ORIGINAL RESEARCH

Biologic Disease-Modifying Antirheumatic Drugs in a National, Privately Insured Population: Utilization, Expenditures, and Price Trends

Christopher B. Atzinger, MS, PhD candidate; Jeff J. Guo, BPharm, PhD

BACKGROUND: Spending on biologic drugs is a significant driver of drug expenditures for payers in private health plans. Biologic disease-modifying antirheumatic drugs (DMARDs) are some of the most effective and costly treatments in a physician's arsenal. Understanding the total annual expenditure, the average cost per prescription, and the impact of cost-sharing is important for drug benefit managers.

OBJECTIVE: To assess drug utilization, expenditures, out-of-pocket (OOP) cost, and price trends of biologic DMARDs in patients with rheumatoid arthritis (RA) in a large managed care organization.

METHODS: We conducted a retrospective database analysis of pharmacy claims data from January 2004 to December 2013 using the Optum Clinformatics Data Mart database, which covers 13.3 million lives. Pharmacy claims for 40,373 patients with RA were identified during the study period. In all, 9 biologic DMARDs approved for the treatment of RA, including infliximab, etanercept, adalimumab, certolizumab, golimumab, tocilizumab, anakinra, abatacept, and rituximab, and 1 nonbiologic oral, small molecule–targeted synthetic drug, tofacitinib, were included in this study. Descriptive statistics were used to analyze the total annual number of prescriptions, the total annual expenditures, the average annual cost per drug (a proxy of drug price), and the average OOP cost (copay plus deductible and coinsurance). All measurements were also stratified by study drugs and by insurance type.

RESULTS: Of the 40,373 patients with RA included in the study, approximately 76% were female (mean age, 55 years at diagnosis). Approximately 77% of the patients were white, and almost 48% lived in the South or Midwest region of the United States. Approximately 62% of patients had a point of service insurance plan. Expenditures on biologic DMARDs increased from $166 million in 2004 to $243 million in 2013, and the number of prescriptions and refills increased from 59,960 in 2004 to 105,295 in 2013. Prescriptions for biologic DMARDs increased more than 20% per patient from 2004 to 2013. The average cost per prescription remained relatively unchanged, at approximately $2300 per prescription, but the OOP expenditures increased from $36 (2.5%) per prescription to $128 (7%) during the study period. The OOP expenditures increased the most in HMO plans and in plans categorized as other (284% and 388%, respectively).

CONCLUSIONS: Spending on biologic DMARDs has been primarily driven by an increase in prescribing rates, as the average amount reimbursed per prescription remained relatively unchanged over time, despite a regular annual increase to the average wholesale acquisition cost of 2% to 10%. The OOP burden for patients has increased, but this does not appear to have limited the use of biologic DMARDs. The entrance of new biologic and nonbiologic DMARDs into the market in the past few years is eroding the market share for several established drugs, and may lead to different results, warranting a study of new trends.

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KEY WORDS: biologic disease-modifying antirheumatic drugs, drug utilization, expenditures, out-of-pocket cost, price trends, rheumatoid arthritis

Mr Atzinger is a graduate student, College of Pharmacy, University of Cincinnati, OH, and Associate Director, Pharmerit International, Bethesda, MD; Dr Guo is Professor, Pharmacoepidemiology & Pharmacoeconomics, College of Pharmacy, University of Cincinnati.

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown cause that primarily affects the peripheral joints in a symmetric pattern.[1-4] RA's effect on other areas of the body, including the skin, heart, lungs, and eyes, can be sub-

KEY POINTS

- Biologic DMARDs are the most effective, and costly, treatments for patients with RA.
- This retrospective database analysis of pharmacy claims data from 40,373 patients with RA calculated the current utilization, expenditures, and pricing trends for biologic DMARDs.
- Expenditures on biologic DMARDs increased from $166 million in 2004 to $243 million in 2013.
- Spending on biologic DMARDs was driven by higher prescribing rates, despite a regular annual increase in average wholesale acquisition cost of 2% to 10%.
- The average reimbursed amount per prescription was stable at approximately $2300, but out-of-pocket spending per prescription increased from $36 (2.5%) to $128 (7%) during the study.
- New biologic and nonbiologic DMARDs are eroding some market share for several established drugs.
- Creating a competitive market for treatments and the introduction of biosimilars will likely help control drug costs.

stantial. The disease also causes joint destruction, and thus often leads to considerable morbidity and mortality.[2] Daily living activities are impaired in most individuals with RA, and spontaneous clinical remission is uncommon (approximately 5%-10%).[5] It is estimated that the annual incidence for RA is approximately 3 cases per 10,000 population.[2]

The prevalence rate of RA is approximately 1%; RA is 3 times more common in women, but this difference narrows as patients age.[2] After 5 years of active disease, approximately 33% of patients are unable to work, and after 10 years, approximately 50% of patients experience substantial functional disability.[6,7] Life expectancy in patients with RA is shortened by 5 to 10 years, although the mortality rate may be lower in those who respond to therapy.[2,8] In the developed world, the prevalence of RA in adults is 0.5% to 1.0%.[8] The incidence of RA globally is 5 to 50 per 100,000, and peaks between ages 35 and 50 years.[9]

The management of RA typically requires a 3-pronged therapy approach that includes (1) symptomatic drugs for pain (ie, nonsteroidal anti-inflammatory drugs, analgesics, and opioids); (2) disease-modifying antirheumatic drugs (DMARDs), which are divided into nonbiologic and biologic drugs; and (3) glucocorticoids for inflammation. Nonbiologic DMARDs, including methotrexate, sulfasalazine, leflunomide, and hydroxychloroquine, are older medications, with established safety profiles and a relatively low cost of between $30 and $900 monthly.[10] Biologic DMARDs are generally newer, powerful medications that are capable of quickly decreasing disease activity in a relatively short time.[11,12] The costs for biologic DMARDs range from $2000 to $5000 monthly.[10]

Biologic DMARDs are divided into several groups, based on which aspect of the immune system they target. There are 5 tumor necrosis factor (TNF)-alpha inhibitors, including infliximab, etanercept, adalimumab, certolizumab, and golimumab; 2 interleukin inhibitors, tocilizumab and anakinra; 1 T-cell activation inhibitor, abatacept; 1 CD-20 activity blocker, rituximab; and 1 oral nonbiologic Janus kinase inhibitor, tofacitinib.

Because of the higher cost and risk profile for newer biologic and nonbiologic DMARDs, the current American College of Rheumatology (ACR) guidelines indicate that patients with early RA should start a treatment regimen of nonbiologic DMARD monotherapy, regardless of disease activity (low, moderate, high).[12] In established RA, after nonresponse to conventional DMARD therapy, the ACR recommends either combination traditional DMARD therapy; a TNF inhibitor, with or without methotrexate; a non-TNF inhibitor biologic, with or without methotrexate; or tofacitinib, with or without methotrexate.[12]

The increased utilization of biologics has had a significant impact on healthcare payers, as a result of the high cost of these novel agents. Analyzing these costs is often difficult, because of the idiosyncrasies of insurance billing and the various drug formulations and routes of administration. Some biologic DMARDs are available as an injectable for at-home use and are reimbursed under drug benefit plans, whereas other biologics are administered via intravenous infusion only in a healthcare facility and are reimbursed under medical plans. To further complicate these analyses, several biologic DMARDs are available for both routes of administration.

Researchers have studied Medicare and Medicaid expenditures for RA per capita and per beneficiary. Doshi and colleagues studied the impact of Medicare Part D coverage, identifying significant increases in payments for infliximab, during a period when payments per patient with RA also increased.[13] The Medicare Modernization Act of 2003 decreased the payments per patient, but infliximab still had a 4% increase in total expenditures.[13] Patient payments for infliximab were slightly decreased once reimbursement was further reduced.[11]

Yazdany and colleagues compared patients who received Medicare's Low-Income Subsidy with those who did not, as well as the cost per beneficiary.[14] The data showed that patients with the Low-Income Subsidy were more likely to receive biologics for at-home use than patients without the Low-Income Subsidy. As expected,

the patients receiving the Low-Income Subsidy also had lower out-of-pocket (OOP) expenditures.[14] In Medicare Part D, at least 1 biologic was covered in 97% of plans.[14] Most plans (81%-100%) required some form of coinsurance rather than a predefined copayment, resulting in an annual OOP cost of $2712 to $2774 before catastrophic benefits take effect.[15] Medicare Advantage plans covered more biologics than standard coinsurance, but had higher premiums compared with nonbiologic DMARDs, which relied on fixed copays of $5 to $10 monthly.[15]

The key drivers for higher expenditures on specialty drugs are increased utilization, approvals for expanded indications, and new biologics entering the market, all of which characterize the biologic DMARD market.[16] Pharmacy benefit managers rely on various control mechanisms, such as benefit design modifications, step-edits, preauthorization, cost-sharing, and adherence counseling and patient education to control spending.[16] The effects of cost-sharing and insurance plan generosity (ie, the percentage of pharmacy costs covered by the insurance plan) have been studied in relation to RA,[17,18] and although healthcare spending is generally elastic, depending on the type of service, spending on specialty drugs, such as biologic DMARDs, is inelastic.[17]

There is a gap in the literature for a comprehensive analysis of payer and patient spending across all 10 currently approved biologic and nonbiologic DMARDs. The objective of this study is to assess drug utilization, expenditures, OOP cost, and pricing trends of biologic DMARDs in patients with RA in a large managed care organization. The results of this research could be significant to the healthcare system (insurance payers, Pharmacy & Therapeutics committee members, healthcare stakeholders, and pharmacy directors) to better understand the overall medication cost for payers and for patients with RA.

Methods

We conducted a retrospective cohort study using the Clinformatics Data Mart database (OptumInsight; Eden Prairie, MN) containing medical and pharmacy claims with linked enrollment information with data covering the period from 2004 to 2013. Data relating to approximately 13.3 million individuals with medical and pharmacy benefit coverage were available. An additional almost 8.7 million enrollees who had medical benefits only was also available for this study. The underlying information from the study database is geographically diverse across the United States and is fairly representative of the US population. Of the approximately 13.3 million individuals, information on race and ethnicity, as well as financial resources, was available for approximately 9 million (65%-70%) of the individuals.[19] Although slightly smaller in terms of lives covered than other commercially available claims databases, the Clinformatics Data Mart database is nationally representative and has all the necessary data fields for this type of analysis.

Table 1 List of Study Biologic and Nonbiologic DMARDs for the Treatment of Rheumatoid Arthritis

Drug	Manufacturer	FDA approval date for RA	HCPCS code
Abatacept (Orencia)	Bristol-Myers Squibb	December 2005	J1029
Adalimumab (Humira)	AbbVie	December 2002	J0135
Anakinra (Kineret)	Sobi	November 2001	J3490
Certolizumab (Cimzia)	UCB	May 2009	J0717
Etanercept (Enbrel)	Amgen	November 1998	J1438
Golimumab (Simponi)	Janssen Biotech	April 2009	J1602
Infliximab (Remicade)	Janssen Biotech	November 1999	J1745
Rituximab (Rituxin)	Genentech	February 2006	J9310
Tocilizumab (Actemra)	Genentech	January 2010	J3262
Tofacitinib (Xeljanz[a])	Pfizer	November 2012	NA

[a]Nonbiologic small-molecule DMARD.
DMARD indicates disease-modifying antirheumatic drug; HCPCS, Healthcare Common Procedure Coding System; NA, not applicable; RA, rheumatoid arthritis.

Target Population and Sample Selection

There were 453,993 patients with an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis code for RA of 714.xx in this national privately insured population. A total of 192,287 patients were aged ≥18 years at diagnosis, with a confirmed diagnosis of RA and at least 3 claims for 714.xx in any billing position at least 45 days apart from each other.[20]

To be included in this study cohort, patients had to start taking at least 1 DMARD during that same period. A total of 129,005 patients met the inclusion criteria of RA diagnosis and at least 1 DMARD for this study. Only 45,923 patients with RA received at least 1 biologic DMARD. Patients were excluded if at any time during the study they had a diagnosis of another disease in which a biologic DMARD may be used as treatment, such as plaque psoriasis (*ICD-9-CM* 696.1x), psoriatic arthritis (696.0x), ankylosing spondylitis (720.0x), juvenile idiopathic arthritis (714.3x), Crohn's disease (555.xx), ulcerative colitis (556.xx), non-Hodgkin lymphoma (200.xx, 202.xx), or chronic lymphocytic leukemia (204.1x).[20]

Based on the inclusion and exclusion criteria, a total of 40,373 patients were identified for this study. The patients' pharmacy claims that were filed between 2004 and 2013 were extracted for this study.

Study Drugs and Costs

All biologics approved for self-injection were identified by their brand name and generic name within the

Table 2 Characteristics of Patients with Rheumatoid Arthritis, 2004-2013

Metric variable	Patients (N = 40,373)
Age, mean, yrs (SD)	55 (12.9)
Age-group, %	
18-24 yrs	1.91
25-34 yrs	5.56
35-44 yrs	12.59
45-54 yrs	24.19
55-64 yrs	32.46
≥65 yrs	23.28
Sex, %	
Female	76.14
Male	23.86
Race, %	
White	76.83
Asian	2.23
Black	7.68
Hispanic	8.86
Unknown	4.40
CMS geography, %	
ME, MA, RI, CT, NH, VT	2.73
NY, NJ, PR, VI	4.68
PA, DE, MD, DC, VA, WV	5.34
KY, TN, NC, SC, GA, AL, MS, FL	27.44
MN, WI, MI, IN, IL, OH	20.44
NM, OK, AR, LA, TX	17.55
NE, IA, MO, KS	6.19
MT, ND, SD, WY, CO, UT	5.73
CA, NV, AZ, HI, GU	7.81
WA, OR, ID, AK	2.06
Insurance type, %	
EPO	11.91
HMO	15.77
FFS	1.84
OTH	0.22
POS	62.28
PPO	7.98
Education level, %	
Bachelor's degree or higher	16.59
High school diploma	29.46
Less than 12th grade	0.66
Less than a bachelor's degree	52.78
Unknown	0.51

CMS indicates Centers for Medicare & Medicaid Services; EPO, exclusive provider organization; FFS, fee for service; OTH, other plan; POS, point of service; SD, standard deviation.

pharmacy database (**Table 1**). All drugs requiring in-facility administration were identified by their Healthcare Common Procedure Coding System code. Costs associated with the administration of in-facility drugs were identified using *Current Procedural Terminology* codes. Drug name, prescription fill date, number of units, and the standard cost were collected and were linked to individual patient records.

To account for the differences in pricing across health plans and provider contracts, OptumInsight applies standard pricing algorithms to the claims data in Clinformatics Data Mart. These algorithms are designed to create standard prices that reflect allowed payments across all provider services. In this way, relative pricing within a therapeutic category and generic indicator is determined by Clinformatics Data Mart information, whereas general pricing levels by therapeutic category and generic indicator are determined by observed payments. To create a standardized cost, the resulting average payment schedule is applied to each pharmacy service based on the National Drug Code listed and the metric quantity for the prescription. All costs are adjusted to 2013 US dollars.

Measures and Definitions

The total number of prescriptions was based on the sum of the prescription fills for all biologic DMARDs and each biologic within each year. The total annual expenditure is based on the sum of the standard cost for each prescription fill within each year. The average cost was based on the total annual expenditure divided by the total number of prescription fills for each drug within each year. The OOP costs represent the sum of the patient's copay, deductible, and coinsurance, if any. The percentage of patient share was calculated by dividing the OOP expenditure by the standard cost. The year-over-year changes were calculated starting with a drug's first full year on the market, then moving forward using the formula $(T_2 - T_1)/T_1$, where T represents the value of a measure at a given time point. The data were also stratified by insurance plan type of exclusive provider organization (EPO), PPO, HMO, point of service (POS), fee for service (FFS), and other uncategorized plans. The study protocol was approved by the University of Cincinnati Institutional Research Board.

Results

Of the 40,373 study patients, 30,740 (76.14%) were female, and the mean age was 55 years (standard deviation, 12.9; **Table 2**). The patients were predominantly white (76.83%), resided in the Southern and Midwestern states (27.44% and 20.44%, respectively), and primarily (62.28%) had POS insurance coverage plans. The majority (52.78%) of patients had less than a bachelor's degree.

The prevalence of biologic DMARD use among patients with RA increased from 16% in 2004, with 7.6 biologic DMARD prescription fills per patient to 39% in 2013, with 9.6 prescription fills per patient (**Table 3**).

Etanercept, infliximab, and adalimumab—3 of the earliest biologics approved for the treatment of RA—were by far the most frequently prescribed therapies in this class of treatments (44%, 16%, and 24%, respectively), accounting for 84% of the prescriptions overall (**Figure 1**).

All drugs have seen a net increase in the total number of prescriptions filled since 2004. With other new biologic DMARDs launched in the market, infliximab has seen a downward trend since 2005, as did adalimumab starting in 2011.

The relatively newer drugs golimumab, certolizumab, tocilizumab, and tofacitinib have shown consistent year-over-year growth since their first full year on the market (certolizumab, 225%; tocilizumab, 72%; and golimumab, 69%). When stratified by insurance plan type, the expenditures followed the pattern of patient plan distribution, with 62% of expenditures incurred by POS plans, 16% by HMO plans, 12% by EPO plans, 8% by PPO plans, and <2% by FFS plans.

Aggregate spending on biologic DMARDs increased 45% from $166 million in 2004 to $242 million in 2013 (**Figure 2**). The most costly biologic DMARDs annually included etanercept (approximately $100 million), adalimumab (approximately $60 million), and infliximab (approximately $50 million-$60 million). Newer biologics, such as certolizumab and tocilizumab, also had strong growth in expenditures. The growth of tofacitinib was unable to be calculated, because it was only on the market for 1 full year.

The average reimbursement amount for each biologic has fluctuated over time, with an increase in average cost each year until 2006 (**Figure 3**). Since 2006, the average cost per prescription has remained relatively unchanged, but costly. The cost for rituximab has been approximately $5000 per prescription fill, and stands out as significantly higher than other approved biologic DMARDs. It's notable that rituximab was initially approved as a chemotherapy agent used to treat cancers of the white blood system (ie, leukemia and lymphomas). Its price may be competitive against other chemotherapy agents, but not against biologic DMARDs.

Other costly biologics include infliximab, at approximately $3800 per fill; adalimumab, at approximately $3000 per fill; etanercept, at approximately $2700 per fill; and certolizumab, at approximately $2600 per fill. In addition, the costs of abatacept and certolizumab had a noticeable decrease between their market entry year and their first full year on the market.

The direct OOP costs and the percentage of cost-sharing increased by more than 10% annually for all biologic DMARDs (**Figure 4**). By 2013, the average OOP cost per prescription was $145, ranging from $34 for anakinra to $222 for infliximab (**Table 4**). Rituximab had the highest (30%) annual increase in OOP expenditure, followed by abatacept (28%), certolizumab (27%), and infliximab (25%).

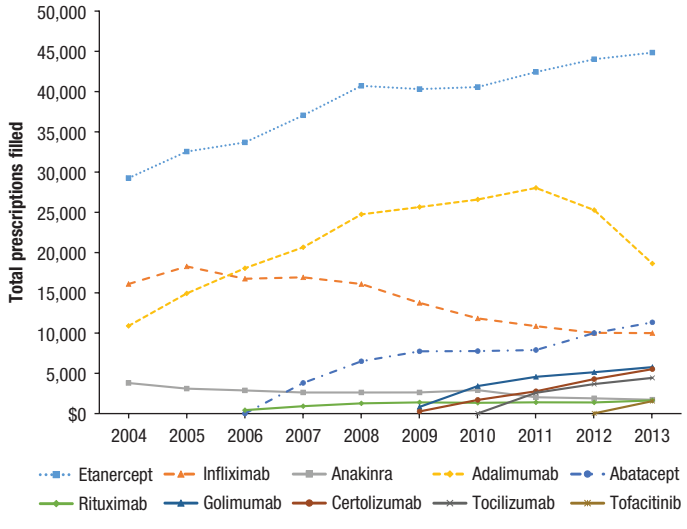
The average OOP expenditure within each plan showed the same pattern of steady increases from 2004 to 2013 (**Figure 5**). HMO plans and uncategorized plans showed the largest increase in OOP spending, for example, the OOP expenditure for a patient with an HMO

Table 3 Trend of Biologic DMARD Use in Patients with RA, 2004-2013

Year	Biologic DMARDs refills, N	Reimbursement amount, $	Patients receiving a biologic DMARD, N	Patients with RA, N	Patients with RA receiving a biologic DMARD, %	Average biologic DMARD prescription fills per patient, N
2004	59,960	166,817,302	9709	40,340	24.1	7.6
2005	68,763	202,565,153	11,574	45,822	25.3	7.3
2006	71,706	213,342,534	12,353	44,832	27.6	7.4
2007	81,858	228,900,255	13,140	47,563	27.6	7.8
2008	91,822	245,026,318	14,127	48,037	29.4	8.1
2009	92,444	238,222,067	14,064	46,875	30.0	8.2
2010	96,011	241,086,264	14,006	45,241	31.0	8.8
2011	102,417	251,319,669	14,502	44,031	32.9	8.9
2012	105,576	255,885,971	14,577	41,250	35.3	9.3
2013	105,295	242,683,714	14,284	37,089	38.5	9.6

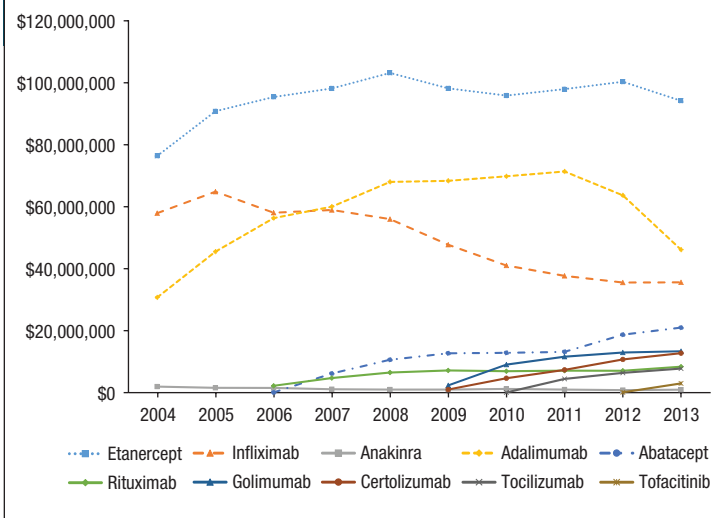
DMARD indicates disease-modifying antirheumatic drug; RA, rheumatoid arthritis.

Figure 1 Annual Number of Biologic DMARD Prescriptions per Drug



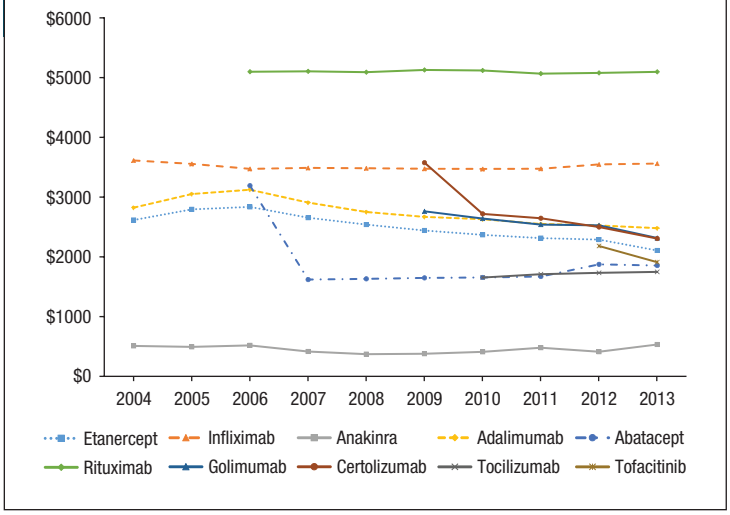
DMARD indicates disease-modifying antirheumatic drug.

Figure 2 Annual Aggregate Spending on Biologic DMARDs per Drug



DMARDs indicates disease-modifying antirheumatic drugs.

Figure 3 Annual Average Cost per Prescription Fill (Price) per Drug



plan increased 288% from $39 to $151 per fill; OOP spending for plans in the "other" category increased 388% from $36 to $180 per fill. FFS plans showed the lowest increase (92%) from 2004 to 2013. EPO and PPO plans consistently had the lowest OOP spending and percentage of cost-sharing (**Figure 6**).

Discussion

The identified cohort in our study matched the descriptions of similar cohorts from other studies of biologic DMARD costs, in being predominantly female, older, and Caucasian.[3,21-26] The data in Table 3 show an annual increase in the percentage of patients who were prescribed a biologic, demonstrating physicians' increased confidence in prescribing these new medications.

It is possible that other factors, such as easier dosing regimens, autoinject syringes for at-home use, oral agents, and direct-to-patient marketing, have contributed to increased utilization of biologic DMARDs. Strong competition from multiple competing therapies may have kept prices in check and relatively similar, with the exception of rituximab, whose price is based off of competing chemotherapy agents, which are generally more expensive than DMARDs. Multiple treatment options targeting several sites have clinical and economic benefits for patients.

However, a recent study reported that more than 50% of patients with RA who were prescribed their first biologic DMARD (88.7% TNF inhibitors) did not fill the prescription via a pharmacy or receive the drug in an outpatient or inpatient setting within 30 days of the index prescription. By 180 days postindex, more than 40% of patients had not yet filled or received a prescription for a biologic DMARD.[27]

There are clear favorites in physicians' prescribing patterns for older drugs (ie, etanercept, infliximab, and adalimumab) that have documented safety profiles. These drugs were also the first to be approved as first-line therapy options for the treatment of RA, and most insurance plans require that patients use at least 2 anti-TNF drugs before moving to a different class of biologic. This leads to the higher utilization and expenditures seen with anti-TNF drugs compared with the newer biologic DMARDs. We did not expect to see the decreases in prescriptions and in spending for these 3 drugs (ie, etanercept, infliximab, and adalimumab) in 2012 and 2013.

There have been 6 biologics approved since 2005 for RA, 4 of which were approved since 2009, which could be eating into the market share of the older RA drugs. There has been a considerable amount of research about switching drugs among biologic DMARDs in recent years. Research suggests that a high proportion of patients who do not respond to their initial anti-TNF therapy are unlikely to have a meaningful response to a second anti-TNF drug,[28] or that dosing for a second anti-TNF drug may need to be increased.[29] Although anti-TNF treatment cycling is common and may be required by some drug benefit plans, this may lead to increased risk for patients who are exposed to therapies without the possibility for a meaningful benefit.

It is possible that with 6 additional treatment options, physicians are more comfortable switching a patient's treatment to another biologic DMARD faster if a patient is not responding as quickly or as completely as they would like, especially with treat-to-target paradigms;

however, these older drugs are still leaders in the industry, because they are approved for multiple indications. It is possible that although the RA market share is going down, these agents are gaining ground in other indications, where there may not be as many approved treatment options, as has happened in the treatment for psoriasis, with the approval of secukinumab and apremilast.

Two drugs are outliers in general. Rituximab, the first US Food and Drug Administration (FDA)-approved CD-20 inhibitor, was first developed for lymphoma and leukemia. As such, it was priced in relation to other chemotherapy agents. The cost per prescription is extremely high by comparison, and the number of annual prescriptions was initially relatively low. It is possible that rituximab was approved by the FDA only for patients with moderate-to-severe RA, because there are lower-cost options with easier routes of administration. Anakinra, 1 of only 2 interleukin-1 receptor antagonists, is another outlier drug, with an extremely low cost per prescription but relatively low utilization, indicating a lack of faith in the drug by physicians. This claim is backed up by Amgen's sale of anakinra to Sobi in 2013, although Sobi has invested in the clinical development of the drug for the treatment of other conditions.[30]

Stratification by insurance plan type clearly demonstrates the drug benefit design of the plan with respect to biologics. EPO and PPO plans, which have more expensive premiums than other plan types, offered the lowest OOP costs and the lowest increase in patient cost-sharing. HMOs, which have lower premiums, ended up with the highest OOP costs and the highest amount of cost-sharing. This puts a disproportionate burden on patients who may not be able to afford the higher premiums of plans with better drug benefits.

Figure 4 Average Out-of-Pocket Expenditure per Prescription, by Year and Drug

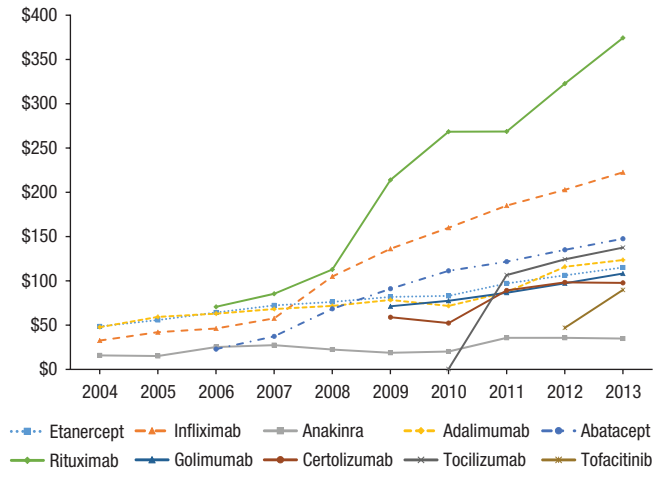
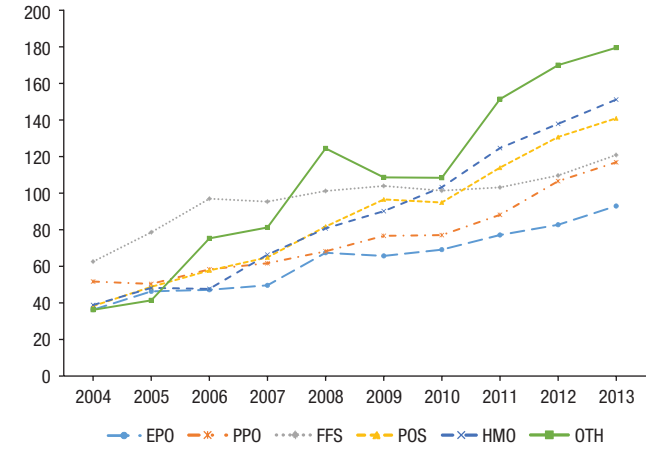


Table 4 Patient Out-of-Pocket Expenditures and Cost-Sharing Percentage for Patients with RA, 2004-2013

OOP cost/cost-sharing percentage	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
By biologic/nonbiologic DMARD, $ (%)										
Etanercept	48 (2.2)	55 (2.4)	63 (2.7)	71 (3.2)	75 (3.8)	81 (4.2)	82 (3.9)	96 (4.5)	105 (4.8)	114 (5.5)
Infliximab	32 (0.9)	41 (1.4)	45 (2.2)	57 (2.3)	10 (3.6)	135 (4.6)	159 (5.3)	184 (5.9)	202 (6.1)	222 (6.6)
Anakinra	15 (4.9)	14 (5.7)	24 (7.4)	26 (11.6)	22 (12.2)	18 (11.5)	19 (10.7)	35 (15.5)	35 (14.8)	34 (14.2)
Adalimumab	47 (1.9)	58 (2.3)	62 (2.5)	67 (2.8)	71 (3.3)	78 (3.6)	71 (3.0)	86 (3.8)	115 (5.0)	123 (5.3)
Abatacept	—	—	22 (11.6)	36 (2.4)	68 (4.4)	90 (5.6)	110 (6.9)	121 (7.4)	134 (7.7)	147 (8.2)
Rituximab	—	—	70 (1.5)	85 (1.8)	11 (2.4)	213 (4.2)	268 (5.3)	268 (5.5)	322 (6.5)	374 (7.5)
Golimumab	—	—	—	—	—	70 (2.9)	77 (3.1)	86 (3.5)	96. (4.0)	107 (4.6)
Certolizumab	—	—	—	—	—	58 (2.2)	51 (2.1)	88 (3.6)	97 (4.1)	97 (4.4)
Tocilizumab	—	—	—	—	—	—	—	106 (7.4)	123 (8.1)	137 (8.9)
Tofacitinib	—	—	—	—	—	—	—	—	46 (2.1)	89 (4.7)
By insurance plan type, $ (%)										
EPO	37 (1.4)	47 (2.2)	48 (2.2)	50 (2.3)	68 (2.9)	66 (3.3)	70 (3.5)	78 (3.7)	83 (3.8)	93 (4.2)
PPO	52 (2.5)	51 (2.1)	59 (2.8)	62 (3.3)	69 (5.9)	77 (5.9)	78 (3.4)	89 (3.9)	107 (4.6)	117 (5.4)
POS	63 (2.6)	79 (4.0)	97 (8.1)	96 (8.5)	102 (7.3)	104 (7.0)	102 (7.2)	104 (7.4)	110 (6.5)	121 (7.1)
FFS	39 (1.9)	49 (2.2)	58 (2.5)	65 (2.9)	82 (3.7)	97 (4.3)	95 (4.4)	114 (5.1)	131 (5.8)	141 (6.4)
HMO	39 (1.8)	49 (2.1)	48 (2.2)	67 (3.0)	81 (3.6)	91 (4.0)	104 (4.9)	125 (5.8)	138 (6.2)	151 (6.7)
Other	37 (1.5)	42 (1.9)	76 (3.2)	82 (3.6)	125 (5.6)	109 (4.7)	109 (5.3)	152 (6.9)	170 (7.2)	180 (8.0)

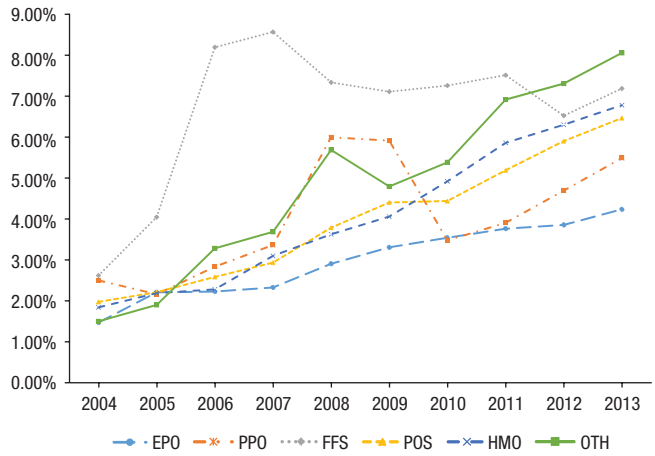
DMARD indicates disease-modifying antirheumatic drug; EPO, exclusive provider organization; FFS, fee for service; OOP, out-of-pocket; POS, point of service; RA, rheumatoid arthritis.

Figure 5 Average Out-of-Pocket Expenditure, by Insurance Plan Type



EPO indicates exclusive provider organization; FFS, fee for service; OTH, other plan; POS, point of service.

Figure 6 Average Patient Cost-Sharing, by Insurance Plan Type



EPO indicates exclusive provider organization; FFS, fee for service; OTH, other plan; POS, point of service.

A recent study of patients covered under the Medicare Advantage plan and Prescription Drug Plan has shown that higher OOP costs affect a patient's decision to initiate treatment with a biologic DMARD or if the patient would continue to use a biologic DMARD.[31] An examination of the OOP expenditures of biologic DMARDs exposes several trends. Patients are being asked to participate in greater cost-sharing year after year, as is evidenced by the increase in average OOP spending, while the average cost of biologic DMARDs decreases. This is in line with a payer's interest to control costs by controlling access to specialty and top-tier drugs. On the surface, these data support the idea that specialty and top-tier drug pricing is very inelastic to demand.

Drug manufacturers, however, have engaged in a series of initiatives through rebates, patient access programs, and other reimbursement schemes to deflect and absorb a patient's direct financial burden and to increase access to biologic DMARDs, thereby invoking a moral hazard. Payers have attempted not to honor rebates or coupons, but little data are available to support that this tactic is effective at controlling cost.

The impact that biosimilar generics in the RA market will have on reducing costs is unclear. The Biologics Price Competition and Innovation (BPCI) Act, which was passed under the Affordable Care Act, lays out a regulatory pathway for generic biologics. The BPCI provisions for biosimilars allow for 2 distinct categories—biosimilars and interchangeable biologic drugs.[32] It is unlikely that any drug will immediately achieve status as an interchangeable biologic drug.[33,34]

Any new biosimilar drug will likely have market penetration similar to that of a novel drug. This will be unlike the impact that generic small-molecule drugs had on brand-name reference drugs, which saw 70% to 80% decreases in costs over time.[34-36] Although it is assumed that there will be some cost-savings, biosimilars are likely to be closer to 20% to 30% of the reference drug.[36]

This is particularly relevant for the new biosimilar approvals, including infliximab, with the April 2016 approval of infliximab-dyyb (Inflectra; Celltrion), a biosimilar to Remicade[37]; the August 2016 approval of etanercept-szzs (Erelzi; Novartis), a biosimilar to Enbrel[38]; and the September 2016 approval of adalimumab-atto (Amjevita; Amgen), a biosimilar to Humira.[39]

Limitations

This study used a large single-payer data set and may not represent the subscriber characteristics of other payers.

Only the cost of biologic DMARDs was included for the intravenously administered medications. The costs associated with the administration and monitoring of the infusion were not included, nor were costs for teaching patients about self-injectables.

Data for tofacitinib were limited, and a detailed analysis was not possible with the current data set, because the drug was only on the market for 1 full year at the time of this analysis.

Furthermore, these current study data were only available from 2004 through 2013, which limits the observation of this study to the more recent market share changes. For example, recently, the utilization of adalumimub was reported to increase in the RA treatment marketplace, and etanercept may lose some market share because of switching patients with RA to adalimumab, as well as from switching patients with psoriasis to apremilast or secukinumab.

Conclusion

Spending on biologic DMARDs has been primarily driven by an increase in prescribing rates, because the cost per prescription remained relatively unchanged over time. The OOP burden for patients has increased, but this does not appear to have limited the use of biologic DMARDs. The entrance of new biologics may be eroding some market share for established drugs through faster rates of treatment switching. Attempts at cost control via cost-sharing have either been ineffective or circumvented. Patients and physicians have a wide array of treatment options with varying treatment targets, and creating a competitive market might help control costs. The introduction of biosimilars will be critical to continued cost control, but the effects of biosimilars are unlikely to be as dramatic as the effects that small-molecule generic drugs have had in their respective markets. ■

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Author Disclosure Statement

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STAKEHOLDER PERSPECTIVE

Rheumatoid Arthritis, Biologic Drugs, and Associated Cost

By Byron C. Scott, MD, MBA

Associate Chief Medical Officer, Truven Health Analytics, an IBM Company, Chicago, IL; and Adjunct Faculty, Isenberg School of Management, University of Massachusetts, Amherst

Like many diseases, rheumatoid arthritis (RA) has significant morbidity and mortality associated with it.[1] What is most striking about RA is that approximately 33% of patients with the disease are unable to work after 5 years of active disease, as Atzinger and Guo note in their study in this issue.[2] Although their study may have limitations, including the use of only 1 payer database and the inclusion of data up to 2013 only, it does highlight the need for additional evaluation of drug costs, prescribing rates, and outcomes in future health outcomes research involving RA.[2] With the development of new advances in treatments for chronic inflammatory conditions, such as RA, we must evaluate all aspects of drug costs and other direct healthcare costs, such as hospitalizations and physician office visits, as well as how these drugs will improve the overall functional status of patients.

PATIENTS: Patients with RA want treatments that can reduce the symptoms of their disease, while also improving their overall functioning, because RA can be very debilitating. One of the most serious impacts of RA is being unable to work. If we measure the overall cost of a person not being able to work, the cost of biologic disease-modifying antirheumatic drugs (DMARDs) may seem very cost-effective, although these agents are as expensive as other RA treatments. We must provide healthcare education and full transparency for patients to make informed treatment decisions with their providers. This means to fully understand the benefits, costs, and side effects of the medicines that are being considered for their treatment, especially for RA, given the cost of treatments such as biologic DMARDs, and the increasing out-of-pocket expense for patients.

PAYERS: With the increasing use of biologic DMARDs and their cost, payers have a high level of interest in these issues, considering that payers are covering most of the cost of these prescriptions for patients. Payers have a vested interest in providing evidence-based treatments, especially if higher-cost biologic DMARDs can ultimately reduce future overall costs, by preventing employees from leaving the workforce, and by helping them to return to the workforce. More studies and evaluations such as the one by Olofsson and colleagues[3] will need to be done in the future to truly look at the cost-effectiveness of various RA treatments and their impact on workforce issues and disability.

PROVIDERS: In the complex world of value-based healthcare, providers want to practice evidence-based medicine that provides effective outcomes for patients in the most cost-effective way possible. Providers also want treatments that result in positive patient satisfaction. One very important aspect of patient satisfaction will hinge on being sure providers can offer treatment options that are affordable, and have high adherence rates. A key component of this in patients with RA is how the treatments will improve their overall functioning status. ■

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