

Managed Care Decision Makers: Understanding the Full Scope of Rheumatoid Arthritis Management

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Rheumatoid arthritis (RA), a chronic, progressive disease, is one of the most common autoimmune diseases in the United States. In addition to other factors, the increasing costs of biologic disease-modifying antirheumatic drugs (DMARDs) are putting increasing pressure on payers to identify opportunities to control costs while providing quality care and improved outcomes.

Burden of Disease

RA exerts a tremendous toll on patients and their families. A study of patient self-reported quality of life found that those with RA were 40% more likely to report fair or poor general health than those without RA. The results also revealed that patients with RA are 30% more likely to need help with personal care and twice as likely to have a health-related activity limitation.¹ Health-related quality of life (HRQoL) is also significantly lower in this population, primarily due to pain, fatigue, disability, and the inability to work.² About 20% of patients stop working full time in the first year after receiving their diagnosis, and within 15 years, half have dropped out of the full-time workforce.³ However, early, aggressive treatment of RA may reduce work-related disability and keep individuals with the disease in the workplace.⁴

Economic Burden of Disease

An analysis of direct medical costs in RA, using government data from 2004 to 2006, estimated per patient annual costs in the first 3 years after diagnosis of \$4422, \$2902, and \$1882, respectively, while a 2005 analysis estimated overall annual medical costs of \$22.3 billion.^{5,6} Meanwhile, a study published in 2011, which used data from between 1999 and 2007 from a large employer database that assessed total healthcare costs in patients receiving a single anti-tumor necrosis factor (TNF) drug or switching from an anti-TNF drug, estimated annual costs of \$20,370 and \$23,388, respectively.⁷ In 2010, Birnbaum et al estimated annual excess healthcare costs of RA at \$8.4 billion.⁸ The disease is responsible for approximately 9100 hospitalizations a year, at an annual cost of \$374 million, as well as 2.9 million ambulatory care visits—65.5% of which are to specialists, such as rheumatologists.⁶

ABSTRACT

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease that affects an estimated 0.5% to 1% of the US population, or approximately 1.5 million individuals. The disease exerts a tremendous toll on patient health-related quality of life, driving many patients out of the workforce as their pain, fatigue, and disability grow. Additionally, with direct medical costs estimated at \$22.3 billion and indirect and intangible costs of another \$50.1 billion, RA also places a significant economic burden on patients, employers, and payers. The advent of disease-modifying antirheumatic drugs in the past 15 years has revolutionized the treatment of RA, slowing progression of the disease and reducing disability. However, the benefits have come with a huge financial cost, as many of these treatments exceed \$20,000 a year. These drug prices have risen by double digits in the past 3 years alone.

Managed care organizations and other payers are implementing numerous approaches to address the challenge of managing the cost of care for patients with RA while improving outcomes. These include utilization review, controlling site-of-care services, shifting coverage of intravenous specialty drugs from the medical to the pharmacy benefit, improving provider adherence to national and international guidelines, and addressing comorbidities in patients with RA. This challenge will become even greater in the next decade with the introduction of new specialty drugs and the growing incidence of the disease.

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Furthermore, RA strikes the working-age population; therefore, indirect costs are very important. An estimated \$252 million per year are costs attributed to just absenteeism.⁹ A 2005 study estimated the annual cost of earnings losses, environmental adaptations in the home and work environments, disability payments, decreased productivity, and the cost of retraining replacement workers at \$10.9 billion. Intangible costs, including premature death and declines in HRQoL added another \$39.2 billion.⁸ Direct medical costs in these patients are twice as high as those without comorbidities.¹⁰

Analysis of an insurance-claims database of 2700 employees with RA and 338,000 without RA found the mean annual cost for workers with RA was \$8700 compared with \$3500 for those without the condition, costing employers an additional \$5.8 billion a year. Direct healthcare costs accounted for 90% of the extra \$5200; the rest was related to absenteeism and short-term disability.¹¹

Comorbidities in RA

The prevalence of comorbidities is higher in patients with RA than in those without RA; however, these comorbidities are underrecognized and undertreated.¹² Patients with RA have an average of 2 comorbidities, and most are related to the chronic inflammation and immune dysfunction of the disease while some are related to the treatment itself. The most common comorbidities in 1 large study were hypertension (31.5%), osteoporosis (17.6%), osteoarthritis (15.5%), and hyperlipidemia (14.2%).¹³

Rising Cost of Specialty Drugs

Today, the majority of the economic burden related to RA comes from the use of biologic DMARDs, which are more than 5 times as expensive as traditional DMARDs, such as methotrexate.^{14,15} One Spanish study revealed that the cost of treating RA tripled between 2000 and 2005 as a result of biologics.¹⁶ An analysis of specialty drug costs in a Midwest healthcare plan's medical and pharmacy administrative claims data between 2008 and 2010 found annual specialty drugs costs consumed 53% of the \$34,163 per person annual costs. From 2008 to 2010, annual growth in the cost of care for patients with RA was 8.0%, 5.6% of which was related to drug cost growth.¹⁴ The price of specialty drugs has skyrocketed since that time. For instance, the price of etanercept has increased 80.3% since 2013, and today, it costs more than \$4000 a month. Adalimumab costs nearly the same, representing a 70% price increase over the past 3 years, while the cost of tofacitinib rose 44.3% to more than \$3100 a month.¹⁷

Overall, the Alliance of Community Health Plans estimates that the annual cost of treating RA in the United States with DMARDs will increase almost 50% from 2013 to 2020, reaching more than \$9 billion a year.¹⁷ Although most manufacturers offer coupons and discounts to help patients meet their out-of-pocket costs, they are limited to commercially insured populations. Therefore,

while coupons and discounts are not available to patients with RA who have Medicare, an estimated 1 in 4 patients with RA on Medicare receive a biologic DMARD.¹⁸ The burden is particularly heavy on this population because Medicare does not cap out-of-pocket expenses as most commercial plans do.^{19,20} Many coupons also have annual or even monthly maximums.²¹ Finally, whereas coupons may save patients money in the short term, they do not reduce the actual cost of the drug to the payer. The coupons can also lead to higher costs by encouraging patients to use higher-cost drugs because they do not have to pay any co-payment.²²

Cost-Effectiveness of Biologics

Even before the recent increase in biologic drug prices, the National Institutes of Health and similar agencies in other countries identified the cost-effectiveness of these medicines as one of the "highest-priority research topics in the pharmacologic treatment of RA."²³ As a result, dozens of studies evaluating the cost-effectiveness of biologics for RA have been published. Such studies are quite heterogeneous, using different willingness-to-pay thresholds (eg, \$50,000 or \$100,000 per quality-adjusted life-year [QALY] gain), perspectives (payer or societal), costs of drugs studied, severity of disease state, outcomes, intensities of treatment, and comparators, making it difficult to determine which drugs are most cost-effective overall.²³⁻³⁵ One systematic review of 18 economic evaluations of biologic monotherapies or combination therapies (eg, adalimumab, etanercept, and infliximab) compared the cost with conventional DMARDs. The authors determined that biologics were not cost-effective in patients with no previous DMARD exposure or those who failed methotrexate combination therapy or sequential DMARD administration. They used a willingness-to-pay threshold of \$50,000 per QALY gain. Some evidence of cost-effectiveness was observed at a willingness-to-pay threshold of \$100,000 per QALY gain, although the results were mixed.²³ It is important to note that most studies were conducted using costs far lower than today's prices.

Managed Care Strategies

Payers have little control over the price of biologics. Therefore, managed care organizations must adopt a rational approach to weigh the direct and indirect costs of RA to make informed decisions regarding costs and benefits. Part of that approach involves addressing the overall costs of the disease and identifying opportunities to reduce costs while maintaining quality. Potential approaches are described below.

Follow Guideline-Recommended Care

Current guidelines from the American College of Rheumatology (ACR) recommend beginning DMARDs in patients with symptomatic RA, regardless of disease activity level.³⁶ Meanwhile, interna-

tional guidelines highlight the importance of treating to target (T2T), with clinical remission, defined as the absence of signs and symptoms of significant inflammatory disease activity, identified as the primary target for treatment. Until the treatment target is met, drug therapy should be adjusted every 3 months.³⁷

Compared with symptomatic treatment, T2T in early RA is cost-effective. An analysis of 2 years of data, in the DREAM (Dutch Rheumatoid Arthritis Monitoring) registry, from 261 patients who received a T2T approach to care and 213 who received usual care found that T2T was associated with higher costs and significantly higher effectiveness. At 3 years, there was a 64% chance that the T2T strategy would result in lower costs with continued higher effectiveness.³⁸

Patients are more likely to receive such guideline-recommended care when seen by a rheumatologist. An analysis of 27 studies published between 2002 and 2012 determined that DMARD use among patients followed by rheumatologists ranged from 77% to 98% compared with 39% to 63% among those seen by other types of physicians (mainly primary care).³⁹ Given the growing shortage of rheumatologists in this country and the increasing number of people with joint-related and autoimmune diseases, this is an important point.^{40,41}

Initiate Early Treatment

Much of the joint damage inherent in RA begins early in the disease. At 2 years after diagnosis, more than 80% of patients demonstrate signs of space narrowing on radiographs of the hands and wrists, and two-thirds show erosions.⁴² A very early window of opportunity exists within the first 12 weeks of the disease during which DMARDs may lead to better outcomes than later treatment, including the prevention of erosions and even complete remission.^{43,44} Thus, early diagnosis and treatment are crucial to slowing the progression and degree of disability in RA.⁴⁵⁻⁴⁷

Several studies found significant gaps in patients receiving early treatment, primarily related to the length of time between disease symptom occurrence, referral to a rheumatologist, and DMARD initiation.⁴⁸ One study revealed that just one-third of patients with RA were assessed less than 12 weeks after their symptoms began, with a median of 13 weeks before they saw a rheumatologist. Patients who saw a rheumatologist within 12 weeks of symptom onset demonstrated a lower rate of progression over 6 years than those whose initial rheumatology visit was delayed ($P = .001$).⁴⁷

Treatment with DMARDs not only improves patient outcomes, but can be cost-effective.^{32,46,49,50} In the United Kingdom's TICORA (Tight Control for Rheumatoid Arthritis) trial, a single-blind, randomized, controlled study conducted in 2 teaching hospitals, 111 patients were randomized to intensive management or usual care. The intervention group was seen monthly and assessed using a validated disease activity score. The usual care group was

seen every 3 months with no formal composite measure of disease activity used in clinical decision making.⁴⁹ More DMARDs were started in the intensive group and fewer were stopped because of toxic effects, with more treatment episodes continuing beyond the trial end. They had a mean reduction in disease activity score of 3.5 versus 1.9 in the usual care group ($P < .0001$), and were more likely to have a good response or reach remission. Total costs were lower in the intensive group as a result of lower inpatient costs, although outpatient and drug-related costs were higher.⁴⁹

Assess Appropriate Use of Biologics

The effectiveness of biologic DMARDs is limited. Between 20% and 50% of adults and adolescents treated with TNF inhibitors fail to achieve a 20% improvement in ACR criteria (the current definition of responsiveness) with these agents.⁵¹ There is also limited benefit to dose escalations of TNF inhibitors.²⁴

One analysis of 5474 patients with RA receiving a biologic DMARD found that, depending on the drug used, the first-line treatments used were effective in 19.0% to 32.7% of patients.²⁴ In addition, between 10% and 50% of patients eventually stopped responding to the drug they were taking, requiring additional therapy, dose escalation, switching to a different drug within the same therapeutic class, or switching to a drug within another class.⁵²⁻⁵⁴

A survey of 100 rheumatologists determined that about half (48%) of their patients cycled through at least 2 biologics during the course of their disease, and 43% cycled through 3 biologics.⁵⁵ Existing guidelines are vague on when and how to switch DMARDs, resulting in significant heterogeneity in the management of patients with RA.²⁹ While current guidelines call for maintaining the target throughout the course of the disease, this does not imply continuing treatment. However, several studies demonstrate the clinical appropriateness of dose reduction and interval increases, and in some instances, the withdrawal of the use of biologics.⁵⁶⁻⁶⁰

Managed care organizations could use the data within their pharmacy and administrative databases to assess the appropriate use of biologic DMARDs in terms of frequency of switching and the length of trial.

Utilization Review and Benefit Design

Utilization review may improve the appropriate use of DMARDs. A 2011 online survey of 100 rheumatologists and 50 health plans covering more than 80 million lives found that payers used tier placement, prior authorization, and contracting as coverage strategies for RA biologics.⁵⁵ For instance:

- **Step therapy.** More than half of all managed care organizations used step therapy, in which a patient has to fail a first-line medication before moving onto other options. Although there are no published studies assessing its effectiveness in

RA, a review of such approaches for antidepressants, antihypertensives, antipsychotics, nonsteroidal anti-inflammatory drugs, and proton pump inhibitors found significant drug cost savings for all except antipsychotics.⁶¹

- **Injectable versus infusion.** Biologic treatment with a self-injectable option versus an infused option is less costly to payers.²⁵ In 2014, about 1 in 4 plans preferred self-administered drugs over those that are provider administered. Eighty-three percent of plans in 1 survey contracted for rebates with the former compared with 57% for the latter.⁶²
- **Prior authorization.** An analysis of 2737 Medicare Part D plan formularies determined that 97% tightly controlled the use of biologic DMARDs through prior authorization approval.⁶³ In 2014, approximately 90% of payers required prior authorization for all immune modulator therapies, with 70% creating coverage guidelines across the pharmacy and medical benefits.⁶²
- **Optimize point-of-care location.** The cost of infusions provided in outpatient hospital settings is up to 40% higher than infusions provided in a physician office. However, in the past 5 years, a substantial percentage of infusions has shifted to the more expensive setting.⁶⁴ A 2014 survey of 70 health plans found that 31% had site-of-service strategies in 2013, while 43% planned to implement them in 2014.⁶²
- **Limiting supplies.** Just 13% of health plans surveyed in 2014 allowed a 90-day supply for patients in remission.⁶²

Shifting coverage of infused specialty drugs from the medical to the pharmacy benefit offers another option for cost management. With this approach, drugs typically come from a specialty pharmacy at negotiated rates versus the buy-and-bill approach, in which physicians or hospitals purchase the drug and are reimbursed an administration fee (and have an incentive to prescribe higher-cost drugs). Obtaining drugs through a specialty pharmacy also provides tighter prior authorization and other cost-management strategies.⁶⁵ In 2013, 27% of plans put infused specialty drugs for RA under the pharmacy benefit compared with 19% in 2011.⁶⁶

Maximize Adherence

Nonadherence to medical therapy is an ongoing problem in RA.⁶⁷⁻⁶⁹ A recent analysis of a commercially insured population determined an average adherence rate of 45.7% among 5 biologics, with intravenous biologics demonstrating the lowest rate.²⁵ A review of 2 years of medical records of 75 patients with early RA found that after 3 years, only 34% of patients were still adherent with their medication. Adherent patients had lower Disease Activity Score 28 (DAS28) values and greater DAS28 improvements, were more likely to reach sus-

tained remission, and had lower Health Assessment Questionnaire scores.⁶⁸ Patients who were nonadherent were 4 times more likely to experience disease flares than those who followed the recommended protocol.⁶⁹ Although there are numerous reasons for nonadherence to synthetic and biologic DMARDs, one barrier is cost^{70,71}: one study revealed that 10.5% to 26.4% of patients were nonadherent with TNF inhibitors if their out-of-pocket expenses were more than \$100 compared with 4.7% when the co-payment was less.⁷¹

Another study found an overall abandonment rate for biologics of 18.2%. Patients with co-payments up to \$250 had the lowest rate (1.3%), while those with co-payments greater than \$550 had an abandonment rate of 32.7% ($P < .0001$).⁷² Out-of-pocket costs also influence whether patients will even start therapy with a DMARD.⁷³ Meanwhile, a survey of 1100 Medicare beneficiaries determined that those with RA were 3.5 times more likely to be nonadherent with their medication because of cost than those without RA and nearly 2.5 times as likely to spend less on basic needs.⁷⁴ Other contributors to nonadherence should also be considered, including patient age, access to rheumatologists, patient-physician communication, and clinical characteristics.^{3,75} Identifying patients at risk of nonadherence and intervening early with medication management efforts could reduce rates of nonadherence and improve outcomes.⁶⁷

Pharmacy Benefit Managers and Specialty Pharmacies

Pharmacy benefit managers and specialty pharmacies have an important role in managing the drug-related costs of RA. Interventions range from negotiating discounts and rebates with manufacturers and identifying financial help for patients to improving medication adherence and managing utilization.^{76,77} Specialty pharmacies can also help train providers in the appropriate use of medications, determine dosing and quantity limits to avoid costly waste, recommend alternative approaches, and provide case management services.⁷⁷ A 2011 survey of 50 payers, representing more than 80 million lives, determined that 80% used specialty pharmacies. The most valuable add-on services they reported were patient education, compliance programs, and the provision of adherence data.⁵⁵

Encourage Interdisciplinary, Coordinated Care

Interdisciplinary, team-based care—composed of physicians, nurses, pharmacists, physical and occupational therapists, and other medical professionals—is becoming a cornerstone of treatment for complex diseases like RA. Studies have found that such approaches can be just as, or more, effective than traditional, physician-led care, and less costly.⁷⁸⁻⁸⁰

Pharmacist-led medication therapy management (MTM) is a cost-effective approach to comprehensive patient management in

several chronic diseases. Pharmacists participating in these programs currently provide an initial assessment and continue with patient-specific interventions designed to identify and resolve medication-related issues. This complements the services delivered by other members of the care team, resulting in improved outcomes.⁸¹

A study published in 2014 found that nurse-led follow-up care in patients with stable, low-activity RA and shared care without scheduled consultations resulted in lower mean scores in disease activity and higher scores for functional status and HRQoL over 2 years compared with patients seen by a rheumatologist. Patients in the nursing group also improved their self-efficacy, confidence, and satisfaction scores compared with those in the rheumatologist group. The patients seen by nurses were also significantly less costly to care for (in terms of direct clinician costs) than the group seen by rheumatologists.⁸² Another study comparing nurse-led care to rheumatologist-led care in 181 adults with RA determined that nurse-led care was noninferior to rheumatology care and was more cost-effective. A Canadian study reported similar results.^{83,84}

Improve Management of Comorbid Conditions

As noted earlier, individuals with RA have a significantly higher burden of comorbidities than those without RA. These conditions are often underdiagnosed and undertreated. A 2010 study that evaluated cardiovascular disease (CVD) risk in 266 patients with RA, but without documented CVD, found that nearly 39% (N = 115) were identified as “high risk,” yet only 7% (8) were receiving statins.⁸⁵ Another study of a 5% random sample of Medicare patients determined that 55% of patients with RA, most of whom received both primary and rheumatology care, did not receive a lipid screening.⁸⁶ Many of these comorbid conditions can be screened for, and managed, in less expensive primary care settings, often with the support of nurses.¹²

Negotiate Value-Based Contracts

Value-based contracting ties outcomes to reimbursement. Such contracts are beginning to take hold in the pharmaceutical industry. They typically involve extra discounts if a drug does not perform as expected or rebate credits to the manufacturer if it does. A recent survey of 42 health plans, representing 161 million covered lives, found that 41% were interested or very interested in negotiating outcomes-based contracts with manufacturers of RA drugs.⁸⁷

Prepare for Biosimilars

Biosimilars are copies of previously approved biologics that have demonstrated a high degree of similarity to the originator reference product.⁸⁸ They have been available in Europe, Japan, and other countries for years, but the FDA did not approve the first biosimilar until 2015. In April 2016, the agency approved the second biosimilar, infliximab-dyyb, whose reference drug is infliximab.

The drug was approved for use in patients with RA and other rheumatic diseases⁸⁹; however, given the legal challenges brought by many manufacturers of the reference drugs, it may take some time before it and other biosimilars reach providers.⁹⁰

Biosimilars in the United States are expected to be priced between 15% and 35% less than the reference drug.⁹¹ In the United Kingdom, Italy, France, and Germany, a recent analysis estimated that the use of the infliximab biosimilar would save €233 million (\$263 million in 2016 US dollars) at a 20% discount and €433.5 million (\$490 million in 2016 US dollars) at a 30% discount over 5 years, as well as increase the number of patients with access to the drug.⁹² In Japan and Norway, the drug is priced 67% and 69% lower, respectively, than infliximab.⁹³ Even the smaller discounts in the United States could lead to substantial savings: a 2014 analysis from Express Scripts estimated savings of \$250 billion if 11 biosimilars for oncology and rheumatology were approved.⁹⁴

Although there is concern in the United States about clinician and patient uptake of biosimilars, in South Korea, one-fifth of all infliximab claims were for the biosimilar just 15 months after its launch. Regulatory agencies in the United Kingdom, Belgium, and Germany are driving the use of biosimilars in RA by requiring that treatment begin with the least expensive drug or with quotas.⁹⁵ Although the impact of biosimilars on the cost of specialty drugs, like those used for RA, remains unclear, they will likely have some effect. Payers can prepare for biosimilars by evaluating and redesigning their formularies, establishing patient registries to track outcomes, and educating clinicians and patients about the drugs.⁹⁵

Conclusion

The introduction of synthetic and biologic DMARDs, and the focus on T2T, has revolutionized the management of RA in the past 15 years, slowing progression of the disease and reducing long-term joint damage and disability. However, those improvements come at a price, with biologics for the disease costing upwards of \$50,000 a year. With both the incidence of RA in the United States and the cost of the specialty drugs used to treat it rising, payers have to identify opportunities to better manage their use, reduce overall costs for RA, and improve outcomes.

To that end, payers are implementing numerous approaches, including utilization management through prior authorization and step therapy; engaging specialty pharmacies and pharmacy benefit managers to provide comprehensive medication management services, ensuring that the drugs are delivered to the most cost-effective site of care; and identifying opportunities to educate clinicians on the optimal use of the drugs.

The role of managed care pharmacists will become more prominent as healthcare reform unfolds. Pharmacy will be forced out of its silo to become a full member of the healthcare team. The introduction of multiple risk models and accountable care organi-

zations will force more integration of pharmacy and medical data. Physicians will no longer be able to be agnostic to costs, regardless of whether they occur within the medical or pharmacy benefit. Aggressive management of the drug benefit and pharmacy network will be critical to the organization's continued ability to provide affordable access to medications. MTM services will become standard practice, pharmacy provider networks will narrow, and specialty drug management will come under increased scrutiny.

Managed care decision makers must prioritize medical and pharmaceutical interventions based on real-world outcomes and tangential costs, and take a long-term approach that looks not only at the potential for national medical cost savings from pharmacotherapy, but also potential benefits to society and dollars saved due to disease prevention.

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