar 2019).
8. European Medicines Agency. Secukinumab (Cosentyx): Summary of product characteristics 2015. www.ema.europa.eu/documents/product-information/cosentyx-epar-product-information_en.pdf (accessed 22 Mar 2019).
9. Woolacott N, Bravo Vergel Y, Hawkins N, et al. Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess* 2006;10:iii–iv, xiii–xvi,1–239.

10. Rodgers M, Epstein D, Bojke L, et al. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess* 2011;15:i–xxi, 1–329.
11. Corbett M, Chehadah F, Biswas M, et al. Certolizumab pegol and secukinumab for treating active psoriatic arthritis following inadequate response to disease-modifying antirheumatic drugs: a systematic review and economic evaluation. *Health Technol Assess* 2017;21:1–326.
12. Wasilewska A, Winiarska M, Olszewska M, et al. Interleukin-17 inhibitors. A new era in treatment of psoriasis and other skin diseases. *Postepy Dermatol Alergol* 2016;33:247–52.
13. Raychaudhuri SP, Wilken R, Sukhov AC, et al. Management of psoriatic arthritis: Early diagnosis, monitoring of disease severity and cutting edge therapies. *J Autoimmun* 2017;76:21–37.
14. Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. *Drugs* 2014;74:423–41.
15. Mease PJ, van der Heijde D, Ritchlin CT, et al. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naïve patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Ann Rheum Dis* 2017;76:79–87.
16. Nash P, Kirkham B, Okada M, et al. Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *Lancet* 2017;389:2317–27.
17. Ali Y, Tom BD, Schentag CT, et al. Improved survival in psoriatic arthritis with calendar time. *Arthritis Rheum* 2007;56:2708–14.

18. Wong K, Gladman DD, Husted J, et al. Mortality studies in psoriatic arthritis: results from a single outpatient clinic. I. Causes and risk of death. *Arthritis Rheum* 1997;40:1868–72.

19. Mease PJ, Antoni CE, Gladman DD, et al. Psoriatic arthritis assessment tools in clinical trials. *Ann Rheum Dis* 2005;64:ii49–54.

20. Fransen J, Antoni C, Mease PJ, et al. Performance of response criteria for assessing peripheral arthritis in patients with psoriatic arthritis: analysis of data from randomised controlled trials of two tumour necrosis factor inhibitors. *Ann Rheum Dis* 2006;65:1373–8.

21. Torre Alonso JC, Díaz Del Campo Fontecha P, Almodóvar R, et al. Recommendations of the Spanish Society of Rheumatology on treatment and use of systemic biological and non-biological therapies in psoriatic arthritis. *Reumatol Clin* 2018;14:254–68.

22. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Galán-Gutierrez M, et al. Eficacia del secukinumab en psoriasis y artritis psoriásica: estudio multicéntrico retrospectivo. *Med Clin* (Barc) 2019; pii:S0025-7753(19)30006-5 doi.org/10.1016/j.medcli.2018.12.009

23. Carretero G, Puig L, Carrascosa JM, et al. Redefining the therapeutic objective in psoriatic patient candidates for biological therapy. *J Dermatolog Treat* 2018;29:334–46.

24. Kobelt G, Jönsson L, Lindgren P, et al. Modeling the progression of rheumatoid arthritis: a two-country model to estimate costs and consequences of rheumatoid arthritis. *Arthritis Rheum* 2002;46:2310–19.

25. Ruyssen-Witrand A, Perry R, Watkins C, et al. Efficacy and safety of biologics in psoriatic arthritis: a systematic literature review and network meta-analysis. *RMD Open 2020*;6:e001117.

26. Ruyssen-Witrand A, Sapin C, Hartz S, et al. THU0290 Effects of biologic dmards on physical function in patients with active psoriatic arthritis: results of network meta-analyses. *Ann Rheum Dis* 2018;77:363–4.

27. Consejo General de Colegios Oficiales de Farmacéuticos. Botplus database 2018. https://botplusweb.portalfarma.com/botplus.aspx (accessed 22 Mar 2019).
28. Oblikue Consulting. Base de datos de costes sanitarios españoles: eSalud 2007. http://www.oblikue.com/bddcostes/ (accessed 22 Mar 2019).
29. Dias S, Sutton AJ, Welton NJ, et al. Evidence synthesis for decision making 6: embedding evidence synthesis in probabilistic cost-effectiveness analysis. *Med Decis Making* 2013;33:671–8.
30. Betteridge N, Boehncke WH, Bundy C, et al. Promoting patient-centred care in psoriatic arthritis: a multidisciplinary European perspective on improving the patient experience. *J Eur Acad Dermatol Venereol* 2016;30:576–85.
31. Gottlieb AB, Strand V, Kishimoto M, et al. Ixekizumab improves patient-reported outcomes up to 52 weeks in bDMARD-naïve patients with active psoriatic arthritis (SPIRIT-P1). *Rheumatology* (Oxford) 2018;57:1777–88.

**Table 1.** Characteristics of the target population of bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis based on the ixekizumab SPIRIT-P1 and -P2 clinical trials.

| Parameter | Mean value |
|---|---|
| Age | 51.0 years |
| Proportion male | 51.8% |
| Proportion female | 48.2% |
| Body weight | 87.0 kg |
| Baseline HAQ-DI score | 1.19 |
| Baseline PASI score | 20.4 |

Patient characteristics based on pooled data from the intent-to-treat trial populations of SPIRIT-P1 and -P2 with ixekizumab. [15,16]

bDMARD, biologic disease-modifying anti-rheumatic drug; HAQ-DI, Health Assessment Questionnaire — Disability Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis.

**Table 2.** Costs for administration and monitoring of treatment in Spain.

| Resource | Cost | Source |
|---|---|---|
| *Drug acquisition costs (list prices)* | | |
| Ixekizumab 80 mg Q4W pre-filled pen | €934.25 per dose | Botplus database [27] minus rebate of 7.5% according to Spanish regulation RDL 8/2010 |
| Secukinumab 300 mg pre-filled pen | €1,057.38 per dose | Botplus database [27] minus rebate of 7.5% according to Spanish regulation RDL 8/2010 |
| *Visits* | | |
| Rheumatologist | €220.62 | Base de datos de costes sanitarios españoles [28] |
| Dermatologist | €100.58 | Base de datos de costes sanitarios españoles [28] |
| GP | €33.86 | Base de datos de costes sanitarios españoles [28] |
| *Monitoring* | | |
| Full blood count | €67.98 | Base de datos de costes sanitarios españoles [28] |
| Erythrocyte sedimentation rate | €1.03 | Base de datos de costes sanitarios españoles [28] |
| Chest X-ray | €42.23 | Base de datos de costes sanitarios españoles [28] |
| Tuberculosis test | €8.95 | Base de datos de costes sanitarios españoles [28] |
| C-reactive protein test | €8.95 | Base de datos de costes sanitarios españoles [28] |

GP, general practitioner; Q4W, every four weeks.

**Table 3.** Results of the base-case analysis comparing ixekizumab and secukinumab in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis.

| Parameter | Ixekizumab | Secukinumab | Difference |
|---|---|---|---|
| *Costs (year 2018 values)* | | | |
| Total costs | €153,901 | €156,559 | −€2,658 |
| Treatment costs | €26,424 | €27,729 | −€1,305 |
| Administration costs | €26 | €24 | €2 |
| Physician visit costs | €4,141 | €4,202 | −€61 |
| Monitoring costs | €797 | €706 | €92 |
| On treatment HAQ-DI/PASI-related costs | €4,608 | €4,115 | €494 |
| BSC costs | €117,904 | €119,784 | −€1,880 |
| *QALYs* | | | |
| Total QALYs | 9.175 | 9.082 | 0.093 |

BSC, best supportive care; HAQ-DI, Health Assessment Questionnaire – Disability Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; QALYs, quality-adjusted life-years.

## Figure Legends and abbreviations

**Figure 1.** Schematic representation of the model structure in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis. Dosage regimens were aligned with the European market authorisation. Although not shown in the figure, patients could transition to death from any state.

BSC, best supportive care; bDMARD, biologic disease-modifying anti-rheumatic drug; PsA, psoriatic arthritis; Q4W, every 4 weeks.

**Figure 2.** A combination of PsARC response and ≥90% improvement in PASI (PASI90) was used to capture both joint and skin response at the end of the induction period.

**Figure 3.** Scenarios for HAQ-DI rebound after the discontinuation of treatment.

HAQ-DI, Health Assessment Questionnaire – Disability Index.

**Figure 4.** Results of the one-way sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

bDMARD, biologic disease-modifying anti-rheumatic drug; CI, confidence interval; FBC, full blood count; HAQ-DI, Health Assessment Questionnaire-Disability Index; ICER, incremental cost-effectiveness ratio; Ixe, ixekizumab; p.a., per annum; PASI90, ≥90% reduction from baseline Psoriasis Area Severity Index score; PsA, psoriatic arthritis; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life-year; Q4W, every 4 weeks; SE, standard error; Sec, secukinumab; Trt, treatment.

**Figure 5.** Results of the probabilistic sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis. Approximately 49.5% of observations were in the south-east quadrant, 28.6% were in the south-west quadrant and 21.9% were in the north-east quadrant of the cost-effectiveness plane.

bDMARD, biologic disease-modifying anti-rheumatic drug; Ixe, ixekizumab; PsA, psoriatic arthritis; QALY, quality-adjusted life-year; Q4W, every 4 weeks; Sec, secukinumab; WTP, willingness to pay.

**Figure 6.** Results of scenario analyses in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

bDMARD, biologic disease-modifying anti-rheumatic drug; PASI75, ≥75% reduction in Psoriasis Area Severity Index score; PASI100, 100% reduction in PASI score; PsA, psoriatic arthritis; PsARC, Psoriatic Arthritis Response Criteria; QALY, quality-adjusted life-year; Resp, response; yrs, years.

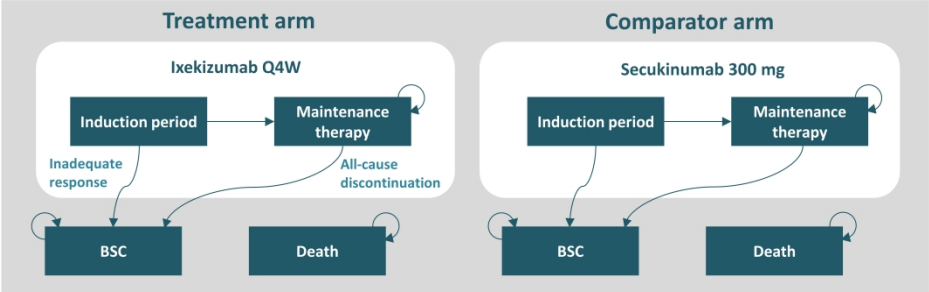


Figure 1. Schematic representation of the model structure in bDMARD-naïve patients with active PsA and concomitant moderate-to-severe psoriasis. Dosage regimens were aligned with the European market authorisation. Although not shown in the figure, patients could transition to death from any state.

228x75mm (600 x 600 DPI)

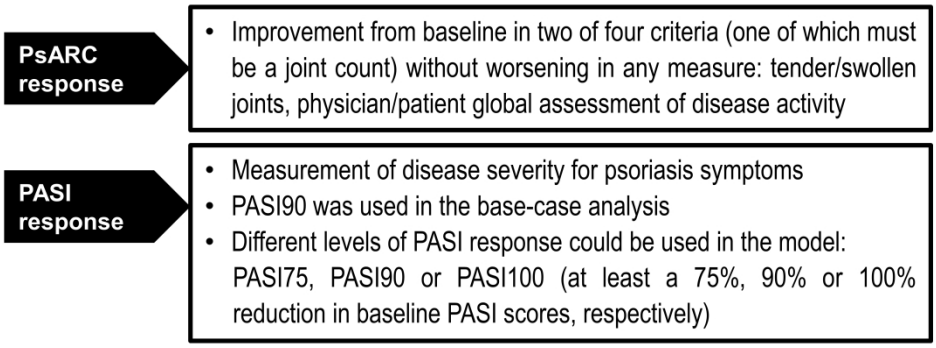


Figure 2. A combination of PsARC response and ≥90% improvement in PASI (PASI90) was used to capture both joint and skin response at the end of the induction period.

178x70mm (600 x 600 DPI)

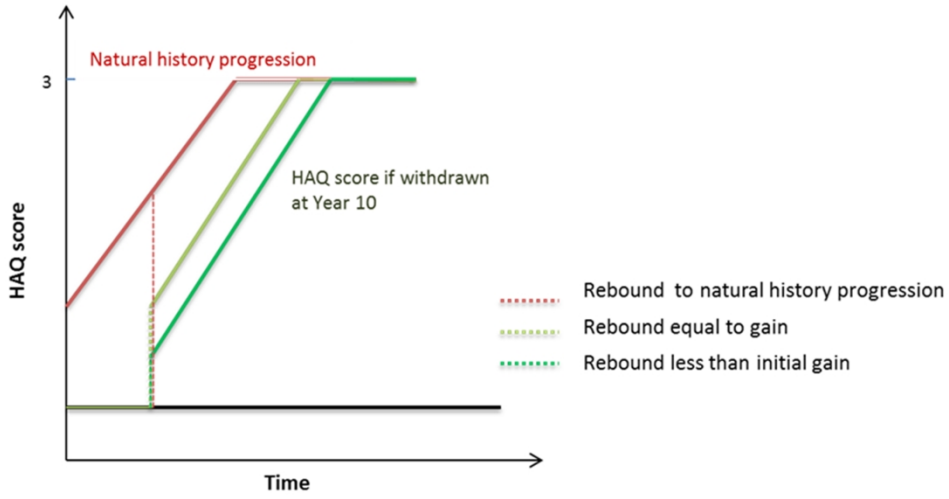


Figure 3. Scenarios for HAQ-DI rebound after the discontinuation of treatment.

228x120mm (600 x 600 DPI)

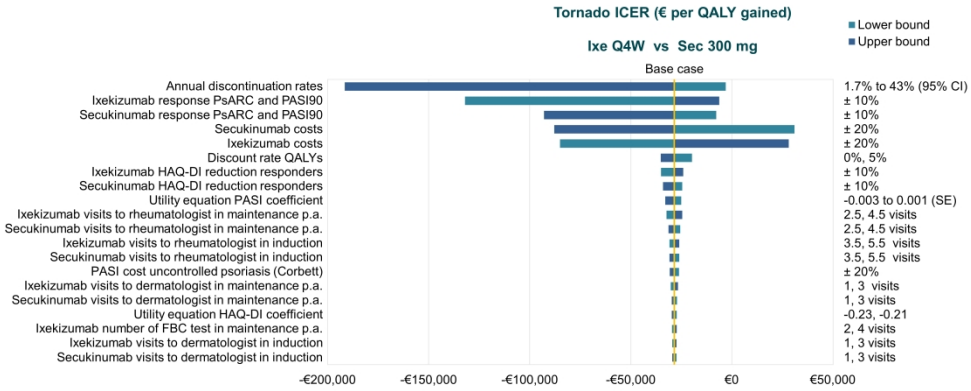


Figure 4. Results of the one-way sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

338x140mm (300 x 300 DPI)

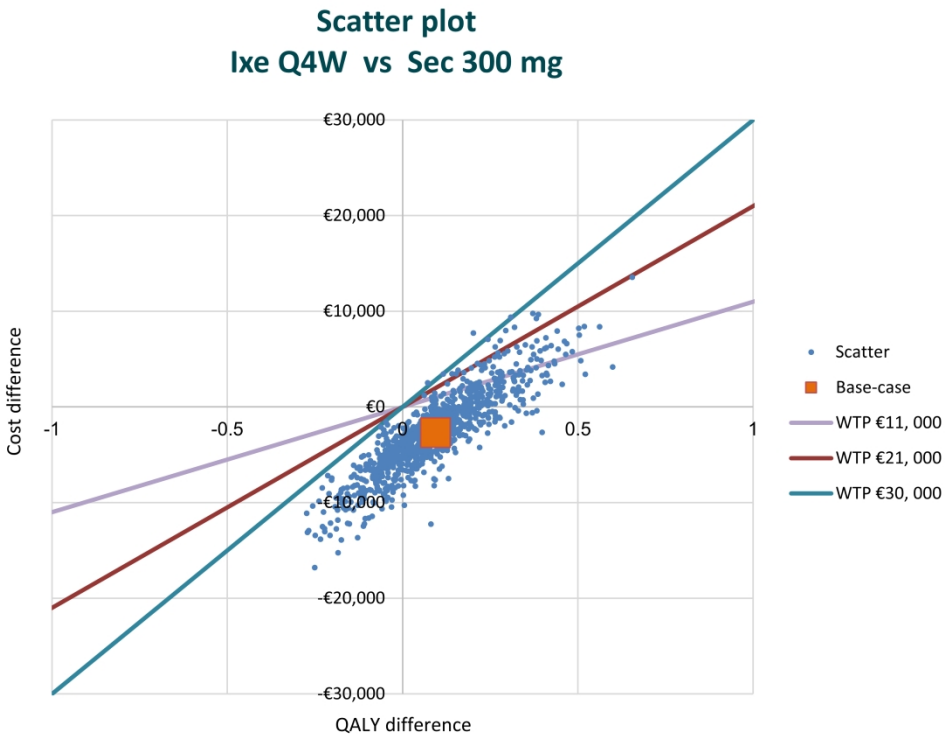


Figure 5. Results of the probabilistic sensitivity analysis in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis. Approximately 49.5% of observations were in the south-east quadrant, 28.6% were in the south-west quadrant and 21.9% were in the north-east quadrant of the cost-effectiveness plane.

168x130mm (600 x 600 DPI)

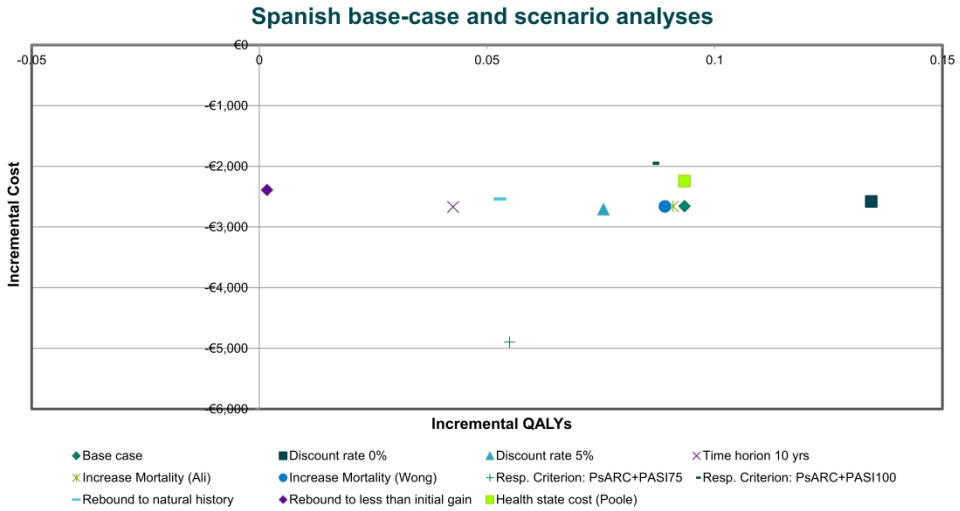


Figure 6. Results of scenario analyses in bDMARD-naïve patients with PsA and concomitant moderate-to-severe psoriasis.

273x145mm (600 x 600 DPI)

**BMJ Open**

# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

Bernd Schweikert, Chiara Malmberg, Mercedes Nuñez, Tatiana Dilla, Christophe Sapin, Susanne Hartz

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**Supplementary Table 1.** Efficacy input data used in the base-case analysis based on data from a related network meta-analysis. [23, 24]

| Treatment | Probability of response for chosen criterion | | HAQ reduction | | PASI response | | | PASI reduction | |
|---|---|---|---|---|---|---|---|---|---|
| | PsARC | PsARC and PASI90 | Responders | Non-responders | PASI75 | PASI90 | PASI100 | Responders | Non-responders |
| Ixe 80 mg Q4W | 53.0% | 34.4% | 0.51 | 0.05 | 70.9% | 52.0% | 35.4% | 18.36 | 9.49 |
| Sec 300 mg | 54.1%[a] | 26.5%[a] | 0.56 | 0.14 | 56.6%[a] | 36.8%[a] | 22.4%[a] | 18.36 | 8.13 |

[a]Data derived from a mixed population of bDMARD-naïve and -experienced patients (due to lack of data reported specifically for bDMARD-naïve patients).
DMARD, biologic disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; Ixe, ixekizumab, PASI, Psoriasis Area and Severity Index; PASI75, 90, 100, ≥75%, ≥90% or 100% reduction from baseline PASI; PsARC, Psoriatic Arthritis Response Criteria; Q4W, every 4 weeks; Sec, secukinumab.

**BMJ Open**

# Cost-effectiveness analysis of ixekizumab versus secukinumab in patients with psoriatic arthritis and concomitant moderate-to-severe psoriasis in Spain

Bernd Schweikert, Chiara Malmberg, Mercedes Nuñez, Tatiana Dilla, Christophe Sapin, Susanne Hartz

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**Supplementary Table 2.** Parameters used in the probabilistic sensitivity analysis

| Parameter | Mean (SE) | Distribution type | CI/assumptions |
|---|---|---|---|
| *Utility regression calculation* | | | |
| Intercept | 0.903 (0.009) | BETA | |
| HAQ | -0.219 (0.010) | NORMAL | |
| PASI | -0.001 (0.002) | NORMAL | |
| Annual HAQ progression | 0.072 (0.018) | GAMMA | Assumption SE=mean/4 |
| Annual discontinuation rate | 0.165 (0.041) | BETA | Assumption SE=mean/4 |
| Mean weight | 87.02 (0.454) | NORMAL | Based on SPIRIT trials |
| Additional annual cost of BSC | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *Monitoring Costs* | | | |
| Cost of full blood count | 67.98 (17.0) | GAMMA | Assumption SE=mean/4 |
| Cost of liver function test | 5.9566 (1.5) | GAMMA | Assumption SE=mean/4 |
| Cost of ESR | 1.03 (0.3) | GAMMA | Assumption SE=mean/4 |
| Cost of urea and electrolytes test | 75.8183 (19.0) | GAMMA | Assumption SE=mean/4 |
| Cost of X-Ray | 42.23 (10.6) | GAMMA | Assumption SE=mean/4 |
| Cost of TB test | 8.95 (2.2) | GAMMA | Assumption SE=mean/4 |
| Cost of ANA test | 8.9507 (2.2) | GAMMA | Assumption SE=mean/4 |
| Cost of dsDNA test | 0 (0.0) | GAMMA | Assumption SE=mean/4 |
| *Admin costs* | | | |
| Cost of subcutaneous injection | 1.11 (0.3) | GAMMA | Assumption SE=mean/4 |
| Cost of intravenous infusion | 81.82 (20.5) | GAMMA | Assumption SE=mean/4 |
| *Physician costs* | | | |
| Cost of rheumatologist visit | 220.62 (55.2) | GAMMA | Assumption SE=mean/4 |
| Cost of dermatologist visit | 100.58 (25.1) | GAMMA | Assumption SE=mean/4 |
| Cost of GP visit | 33.86 (8.5) | GAMMA | Assumption SE=mean/4 |
| *AEs hospital costs* | | | |
| NMSC | 3858.07 (964.5) | GAMMA | Assumption SE=mean/4 |
| Lymphoma | 10345.71 (2586.4) | GAMMA | Assumption SE=mean/4 |
| Melanoma | 3966.44 (991.6) | GAMMA | Assumption SE=mean/4 |
| Sepsis | 7769.76 (1942.4) | GAMMA | Assumption SE=mean/4 |

| | | | |
|---|---|---|---|
| TB | 7110.13 (1777.5) | GAMMA | Assumption SE=mean/4 |
| Pneumonia | 4558.02 (1139.5) | GAMMA | Assumption SE=mean/4 |
| Skin and soft tissue infection | 4171.03 (1042.8) | GAMMA | Assumption SE=mean/4 |
| one and joint infection | 7245.83 (1811.5) | GAMMA | Assumption SE=mean/4 |
| Urinary tract infection | 3347.43 (836.9) | GAMMA | Assumption SE=mean/4 |
| *Health state costs* | | | |
| Kobelt HAQ regression constant | 636.56 (410.7) | NORMAL | Kobelt |
| Kobelt HAQ regression intercept | 2101.70 (739.7) | NORMAL | Kobelt |
| Corbett PASI cost uncontrolled psoriasis | 2871.95 (718.0) | GAMMA | Assumption SE=mean/4 |
| Corbett PASI cost controlled psoriasis | 81.03 (2.03) | GAMMA | Assumption SE=mean/4 |
| Kobelt cost adjustment factor | 0.85 (0.2) | BETA | Assumption SE=mean/4 |
| *Efficacy of BSC* | | | |
| PsARC | 30.60% | CODA | |
| PsARC and PASI75 | 5.04% | CODA | |
| PsARC and PASI90 | 1.77% | CODA | |
| PsARC and PASI100 | 0.61% | CODA | |
| HAQ reduction responders | 0.257 | CODA | |
| HAQ reduction non-responders | -0.009 | CODA | |
| PASI50 response | 17.40% | CODA | |
| PASI75 response | 6.40% | CODA | |
| PASI90 response | 2.20% | CODA | |
| PASI100 response | 0.70% | CODA | |
| *Treatment specific costs - Ixekizumab Q4W* | | | |
| PsARC | 53.00% | CODA | |
| PsARC and PASI75 | 46.65% | CODA | |
| PsARC and PASI90 | 34.40% | CODA | |
| PsARC and PASI 100 | 23.01% | CODA | |
| HAQ reduction responders | 0.506 | CODA | |
| HAQ reduction non-responders | 0.052 | CODA | |
| PASI50 response | 87.20% | CODA | |
| PASI75 response | 70.90% | CODA | |
| PASI90 response | 52.00% | CODA | |
| PASI100 response | 35.40% | CODA | |
| *Physician Visits - Induction period* | | | |
| Rheumatologist | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Dermatologist | 6.00 (1.50) | GAMMA | Assumption SE=mean/4 |
| GP | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Physician Visits - Maintenance therapy* | | | |
| Rheumatologist (annually) | 3.50 (0.875) | GAMMA | Assumption SE=mean/4 |
| Dermatologist (annually) | 2.00 (0.50) | GAMMA | Assumption SE=mean/4 |
| GP (annually) | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Induction period* | | | |
| Number of FBC | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of ESR | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |

| | | | |
|---|---|---|---|
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of dsDNA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Maintenance therapy* | | | |
| Number of FBC | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of ESR | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of dsANA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *AEs* | | | |
| Rate NMSC/patient year | 0.00 (0.000) | BETA | Assumption SE=mean/4 |
| Rate of malignancies/patient year | 0.00 (0.000) | BETA | Assumption SE=mean/4 |
| Rate of severe infections/patient year | 0.02 (0.004) | BETA | Assumption SE=mean/4 |
| *Treatment specific costs - Secukinumab 300 mg* | | | |
| PsARC | 54.10% | CODA | |
| PsARC and PASI75 | 40.50% | CODA | |
| PsARC and PASI90 | 26.50% | CODA | |
| PsARC and PASI 100 | 15.82% | CODA | |
| HAQ reduction responders | 0.561 | CODA | |
| HAQ reduction non-responders | 0.139 | CODA | |
| PASI50 response | 77.30% | CODA | |
| PASI75 response | 56.60% | CODA | |
| PASI90 response | 36.80% | CODA | |
| PASI100 response | 22.40% | CODA | |
| *Physician Visits - Induction period* | | | |
| Rheumatologist | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Dermatologist | 6.00 (1.50) | GAMMA | Assumption SE=mean/4 |
| GP | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Physician Visits - Maintenance therapy* | | | |
| Rheumatologist | 3.50 (0.875) | GAMMA | Assumption SE=mean/4 |
| Dermatologist (annually) | 6.50 (1.625) | GAMMA | Assumption SE=mean/4 |
| GP (annually) | 10.80 (2.70) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Induction period* | | | |
| Number of FBC | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of ESR | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 4.50 (1.125) | GAMMA | Assumption SE=mean/4 |
| Number of dsANA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *Monitoring - Maintenance therapy* | | | |
| Number of FBC | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of LFT | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |

| | | | |
|---|---|---|---|
| Number of ESR | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of U&E | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of X-Ray | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| Number of TB test | 1.00 (0.250) | GAMMA | Assumption SE=mean/4 |
| Number of ANA | 3.00 (0.750) | GAMMA | Assumption SE=mean/4 |
| Number of dsANA tests | 0.00 (0.000) | GAMMA | Assumption SE=mean/4 |
| *AEs* | | | |
| Rate NMSC/patient year | 0.00 (0.000) | BETA | Assumption SE=mean/4 |
| Rate of malignancies/patient year | 0.01 (0.001) | BETA | Assumption SE=mean/4 |
| Rate of severe infections/patient year | 0.02 (0.005) | BETA | Assumption SE=mean/4 |

AEs, adverse events; ANA, antinuclear antibody; BSC, best supportive care; CODA, convergence diagnostics and output analysis; dsDNA, double-stranded deoxyribonucleic acid; ESR, erythrocyte sedimentation rate; FBC, full blood count; HAQ, Health Assessment Questionnaire; LFT, liver function test; MD, medical doctor; NMSC, nonmelanoma skin cancers; PASI, Psoriasis Area and Severity Index; PASI50, 75, 90, 100, ≥50%, ≥75%, ≥90% or 100% reduction from baseline PASI; PsARC, Psoriatic Arthritis Response Criteria; Q4W, every 4 weeks; SE, standard error; TB, tuberculosis; U&E, urea and electrolyte.

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

| Section/item | Item No | Recommendation | Reported on page No/line No |
|---|---|---|---|
| **Title and abstract** | | | |
| Title | 1 | Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared. | Page 1/Lines 1-3 |
| Abstract | 2 | Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions. | Pages 2-3/Lines 33-58 |
| **Introduction** | | | |
| Background and objectives | 3 | Provide an explicit statement of the broader context for the study. | Page 5/Lines 75-97 |
| | | Present the study question and its relevance for health policy or practice decisions. | Pages 5-6/Lines 98-106 |
| **Methods** | | | |
| Target population and subgroups | 4 | Describe characteristics of the base case population and subgroups analysed, including why they were chosen. | Page 6/Lines 109-111 |
| Setting and location | 5 | State relevant aspects of the system(s) in which the decision(s) need(s) to be made. | Page 6/Lines 109-121 |
| Study perspective | 6 | Describe the perspective of the study and relate this to the costs being evaluated. | Page 9 /Line 182-184 |
| Comparators | 7 | Describe the interventions or strategies being compared and state why they were chosen. | Pages 5-6/Lines 98-106 |
| Time horizon | 8 | State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate. | Page 6 /Lines 115-117 |
| Discount rate | 9 | Report the choice of discount rate(s) used for costs and outcomes and say why appropriate. | Page 9/Lines 200-201<br>Page 10/Line 207 |
| Choice of health outcomes | 10 | Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed. | Page 8/Lines 152-180 |
| Measurement of effectiveness | 11a | *Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data. | N/A |
| | 11b | *Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data. | N/A |
| Measurement and valuation | 12 | If applicable, describe the population and methods used to elicit preferences for outcomes. | N/A |

| Section/item | Item No | Recommendation | Reported on page No/line No |
|---|---|---|---|
| of preference based outcomes | | | |
| Estimating resources and costs | 13a | *Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | N/A |
| | 13b | *Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. | Page 9/Lines 182-200 |
| Currency, price date, and conversion | 14 | Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate. | Page 9/Lines 182-200<br>Table 2 |
| Choice of model | 15 | Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended. | Page 6/Lines 115-123<br>Figure 1 |
| Assumptions | 16 | Describe all structural or other assumptions underpinning the decision-analytical model. | Page 6/Lines 112-113<br>Page 7/ Lines 141-148<br>Page 8/Lines 156-172 |
| Analytical methods | 17 | Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty. | Pages 9-10/Lines 202-220 |
| **Results** | | | |
| Study parameters | 18 | Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended. | Table 1<br>Supplementary Table 1 |

| Section/item | Item No | Recommendation | Reported on page No/line No |
|---|---|---|---|
| Incremental costs and outcomes | 19 | For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios. | Page 10/Lines 222-227<br>Table 3 |
| Characterising uncertainty | 20a | *Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective). | N/A |
| | 20b | *Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions. | Pages 10-11/Lines 228-241<br>Figures 4-6 |
| Characterising heterogeneity | 21 | If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information. | N/A |
| **Discussion** | | | |
| Study findings, limitations, generalisability, and current knowledge | 22 | Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge. | Pages 11-12/ Lines 243-274 |
| **Other** | | | |
| Source of funding | 23 | Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support. | Page 14/Line 288 |
| Conflicts of interest | 24 | Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations. | Page 14/Lines 290-292 |

For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement checklist