MANAGED CARE BIOSIMILARS UPDATE:
2017 POLICY INITIATIVES & FORMULARY IMPACT

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About the Faculty

Steven G. Avey, MS, RPh, FAMCP

Steven Avey is a distinguished expert in managed care and namesake of the Academy of Managed Care Pharmacy (AMCP) Foundation’s prestigious lifetime achievement award, the Steven G. Avey Award. AMCP renamed their award in recognition of his achievements in quality measurement programs and improving drug assessment processes in the U.S. As Vice President of Specialty Programs at MedImpact, Steven is responsible for setting the overall business strategy in the specialty arena.

For the past 5 years, Steve has devoted his full attention to the appropriate management of specialty medications. His passion is working with clinicians and health outcomes researchers to better understand the value each specialty medication brings to a patient population and given their high cost, determine when and how they should be utilized. Due to the relatively small number of patients that must take a specialty medication, it leaves many opportunities for contracted pharmacies to directly influence the health status of these patients and better manage their care.

Steve began his career in retail practice, but following graduate school, managed care pharmacy became his focus. He initially started with Prospective Health (now Relay Health), where he helped establish and run its data services division. In 2000, after serving as treasurer and president of AMCP, he was hired as the executive director of the Foundation for Managed Care Pharmacy. This foundation presented education programs across the country training physicians and pharmacists how to better assess the value of new therapies. In 2005, Steve left AMCP to become Vice President of Managed Care at Partners Rx Management. Six years later he joined RegenceRx where we worked to assess the company’s services, networks and rebates to determine how RegenceRx could better service its health plan.

In January 2013, Avey was named Vice President, Specialty Pharmacy Programs for MedImpact in San Diego, California. In this role, he is setting the overall business and clinical strategy in the specialty arena and developing a team to support MedImpact’s clients as they forge into the new era of substantial specialty usage and spend.

Steve holds a Bachelor of Science degree in pharmacy and a Master of Science degree in pharmacy administration from the University of Utah. He was named the College of Pharmacy’s outstanding alumnus in 2003.

Steven Lucio, PharmD, BCPS

Steven Lucio is Associate Vice President for Clinical Solutions and Pharmacy Program Development at Vizient, a health care supply chain and analytics company in Irving, Texas. During his tenure, he has had responsibility for providing clinical education to member organizations on practice topics including improving medication safety, mitigating the impact of drug shortages, benchmarking pharmacy costs for key drug classes, evaluating the expense of high cost biologics and specialty drugs and preparing for future trends such as the development of biosimilars. Prior to joining Vizient, Steven practiced for almost 10 years within the Baylor Health Care System in both inpatient and ambulatory care. Steven received his Doctor of Pharmacy degree from Creighton University, his Bachelor of Science in Pharmacy from the University of Texas at Austin, and is a Board Certified Pharmacotherapy Specialist. He is author of several recent publications and a frequent presenter on the topic of biosimilars.
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Learning Objectives

• Summarize the current status of biosimilar development in United States, including FDA approval pathway, FDA guidance documents, and the approval status and pipeline for biosimilars
• Describe the use of extrapolation/interchangeability in the FDA approval process for biosimilars and their indications, and how this may impact formulary diagnostic criteria and tier placement

Learning Objectives

• Recognize how conflicts between state legislative initiatives and FDA guidance may impact managed care policy
• Identify economic and formulary implications surrounding the uptake and use of biosimilar agents in clinical practice
• List the clinical, legal, and operational implications that institutions must consider when preparing to add biosimilars to formularies
Polling Question #1

How many interchangeable biosimilars have been approved for marketing in the US?
A. 2
B. 4
C. 5
D. 6
E. None

Polling Question #2

Which of the following is a correct non-proprietary name for a currently approved biosimilar?
A. Infliximab-cool
B. Adalimumab-best
C. Etanercept-ASAP
D. Infliximab-atto
E. Infliximab-dyyb
Polling Question #3

Which of the following attributes could impact the requirements to determine the interchangeability status of a biosimilar?

A. Size of molecule  
B. Complexity of the molecule  
C. Risk of immunogenicity  
D. Degree of analytical characterization  
E. All of the above

WHERE DO WE CURRENTLY STAND WITH BIOSIMILARS

February 2017 Update
It’s Been a Busy Couple of Months!

- November 2016
  - Launch of Inflectra (infliximab-dyyb)
- December 2016
  - Finalization of biologic clinical pharmacology and naming guidances
- January 2017
  - Supreme Court to hear biosimilar litigation
  - Publication of draft interchangeability guidance
  - Acceptance of applications for biosimilar versions of trastuzumab and adalimumab

And Then There Were Four (Approved Biosimilars)

- First biosimilar - Filgrastim-sndz (Zarxio; Sandoz)
  Approved March 6, 2015
  Launched September 3, 2015
- Second biosimilar - Infliximab-dyyb (Inflectra; Celltrion/Pfizer)
  Approved April 5, 2016
  Launch date = November 2016 (15% discount off of Remicade WAC)
- Third biosimilar – etanercept-szsz (Erelzi; Sandoz)
  Approved August 30, 2016
  Estimated launch date: ?????? 
- Fourth biosimilar – adalimumab-atto (Amjevita; Amgen)
  Approved September 23, 2016
  Estimated launch date: ??????

PDUFA = Prescription Drug User Fee Act
The Pink Sheet, FDA Performance Tracker, Pending Biosimilars (subscription), accessed January 20, 2017; Drugs@FDA, accessed October 5, 2016
Managed Care Biosimilars Update: 2017 Policy Initiatives and Formulary Impact

Biosimilar Pipeline

<table>
<thead>
<tr>
<th>INN</th>
<th>Manufacturer</th>
<th>Application Submitted</th>
<th>Estimated FDA Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab (SB2)</td>
<td>Samsung Bioepis</td>
<td>3/2016</td>
<td>1/2017</td>
</tr>
<tr>
<td>Pegfilgrastim (CHS-1701)</td>
<td>Coherus</td>
<td>8/2016</td>
<td>6/2017</td>
</tr>
<tr>
<td>Trastuzumab (MYL-1401O)</td>
<td>Mylan and Biocon</td>
<td>11/2016</td>
<td>9/2017</td>
</tr>
<tr>
<td>Bevacizumab (ABP 215)</td>
<td>Amgen and Allergan</td>
<td>11/2016</td>
<td>9/2017</td>
</tr>
</tbody>
</table>

- Also, Adalimumab biosimilar from Boehringer accepted for review (1/2017), but estimated approval date still pending
- Sandoz (pegfilgrastim), Apotex (filgrastim, pegfilgrastim), and Hospira (epoetin) working on refiling previously submitted applications
- Ongoing litigation will determine the exact date of biosimilar launch

The Pink Sheet, FDA Performance Tracker, Biosimilars, accessed 1/20/2017

LEGAL ACTIVITIES AND REGULATORY GUIDANCE
Ongoing Litigation

• Ongoing Litigation
  – Issues: patent dance; 180 day notification
    • Amgen vs. Sandoz (filgrastim)
    • Janssen vs. Celltrion (infliximab)
    • Amgen vs. Apotex (pegfilgrastim)
    • Amgen vs. Hospira (epoetin)
    • Immunex vs. Sandoz (etanercept)
    • Amgen vs. Sandoz (pegfilgrastim)
    • AbbVie vs. Amgen (adalimumab)
  – Supreme Court to hear Amgen vs. Sandoz


Biosimilar Guidances

• 11 published guidances
  – 6 finalized
    • Scientific considerations
    • Quality considerations
    • Questions and answers
    • Formal meetings with FDA
    • Clinical pharmacology
    • Non-proprietary naming

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm290967.htm;
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm065010.htm
What’s in a Name?

- Two names for biologics
  - Core name = (e.g. infliximab)
  - Proper name = core name plus four letter suffix (e.g. infliximab-dyyb)
    - Suffix must be unique and devoid of meaning
  - Will ultimately apply to all biologics
- Why?
  - Prevent inadvertent substitution
  - Improve pharmacovigilance
  - Encourage use of FDA-designated suffixes
  - Advance accurate perceptions about biologicals


Naming in Practice

<table>
<thead>
<tr>
<th>Current</th>
<th>Proposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filgrastim</td>
<td>Filgrastim-jcwp</td>
</tr>
<tr>
<td>Filgrastim-sndz</td>
<td>Filgrastim-bflm</td>
</tr>
<tr>
<td>Tbo-filgrastim</td>
<td>Filgrastim-vkzt</td>
</tr>
<tr>
<td>Epoetin alfa</td>
<td>Epoetin alfa-cgkn</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Infliximab-hjmt</td>
</tr>
</tbody>
</table>

Approved biosimilars with proper name completed: infliximab-dyyb, etanercept-szss, adalimumab-atto

Interchangeability Guidance (FINALLY!)

- Key elements
- Interchangeability requires switching study (or studies) and possibly post-marketing data
- Requirements affected by complexity of molecule, analytical characterization, and likelihood of immunogenicity adverse events
- Cannot use non-US licensed data in switching study
  - 60 day comment period
  - Submit comments at https://www.regulations.gov/


State Biosimilarity Legislation Continues

- 36 states have considered legislation
- 25 states, plus Puerto Rico have been signed into law
- Common features
  - FDA determination as interchangeable – “Purple Book”
  - Physician dispense as written authority
  - Physician notification, patient notification and consent of substitution
  - Record keeping requirements
  - Cost information to the patient

PERSPECTIVES ON APPROVALS TO DATE

The ABC’s and E’s of Biosimilars

- Accept the Accuracy of Analytics
- Build a Bridge with non-US licensed biosimilars
- Curb the expectation of clinical trials in every indication
  – (embrace extrapolation)
- See example of bridging and extrapolation on next slide
### The Utility of Bridging

<table>
<thead>
<tr>
<th>Study (Dates)</th>
<th>Design (Objectives)</th>
<th>Patient Population (Total Number)</th>
<th>Treatment Arms</th>
<th>Number per arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT-P13 3.1 (Global, ex-US) 54 weeks (12/10 to 07/12)</td>
<td>R, DB, PG Comparative Clinical Study: Efficacy, Safety, PK, Immunogenicity</td>
<td>Moderate to Severe RA, MTX-IR N=606</td>
<td>CT-P13 3 mg/kg + MTX EU-approved infliximab</td>
<td>n = 302 n = 300</td>
</tr>
<tr>
<td>CT-P13 1.1 (Global, ex-US) 54 weeks (12/10 to 07/12)</td>
<td>R, DB, PG PK, Efficacy, Safety, Immunogenicity</td>
<td>Moderate to Severe AS N = 250</td>
<td>CT-P13 5 mg/kg EU-approved infliximab</td>
<td>n = 128 n = 122</td>
</tr>
<tr>
<td>CT-P13 1.4 Single Dose (10/13 to 02/14)</td>
<td>R, DB, PG, SD 3-way PK bridging: PK, Safety, Immunogenicity</td>
<td>Healthy volunteers N = 213</td>
<td>CT-P13 5 mg/kg EU-approved Remicade 5 mg/kg US-licensed Remicade 5 mg/kg</td>
<td>n = 71 n = 71 n = 71</td>
</tr>
</tbody>
</table>


### Biosimilar Approval and Extrapolation

<table>
<thead>
<tr>
<th>Zarxio</th>
<th>Inflectra</th>
<th>Erelzi</th>
<th>Amjevita</th>
</tr>
</thead>
</table>
| **Name** | • Filgrastim-sndz (place holder)  
• Proposed name: filgrastim-bfim | • Infliximab-dyyb | • Etanercept-szss | • Adalimumab-atto |
| **Indications studied** | Myelosuppressive chemotherapy | Rheumatoid arthritis  
Ankylosing spondylitis | Plaque psoriasis | Rheumatoid arthritis  
Plaque psoriasis |
| **Indication coverage** | All non-orphan indications | All non-orphan indications | All indications  
However, no weight based dosing for children less than 63 kg (product only available in prefilled syringe) | All non-orphan indications |

[http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM484859.pdf](http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM484859.pdf);  
Approval Summaries

• Four products approved to date
• FDA comfortable with extrapolation and bridging of data
• 2017 could bring the first instance of a second biosimilar for the same reference product and the first biosimilar for oncology indications
• Will have to monitor for impact of interchangeability guidance

Section Summary

• Several additional developments in the biosimilars market should make the approval methodology clearer
  – More approvals
  – Regulatory actions
  – Outcome of litigation
• Substantial education is required for all stakeholders given the continued evolution of this market
FORMULARY CONSIDERATIONS AND POSITIONING

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The Specialty Drug Spend Challenge
Specialty Trend Example for a 50,000 Life Group

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Specialty Rxs</th>
<th>Avg. Cost of a Specialty Rx</th>
<th>Specialty Spend</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>2,500</td>
<td>$1,500</td>
<td>$3,875,000</td>
</tr>
<tr>
<td>2012</td>
<td>2,895</td>
<td>$1,755</td>
<td>$5,080,725</td>
</tr>
<tr>
<td>2013</td>
<td>3,195</td>
<td>$2,210</td>
<td>$7,060,950</td>
</tr>
<tr>
<td>2014</td>
<td>3,451</td>
<td>$2,840</td>
<td>$9,800,840</td>
</tr>
<tr>
<td>2015</td>
<td>3,580</td>
<td>$3,490</td>
<td>$12,339,258</td>
</tr>
<tr>
<td>2020</td>
<td>5,604</td>
<td>$6,719</td>
<td>$37,656,426</td>
</tr>
</tbody>
</table>

Source: Example based on a model built utilizing national trend data of utilization and cost increases plus influence of drug mix; not actual client experience.
Polling Question #4

All of the following are key formulary and legal implications for utilization of biosimilar products, EXCEPT:

A. The net cost of the biosimilar compared to the reference drug
B. The co-pay amount the member will pay for the biosimilar
C. The PK data shows that the biosimilar molecule is very similar
D. A patient group opposes any biosimilar use over reference drug
E. The P&T Committee places the new biosimilar on the formulary

Polling Question #5

All of the following criteria are important when considering PK data in the evaluation of a new biosimilar product, EXCEPT:

A. Area under the curve
B. C max – peak concentration
C. K (elim) – rate of elimination
D. Absorption vs. elimination
E. PK data from European submissions
Managed Care Biosimilars Update: 2017 Policy Initiatives and Formulary Impact

Key Formulary and Positioning Issues

- Latest information about:
  - Interchangeability and biosimilarity
  - Issues around litigation

- Influence of the European Experience
  - What did we learn from Europe that we can consider in the US

- Evidential criteria
  - PK data impact
  - Clinical data impact

- Formulary and positioning
  - Considerations
  - Proactive response

Latest information about:
- Interchangeability and biosimilarity
- Issues around litigation
Interchangeability – From 2015

Biosimilars - FDA: Interchangeability Finding In Original 351(k) Application Possible
5/26/2015 - Inside Health Policy, Erin Durkin

FDA clarifies in a recent guidance document that interchangeability determinations can be made in an original biosimilar application, but cautions that it would be extremely challenging for biosimilar sponsors to do so. The agency last week issued guidance that contains additional questions and answers regarding implementation of the biosimilar pathway, including how to fulfill requirements under the Pediatric Research Equity Act (PREA) by extrapolating information from the reference product.

Latest FDA Guidance – 2017

Bad news for Biosim makers: FDA sets 'high bar' in interchangeability guidance
FiercePharma - by Eric Sagonowsky | Jan 18, 2017

The FDA rolled out much-awaited biosimilar interchangeability draft guidelines Tuesday, tipping its hand to developers looking to challenge sales of the world’s top biologics. The gist? Winning the designation won’t be easy, but a big payoff could await for those who do.

Together, the guidelines (PDF) outline requirements for biosimilar developers looking to prove that their versions are interchangeable with the original brands. If deemed so, branded scripts could be filled with biosims instead without the prescribing doctor’s approval, similar to generic versions of traditional meds.

But the requirements for that designation, according to analysts, appear to be more stringent than biosim makers would like. The current draft would require switching studies more complicated than many now in the works, for instance.
Why Are All of these People Smiling?

Impact of Litigation on Formulary Process

U.S. Supreme Court agrees to hear dispute over biologic drug sales

Health News | Fri Jan 13, 2017 |
By Andrew Chung | NEW YORK

The U.S. Supreme Court on Friday agreed to hear a dispute over whether companies that make copycat versions of biologic drugs must wait six months after winning federal approval to begin selling them.

The justices will take up an appeal by Novartis AG of a 2015 federal appeals court decision that prevented the Swiss pharmaceutical company from selling its biosimilar version of California-based Amgen Inc’s $1-billion-a-year Neupogen until six months after the Food and Drug Administration approved it. The case could determine how quickly patients have access to biosimilar medicines at potentially cheaper prices.
Sandoz head: Enbrel biosimilar Erelzi won't launch before 2018, delayed by legal battle

Reuters – Jan 25, 2017

Richard Francis, head of Novartis’s Sandoz generics business, told Reuters today that approval or not, it takes a long time to fight these battles.

“That won’t really reach a conclusion until 2018,” Francis said. “That’s the frustration sometimes of the legal situation, but the way I look at that, we’re carving the landscape out as we go.”

It has been nearly 5 months since Novartis won FDA approval for Erelzi as a replacement for Enbrel. Once on the market, doctors can prescribe it in place of Amgen’s drug for any of its indications—including rheumatoid arthritis, plaque psoriasis and psoriatic arthritis.

Litigation – Influence on Biosimilars

- Reference manufacturers insist they need to protect their patents and company profitability
- Biosimilar manufacturers insist lengthy delays harm them from marketing products and protecting their investments
- Managed care and payers want RELIEF from the +20% trends in specialty medication spend
- When biosimilar launches are delayed, the spend RELIEF is delayed
Influence of the European Experience

- What did we learn from Europe that we can consider in the US

Lessons from the European Experience

- Manage expectations – under-promise and over-deliver
- Keep the market healthy – unlike our generic market today, we need multiple options
- Plan ahead and be proactive
- Do not over-regulate – could be an issue in the U.S.
Evidential criteria
  - PK data impact
  - Clinical data impact

Pharmacokinetics and Pharmacodynamics

Biologic Drug
Specific Data Elements

- Area under the curve – absorption vs elimination
- C max – peak concentration
- K (elim) – rate of elimination
- Biomarker – identification for comparison
- Hydroxylation – molecule folding
- Immunogenicity – comparison of immune response

Source: U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER) December 2016 Biosimilars

Clinical Trial Information – How Much?
Issues Regarding Clinical Trials

- Biosimilar manufacturers appear to be moving in the direction of providing clinical trial data.
- With drugs like Humira that have multiple approved indications, will clinical trial data on one indication suffice for all others?
- If the molecule looks very similar and a clinical study shows equal efficacy, will that be enough?
- Will we treat everyone or just new patients?

Formulary and Positioning

- Considerations
- Proactive response
Biosimilar State Legislation

Legislation on Biologics and Biosimilar Substitution, 2013-2016

LEGEND
- Enacted law: 2013-16
- Passed legislature: not law
- Filed: failed/adjourned 2013-16 (most recent action)
- Bill filed: pending or carryover, 2015-16
- Other regulation: stop therapy enacted law

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See NCSP reports for details at www.ncsl.org

Considerations for Formulary

Drug Technology

Patient Concerns

How Many and When?

Data from SPs

Prescriber Concerns

Savings?

Issues
**AMCP Format for Formulary Submissions**

**Version 4.0**

**BIOLOGICS, BIOSIMILARS AND THE AMCP FORMAT**

Many specialty pharmaceuticals are classified as biologicals which are typically large protein molecules or blood products. Due to the nature of biologicals, the current FDA evaluation process for authorizing a generic version of the innovator product is impractical. The exact chemical structure of the biological is likely unknown, thus preventing FDA from analyzing exact comparison data between the two products. Therefore, biosimilars do not fit the definition of a generic equivalent product, i.e., identical -- or bioequivalent -- to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. In summary, biosimilars are not generic biologics.

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Contracting and Rebate Issues

1. When the innovator company comes back with a higher rebate, how will you respond?

2. Do we support the biosimilar companies? Long term vs short term

3. Managed Medicaid plans vs other payers due to significant rebates

4. Medical vs pharmacy benefit

Post-Marketing Surveillance of Biosimilars

The Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

The BBCIC is a multi-stakeholder research consortium focused on generating the scientific evidence on Biologics and Biosimilars. The consortium is establishing a science driven approach using real world data to counter anecdotal reports of lack of safety or efficacy.

Source: AMCP document at www.bbcic.org
**Being Proactive in the Biosimilar Space**

**Goals**
- Monitor the market
- Designate a reviewer
- Review the evidence
- Price negotiations
- Formulary placement
- Prepare materials for the 3 P’s
- Post marketing surveillance

**The Unknowns**
- What designation will each biosimilar have?
- When will the litigation end?
- Can manufacturers deliver significant discounts on biosimilars?
- How will innovator companies respond?
- How will prescribers and patients react?

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**Biosimilar Management Considerations**

**Communicate with payers on individual product status**
- Display evidence of biosimilarity of molecule
- Continue to reassess pricing and overall impact
- Monitor each biosimilar’s performance

**Aggressive formulary options:**
- Place Biosimilar as the mandatory agent against the innovator product
  Savings ~ XX% of Humira
- Place the Biosimilar as the mandatory agent against all other drugs in the therapy class
  > Savings of entire autoimmune class
Questions & Answers

Thank You!

To Receive CE Credit

- Complete the Post-Test and Evaluation
- Score of ≥ 70% is required to receive credit