An Analysis of Treatment Options, Comparative Effectiveness Research, and Benefit Designs for Rheumatoid Arthritis

Supported by an independent educational grant from Lilly. For further information concerning Lilly grant funding visit www.lillygrantoffice.com
The Managed Care Review Board™

• The first curriculum of its kind, The Managed Care Review Board™ is specifically designed and developed for managed care professionals
• It uses a multidisciplinary, evidence-based process for decision-making that contributes to the optimization of patient outcomes to enhance managed care stakeholders' ability to compare the effects of various treatment options on clinical outcomes, perceived value, and economic implications for the entire health care system
• www.ManagedCareReviewBoard.com is a website devoted to delivering these CE activities
6:10 PM   Assessing the Clinical Benefits of Current and Evolving RA Therapies in a Managed Care Setting  
          *Brian Kaye, MD*

6:30 PM   Current Practice Guidelines Review  
          *Neil Minkoff, MD*

6:45 PM   Faculty Idea Exchange

6:50 PM   Current and Emerging CER for Evidence-Based Treatment and Benefit Design Decision Making  
          *Jeffrey Dunn, PharmD, MBA*

7:05 PM   Analyzing the Available Data to Assess the Value of Current and Emerging Treatment Options  
          *Fadia Tohme-Shaya, PhD, MPH*

7:25 PM   Plan Benefit Designs: Maximizing Value for Current and Emerging RA Therapies  
          *Jeffrey Dunn, PharmD, MBA*

7:40 PM   Faculty Idea Exchange and Audience Q&A

7:55 PM   Closing Comments, Post-survey, and Evaluations  
          *Neil Minkoff, MD*
After completing this activity, the participant should be better able to:

• Discuss the current clinical practice guidelines to improve outcomes for patients with RA
• Explain the unique role and utility of CER to improve outcomes for the treatment of RA within a managed care setting
• Cite currently available RA data and interpret the results for enhanced managed care decision-making for the treatment of RA
• Apply the use of CER for the treatment of RA within a managed care setting
• Provide accurate and appropriate counsel as part of the managed care treatment team
An Analysis of Treatment Options, Comparative Effectiveness Research, and Benefit Designs for Rheumatoid Arthritis
Assessing the Clinical Benefits of Current and Evolving RA Therapies in a Managed Care Setting

Brian Kaye, MD, FACP
Rheumatologist
Sutter East Bay Medical Foundation
Clinical Professor of Medicine
University of California at San Francisco
Adjunct Professor
College of Education and Health Sciences
Touro University
The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Brian Kaye, MD, FACP

No financial interest/relationships relating to the topic of this activity
• Overview of RA treatment
  • Principles
  • Goals
  • Strategy
• Measures of disease progression
• Pharmacologic management
  • Approved therapies
  • Emerging therapies
RA Treatment Goals

- Maximize long-term health-related quality of life
- Control of symptoms
- Prevention of structural damage
- Normalization of function
- Social participation

RA Treatment Strategy

Early and aggressive treatment
• Attenuate inflammation quickly

Treat-to-target (remission)
• Achieve minimal or no signs or symptoms of active inflammation

Achieve tight control
• Maintain a low level of disease activity over time through individualized therapy

Early and Aggressive Treatment Elicits Greater Disease Control

A higher proportions of patients with very early RA achieved low disease activity and remission when treated more aggressively.

Disease Activity and DAS28 Remission at 52 Weeks
(Data from the COMET Trial)

- **VERA; ETN + MTX (n = 263)**
  - Low Disease Activity: 79%*
  - Remission: 47%

- **ERA; ETN + MTX (n = 263)**
  - Low Disease Activity: 70%*
  - Remission: 48%

- **VERA; MTX (n = 263)**
  - Low Disease Activity: 62%
  - Remission: 47%

- **ERA; MTX (n = 263)**
  - Low Disease Activity: 35%
  - Remission: 32%

*P < .05

**Randomized, double-blind, parallel treatment trial of MTX-naïve patients with moderate to severe early RA (n = 542)**

COMET=combination of methotrexate and etanercept in active early RA; DAS28=28-joint Disease Activity Score; DMARD=disease-modifying antirheumatic drug; ERA=early rheumatoid arthritis; ETN=etanercept; MTX=methotrexate; TNF=tumor necrosis factor; VERA=very early rheumatoid arthritis.

Treat-to-Target Elicited Remission in 65% of RA Patients

Data from the TICORA Study

- **ACR20**: American College of Rheumatology 20% improvement criteria
- **ACR50**: American College of Rheumatology 50% improvement criteria
- **ACR70**: American College of Rheumatology 70% improvement criteria
- **Remission†**: Disease activity score < 1.6

Intention-to-treat population; n = 111 patients with RA duration < 5 years.

- Intensive Treatment
- Routine Treatment

* indicates *P < .0001 vs routine care
† indicates Disease activity score < 1.6

Barriers to RA Disease Control

• Factors associated with no adjustment in RA therapy despite documented high or moderate disease activity

<table>
<thead>
<tr>
<th>Barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irreversible joint damage</td>
</tr>
<tr>
<td>Patient-driven preference for current therapy</td>
</tr>
<tr>
<td>Non-inflammatory muscle pain</td>
</tr>
<tr>
<td>Insufficient time to assess effect of recently initiated RA therapy</td>
</tr>
<tr>
<td>Safety concerns</td>
</tr>
<tr>
<td>Presence of comorbid conditions</td>
</tr>
<tr>
<td>Resistant disease</td>
</tr>
</tbody>
</table>

Measures of Disease Activity and Progression Guide Treatment Decisions

Use validated measurements of disease activity/progression to guide treatment decisions and achieve tight control of RA

Biomarkers of inflammation

- ESR and CRP are acute-phase response measures scored as normal or abnormal based on local laboratory standards
- If results of at least 1 of these 2 tests are abnormal, patient should be scored as having an abnormal acute-phase response

Disease activity scales

- American College of Rheumatology 20% improvement criteria (ACR20)
- Disease Activity Score-28 (DAS28)
- Simplified Disease Activity Score (SDAI)
- Clinical Disease Activity Score (CDAI)
- Easy Rheumatoid Arthritis Measure (ERAM)
- Global Arthritis Scale (GAS)
- Routine Assessment of Patient Index Data 3 (RAPID3)

CRP=C-reactive protein; ESR=erythrocyte sedimentation rate.
Disease Activity Measures Provide Insight on Patient Response to Treatment

<table>
<thead>
<tr>
<th></th>
<th>ACR20</th>
<th>DAS28</th>
<th>SDAI</th>
<th>CDAI</th>
<th>ERAM</th>
<th>GAS</th>
<th>RAPID3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Function</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Patient Pain</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Patient Global</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Physician Global</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Tender Joints</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Number of Swollen Joints</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute Phase Response</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

ACR20=American College of Rheumatology 20% improvement criteria; CDAI=Clinical Disease Activity Index; CRP=C-reactive protein; DAS28=Disease Activity Score in 28 joints; ERAM=Easy Rheumatoid Arthritis Measure; ESR=erythrocyte sedimentation rate; GAS=Global Arthritis Score; RAPID3=Routine Assessment of Patient Index Data 3; SDAI=Simplified Disease Activity Index.

## Routine Objective Measurement of Disease Activity Associated with Remission

<table>
<thead>
<tr>
<th>Trial</th>
<th>Factors Associated With Remission</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>TICORA(^1)</td>
<td>• Intense treatment&lt;br&gt;• Frequent assessments&lt;br&gt;• Predetermined thresholds for escalation of therapies</td>
<td>10x higher rate of remission in patients receiving frequent objective assessment and intense therapy vs routine care</td>
</tr>
<tr>
<td>BeST(^2)</td>
<td>• Frequent assessments&lt;br&gt;• Early escalation to combination therapy</td>
<td>Greater number of patients receiving frequent objective assessment and early escalation of therapy achieved remission vs. routine care</td>
</tr>
</tbody>
</table>

BeST=The Dutch Behandel Strategieen study; TICORA=tight control for rheumatoid arthritis study.

Treat-to-Target Algorithm

**ACTIVE RA**
- MAIN TARGET
  - Adapt therapy according to disease activity
  - Use a composite measure of disease activity every 1-3 months
- ALTERNATIVE TARGET
  - Adapt therapy according to disease activity

**REMISION**
- Adapt therapy if state is lost
- Assess disease activity every 3-6 months

**SUSTAINED REMISSION**
- SUSTAINED LOW DISEASE ACTIVITY
  - Adapt therapy if state is lost

Pharmacologic Management of RA: Guiding Principles

Duration of therapeutic response varies

Long-term RA treatment often involves a sequence of different therapies

Optimal sequencing determined by response to therapy, disease progression, and effect of different therapies on disease pathways

Pharmacologic Interventions

<table>
<thead>
<tr>
<th>Corticosteroids</th>
<th>Non-biologic DMARDs</th>
<th>Biologics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone</td>
<td>Azathioprine</td>
<td>TNF inhibitors</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Hydroxychloroquine</td>
<td>IL-1 inhibitors</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Leflunomide</td>
<td>B-cell agents</td>
</tr>
<tr>
<td></td>
<td>Methotrexate</td>
<td>T-cell agents</td>
</tr>
<tr>
<td></td>
<td>Sulfasalazine</td>
<td>IL-6 inhibitors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JAK inhibitors</td>
</tr>
</tbody>
</table>

DMARD=disease modifying anti-rheumatic drugs; JAK=Janus Kinase inhibitor; TNF=Tumor Necrosis Factor.
Corticosteroids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial US Approval</th>
<th>Brand Name</th>
<th>Route of Administration</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>1955</td>
<td>Generic</td>
<td>Oral</td>
<td>Anti-inflammatory and immunomodulator</td>
</tr>
<tr>
<td>Prednisolone¹</td>
<td>1955</td>
<td>Orapred ODT®</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone²⁴</td>
<td>1957</td>
<td>Medrol®, Solu-Medrol®, Depo-Medrol®</td>
<td>Oral, IV infusion or IM injection (in office), IA, IL, IM, or soft tissue injection (in office)</td>
<td>Anti-inflammatory and immunomodulator</td>
</tr>
</tbody>
</table>

IA=intraarticular; IL=intraleosional; IM=intramuscular; IV=intravenous, ODT=orally disintegrating tablet.

Nonbiologic Disease Modifying Antirheumatic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial US Approval</th>
<th>Brand Name</th>
<th>Route of Administration</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine¹</td>
<td>1950</td>
<td>Azulfidine®</td>
<td>Oral</td>
<td>Not well defined</td>
</tr>
<tr>
<td>Methotrexate²,³</td>
<td>1953</td>
<td>Generic</td>
<td>Oral</td>
<td>Dihydrofolate acid reductase inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Otrexup™</td>
<td>SC injection</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine⁴</td>
<td>1955</td>
<td>Plaquenil®</td>
<td>Oral</td>
<td>Not well defined</td>
</tr>
<tr>
<td>Azathioprine⁵,⁶</td>
<td>1968</td>
<td>Imuran®</td>
<td>Oral or IV infusion</td>
<td>Immunosuppressant</td>
</tr>
<tr>
<td>Leflunomide⁷</td>
<td>1998</td>
<td>Arava®</td>
<td>Oral</td>
<td>Pyrimidine synthesis inhibitor</td>
</tr>
</tbody>
</table>

Currently Available Biologic Agents Indicated for the Treatment of RA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial US Approval</th>
<th>Brand Name</th>
<th>Route of Administration</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>1998</td>
<td>Enbrel®</td>
<td>SC injection</td>
<td>TNF inhibitor</td>
</tr>
<tr>
<td>Infliximab</td>
<td>1998</td>
<td>Remicade®</td>
<td>IV infusion</td>
<td>TNF inhibitor</td>
</tr>
<tr>
<td>Anakinra</td>
<td>2001</td>
<td>Kineret®</td>
<td>SC injection</td>
<td>IL-1 receptor inhibitor</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>2002</td>
<td>Humira®</td>
<td>SC injection</td>
<td>TNF inhibitor</td>
</tr>
<tr>
<td>Certolizumab pegol®</td>
<td>2008</td>
<td>Cimzia®</td>
<td>SC injection</td>
<td>TNF inhibitor</td>
</tr>
<tr>
<td>Golimumab</td>
<td>2009</td>
<td>Simponi®</td>
<td>SC injection</td>
<td>TNF inhibitor</td>
</tr>
<tr>
<td>Rituximab</td>
<td>1997</td>
<td>Rituxan®</td>
<td>IV infusion</td>
<td>B-cell agent (anti-CD20 antibody)</td>
</tr>
<tr>
<td>Abatacept</td>
<td>2005</td>
<td>Orencia®</td>
<td>IV infusion or SC injection</td>
<td>T-cell agent (selective costimulator inhibitor)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>2010</td>
<td>Actemra®</td>
<td>IV infusion or SC injection</td>
<td>IL-6 inhibitor</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>2012</td>
<td>Xeljanz®</td>
<td>Oral</td>
<td>JAK inhibitor</td>
</tr>
</tbody>
</table>

IL=interleukin; IV=intravenous; JAK=Janus kinase; SC=subcutaneous; TNF=tumor necrosis factor.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Dosing and Administration</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baricitinib (LY3009104)</td>
<td>JAK1/2 inhibitor</td>
<td>Once daily oral dosing</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Secukinumab (Cosentyx®)</td>
<td>IL-17A antagonist</td>
<td>Monthly subcutaneous injection</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Ixekizumab (LY2439821)</td>
<td>IL-6 receptor antagonist</td>
<td>Subcutaneous injection</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Sarilumab</td>
<td>IL-6 receptor antagonist</td>
<td>Subcutaneous injection</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Sirukumab</td>
<td>IL-6 receptor antagonist</td>
<td>Subcutaneous injection</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

IL=interleukin; JAK=Janus kinase; RA=rheumatoid arthritis.

## Summary

<table>
<thead>
<tr>
<th>Treatment Goals</th>
<th>• Achieve remission, relieve symptoms, prevent joint and organ damage, improve physical function and well-being, and reduce long-term complications</th>
</tr>
</thead>
</table>
| Treatment Strategy | • Early and aggressive treatment  
• Treat-to-target (remission)  
• Achieve tight control through individualized therapy |
| Measures of Disease Activity/Progression | • Use validated measurements to guide treatment decision-making |
| Pharmacologic Management | • Long-term treatment often involves a sequence of different therapies  
• Optimal sequencing is determined by response, disease progression, and effects of therapies on disease pathways |
Current Practice Guidelines Review

Neil Minkoff, MD
Principal, FountainHead HealthCare
Chief Medical Officer, EmpiraMed, Inc.
• The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
  Neil Minkoff, MD
Outline

• Current American College of Rheumatology (ACR) RA Treatment Guidelines
• Principles guiding the 2015 revision of the document
• Anticipated revisions
American College of Rheumatology RA Treatment Recommendations

DMARDs=disease-modifying antirheumatic drugs.
Principles Guiding the 2015 Updates

- Focus on common or everyday patients, not exceptional cases
- Optimal dose of medication should be given for 3 months before escalating dose or switching to a new therapy
- Disease activity measurement using one of the ACR recommended measures should be performed in a majority of encounters
- Cost is considered as one of the many possible conditions for the recommendations
- MTX is the initial therapy prescribed for most RA patients
- All RA patients should see a rheumatologist
- Limit corticosteroid treatment to the lowest effective dose for shortest possible time

ACR=American College of Rheumatology; MTX=methotrexate.
Anticipated 2015 ACR Guideline Updates: Employ a Treat-to-Target Approach

**Targets**
- Low disease activity
- Remission
- Other appropriate target selected by the clinician and patient

**Functional Assessment**
- Routine functional assessment using standardized, validated tools
- Conducted at least once per year and more often in active RA

Anticipated 2015 ACR Guideline Updates: RA Treatment and Comorbidities

• Guidance is anticipated on the approach to treatment in RA patients with
  • Melanoma
  • Lymphoproliferative disorders
  • Hepatitis infection
  • Congestive heart failure

• Guidance will also be provided on the use of biologic therapy and the timing of vaccination

Anticipated 2015 ACR Guideline Updates: Therapeutic Selection and Sequencing

• Methotrexate remains first-line therapy for all patients
• Corticosteroids should be used at the lowest possible dose for the shortest possible time
• DMARD failure → combination of traditional DMARDs, TNF inhibitor, non-TNF-inhibitor biologic, or tofacitinib (± methotrexate)
• TNF failures
  • Failure of a single TNF inhibitor → another TNF inhibitor or a non-TNF biologic (± methotrexate)
  • Failure of multiple TNF inhibitors → non-TNF-inhibitor biologic or tofacitinib (± methotrexate)

• Non-TNF biologic failure
  • Failure of a single non-TNF inhibitor biologic → another non-TNF inhibitor biologic or tofacitinib (± methotrexate)
  • Failure of multiple non-TNF inhibitor biologics → tofacitinib or TNF inhibitor biologic (± methotrexate)
• Switching from one therapy to another should only be done at the discretion of the treating physician in consultation with the patient
• Patients with established RA in remission continuing on methotrexate can taper traditional DMARD therapy, TNF inhibitor, non-TNF biologic, or tofacitinib

The updated ACR RA treatment guidelines are expected to emphasize:

- Treating-to-target in both early and established RA.
- Goal is to achieve low disease activity or remission.
- Individualizing treatment.
- Using an optimal dose for 3 months before escalating or switching therapy.
- Routinely assessing disease activity.
- Treating patients with comorbid conditions.
- Tapering of therapy in patients in established remission.
An Analysis of Treatment Options, Comparative Effectiveness Research, and Benefit Designs for Rheumatoid Arthritis

Supported by an independent educational grant from Lilly. For further information concerning Lilly grant funding visit www.lillygrantoffice.com
Current and Emerging CER for Evidence-Based Treatment and Benefit Design Decision Making

Jeffrey Dunn, PharmD, MBA
Chief Clinical Officer
Senior Vice President
VRx Pharmacy Services, LLC
The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Jeffrey Dunn, PharmD, MBA

- Consulting Fees: Amgen Inc., Pfizer Inc.
Outline

• Overview of comparative effectiveness research (CER)
• Data sources
• Application of CER as a decision support tool
Why Don’t Patients Receive the “Best” Treatments?

Confounding variables include:
- Presence of comorbidities
- Patient age
- Health reimbursement system
- Year in which costs are determined
- Variation in study design

Differing underlying assumptions and study designs make comparison of clinical trial results difficult.
Why Comparative Effectiveness Research (CER)?

• Pharmacists, physicians, payers, policy makers, and patients must often rely on incomplete data when making health care decisions.

• Lack of head-to-head comparisons of competing treatment alternatives can lead to a “trial and error” approach to decision-making.

• If effectively designed and conducted, CER can help fill data gaps.
  • Used to compare drug therapies in the absence of head-to-head data.
  • Applicable to a wide variety of practice settings and diversity of patients.

Brixner DI, Oderda G. *J Manag Care Pharm.* 2012;18(Suppl. 4-a):S3-S4.
CER is Not a New Phenomenon

- CER existed before the recent legislative push for health care reform
- Health care decision makers have always compared one treatment with another
- The rise in health care costs has led to renewed emphasis on comparative effectiveness and cost-effectiveness
- Introduction of novel, efficacious, and expensive treatments has led to an increased emphasis on comparing treatments
  - Medications with each other
  - Procedures with each other
  - Procedures compared with medications or physical treatments (exercise, physical therapy, etc)
CER Utilized to Differentiate the Effectiveness vs Efficacy of Treatment Alternatives

**CAN IT WORK?**
- Randomized Controlled Trials

**DOES IT WORK?**
- Comparative Effectiveness Research
- Accumulated Evidence
- Clinical Guidelines
- Treatment Pathways

**IS IT WORTH IT?**
- Health Technology Assessments
- Informed Decision Making
- Benefit Design
- Formulary Positioning
- Coverage Decisions

CER Consolidates Evidence From Multiple Sources

• Prospective observational studies
• Peer-reviewed and published retrospective analyses of healthcare data including:
  • Medical or pharmacy claims
  • Electronic health records
  • Registries

CER Consolidates Evidence From Multiple Sources (cont’d)

- Systematic reviews/meta-analyses
- Agency for Healthcare Research and Quality (AHRQ) CER reviews
- Cochrane reviews
- Accessible health technology assessment reports (eg, the National Institute for Health and Clinical Excellence [NICE])
- Tailored reviews (technology assessments) using published data
- In-house data analysis

CER: How Can it Change Practice?

- Establishing parameters to measure improvements
  - Outcomes
  - Reduction in costs
  - Increase in value
- Determining threshold of positive effect to alter current behavior
  - Patients
  - Providers
  - Payers

Application of CER to Rheumatoid Arthritis
RA is a Prime Target for Comparative Effectiveness Research

High Budget Impact and Lack of Clear Clinical Superiority Among Biologic Alternatives Makes RA an Attractive Target for CER

Potential Budget Impact (Revenues, pipeline intensity)

Comparable Alternatives (Number of agents, degree of genericization)

Clinical questions addressed include:

- Do drug therapies for RA differ in their ability to reduce disease activity, to slow or limit the progression of joint damage, or to maintain remission?
- Do RA drugs differ in their ability to improve patient-reported symptoms, functional capacity, or quality of life?
- Do RA drugs differ in harms, tolerability, patient adherence, or adverse effects?
- What are the comparative benefits and harms of drug therapies for RA in subgroups of patients, based on stage of disease, prior therapy, demographics, concomitant therapies, or comorbidities?
### CER Results: Biologic DMARDs

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologic DMARDs provide greater symptom response and remission rate vs. oral DMARDs for patients with longstanding active RA requiring a change in therapy.</td>
<td>Risk of serious infections increases when patients are treated with biologic DMARDs.</td>
</tr>
<tr>
<td>Combining two biologic DMARDs (etanercept with abatacept or anakinra) does improve disease activity, functional capacity, or symptom response more than one biologic DMARD and increases the risk of serious adverse effects.</td>
<td>Combining two biologic DMARDs leads to substantially higher rates of serious adverse events (AEs) than monotherapy.</td>
</tr>
<tr>
<td>Comparisons across studies of patients resistant to MTX suggest that there may be clinically observable differences in the efficacy of the biologic DMARDs.</td>
<td>Rate of AEs did not increase over time in long-term studies of adalimumab, anakinra, etanercept, and infliximab.</td>
</tr>
<tr>
<td></td>
<td>No consistent evidence of elevated risk of lymphoma or other cancer types associated with biologic DMARDs (vs oral DMARDs or placebo); actual risk not clear.</td>
</tr>
<tr>
<td></td>
<td>Evidence is insufficient to permit conclusions about differences in risks for rare but serious AEs among biologic DMARDs (demyelination, autoimmunity, hepatotoxicity).</td>
</tr>
</tbody>
</table>

CER Results: Combining Oral and Biologic DMARDs

### Benefits
- In patients with inadequate disease control who required a change in treatment, combination therapy with a biologic DMARD and MTX achieved greater improvements in some outcomes than either a biologic DMARD or MTX alone.
- In patients whose RA failed to respond to first-line MTX, combination therapy with MTX and a biologic DMARD was not more successful than monotherapy with a biologic DMARD.
- In MTX-naive patients or those not recently on MTX, combination therapy is superior to monotherapy with a biologic DMARD for functional capacity and quality of life.

### Adverse Events
- Combining MTX or other oral DMARDs with a biologic DMARD does not alter the adverse event (AE) rate found with the biologic DMARD alone.
- Combining MTX and biologic DMARDs demonstrates a better tolerability profile than MTX alone.
- The evidence is insufficient to estimate differences in rates of specific AEs between the biologic and oral DMARDs.

## CER Results:
### DMARDs For Patients With Early RA

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination strategies that use corticosteroids plus 2 to 3 oral DMARDs are more effective than oral DMARD monotherapy for improving symptom response, disease activity, and functional capacity in the short-term and reducing radiographic evidence of progression and joint erosion in the longer term (≥1 year).</td>
<td>Adding prednisone to treatment with one or multiple oral DMARDs does not increase treatment discontinuation rates.</td>
</tr>
<tr>
<td>Combining one oral DMARD with prednisone reduces radiographic progression and joint erosion more than the DMARD alone.</td>
<td>Combining oral DMARDs (sulfasalazine and MTX) increases withdrawal from treatment due to adverse events.</td>
</tr>
</tbody>
</table>

For MTX-naive patients with early, aggressive RA, combining MTX with a biologic DMARD (abatacept, adalimumab, etanercept, or infliximab) provides greater improvement than biologic DMARD monotherapy for symptom response, clinical remission rates, and radiographic progression.

CER in Formulary and Benefit Design: How to Evaluate Without Head-to-Head Trials

• Identify and target key trials with similar patient characteristics, outcome measures, inclusion/exclusion criteria, etc.
• Evaluate drug benefit minus placebo benefit over defined time frame of defined and appropriate outcome measure(s)
• Determine appropriate costs over same time period
• Divide cost into drug benefit
• Compare cost to achieve predefined response
  • “How much do we pay for an outcome with all of the drugs?”
• Have to hold industry accountable
Summary

• Incomplete data can impact decision-making in health care decisions
• Comparative effectiveness research can be utilized to generate and/or synthesize data to support health care decision-making
  • Intent of CER is to describe whether a treatment works for the average patient in the average practice
• CER requires valid and feasible data from multiple sources
• A comprehensive CER analysis of 211 studies of drugs used to treat RA was conducted by the AHRQ
An Analysis of Treatment Options, Comparative Effectiveness Research, and Benefit Designs for Rheumatoid Arthritis

Supported by an independent educational grant from Lilly. For further information concerning Lilly grant funding visit www.lillygrantoffice.com
Analyzing the Available Data to Assess the Value of Current and Emerging Treatment Options

Fadia Tohme-Shaya, PhD, MPH
Professor and Vice Chair for Academic Affairs PHSR
University of Maryland School of Pharmacy
Faculty Disclosure

• The faculty reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:
  Fadia Tohme-Shaya, PhD, MPH
  • No financial interest/relationships relating to the topic of this activity
• Clinical and economic burden of rheumatoid arthritis (RA)
• Determining the value of current and emerging RA treatment regimens
• Application to patient care and managed care decision-making
RA Disease Burden Extends Beyond the Joint

Articular disease
- Joint inflammation
- Cartilage degradation
- Bone erosion
- Loss of joint function

Psychosocial aspects
- Impaired HRQOL
- Fatigue
- Depression
- Cognitive dysfunction
- Reduced work performance
- Work disability

Comorbidities
- Cardiovascular disease
- Osteoporosis
- Lung disease
- Infection
- Malignancy

Physical inactivity
- Treatment effects
Clinical Burden of RA

- **Prevalence**: ~0.5 to 1.0% of the US population\(^1\)
- **Ambulatory care events**: 2.9 million ambulatory care visits
- **Hospitalizations**: >15,000 hospitalizations with RA listed as the principle diagnosis
- **Cardiovascular (CV) risk**: 5x higher CV event rate vs general population
- **Disability**: Many RA patients are unable to work within 10 years of onset
  - Pre-biologic era: 50%\(^2\)
  - Current: 26%\(^3\)
- **Excess deaths**: Mortality rate is 1.5 to 1.6-fold higher in RA patients vs general population

---

Economic Burden of RA

• RA exerts considerable incremental economic burden on the health care system

• Excess costs include expenditures on
  • Pharmacy
  • Office visits
  • Emergency care
  • Inpatient stays

• Total incremental expenditure of all RA patients: ~$22.3 billion

Cost of RA Treatment Increases Over Time as Function Declines


*50% rates of loss of function based on Health Assessment Questionnaire (HAQ) scores.*
Medical Resource Utilization is Highest in Patients with Highly Active RA

Total Medical Resource Use over 6 Months

- Low Disease Activity: $4000
- High Disease Activity: $7900
- Remission: $5500

Determining the Value of RA Treatment Options
Determining the Value of RA Treatments

• The relatively high cost and expanding use of biologics make them an important target for economic evaluation

• Economic evaluation tools include
  • Cost-effectiveness analysis (CEA) compares the cost and effectiveness of two or more treatments
  • Cost-utility analysis (CUA) is a subtype of CEA, applying quality-adjusted life-years (QALY) as a measure of effectiveness
    • Primary outcome measure in CUA is the incremental cost-effectiveness ratio (ICER)
    • ICER describes the ratio of the additional costs of a treatment (vs an alternative) to QALYs gained
Biologics Do Not Appear to be Cost-Effective as First Line Therapy

• Anti-TNF agents are less cost-effective vs conventional DMARDs for newly diagnosed, treatment-naïve patients\(^1,2\)

BeST=The Dutch Behandel Strategieen study.
ICERs Favor Treatment with Conventional DMARDs in the First Line

Cost Utility Analyses

<table>
<thead>
<tr>
<th>Conventional DMARD vs</th>
<th>ICER ($/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Payer Perspective</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>$63,281 to $382,982/QALY</td>
</tr>
<tr>
<td>Infliximab</td>
<td>$71,936 to $1,464,344/QALY</td>
</tr>
<tr>
<td>Etanercept</td>
<td>$110,389 to $175,721/QALY</td>
</tr>
<tr>
<td>TNFa inhibitors (class)</td>
<td>$139,744</td>
</tr>
<tr>
<td></td>
<td>Societal Perspective</td>
</tr>
<tr>
<td>Infliximab</td>
<td>$141,827</td>
</tr>
<tr>
<td>TNFa inhibitors (class)</td>
<td>$137,843</td>
</tr>
</tbody>
</table>

- These (and similar) findings lead most payers to require a trial of conventional DMARDs in treatment-naïve patients

Biologics Begin to Be Cost Effective After Failure of a Conventional DMARD

- Early treatment should be with nonbiologic therapies
- Biologic treatments become cost effective after failure of therapy a conventional DMARD

ICERs Favor Treatment with Biologics in DMARD Inadequate Responders (IR)

<table>
<thead>
<tr>
<th>Sequential use/switching to another DMARD vs</th>
<th>ICER ($/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab</td>
<td>$29,654/QALY</td>
</tr>
<tr>
<td>Abatacept</td>
<td>$58,376/QALY</td>
</tr>
<tr>
<td>Etanercept</td>
<td>$32,465 to $154,057/QALY</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>$33,396 to $317,650/QALY</td>
</tr>
<tr>
<td>Infliximab</td>
<td>$37,225 to $313,144/QALY</td>
</tr>
<tr>
<td>TNFa inhibitors (class)</td>
<td>$53,802 to $291,531/QALY</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Societal Perspective</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>$59,924/QALY</td>
</tr>
<tr>
<td>Etanercept</td>
<td>$25,727 and $76,089/QALY</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>$34,183/QALY</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>$29,707/QALY</td>
</tr>
</tbody>
</table>

Cost-effective Strategy in the Treatment of TNF-IR Patients

• Anti-TNF agents are frequently used sequentially in case of an inadequate response (IR) or intolerance to another anti-TNF agent.

• Switching between biologic agents is common in medical practice.
  • However, there is limited evidence that compares the overall costs and effectiveness of such a strategy.

## Cost-effective Strategy in the Treatment of TNF-IR Patients

<table>
<thead>
<tr>
<th>Sequential use/switching to another anti-TNF vs</th>
<th>ICER ($/QALY)</th>
<th>Payer Perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abatacept</td>
<td>$78,303 to $270,539/QALY</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>$26,314 to $40,868/QALY</td>
<td></td>
</tr>
</tbody>
</table>

- Rituximab was found to be the most cost-effective alternative compared to other biologics among the patients with an insufficient response to an anti-TNF agent

Cost-effectiveness of JAK Inhibitors as First Line Therapy

- Comparison of treatment of patients with moderate-to-severe RA using an anti-TNF agent or an oral JAK inhibitor
- Cost-utility analysis (societal perspective) of the phase 3 placebo-controlled Oral Rheumatoid Arthritis Trial (ORAL)
  - Efficacy assessed using ACR response rates, converted to the changes in Health Assessment Questionnaire-Disability Index (HAQ-DI) score
  - HAQ-DI scores were mapped onto utility values to calculate outcomes in terms of quality-adjusted life-years (QALYs)
  - Costs were analyzed from a societal perspective
  - Cost-effectiveness is presented in ICERs

1st Line Treatment with Oral JAK Inhibitors in Moderate-to-Severe RA Appears to be Cost-effective

• 1st line use of oral JAK inhibitors increased QALYs gained vs standard-of-care, resulting in an ICER of ~$13,000 per QALY
  • Treatment with the oral JAK inhibitor also increased costs and QALYs gained when incorporated as a 2nd, 3rd, or 4th line therapy
• JAK inhibitor-associated increases in costs were attributable to the increased lifetime drug costs
• Sensitivity analyses yielded ICERs in the range of ~$6,000 to $32,000/QALY
• From a societal perspective, the inclusion of an oral JAK inhibitor as a treatment strategy for moderate-to-severe RA is cost-effective

• RA is associated with significant clinical and economic costs
• Anti-TNF agents are less cost-effective options for 1st line treatment vs conventional DMARDs
• Treatment with an anti-TNF agent in patients refractory to previous DMARD therapies is more cost-effective, vs switching to another conventional DMARD
• In TNF-IR patients, rituximab appears to be more cost-effective than switching to another anti-TNF agent
• Treatment with an oral JAK inhibitor for moderate-to-severe RA appears to be cost-effective across the treatment sequence
An Analysis of Treatment Options, Comparative Effectiveness Research, and Benefit Designs for Rheumatoid Arthritis
Plan Benefit Designs:
Maximizing Value for Current and Emerging RA Therapies

Jeffrey Dunn, PharmD, MBA
Chief Clinical Officer
Senior Vice President
VRx Pharmacy Services, LLC
• Coverage strategies for current RA therapies
• Impact of advances in RA therapeutics on benefit design
Sales of Specialty Drugs Continues to Grow

Spending on Specialty Drugs Projected to Surpass Sales of Traditional Agents by 2018

Forecasts PMPY net drug spend ($)

- **2012**: $290 (Traditional $665, Specialty $348)
- **2013**: $348 (Traditional $675, Specialty $348)
- **2014**: $425 (Traditional $694, Specialty $425)
- **2015**: $514 (Traditional $722, Specialty $514)
- **2016**: $612 (Traditional $751, Specialty $612)
- **2017**: $722 (Traditional $789, Specialty $722)
- **2018**: $845 (Traditional $836, Specialty $845)

PMPY=per member per year

Growth of Pharmacy Spending on Specialty Drugs in Commercial Plans Expected to Grow as Coverage is Shifted Out of the Medical Benefit

Forecasted net prescription drug spend (%)

<table>
<thead>
<tr>
<th>Year</th>
<th>Traditional</th>
<th>Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>2013</td>
<td>66%</td>
<td>34%</td>
</tr>
<tr>
<td>2014</td>
<td>62%</td>
<td>38%</td>
</tr>
<tr>
<td>2015</td>
<td>58%</td>
<td>42%</td>
</tr>
<tr>
<td>2016</td>
<td>55%</td>
<td>45%</td>
</tr>
<tr>
<td>2017</td>
<td>52%</td>
<td>48%</td>
</tr>
<tr>
<td>2018</td>
<td>50%</td>
<td>50%</td>
</tr>
</tbody>
</table>

### Specialty Categories Under the Pharmacy Benefit

<table>
<thead>
<tr>
<th>RANK</th>
<th>THERAPY CLASS</th>
<th>PMPY SPEND</th>
<th>UTILIZATION</th>
<th>UNIT COST</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inflammatory Conditions</td>
<td>$80.03</td>
<td>8.5%</td>
<td>15.7%</td>
<td>24.3%</td>
</tr>
<tr>
<td>2</td>
<td>Multiple Sclerosis</td>
<td>$52.36</td>
<td>3.2%</td>
<td>9.7%</td>
<td>12.9%</td>
</tr>
<tr>
<td>3</td>
<td>Oncology</td>
<td>$41.64</td>
<td>8.9%</td>
<td>11.7%</td>
<td>20.7%</td>
</tr>
<tr>
<td>4</td>
<td>Hepatitis C</td>
<td>$37.95</td>
<td>76.1%</td>
<td>666.6%</td>
<td>742.6%</td>
</tr>
<tr>
<td>5</td>
<td>HIV</td>
<td>$27.24</td>
<td>4.5%</td>
<td>10.3%</td>
<td>14.8%</td>
</tr>
<tr>
<td>6</td>
<td>Miscellaneous Specialty Conditions</td>
<td>$11.10</td>
<td>27.3%</td>
<td>8.2%</td>
<td>35.6%</td>
</tr>
<tr>
<td>7</td>
<td>Growth Deficiency</td>
<td>$9.98</td>
<td>-0.9%</td>
<td>7.5%</td>
<td>6.6%</td>
</tr>
<tr>
<td>8</td>
<td>Hemophilia</td>
<td>$5.49</td>
<td>-0.8%</td>
<td>17.6%</td>
<td>16.9%</td>
</tr>
<tr>
<td>9</td>
<td>Pulmonary Arterial Hypertension</td>
<td>$5.41</td>
<td>7.6%</td>
<td>6.2%</td>
<td>13.8%</td>
</tr>
<tr>
<td>10</td>
<td>Transplant</td>
<td>$5.13</td>
<td>0.8%</td>
<td>-3.1%</td>
<td>-2.3%</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL SPECIALTY</strong></td>
<td><strong>$311.11</strong></td>
<td><strong>5.8%</strong></td>
<td><strong>25.2%</strong></td>
<td><strong>30.9%</strong></td>
</tr>
</tbody>
</table>

PMPY=per member per year.
## RA Management Challenges: Drug and Disease Cost Issues and Trends

### Drug Costs
- Drug acquisition
- Pipeline burgeoning with novel biologic agents
- Price increases vs rebates

### Administrative Burden
- Elusiveness of data to determine total costs due to lack of transparency driven by medical/pharmacy benefit designs
- Parity laws
- Patient education/health management programs
- Management of safety monitoring

### Total Costs to be Evaluated
- Direct and indirect
- Contract implications of indications
- Role of Patient Assistance Programs
RA Management Challenges: Increasing Number of Biologic Agents

- No standardized outcomes measures used in clinical practice
- Growing number of biologic agents for the treatment of RA
  - Not every biologic agent works for every RA patient
  - Little understanding of the cause of variation of drug efficacy between patients
- Guidelines on how biologics should be used to optimize RA treatment outcomes are lacking
  - Importance of understanding the optimal use of these agents magnified by their high cost
- Physicians, patients, and plan managers need better data to compare the effectiveness of the different biologics

Benefit Design: Multi-tier Structure

• All specialty is NOT created equal
• 12 of 36 health plans with specialty strategy have multi-tier specialty cost share
  • Accounts for 45% of covered lives
• 93% of PBMs plan to increase use of specialty tier in next 24 months

• Proposal:
  • Multi-tier specialty formulary
    • Generic specialty tier
    • Preferred specialty tier
    • Non-preferred specialty tier
• Optional to clients but structure in place for those that want to participate in specialty strategy

EMD Serono Specialty Digest, 9th Edition. Managed care strategies for specialty pharmaceuticals
Benefits

• Further differentiation of specialty class
  • Cost management
  • Ability to manage specialty classes
• Contracting benefits
• Provides a strategy solution for employer groups and health plans

Possible Difficulties

• Multiple layers adds confusion
  • Client
  • Member
  • Customer Service
  • Internal
• More time spent managing the formulary

<table>
<thead>
<tr>
<th>Tier</th>
<th>Specialty “Opt In”</th>
<th>“Opt out”</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (generic)</td>
<td>10%</td>
<td>20%</td>
</tr>
<tr>
<td>5 (preferred)</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>6 (non-preferred)</td>
<td>40%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Contracting and Rebates for Preferred Products

10-15% Savings

Contracting Activities

Specialty Drug Management

Drug Dispensing

Utilization Management

Coordination of Care
Contracting and Rebates

• Create “preferred” products within key therapeutic classes
  • Maximize rebate potential
  • Control utilization
• 2013 EMD Serono Specialty Report identifies 15 therapeutic classes where health plans have preferred products

<table>
<thead>
<tr>
<th>Preferred Product Categories</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MS (IM/SC)</td>
<td>Growth hormone</td>
</tr>
<tr>
<td>RA/CD (SC)</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>HCV (oral)</td>
<td>HCV (SC)</td>
</tr>
<tr>
<td>ESAs</td>
<td>PAH (oral/inhaled)</td>
</tr>
<tr>
<td>RA/CD (IV)</td>
<td>HA derivatives</td>
</tr>
</tbody>
</table>

Channel Management: Drug Dispensing

1-3% Savings
Channel Management (Medical to Pharmacy) 5-10% savings

Drug Dispensing

Specialty Drug Management

Utilization Management

Coordination of Care

Contracting Activities
Drug Dispensing

• Channel management
  • Medical claim Site-of-Care Optimization
  • Pharmacy channel management

<table>
<thead>
<tr>
<th>Place of Service</th>
<th>Cost per Unit</th>
<th>Units</th>
<th>Cost Per Claim</th>
<th>Claims per Year</th>
<th>Annual Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD office or home infusion</td>
<td>$70</td>
<td>50</td>
<td>$3,500</td>
<td>7</td>
<td>$24,500</td>
</tr>
<tr>
<td>HOPD (average)</td>
<td>$111</td>
<td>50</td>
<td>$5,500</td>
<td>7</td>
<td>$38,850</td>
</tr>
<tr>
<td>HOPD (highest cost hospital)</td>
<td>$360</td>
<td>50</td>
<td>$18,000</td>
<td>7</td>
<td>$126,000</td>
</tr>
</tbody>
</table>

HOPD = hospital outpatient department.
Internal utilization and pricing data.
Channel Management: Utilization Management

- Drug Dispensing
- Specialty Drug Management
- Utilization Management
- Contracting Activities
- Coordination of Care

5-7% Savings
Utilization Management

- Prior authorizations
- Step-therapy
- Quantity limits
- Reporting

Use of Prior Authorizations by Disease State

GH Disorders
RA/Crohn's Disease (SC)
Hepatitis C (Oral)
MS (Oral)
Hepatitis C (SC)
ESAs
MS (SC)
RA/Crohn's Disease (IV)
Psoriasis
Botulinum Toxins
RSV
MS (IV)
Immune Globulin (IV)
Immune Globulin (SC)

Utilization Management (cont’d)

Analysis
- Review of specialty database for clinically appropriate quantity limits and PAs
  - Opportunities exist to further control utilization by implementing PAs and QLs on medications
- Evaluate PA/step-therapy effectiveness

Actions
- Multiple layers adds confusion
  - Client
  - Member
  - Customer Service
  - Internal
- More time spent managing the formulary

PA=prior authorization; QL=quantity limits.
Utilization Management (cont’d)

Plan

• Reporting
  • Control utilization through analysis of medications that require special dosing
    • Medical therapy management (MTM) outreach/education on these medications

Actions

• Create list of targeted medications
• Develop reporting system in claims system
• Implement intervention in MTM program
Channel Management: Care Management

- Drug Dispensing
- Specialty Drug Management
- Utilization Management
- Contracting Activities
- Coordination of Care

5-10% Savings
**Care Management**

- **Opportunity**
  - Costs will continue to rise (How to get the most out of drug spend?)

- **Fill the specialty pharmacy “gap”**
  - Education on use
  - Education on side effects
  - Adherence
  - Site-of-care optimization

---

Specialty Care Management

**Program**
- Specialty Pharmacy MTM
  - Integration with care management
  - Coordinate site-of-care
  - Ensure appropriate dosing
  - Adherence
  - Education on use
  - Expectation management

**Actions**
- Design program workflow and integration with care management
- Analyze utilization to select targeted drugs/disease states
- Train personnel:
  - Specialty diseases
  - Medications
  - Site-of-care logistics
What is a Biosimilar (Then)?

Close, but...?
What is a Biosimilar (Now)?

Close, but...?
Issues with Biosimilars

- Rating/interchangeability
- Data extrapolation/indications
- Safety

- Manufacturing
- Cost

**Best selling Biologics Patent Cliff**

<table>
<thead>
<tr>
<th>Year</th>
<th>Enbrel®</th>
<th>NovoLog®</th>
<th>Lantus®</th>
<th>Neulasta®</th>
<th>Humira®</th>
<th>Rituxan®</th>
<th>Remicade®</th>
<th>Avastin®</th>
<th>Herceptin®</th>
<th>Lucentis®</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>Amgen</td>
<td>Novo Nordisk</td>
<td>Sanofi-Aventis</td>
<td>Amgen</td>
<td>Abbott</td>
<td>Genentech</td>
<td>Centocor</td>
<td>Genentech</td>
<td>Genentech</td>
<td>Genentech</td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2010</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2015</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>2020</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sales

- 2011: $7.9
- 2015: $3.9
- 2020: $3.8

**Sales**

- Amgen: $7.9
- Novo Nordisk: $2.4
- Sanofi-Aventis: $5.4
- Genentech: $6.0
- Genentech: $6.8
- Genentech: $7.2
Summary

• Spending on specialty drugs projected to surpass sales of traditional agents by 2018
• RA drugs represent a significant proportion of the specialty spend and the number of available biologic agents continues to increase
• Strategies include multi-tier specialty formularies, contracting activities, channel management, utilization management, care management, and specialty pharmacy management
• Biosimilars are poised to enter the RA biologic market
• It remains challenging to identify the most effective allocation of agents for optimal RA management
An Analysis of Treatment Options, Comparative Effectiveness Research, and Benefit Designs for Rheumatoid Arthritis

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