Treatment Patterns and Annual Drug Costs of Biologic Therapies Across Indications from the Humana Commercial Database

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ABSTRACT

BACKGROUND: A variety of biologic therapies are currently used for the treatment of inflammatory autoimmune diseases, including rheumatoid arthritis (RA), psoriasis (PsO), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). These diseases require long-term treatment, and information regarding the use and costs of biologic therapies can be valuable in making treatment and formulary decisions for clinicians and payers.

OBJECTIVE: To evaluate current utilization and annual costs of biologic therapies for treatment of RA, PsO, PsA, and AS in a real-world setting.

METHODS: This retrospective observational cohort analysis utilized data from the Humana commercial claims database. Eligible patients had an index (first) claim between February 1, 2008, and September 30, 2011, for abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, or ustekinumab and a diagnosis of RA, PsO, PsA, AS, or combination of these diseases. Patients with and without a claim for their index therapy within 180 days prior to their index dates were defined as continuing and new patients, respectively. Outcomes included 1-year rates of persistence; rates of restarting, discontinuing, or switching for patients who were not persistent; and annual costs. Costs were based on dose and the October 2013 wholesale acquisition cost (WAC). Total expenditure was calculated as the (total index biologic drug utilization × WAC) + (number of administrations × Medicare fee schedule) + Σ(biologic dose after discontinuation × associated WAC price).

RESULTS: Of 2,721 patients analyzed, 1,308 (48%) were new patients, and 1,413 (52%) were continuing patients. Across approved indications, the most commonly used biologics were adalimumab, etanercept, and infliximab. Continuing patients had higher rates of persistence on index therapy than new patients. The mean annual cost [SD] per treated patient for new patients across all indications was numerically lowest for adalimumab ($20,916 [$7,572]), followed by infliximab ($22,516 [$8,460]) and etanercept ($23,567 [$8,314]). The mean annual cost [SD] per treated patient for continuing patients across all indications was numerically lowest for etanercept ($21,508 [$6,769]), followed by infliximab ($22,852 [$11,674]) and adalimumab ($24,341 [$8,906]).

CONCLUSIONS: The tumor necrosis factor blockers adalimumab, etanercept, and infliximab were the most commonly used biologics across indications. New patients were less persistent than those continuing on therapy. Among new patients, adalimumab had the lowest mean annual cost per treated patient, and etanercept had the lowest mean annual cost per treated patient among those continuing on therapy.

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What is already known about this subject

- Treatment patterns and annual cost of therapies for the treatment of rheumatoid arthritis (RA) and psoriasis (PsO) using commercial claims data have been reported for the most commonly used biologic agents.
- Biologic therapies included in this study are also approved for the treatment of psoriatic arthritis (PsA) and ankylosing spondylitis (AS); however, few studies have reported on the treatment patterns and annual costs of treatment for these indications and therapies in a commercial claims-based data setting.

What this study adds

- This study reports treatment patterns and annual cost per treated patient for RA, PsO, PsA, and AS, and various combinations of these diseases for patients enrolled in a large commercial claims database.
- This study also reports data for biologic therapies that are recently approved for the indications in addition to the established biologics, which had lower utilization than established biologics in this analysis.

Rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and plaque psoriasis (PsO) are chronic, inflammatory, autoimmune diseases. Although these diseases are systemic in nature, tissue destruction is the result of dysregulation of innate and adaptive immunity in specific organs, such as joints and skin.[1,2] In addition to symptoms of tissue destruction, these autoimmune diseases have substantial negative impact on health-related quality of life.[3-5] Several biologic therapies that target specific components of the immune system are approved by the U.S. Food and Drug Administration (FDA) for the treatment of autoimmune diseases, including agents that target tumor necrosis factor (TNF; adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab); Cluster of Differentiation (CD) 20 (rituximab); interleukin (IL)-12 and IL-23 (ustekinumab); and CD80 and CD86 (abatacept; Table 1).

RA, PsA, AS, and PsO require long-term treatment and represent a significant clinical and economic burden for patients and payers. Patients with these chronic illnesses suffer from disability, loss of productivity, and a lifetime of expenses for

TABLE 1 Year of FDA Approval for Each Indication at the Time of Study and Mode of Administration for Biologic Agents Evaluated in Study

	Indication				
	RA	PsO	PsA	AS	Administration
Abatacept	2005				SC or IV
Adalimumab	2002	2008	2005	2006	SC
Certolizumab pegol	2008				SC
Etanercept	1998	2004	2002	2003	SC
Golimumab	2009		2009	2009	SC
Infliximab	1999	2006	2005	2004	IV
Rituximab	2006				IV
Ustekinumab		2009			SC

AS = ankylosing spondylitis; FDA = U.S. Food and Drug Administration; IV = intravenous; PsA=psoriatic arthritis; PsO = psoriasis; RA=rheumatoid arthritis; SC = subcutaneous.

their diseases.[6-8] Mean response rates to biologic therapies in patients with RA are 60% to 70%,[9] resulting in a substantial number of patients discontinuing therapy and switching to other biologic or nonbiologic therapies. Response rates vary by biologic agent and by indication. An evaluation of utilization patterns with biologic therapies in a real-world claims setting would assist payers with estimating the annual costs of discontinuing, restarting, and switching therapies in patients with these autoimmune diseases.

The purpose of this study was to describe 1-year utilization of the biologic agents abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, and ustekinumab for the treatment of RA, PsA, AS, and PsO. Administrative claims data were used to assess utilization patterns for commercially insured patients in the Humana commercial claims database, and annual costs were estimated using wholesale acquisition cost (WAC) based on utilization.

Methods

Study Design and Setting

This study utilized data from Humana Inc., a large U.S. health insurance company. The Humana database consists of claims data from approximately 12 million former or current members of health plans (medical and pharmacy coverage). Most members reside in the midwestern and southern regions of the United States; the West and Northeast are sparsely represented. Humana's Statistical Analysis System database, containing enrollment, medical, and pharmacy claims data, was the source for all study data. All data sources were merged using de-identified member identification. The finalized protocol was approved by an independent institutional review board, Schulman Associates IRB, Cincinnati, Ohio.

Data from August 1, 2007, through September 30, 2012, were used in the analysis (Appendix A, available in online article). The index date was defined as the date of the first pharmacy or medical claim for abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, or ustekinumab during the identification period (February 1, 2008, through September 30, 2011) preceded by at least 6 months of continuous medical and pharmacy enrollment (August 1, 2007, through January 31, 2008). The follow-up period was 1 year following the index date (February 1, 2008, through September 30, 2012).

Eligibility Criteria

To be eligible for inclusion in this analysis, patients were aged 18 to 63 years and had at least 1 (index) claim for 1 of the biologic agents of interest between February 1, 2008, and September 30, 2011. Eligible patients had a diagnosis of RA (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code: 714.0x), PsO (ICD-9-CM: 696.1), PsA (ICD-9-CM: 696.0), AS (ICD-9-CM: 720.0), or a combination of these conditions within the 180 days prior to or 30 days after the index date. Patients were categorized by diagnosis or combination of diagnoses. Patients were required to have continuous enrollment in the same plan for at least 360 days following the index date. Patients with claims for their index biologics in the 180 days prior to their index dates were considered continuing on therapy, and patients without claims in the 180 days prior to their index dates were considered new initiators. Patients were ineligible for the study if they had index claims for a biologic before it received FDA approval for the indication (which was assumed to be an off-label use); had a diagnosis for another condition for which any of these biologics are approved, including juvenile idiopathic arthritis (ICD-9-CM: 714.3x), non-Hodgkin lymphoma (ICD-9-CM: 200.xx, 202.xx), or chronic lymphocytic leukemia (ICD-9-CM: 204.1x) within 180 days prior to or 30 days after the index date; had a claim for >1 biologic of interest on the index date; or had incomplete demographic information. Patients whose doses exceeded twice the maximum recommended dose for any indication were excluded from the analysis, since these were considered to be data errors in the claims database.

Outcomes

Study outcomes included the proportions of new and continuing patients receiving biologic agents of interest and the calculated annual cost per treated patient. Patients who continued on their index biologics without a ≥45-day gap in therapy until the end of the follow-up period (360 days based on 30-day months, or approximately 1 year) and without a switch to another biologic agent were considered persistent.

Patients who were not persistent on their index biologics were classified as either restarting their index therapy if they had a gap in therapy of ≥45 days after the end of the days' supply of the last dispensed prescription and then had another claim for the index biologic, discontinuing biologic therapy completely, or switching to another biologic of interest. This gap length was selected based on the most common prescription period (30 days) plus 15 days to avoid misclassification of patients who had a break in therapy but did not discontinue treatment. The expected clinical benefit (ECB) was determined based on days' supply for self-administered agents and the longest recommended dosing interval for physician-administered agents. Only the first episode of restarting, discontinuing, or switching was considered for this analysis.

The mean annual cost per treated patient included the cost of the index biologic and the cost of any biologic used after discontinuation of the index agent. It was calculated as the total expenditures divided by the number of treated patients for each agent. Drug prices were based on the October 2013 WAC[10] (Appendix B, available in online article), and drug administration costs were based on the 2012 Medicare fee schedule.[11] Total expenditure was calculated as the following: (total index biologic drug utilization × WAC) + (number of administrations × Medicare fee schedule) + Σ(biologic dose after discontinuation × associated WAC price). Dose per claim was calculated based on the quantity (for National Drug Code [NDC] claims) or service units (for J-Code claims). Doses were expressed as follows: abatacept—250 milligram (mg) unit with ECB of 28 days; adalimumab—20 mg unit with ECB of 14 days for each 40 mg syringe; certolizumab pegol—400 mg unit with ECB of 28 days; etanercept—25 mg unit with ECB of 7 days for 50 mg syringe; golimumab—50 mg unit with ECB of 28 days; infliximab—100 mg unit with ECB of 56 days for RA, PsO, and PsA and ECB of 42 days for AS based on maintenance dose; rituximab—100 mg unit with ECB of 168 days; and ustekinumab—45 mg unit with ECB of 84 days.

Statistical Considerations

Descriptive analyses were conducted for patients in the abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab, and ustekinumab cohorts by indication. Additional analyses were conducted for new initiators and for continuing patients. For categorical measures, the distribution of patients across the categories of each characteristic was described using cross-tabulation analysis, showing the frequency and percentage of the total number of study patients observed in each category by biologic, new initiators, continuing patients, and for each disease category. For quantitative and count measures, descriptive statistics (means, standard deviations [SD]) were computed.

Results

Patients

A total of 2,721 patients were eligible for inclusion in the analysis (Figure 1). Of these, 1,308 (48.1%) patients were new to biologic therapy, and 1,413 (51.9%) were continuing on biologic therapy. Over half of the patients had a diagnosis of RA only (53.1%), followed by PsO only (21.2%), PsO with PsA (7.6%), and PsA only (6.3%). The percentage of females was 80% for RA, 43% for PsO, 51% for PsA, and 27% for AS. Most patients were enrolled in a preferred provider organization, and most were from the southern region of the United States (Table 2).

Treatment Patterns

The most commonly used biologics were etanercept (prescribed to 48.3% of all patients), adalimumab (prescribed to 34.7% of all patients), and infliximab (prescribed to 11.2% of all patients), which were prescribed to 92.6% of new patients and 95.6% of continuing patients across approved indications (Table 3). Most continuing patients were persistent on their index biologic at 1 year (range 56% to 64% for treatment groups with >50 patients), and rates of discontinuation from the index biologic were higher for new patients (range 30% to 35% for treatment groups >50 patients) than for continuing patients (range 11% to 18% for treatment groups >50 patients). The proportion of patients who restarted their index biologics after a 45-day gap in therapy varied by agent and indication and, with some exceptions, appeared to be similar between new and continuing patients. Relatively few patients switched from their index biologics to another biologic.

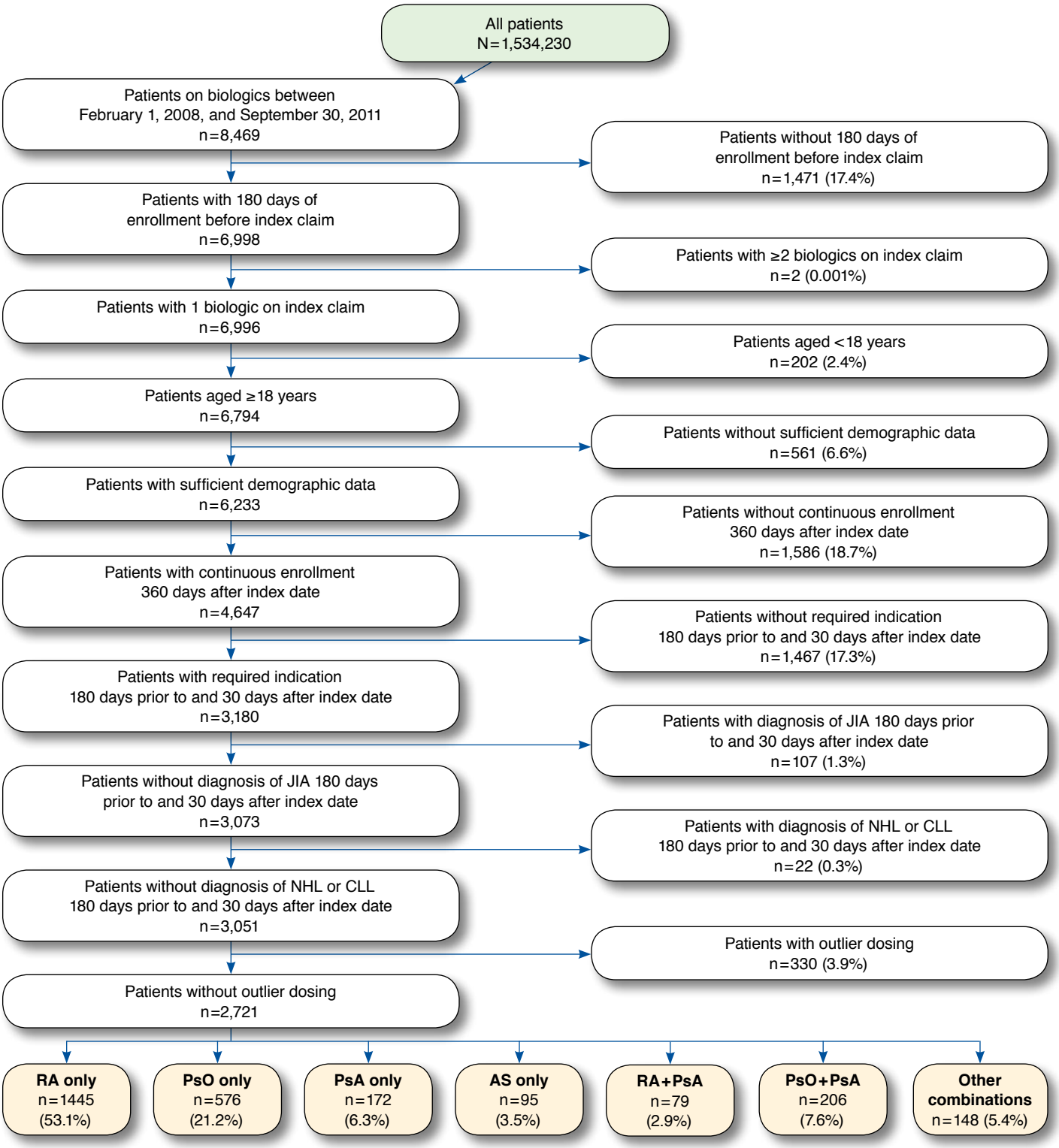
Duration of Treatment

The duration of treatment over 1 year varied for each treatment group across indications and tended to be numerically longer for continuing patients (Table 4). Across indications for all new patients, the range of mean treatment duration was 5.8 to 8.2 months for etanercept, 7.3 to 8.1 months for adalimumab, and 1.8 to 10.3 months for infliximab. Across all indications for continuing patients, the mean treatment duration ranged from 7.7 to 9.5 months for etanercept, 7.8 to 9.3 months for adalimumab, and 9.2 to 11.3 months for infliximab.

Annual Cost Per Treated Patient

The mean annual cost per treated patient for new patients across all indications ranged from $8,930 to $47,701 (Table 5). For continuing patients, the mean annual cost per treated patient ranged from $14,894 to $180,881. For patients with RA, the mean annual cost per treated patient for new patients ranged from $8,930 to $21,638 and for continuing patients ranged from $14,894 to $30,414. For patients with PsO, the mean annual cost per treated patient for new patients ranged from $22,122 to $47,701 and for continuing patients ranged

FIGURE 1 Patient Selection



AS = ankylosing spondylitis; CLL = chronic lymphocytic leukemia; JIA = juvenile idiopathic arthritis; NHL = non-Hodgkin lymphoma; PsA = psoriatic arthritis; PsO = psoriasis; RA = rheumatoid arthritis.

TABLE 2 Patient Demographics and Health Plan Characteristics at Index Date

	RA Only N = 1,445	PsO Only N = 576	PsA Only N = 172	AS Only N = 95	RA + PsA N = 79	PsO + PsA N = 206	Other Combinations N = 148
Age, mean years [SD]	49.5 [10.6]	44.0 [11.4]	48.3 [8.9]	42.1 [11.3]	48.5 [10.2]	46.5 [11.2]	47.0 [10.5]
Sex, n female (%)	1,156 (80.0)	247 (42.9)	87 (50.6)	26 (27.4)	45 (57.0)	94 (45.6)	86 (58.1)
Plan type, n (%)							
PPO	659 (45.6)	274 (47.6)	78 (45.3)	48 (50.5)	29 (36.7)	104 (50.5)	63 (42.6)
HMO	389 (26.9)	119 (20.7)	35 (20.3)	15 (15.8)	26 (32.9)	43 (20.9)	37 (25.0)
POS	342 (23.7)	151 (26.2)	50 (29.1)	28 (29.5)	21 (26.6)	48 (23.3)	41 (27.7)
Indemnity plan	55 (3.8)	32 (5.6)	9 (5.2)	4 (4.2)	3 (3.8)	11 (5.3)	7 (4.7)
Geographic region, n (%)							
Northeast	5 (0.3)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.4)
Midwest	398 (27.5)	140 (24.3)	39 (22.7)	32 (33.7)	15 (19.0)	42 (20.4)	30 (20.3)
South	960 (66.4)	389 (67.5)	124 (72.1)	57 (60.0)	61 (77.2)	152 (73.8)	109 (73.6)
West	82 (5.7)	45 (7.8)	9 (5.2)	6 (6.3)	3 (3.8)	12 (5.8)	7 (4.7)
Prescribing physician specialty, n (%)							
FP/GP	8 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Internal medicine	112 (7.8)	10 (1.7)	15 (8.7)	10 (10.5)	5 (6.3)	9 (4.4)	8 (5.4)
Dermatology	5 (0.3)	382 (66.3)	4 (2.3)	0 (0.0)	0 (0.0)	58 (28.2)	8 (5.4)
Rheumatology	932 (64.5)	10 (1.7)	114 (66.3)	65 (68.4)	56 (70.9)	84 (40.8)	87 (58.8)
Other	178 (12.3)	106 (18.4)	24 (14.0)	10 (10.5)	9 (11.4)	33 (16.0)	25 (16.9)
Unknown	210 (14.5)	67 (11.6)	15 (8.7)	10 (10.5)	9 (11.4)	21 (10.2)	20 (13.5)
Treatment status, n (%)							
New	676 (46.8)	289 (50.2)	66 (38.4)	45 (47.4)	37 (46.8)	109 (52.9)	86 (58.1)
Continuing	769 (53.2)	287 (49.8)	106 (61.6)	50 (52.6)	42 (53.2)	97 (47.1)	62 (41.9)

AS = ankylosing spondylitis; FP/GP = family practice/general practice; HMO = health maintenance organization; POS = point of service; PPO = preferred provider organization; PsA = psoriatic arthritis; PsO = psoriasis; RA = rheumatoid arthritis; SD = standard deviation.

from $22,474 to $10,881. For patients with PsO + PsA, the mean annual cost per treated patient for new patients ranged from $19,920 to $26,608 and for continuing patients ranged from $14,690 to $25,672. Treatment with certolizumab pegol was associated with lower cost per treated patient than the other biologics; however, it was only used by 11 patients.

Discussion

In this analysis of real-world utilization data for biologic agents used in the treatment of RA, PsO, PsA, and AS, etanercept was the most commonly used agent, followed by the TNF blockers adalimumab and infliximab. Despite the availability of multiple options for patients with RA, these TNF blockers were used to treat the majority of patients. For patients with PsO, the only FDA-approved biologic therapies that were available during the course of the study consisted of the TNF blockers adalimumab, etanercept, and infliximab, and the IL-12/IL-23 blocker ustekinumab. Across new and continuing patients with PsO, only 4 patients received infliximab, and 8 patients received ustekinumab. One potential reason for low utilization of infliximab could be the route of administration, since intravenous dosing requires clinic visits, whereas the other TNF blockers are self-administered at home. In this study, newer biologic therapies (certolizumab pegol, golimumab, and ustekinumab) were not utilized to the same extent as the older, established TNF blockers (adalimumab, etanercept, and infliximab).

This study examined rates of persistence, restarting, discontinuing, and switching from index biologic therapy. Caution is warranted in the interpretation of these results because of the low rate of utilization for non-TNF blockers. Among the most commonly used TNF blockers, utilization patterns were generally similar for new and continuing patients with RA. Rates of switching from index TNF blocker were low across indications. Treatment duration by diagnosis among the agents must be interpreted with caution because there were relatively few patients utilizing specific drugs for some diagnoses (e.g., rituximab for RA and infliximab for some disease combinations).

We used a cost analysis to evaluate biologic utilization data from a national health plan across multiple disease indications. This approach is useful for payers because of the comparison of utilization by indication. In addition, these analyses are useful for specialty pharmacy products rather than traditional per-member-per-month (PMPM) methodologies because utilization may substantially influence PMPM analyses. For example, greater utilization and duration of use for a specific medication will increase the PMPM cost for that medication, whereas lower utilization and duration of use will lower the PMPM cost. This is particularly important in the current era of comparative effectiveness research in which PMPM may fall out of favor

TABLE 3 Index Biologic Therapies and Treatment Patterns by Each Biologic over 360 Days

	ABA	ADA	CZP	ETN	GLB	INF	RTX	UST
New patients								
RA only, n	42	238	9	280	10	71	26	NI
Persistent,[a] n (%)	17 (40.5)	102 (42.9)	2 (22.2)	128 (45.7)	2 (20.0)	29 (40.8)	11 (42.3)	
Restarted, n (%)	8 (19.0)	29 (12.2)	2 (22.2)	56 (20.0)	2 (20.0)	14 (19.7)	5 (19.2)	
Discontinued, n (%)	15 (35.7)	85 (35.7)	5 (55.6)	85 (30.4)	5 (50.0)	24 (33.8)	10 (38.5)	
Switched, n (%)	2 (4.8)	22 (9.2)	0 (0.0)	11 (3.9)	1 (10.0)	4 (5.6)	0 (0.0)	
PsO only, n	NI	126	NI	155	NI	1	NI	7
Persistent,[a] n (%)		63 (50.0)		52 (33.5)		0 (0.0)		2 (28.6)
Restarted, n (%)		19 (15.1)		46 (29.7)		1 (100.0)		5 (71.4)
Discontinued, n (%)		39 (31.0)		51 (32.9)		0 (0.0)		0 (0.0)
Switched, n (%)		5 (4.0)		6 (3.8)		0 (0.0)		0 (0.0)
PsA only, n	NI	36	NI	24	1	5	NI	0
Persistent,[a] n (%)		13 (36.1)		12 (50.0)	1 (100.0)	1 (20.0)		
Restarted, n (%)		7 (19.4)		5 (20.8)	0 (0.0)	0 (0.0)		
Discontinued, n (%)		15 (41.7)		5 (20.8)	0 (0.0)	3 (60.0)		
Switched, n (%)		1 (2.8)		2 (8.4)	0 (0.0)	1 (20.0)		
AS only, n	NI	23	NI	20	1	1	NI	NI
Persistent,[a] n (%)		10 (43.5)		12 (60.0)	1 (100.0)	0 (0.0)		
Restarted, n (%)		6 (26.1)		4 (20.0)	0 (0.0)	0 (0.0)		
Discontinued, n (%)		6 (26.1)		4 (20.0)	0 (0.0)	1 (100.0)		
Switched, n (%)		1 (4.3)		0 (0.0)	0 (0.0)	0 (0.0)		
RA+PsA, n	NI	15	0	14	0	8	0	NI
Persistent,[a] n (%)		6 (40.0)		4 (28.6)		3 (37.5)		
Restarted, n (%)		4 (26.7)		2 (14.3)		2 (25.0)		
Discontinued, n (%)		3 (20.0)		8 (57.1)		2 (25.0)		
Switched, n (%)		2 (13.3)		0 (0.0)		1 (12.5)		
PsO+PsA, n	NI	49	NI	52	0	8	NI	0
Persistent,[a] n (%)		24 (49.0)		26 (50.0)		4 (50.0)		
Restarted, n (%)		9 (18.4)		10 (19.2)		1 (12.5)		
Discontinued, n (%)		14 (28.6)		9 (17.3)		2 (25.0)		
Switched, n (%)		2 (4.0)		7 (13.4)		1 (12.5)		
Other combinations, n	1	47	0	29	0	9	0	0
Persistent,[a] n (%)	1 (100.0)	21 (44.7)		13 (44.8)		4 (44.4)		
Restarted, n (%)	0 (0.0)	9 (19.1)		4 (13.8)		1 (11.1)		
Discontinued, n (%)	0 (0.0)	15 (31.9)		11 (37.9)		4 (44.4)		
Switched, n (%)	0 (0.0)	2 (4.3)		1 (3.4)		0 (0.0)		
Continuing patients								
RA only, n	37	231	2	338	4	145	12	NI
Persistent,[a] n (%)	22 (59.5)	138 (59.7)	1 (50.0)	204 (60.4)	1 (25.0)	92 (63.4)	6 (50.0)	
Restarted, n (%)	5 (13.5)	46 (19.9)	0 (0.0)	85 (25.1)	2 (50.0)	27 (18.6)	5 (41.7)	
Discontinued, n (%)	9 (24.3)	42 (18.2)	0 (0.0)	40 (11.8)	1 (25.0)	18 (12.4)	1 (8.3)	
Switched, n (%)	1 (2.7)	5 (2.2)	1 (50.0)	9 (2.7)	0 (0.0)	8 (5.5)	0 (0.0)	
PsO only, n	NI	69	NI	214	NI	3	NI	1
Persistent,[a] n (%)		43 (62.3)		102 (47.7)		2 (66.7)		1 (100.0)
Restarted, n (%)		15 (21.7)		64 (29.9)		0 (0.0)		0 (0.0)
Discontinued, n (%)		9 (13.0)		39 (18.2)		0 (0.0)		0 (0.0)
Switched, n (%)		2 (2.9)		9 (4.2)		1 (33.3)		0 (0.0)
PsA only, n	NI	28	NI	67	3	8	NI	NI
Persistent,[a] n (%)		14 (50.0)		37 (55.2)	3 (100.0)	5 (62.5)		
Restarted, n (%)		6 (21.4)		19 (28.4)	0	2 (25.0)		
Discontinued, n (%)		7 (25.0)		10 (14.9)	0	1 (12.5)		
Switched, n (%)		1 (3.6)		1 (1.5)	0	0 (0.0)		

TABLE 3 Index Biologic Therapies and Treatment Patterns by Each Biologic over 360 Days *(continued)*

	ABA	ADA	CZP	ETN	GLB	INF	RTX	UST
Continuing patients								
AS only, n	NI	14	NI	28	0	8	NI	NI
Persistent,[a] n (%)		7 (50.0)		19 (67.9)		6 (75.0)		
Restarted, n (%)		5 (35.7)		4 (14.3)		1 (12.5)		
Discontinued, n (%)		2 (14.3)		5 (17.9)		0 (0.0)		
Switched, n (%)		0 (0.0)		0 (0.0)		1 (12.5)		
RA+PsA, n	1	14	0	14	0	13	0	NI
Persistent,[a] n (%)	1 (100.0)	8 (57.1)		10 (71.4)		8 (61.5)		
Restarted, n (%)	0 (0.0)	3 (21.4)		2 (14.3)		2 (15.4)		
Discontinued, n (%)	0 (0.0)	1 (7.1)		1 (7.1)		1 (7.7)		
Switched, n (%)	0 (0.0)	2 (14.2)		1 (7.1)		2 (15.4)		
PsO+PsA, n	NI	39	NI	50	1	7	NI	0
Persistent,[a] n (%)		24 (61.5)		25 (50.0)	0 (0.0)	6 (85.7)		
Restarted, n (%)		8 (20.5)		11 (22.0)	0 (0.0)	1 (14.3)		
Discontinued, n (%)		7 (17.9)		12 (24.0)	1 (100.0)	0 (0.0)		
Switched, n (%)		0 (0.0)		2 (4.0)	0 (0.0)	0 (0.0)		
Other combinations, n	0	15	0	28	1	18	0	0
Persistent,[a] n (%)		10 (66.7)		17 (60.7)	0 (0.0)	10 (55.6)		
Restarted, n (%)		0 (0.0)		8 (28.6)	1 (100.0)	5 (27.8)		
Discontinued, n (%)		4 (26.7)		3 (10.7)	0 (0.0)	3 (16.7)		
Switched, n (%)		1 (6.7)		0 (0.0)	0 (0.0)	0 (0.0)		

[a]*Data represent patients who were persistent on index medication for 1 year.*

ABA = abatacept; ADA = adalimumab; AS = ankylosing spondylitis; CZP = certolizumab pegol; ETN = etanercept; GLB = golimumab; INF = infliximab; NI = not indicated; PsA = psoriatic arthritis; PsO = psoriasis; RA = rheumatoid arthritis; RTX = rituximab; UST = ustekinumab.

TABLE 4 Duration of Treatment with Index Biologic Therapies

Duration of Treatment, Mean Months [SD]	ABA	ADA	CZP	ETN	GLB	INF	RTX	UST
New patients								
RA only	8.0 [3.8]	7.5 [3.9]	5.8 [4.5]	7.9 [3.9]	5.4 [3.7]	10.5 [5.2]	17.2 [7.0]	NI
PsO only	NI	8.1 [3.6]	NI	7.1 [3.5]	NI	6.4 [0.0]	NI	7.3 [3.3]
PsA only	NI	7.3 [3.9]	NI	7.7 [3.6]	11.5 [0.0]	9.5 [3.5]	NI	NI
AS only	NI	7.9 [3.7]	NI	8.2 [3.8]	11.1 [0.0]	1.8 [0.0]	NI	NI
RA+PsA	IBNP	7.7 [4.1]	IBNP	5.8 [4.2]	IBNP	10.2 [4.0]	IBNP	NI
PsO+PsA	NI	8.2 [4.0]	NI	8.2 [3.6]	IBNP	11.2 [3.3]	NI	IBNP
Other combinations	12.9 [0.0]	8.0 [3.5]	IBNP	7.6 [3.6]	IBNP	10.5 [3.5]	IBNP	IBNP
Continuing patients								
RA only	9.1 [3.4]	8.8 [3.4]	7.3 [9.1]	8.5 [3.2]	8.1 [1.9]	11.9 [4.4]	20.7 [7.8]	NI
PsO only	NI	9.5 [3.2]	NI	7.7 [3.6]	NI	13.5 [9.2]	NI	11.2 [0.0]
PsA only	NI	8.0 [3.7]	NI	8.4 [3.4]	11.5 [0.5]	11.5 [2.4]	NI	NI
AS only	NI	7.9 [4.4]	NI	9.2 [3.3]	IBNP	12.4 [4.1]	NI	NI
RA+PsA	11.0 [0.0]	8.3 [4.1]	IBNP	9.8 [3.5]	IBNP	12.4 [4.8]	IBNP	NI
PsO+PsA	NI	8.8 [3.5]	NI	8.2 [3.3]	8.9 [0.0]	12.1 [2.0]	NI	IBNP
Other combinations	IBNP	8.3 [4.0]	IBNP	8.6 [2.9]	9.2 [0.0]	11.9 [3.2]	IBNP	IBNP

ABA = abatacept; ADA = adalimumab; AS = ankylosing spondylitis; CZP = certolizumab pegol; ETN = etanercept; GLB = golimumab; IBNP = indicated but not prescribed; INF = infliximab; NI = not indicated; PsA = psoriatic arthritis; PsO = psoriasis; RA = rheumatoid arthritis; RTX = rituximab; SD = standard deviation; UST = ustekinumab.

because of increased demands for more sophisticated and precise analyses as part of the formulary decision-making process. Many payers must resort to using pharmacy claims data only, which do not provide information on diagnosis. In our study, rituximab use was low, but this drug has other indications (i.e., cancer) that may not be filtered out of traditional pharmacy claims utilization analyses.

Other recent analyses also used claims data to examine annual costs of TNF-blocker therapy for patients with RA, PsO, PsA, and AS utilizing methodologies similar to ours.[12-14] The most recent of

TABLE 5 Mean Annual Cost Per Treated Patient with Biologic Therapies[a]

Mean Cost [SD]	ABA	ADA	CZP	ETN	GLB	INF	RTX	UST
New patients								
RA only	13,657 [6,873]	19,936 [7,829]	8,930 [9,251]	20,690 [7,416]	15,787 [7,058]	21,638 [9,045]	20,711 [8,627]	NI
PsO only	NI	22,761 [7,521]	NI	29,122 [9,590]	NI	47,701[b]	NI	35,490 [15,441]
PsA only	NI	20,845 [7,765]	NI	24,896 [6,584]	29,486[b]	20,351 [4,994]	NI	NI
AS only	NI	18,691 [7,100]	NI	20,068 [6,809]	29,403[b]	19,553[b]	NI	NI
RA + PsA	IBNP	20,984 [7,166]	IBNP	15,504 [7,315]	IBNP	26,135 [7,452]	IBNP	NI
PsO + PsA	NI	24,280 [7,268]	NI	26,608 [8,388]	IBNP	19,920 [6,493]	NI	IBNP
Other combinations	22,164[b]	18,552 [6,552]	IBNP	21,417 [6,119]	IBNP	27,269 [8,281]	IBNP	IBNP
Continuing patients								
RA only	16,596 [6,973]	23,169 [8,099]	14,894[18,231[c]]	20,677 [5,783]	19,990 [4,242]	21,992 [11,893]	30,414 [12,976]	NI
PsO only	NI	26,229 [7,082]	NI	22,474 [8,230]	NI	31,094 [17,188]	NI	180,881[b]
PsA only	NI	23,183 [11,655]	NI	20,437 [6,673]	28,713 [1,320]	19,548 [3,139]	NI	NI
AS only	NI	22,522 [8,590]	NI	23,609 [7,154]	IBNP	25,608 [9,056]	NI	NI
RA+PsA	19,911[b]	24,195 [11,376]	IBNP	23,070 [6,345]	IBNP	30,168 [11,542]	IBNP	NI
PsO+PsA	NI	25,762 [11,550]	NI	22,721 [5,994]	22,407[b]	14,690 [7,334]	NI	IBNP
Other combinations	IBNP	34,006 [13,096]	IBNP	21,676 [6,357]	9,959[b]	26,549 [11,831]	IBNP	IBNP

[a]*Data represent mean annual cost per treated patient in U.S. dollars.*
[b]*Data are from a single patient so SD was not calculated.*
[c]*Data are from only 2 patients so SD was higher than the mean cost.*
ABA = abatacept; ADA = adalimumab; AS = ankylosing spondylitis; CZP = certolizumab pegol; ETN = etanercept; GLB = golimumab; IBNP = indicated but not prescribed; INF = infliximab; NI = not indicated; PsA = psoriatic arthritis; PsO = psoriasis; RA = rheumatoid arthritis; RTX = rituximab; SD = standard deviation; UST = ustekinumab.

these analyses showed that annual costs for new RA patients were $15,828 for etanercept, $17,250 for adalimumab, and $19,397 for infliximab.[13] These annual costs were significantly lower compared with the Humana claims data presented here. One potential explanation may be price changes, since the Humana claims database included more recent data (2008-2012) than the dataset used by Schabert et al. (2008-2010).[13] Additionally, patients in the prior study may have had different rates of persistence or higher rates of dose escalation than those in our study. Results from an earlier study (using 2005-2009 data) showed similar trends in ranking of TNF blockers by annual cost.[12]

Health plans must manage both new and continuing patients (patient churn) for any disease, which is especially important in high cost, high impact, specialty pharmacy medications. The ratio of new and continuing patients may impact persistence and therefore ultimately impact costs. In our study, continuing patients across all indications had higher rates of persistence on their index agents than new patients, but annual costs were not necessarily higher.

A strength of this analysis was that dosing was based on real-world utilization. In addition, the use of total units dispensed as the basis of calculating costs captures dose changes over time. This methodology also allows for the incorporation of gaps to adjust for missed refills and costs that may not always be reported in studies with rigorous dosing schedules. In addition, algorithms were created for each drug to allow for the route of administration in order to minimize errors associated with claims adjudication for infusion products. These considerations within the confines of a budget impact model can help inform formulary decision makers to compare results from the budget impact model and their own analyses.

Limitations

A limitation of this analysis was our inability to document disease severity from the pharmacy claims data, nor did our analysis compensate for clinical and demographic differences in patients across indications. Approximately one-third of the population of patients on biologics during the study period were excluded because they did not have a qualified indication 180 days prior to and 30 days after the index date. The reason for lack of diagnosis was unknown but could have been because patients did not have a medical visit during that window. Data for duration of treatment were censored at 1 year and could not be extrapolated to longer periods based on this analysis. The study was limited to a U.S. managed care population and may not be generalizable to patients on Medicare or non-U.S. payers and patients. In addition, we did not account for estimates of drug acquisition costs including rebates, discounts, and price concessions that are common with branded products. Actual costs to a plan may vary based on negotiated prices. In addition, the limited utilization of newer agents led to very small sample sizes for these medications, and thus, the estimates of cost per treated patient for those agents may not be as robust as for the agents with larger sample sizes.

Conclusions

Treatment patterns for biologic therapies based on commercial claims data provide useful information to payers for formulary cost management. Cost should be an important consideration in making formulary decisions, and the results of this study may be useful to payers to evaluate annual costs in the real-world setting. Utilization of new biologic agents was very low in this analysis, whereas the established TNF blockers adalimumab, etanercept, and infliximab were commonly used for the treatment of RA, PsO, PsA, AS, and combinations of these conditions.

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DISCLOSURES

This study was sponsored by Immunex, a wholly owned subsidiary of Amgen Inc., and by Wyeth, which was acquired by Pfizer in October 2009. Dufour is a current employee of Comprehensive Health Insights, Inc., and at the time of this study, Howe and Ten Eyck were employed by Comprehensive Insights, which received funding from Amgen Inc. for this study. Shah and Harrison are employees and shareholders of Amgen Inc.

Study concept and design were contributed by Shah, Harrison, Howe, and Ten Eyck, with assistance from Dufour. Data were collected by Ten Eyck and Dufour and interpreted by Howe, Harrison, Ten Eyck, and Shah, with assistance from Dufour. The manuscript was written by Howe, Shah, and Harrison, with assistance from Ten Eyck and Dufour, and revised by Howe, Shah, Harrison, Dufour, and Ten Eyck.

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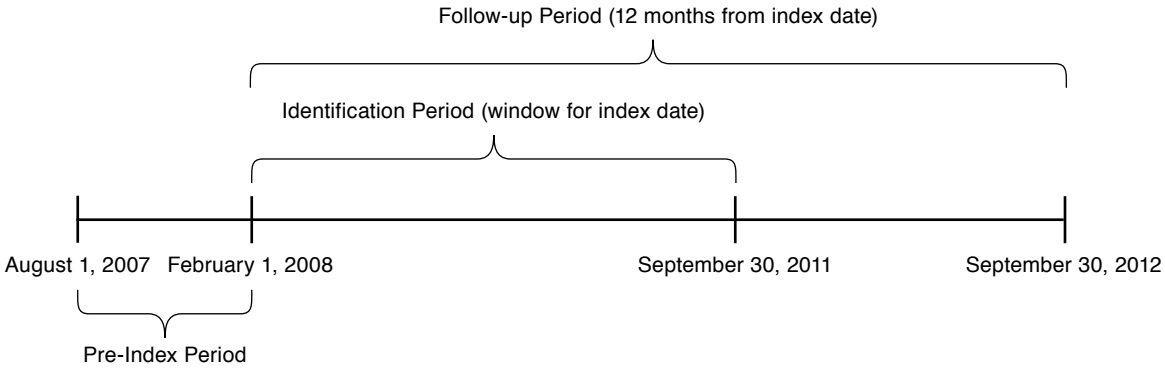
APPENDIX A Identification of Study Periods



APPENDIX B October 2013 Wholesale Acquisition Costs Used in Study

Biologic Agent	Package Size (mg)	Price Per Package ($)
Abatacept	250	643.68
Adalimumab	80	2,341.08
Certolizumab pegol	400	2,519.70
Etanercept	200	2,363.60
Golimumab	50	2,535.60
Infliximab	100	843.55
Rituximab	100	667.73
Ustekinumab	45	6,897.65