OPTUMRx®

Drug Class Insight

RHEUMATOID ARTHRITIS

Background, new developments, key strategies

INTRODUCTION

- About **1.5 million adults** in the U.S. have RA[1]
- **75% of RA patients are women**[1]
- RA consistently ranks #1 or #2 in PBM specialty spending[2,3,4,5]

Rheumatoid arthritis (RA) is an incurable inflammatory disease that is especially damaging to working-age adults, causing pain, swelling, stiffness, and loss of function in the joints. RA is one of the highest-cost conditions for employers, with estimated direct medical expenditures in the US totaling over $73 billion.[6]

Overall, RA accounts for **one fourth of all specialty drug spending** in the US and is expected to account for around **one fifth of all health plan drug spending** by the end of 2014.[7]

RA occurs when the immune system mistakenly attacks the membrane lining the joints. This causes the inflammation that characterizes RA, which most often affects joints of the hands and feet.[1]

RA is distinguished from other forms of arthritis, such as **osteoarthritis**, which is more commonly associated with the wear and tear on joints from aging.[1]

JOINT DAMAGE

RA attacks the synovium and can destroy the cartilage and bone within the joints.

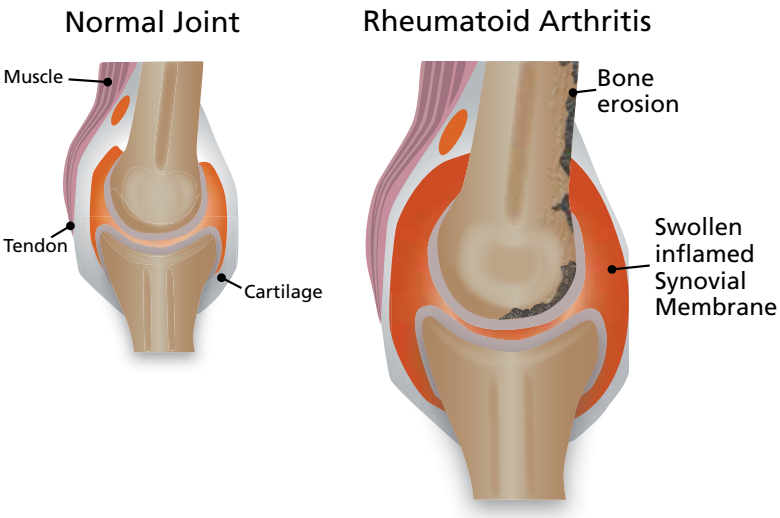
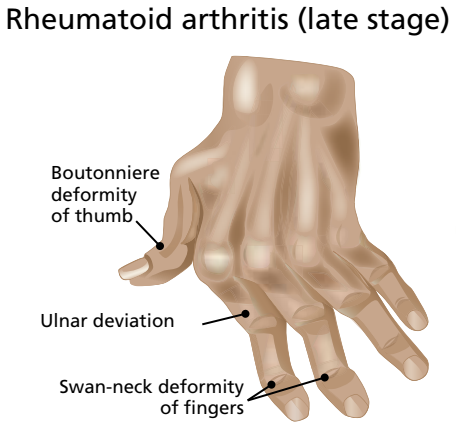


Image adapted from: Advanced Research Institute. Rheumatoid Arthritis. Accessed at: http://www.advresearch.org/rheumatoid-arthritis/

RA progressively weakens the surrounding muscles, ligaments, and tendons that ordinarily support and stabilize the joints. This can cause joints to deform and shift out of place.[1]



Source: Arthritis Research UK. Why do joints become damaged? Available at: http://www.arthritisresearchuk.org/

TREATING RA

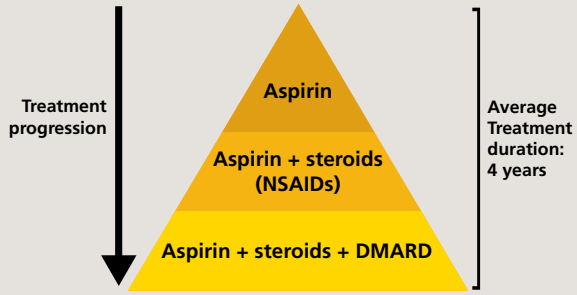
While there is no cure for RA, therapy for RA has improved greatly in the past 30 years. Today, patients usually begin their treatment with **disease-modifying anti-rheumatic drugs, or DMARDs**. These drugs not only relieve symptoms, but also slow the progression of the disease. DMARDs have greatly improved the symptoms, function and quality of life for nearly all patients with RA.[1]

Early Failure

1

Early treatment models followed a "pyramid" pattern. This meant that patients were treated conservatively for years and only slowly graduated to more intensive treatment, including DMARDs, at the end.[9]

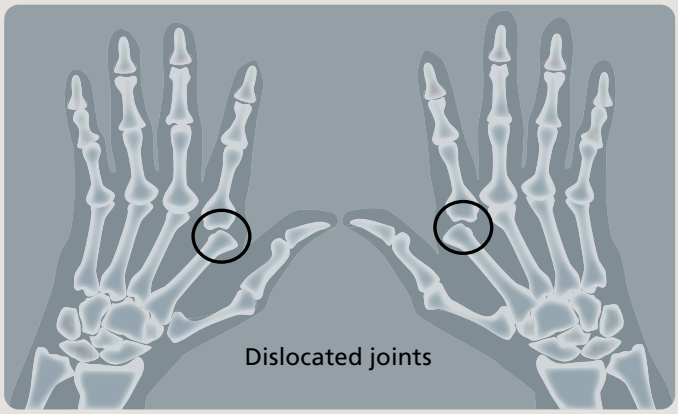
Original RA treatment pyramid: 1950's-1980's



Rheumatology. Evolution of treatment for rheumatoid arthritis. Volume 51, Issue suppl 6. Sept. 14, 2012.

2

The original pyramid model was ineffective. But it took new radiographic analysis to reveal the true speed of RA's destructive power: most joint damage occurs within the first 2 years. In the meantime, these failed treatments caused considerable – and unnecessary – pain and disability among RA patients.[10]

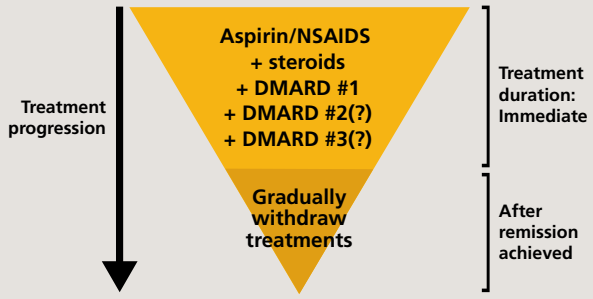


Adapted from American College of Rheumatology image.

3

New treatment standards essentially "inverted" the old pyramid with much more aggressive treatment – right after initial diagnosis. The new goal for treatment is to achieve maximum clinical success as quickly as possible to slow or stop disease progression and prevent permanent damage to the joints.[11]

RA treatment pyramid: 1990's-present



Rheumatology. Evolution of treatment for rheumatoid arthritis. Volume 51, Issue suppl 6. Sept. 14, 2012.

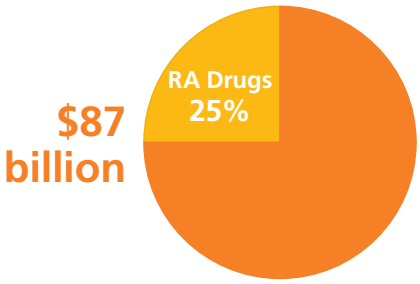
RA treatment is complicated. It is common for patients to switch therapies multiple times in their lives, between the conventional and biologic DMARDs, plus more common medications such as ibuprofen and corticosteroids.[12]

CURRENT RA SPENDING

RA is one of the highest-cost conditions for employers, with estimated direct medical expenditures in the US totaling over $73 billion.[6]

RA accounts for **one fourth of all specialty drug spending** in the US and may be responsible for up to **one fifth of all health plan drug spending** by the end of 2014.[6]

RA Drugs Account for 1/4 of all Specialty Spend



UnitedHealth Center for Health Reform & Modernization. Issue Brief. The Growth of Specialty Pharmacy: Current trends and future opportunities. April 2014. American Health & Drug Benefits. Trends in Biologic Therapies for Rheumatoid Arthritis. March/April, 2012.

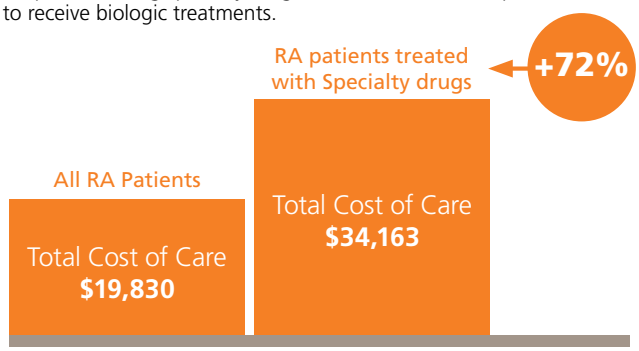
So why are RA costs so high? The answer is the extremely high cost of biologic DMARDs – **over 9,000% higher than the conventional kind.**

CONVENTIONAL OR BIOLOGIC?

As noted, RA patients can receive a variety of treatments – including even over-the-counter drugs – depending on the stage and severity of their illness. Their costs jump dramatically once specialty drugs are added to their treatment:

Average Annual Cost of Care

RA patients using specialty drugs are sicker and more apt to receive biologic treatments.



Journal of Managed Care Pharmacy. Health Plan Utilization and Costs of Specialty Drugs within 4 Chronic Conditions. Sept. 2013.

The question of when to use conventional DMARDs versus biologics is extremely complex.

Ideally, expensive biologically engineered RA medications are reserved for more severe forms/phases of the disease.[13]

Large-molecule bioengineered DMARDs

Guidelines suggest that, except for specific exceptions, these costly medications should be used when conventional DMARDs fail or lose their effectiveness for a patient.

Small-molecule-small cost

Conventional DMARDs have been proven to be safe and effective, especially when used in various combinations including methotrexate.

Retail prices via GoodRx.com, Aug. 13, 2014. Top 4 biologics via: IMS Health White Paper: Succeeding In the Rapidly Changing U.S. Specialty Market. 2014.

PRIMARY COST DRIVERS

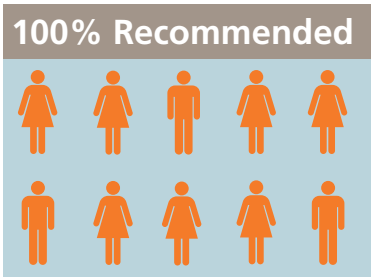
RA drug costs are increasing due to three main factors:

Innovation – RA is being treated with increasingly more complex and costly drugs

Successful new treatment options have significantly raised expectation for what RA patients can expect in terms of their symptoms and quality of life.[7]

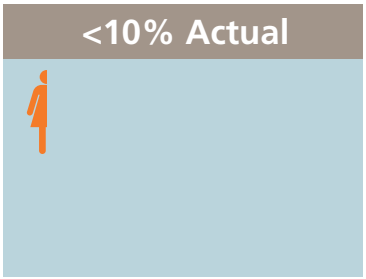
Utilization – The number of people being treated with expensive new medications has grown rapidly

RA patients have quickly replaced cheaper drugs with vastly more expensive ones. Biologics use grew 100% in just 6 years.[14]



American College of Rheumatology recommends that all* RA patients begin treatment with conventional DMARDs

*Subject to clinical indications.
Arthritis Care & Research. Vol. 65, No. 3, March 2013.



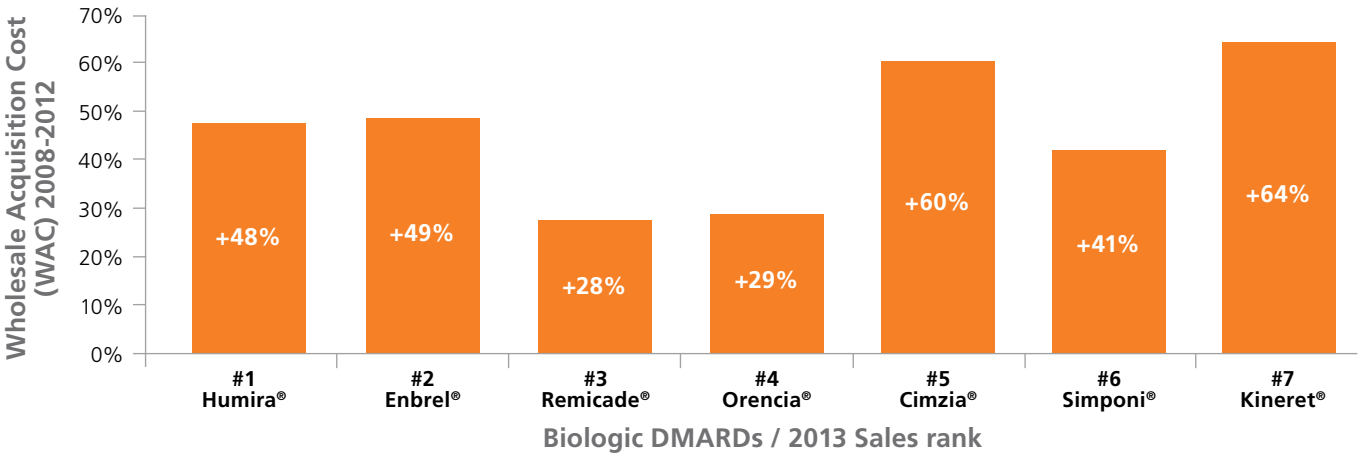
Fewer than 10% of all patients begin RA treatment with recommended conventional treatment.

MedPage Today Methotrexate Use Falls Short in RA. Jun 19, 2014.

Inflation – Prices for RA drugs are increasing rapidly

Not only was biologic utilization growing, but drug prices were also rising fast. The chart below illustrates the rapid rise in biologic prices over a five year period for this basket of top-selling biologic DMARDs.

Wholesale Acquisition Cost (WAC)



Sales rank: Fierce Pharma.Top 10 rheumatoid arthritis drugs 2013. Sept 16, 2013. WAC increase: Poster: Academy of Managed Care Pharmacy. Rheumatoid Arthritis Specialty Drug Utilizers Cost of Care Trends 2008 to 2010: An Integrated Medical and Pharmacy Claims Analysis. April, 2013.

Where to from here?

Like other chronic diseases, RA could benefit from cheaper generic drugs and enhanced adherence among patients to limit waste. However, these concerns, while valid, cannot by themselves really control RA spending. Far more important is bringing doctors and patients to understand the very real clinical value that the conventional DMARDs still have, in addition to their economic advantage.[15]

The American College of Rheumatology is taking steps to promote the wise use of biologics and conventionals alike. OptumRx supports these steps with intelligent management strategies that reinforce professional guidelines.[13]

Where are the biosimilars?

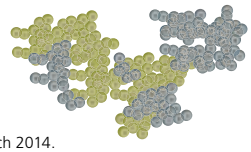
Two of the biggest-selling RA drugs (Humira and Enbrel) are scheduled to lose their patent protection in 2016. Their huge revenues make them lucrative targets for biosimilar competition. Accordingly, nearly a dozen pharmaceutical manufacturers have versions of these and other RA drugs in development.[16]

But the greater complexity of biologic & biosimilar drugs impacts the entire range of the production cycle, as shown below. Ultimately, these difficulties may delay the arrival of biosimilars, significantly reduce their cost-savings potential, and even make physicians more cautious about prescribing them.[17]

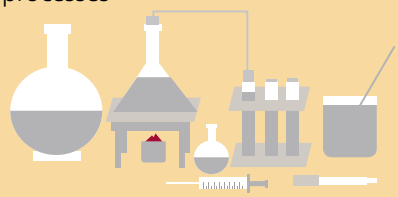
Biologics Bigger, More Complex

Aspirin (acetylsalic acid) Acetylsalicylic acid
21 atoms

Biologically engineered antibody
> 20,000 atoms



Adapted from: Amgen Inc. Biologics and biosimilars: An overview. March 2014.

Small Molecule (conventional) generic	Biosimilar
1.) Biologics & Biosimilars are much more difficult to manufacture	
Conventional drugs can be simply mass-produced[17] 	Biologics require extremely sophisticated production processes[17] 
2.) Biosimilars require more time and investment	
Conventionals can be copied quickly and inexpensively[17] Development time: 2-3 years Development costs: $2-5 million	Complex biologics take longer & cost more to duplicate[17] Development time: > 5 years Development costs: $100 million
Lower up-front investment means greater savings Conventional generic $ Avg. savings for generics: -75%	Lower up-front investment means greater savings Biosimilar $ Avg. savings for biosimilars (est.): ~20%
3.) Biosimilars are struggling with the FDA Approval Process	
Conventional drugs benefit from a well-established approval process[17] **Chemical Generics** FDA Interchangeable ☑ 	Many questions remain concerning what the FDA will require to approve biosimilars[17] **Biosimilars** • FDA Marketing Approval Process ? • FDA Biosimilar Standard for Interchangeability ? • Post-Approval Data Required ? • Safety & Efficacy Studies Required ?

A COMPREHENSIVE APPROACH TO MANAGING RA

End-to-End Programs

As we have detailed here, the use of biologic DMARDs spread quickly throughout the RA space after they were introduced. In fact, the evidence shows that biologics have displaced the use of conventional DMARDs even in cases where conventional DMARDs are the preferred treatment option.

The OptumRx strategy deploys end-to-end programs deliver value through appropriate clinical management and adherence programs, so we can be sure each patient is getting on the right drug at the right dose, the right duration and the right response.

What you can do

Our **total approach** to RA combines a robust drug management strategy together with clinical management and adherence programs:

- **Actively managed Prescription Drug List (PDL):** Lowest-cost products through appropriate reimbursement, rebates and preferred product strategies
- **ONE care team:** Synchronized support for complex conditions like RA helps improve outcomes
- **Medical Necessity:** Helps guard against treatments that could be ineffective or cause an adverse reaction
- **Step therapy:** Promotes the use of clinically appropriate medications
- **Prior authorization:** Helps ensure that high-cost medications are used only for patients who can benefit from them
- **Supply limits:** Prevents needless waste when treatment regimens change frequently, as in RA
- **Price protection:** Our negotiated arrangements lock-in drug prices

We automatically apply these strategies for our Fully Insured clients who combine UnitedHealthcare medical policies with pharmacy benefits administered by OptumRx. **We encourage, but do not require, our carve-out ASO customers to adjust their plans in this way. Consult with your representative for details.**

TOTAL RA CARE COORDINATION

We use the power of **synchronization** to surround RA patients with the power of ONE. ONE streamlined member experience comes from ONE common platform supporting ONE care team to deliver lower cost and better health.

ONE Experience	ONE System	ONE Team
• **Streamlined touch points** for a better experience • 1 to 1 consultations • Reducing total costs by promoting lower cost medications, mail service, and care management programs • Making the most of interactions by engaging on health and savings opportunities	• **360° total health view** of each member (Medical, Rx, lab, wellness) • Real-time data vs. monthly feeds • 64% of health and savings opportunities driven by pharmacy data	• **Up to 30 days faster** engagement on health and savings opportunities • Pharmacists, nurses, case managers and member services share information and expertise. • Depression screening and referrals

ONE System for earlier interventions & better support

The ONE system captures hundreds of data points and scores them against over 500 care standards and rules. For example, a medication adherence score triggers an automatic alert to a nurse if a member is not refilling their medication. A unique pharmacy risk score for each member helps nurses prioritize risks and expand care connections.

The ONE care team uses targeted data to help members take control of their health and medical costs in many ways, including:

- Directing to premium providers
- Flagging prescription duplications and contraindications
- Addressing adherence issues
- Shifting to lower tier or lower-cost medications

The synchronized care management model described here depends on a minimum specific set of OptumHealth care management services, plus OptumRx pharmacy services. Please speak to your OptumRx or UnitedHealthcare representative for more information about how synchronization can work for you.

SPECIALTY PHARMACY PROGRAMS

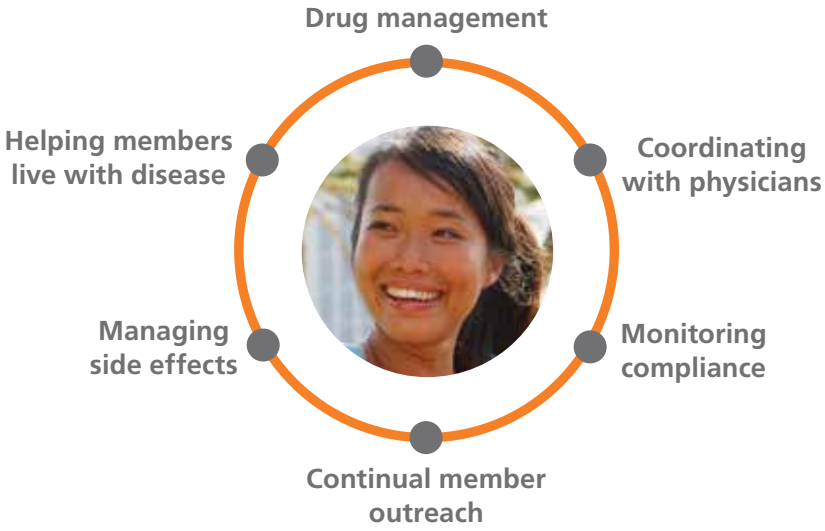
Our Clinical Management Programs combine disease self-management with medication therapy management, including telephone consultations, educational materials, and a personalized care plan.

Studies* show that our Specialty Pharmacy Program out-performs retail pharmacies with:

- Higher Adherence Rates
- Reduced Drug Waste
- Lower Medical Costs
  - Fewer ER & Office Visits
  - Less Hospitalization

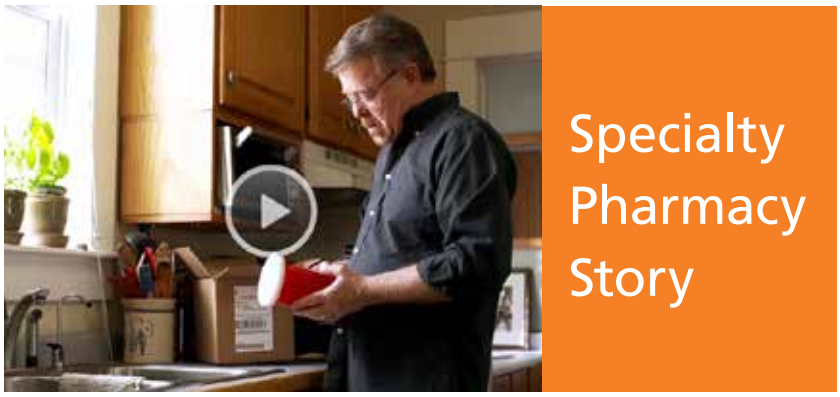
Total UM Savings for all Inflammatory Conditions: **13%****

Total Care Management = Better Health, Lower Costs



See how OptumRx specialty pharmacy is lowering costs and improving health for specialty patients.

If you are viewing this online, click on the play button to begin.



*__Managing Specialty Medications Through a Network of Specialty Pharmacies.__ A Four-Year Evaluation of Medication Adherence. Suzanne Tschida, PharmD; John Smolskis, MA; Brett Sahli, PharmD, Jon C Montague-Clouse, BS, MS; Saad Aslam, PhD. Poster and Abstract accepted for presentation at the October 2103 AMCP conference, San Antonio, TX.

**UM program outcomes based on UHC commercial membership in 2013. Individual plan results may vary.

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For more information about how you can manage the cost of RA, please contact your OptumRx representative.

www.optum.com

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