Biosimilars:

Changes, Challenges and Choices for Managed Care Healthcare Professionals and Their Patients

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- Dr. Johnson serves as President and Scientific Content Expert for her own J³ Consulting, LLC. Expertise includes scientific platform and content development, educational narrative composition, data and evidence gap analysis, emerging area and trend identification, external landscape evaluation and strategic plan support.

- Dr. Johnson previously held the position of Executive Medical Science Liaison for AstraZeneca Pharmaceuticals - one of the first in this position. While serving in this role, Dr. Johnson was presented with the highest award in her Scientific Affairs division – the Dave Haack Award.

- Additionally, Dr. Johnson makes time to serve the community and to support health-related causes, such as the annual Hope Health Clinic that provides health services to medically underserved Georgia counties, the Jordan D. Savage Foundation (Board of Directors) and the Lupus Foundation.

- Dr. Johnson has no conflicts of interest to disclose.
Accreditation Statement

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• ACPE program numbers are:
  0459-0000-18-007-L04-P & 0459-0000-18-007-L04-T

• Initial release date is 3/3/2018.
Learning Objectives

1. Differentiate between biologic product, biosimilar product and generic product including how each relates to interchangeability
2. List 3 key benefits of biosimilar medications
3. Describe why an abbreviated approval pathway and a stepwise approach are needed for biosimilar products
4. Articulate the clinical and financial implications for biosimilars for payers, clinicians, pharmacists and patients
5. Identify and explain key challenges and benefits surrounding the uptake and use of biosimilar agents
Pre-Test Questions

1. A biosimilar product is also a biologic product
   a. True
   b. False

2. To develop the data and information needed to support a demonstration of biosimilarity, the FDA recommends that sponsors use a stepwise approach which includes:
   a. Analytical studies
   b. Animal studies
   c. Clinical PK/PD studies
   d. Clinical immunogenicity assessment
   e. Large clinical studies that establish safety and efficacy
   f. All except (e)
   g. All of the above

3. Pharmacists play a key role in biosimilar uptake and utilization by leading the education of team members and patients about:
   a. Manufacturing differences
   b. Interchangeability
   c. Principles of biosimilar development and evolving regulatory guidelines
   d. All of the above
Pre-Test Answers

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Outline
Outline

• Introduction to Biosimilars
• Nomenclature
• FDA
• Medications
• Perspectives
• Challenges
• Benefits
• Resources
• Concluding Observations
Paradigm Shift: A Place for Biosimilars

As the first biosimilars for today’s revolutionary and expensive biologic drugs enter the market, payers and manufacturers are poised for what could be a great paradigm shift in the pharmacy world¹

Ideally the biosimilar movement afoot today will affect health care much like the introduction of generic drugs did years ago²

Increasing competition²

Driving down costs²

Maintaining optimal patient outcomes²

2. Oskouei S. Following the biosimilar breadcrumbs: When health systems and manufacturers approach forks in the road. JMCP. 2017;23(12):1245-1248
Paradigm Shift:
A Place for Biosimilars

Key Drivers:
Crucial for facilitating widespread use of these products and optimizing their value:

1. Biosimilars must be positively perceived and adopted by numerous stakeholders
   • Competitive landscape
   • Management of costs of care

2. Efforts to ensure safe and effective use, including pharmacovigilance and bidirectional communication
   • Prioritize to limit risks to patients and improve care

3. Ongoing collaboration with and education targeting a variety of stakeholders
   • Providers, patients, payers and policymakers

4. Pharmacists important contributors to the biosimilar information cascade shared with prescribers and patients as they make product decisions
   • Experts on biosimilars
   • Education to healthcare professionals about safe prescribing and use which ultimately affects patient care

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Paradigm Shift: A Place for Biosimilars

Between 2013 and 2014, spending on specialty drugs, including biologics, increased 32.4% \(^1\)

- While spending on small-molecule drugs increased just 6.8%\(^1\)

The current healthcare landscape demands additional therapeutic choices for healthcare providers and patients

- Opportunities for competition in key therapeutic areas
- Potential to significantly decrease healthcare costs in the U.S.
- Improving access to treatment for patients\(^2\)

Evolution of the U.S. Biosimilar Market

- **JULY**
  - FDA accepts application for first biosimilar in the U.S.

- **MARCH**
  - FDA approves the first biosimilar in the U.S.
  - CMS issues guidance documents on the treatment of biosimilar products under Medicare Part B, Medicare Part D and Medicaid Drug Rebate Program

- **DECEMBER**
  - Six active filings for biosimilars pending review as of December 31, 2015

2014

- **DECEMBER**
  - Three active filings for biosimilars pending review by December 31, 2014

2015

- **APRIL**
  - FDA issues two final guidance documents on Scientific and Quality Considerations in Demonstrating Biosimilarity to a Reference Product

- **OCTOBER**
  - CMS finalizes reimbursement provisions for biosimilars

- **SEPTEMBER**
  - Launch of first biosimilar in the U.S.

Amgen. 2017 Trends in biosimilars report: Navigating the path to biosimilars.
**JULY**
U.S. Court of Appeals for the Federal Circuit rules 180-day notice must be given to reference product sponsor before commercial marketing of biosimilar may begin.

**APRIL**
FDA approves second biosimilar, first monoclonal antibody (mAb).

**AUGUST**
FDA approves third biosimilar.

**SEPTEMBER**
FDA approves fourth biosimilar.

**JANUARY**
- FDA finalizes guidance on Nonproprietary Naming of Biological Products.
- FDA releases draft guidance on Considerations in Demonstrating Interchangeability with a Reference Product.

**2016**
- **JULY** U.S. Court of Appeals for the Federal Circuit rules 180-day notice must be given to reference product sponsor before commercial marketing of biosimilar may begin.

**2017**
- **DECEMBER**
  - FDA issues final guidance on Clinical Pharmacology Data to Support Demonstration of Biosimilarity to a Reference Product.
  - Six active FDA filings for biosimilars pending review as of December 31, 2016.

Amgen. 2017 Trends in biosimilars report: Navigating the path to biosimilars.
Growth in Enrollment in the Biosimilar Product Development (BPD) Program

![Bar chart showing growth in enrollment in the BPD program by fiscal year]

Note: A biosimilar product is no longer in the BPD program after a 351(k) BLA is accepted for review (i.e., filed)

The Potential

- Significant potential exists for biosimilars to revolutionize biologic therapy by widening patient access across therapy areas
- Biosimilars are viewed as a future source of value and potential savings for the healthcare system
- Cannot offer a “magic bullet” solution to the current issues being debated in the US healthcare system
- Can provide much-needed relief upon successful existence
Nomenclature
Biologics are one of the fastest growing segments of the prescription product market.
Biologics Compared to Conventionals

**Conventional Medications** *(known to most):*

- Small-molecule drugs
- Made from pure chemical substances
- Structure identified and characterized relatively easily
- Usually synthesized through a predictable chemical process according to a reproducible “recipe”

**Biologic Medications:**

- Large, more complex molecules or mixtures of molecules (200-1000x)
- Made from material that comes from living cells or organisms
  - Humans, animals and microorganisms (bacteria or yeast)
- Not as easily characterized or identified
- Usually manufactured using biotechnology methods (recombinant DNA technology) or other cutting-edge technologies
- Cannot be made by following a reproducible recipe
  - Manufacturing process more complicated, expensive, costly
  - Average cost for a biologic is 22 times greater than the cost for a conventional medication

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### Reference Product

**Originator Product, Innovator Product**

### Biological Product:

- Approved by the FDA in a “standalone” application that must contain all data and information necessary to demonstrate its safety and effectiveness\(^1\)
- Approval based on full complement of product-specific data, including nonclinical and clinical data\(^2\)

### Reference Product:

- Compared against a proposed biosimilar product\(^1\)

Biosimilar

• Highly similar to an already FDA-approved biological product (its reference product)

• No clinically meaningful differences in terms of potency (safety and effectiveness) and purity from its reference product

• Same mechanism of action, route of administration, dosage form, and strength as the reference product

• Only minor differences in clinically inactive components allowed
  • Because of the complexity and inherent variability of biological products
  • Differences must not preclude a demonstration of highly similar
  • Differences must not be clinically meaningful
What is a Biosimilar?

› A biosimilar is a biological product

FDA-approved biosimilars have been compared to an FDA-approved biologic, known as the reference product. Reference and biosimilar products are:

- Large and generally complex molecules
- Produced from living organisms
- Carefully monitored to ensure consistent quality
- Carefully monitored to ensure consistent quality

A biosimilar is highly similar to a reference product

For approval, the structure and function of an approved biosimilar were compared to a reference product, looking at key characteristics such as:

- Purity
- Molecular structure
- Bioactivity

The data from these comparisons must show that the biosimilar is highly similar to the reference product.

A biosimilar has no clinically meaningful differences from a reference product

Studies were performed to show that biosimilars have no clinically meaningful differences in safety, purity, or potency (safety and effectiveness) compared to the reference product:

- Pharmacokinetic and, if needed, pharmacodynamic studies
- Immunogenicity assessment
- Additional clinical studies as needed

Studies may be done independently or combined.

A biosimilar is approved by FDA after rigorous evaluation and testing by the applicant

Prescribers and patients should have no concerns about using these medications instead of reference products because biosimilars:

- Meet FDA’s rigorous standards for approval
- Are manufactured in FDA-licensed facilities
- Are tracked as part of post-market surveillance to ensure continued safety

www.FDA.gov
Biosimilar Compared to Generic\textsuperscript{1,2}

**Generic Medications (Conventional)**

1. Small molecules
2. Simple and well-defined structure
3. Made through predictable chemical processes so **identical copies made**
4. **Lower** immunogenicity potential
5. Approved for all indications of brand
6. ANDA for approval
7. Designated as pharmaceutical equivalents and bioequivalent
8. Can be **substituted** for the brand product
9. **Orange Book** governs substitution
10. Relatively stable
11. **Lower research and development costs**

**Biosimilar Medications**

1. Large molecules (200 to 1000x)
2. Far more complex structure
3. **Grown in living cells instead of via chemical synthesis so similar but not identical copies**
4. Higher immunogenicity potential
5. Extrapolation of indications possible
6. 351(k) for approval
7. Designated as biosimilar (no clinically meaningful differences)
8. Cannot be substituted for the reference product: no FDA interchangeability designation
9. **Purple Book** governs substitution
10. Sensitive to handling and storage conditions
11. **Higher research and development costs**

\textsuperscript{2} Stevenson J. Clinical data and regulatory issues of biosimilar products. Pharmacy Times Continuing Education. Dec 2015-2016.
Comparison of Generic/Biosimilar/Reference Biologic

Development and Manufacturing of Biosimilars Is Different from Generic Small Molecules or Originator Biologics

<table>
<thead>
<tr>
<th></th>
<th>Generics</th>
<th>Biosimilars</th>
<th>Reference Biologics</th>
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</thead>
<tbody>
<tr>
<td><strong>Scientific Difficulty</strong></td>
<td>Low(^1)</td>
<td>High(^1)</td>
<td></td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>Short (3–4 years)(^2)</td>
<td>~ 8 Years(^2)</td>
<td>Long (10+ years)(^3)</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>Low (&lt; $5M) Bioequivalence(^2)</td>
<td>~ $200 M(^2)</td>
<td>High (&gt; $1.2B) Full clinical development(^3)</td>
</tr>
<tr>
<td><strong>Ops</strong></td>
<td>Simple, short(^4)</td>
<td>Complex</td>
<td>Long, complex(^4)</td>
</tr>
</tbody>
</table>

**Ops = operations.**

Biosimilars Are Not…

<table>
<thead>
<tr>
<th>“Biobetters”(^1)</th>
<th>Improved versions of the originator biologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Biomimics” or “biocopies”(^2)</td>
<td>Copies of licensed biologic medicines that have not been subjected to rigorous clinical testing or evaluated according to the biosimilar regulatory pathway</td>
</tr>
<tr>
<td><strong>Generic drugs</strong>(^3,4)</td>
<td>Small-molecule, chemically synthesized drugs using the same active ingredient, strength, dosage form, route of administration, and conditions of use as the reference product</td>
</tr>
</tbody>
</table>

Biobetter

• Biosimilar
  • Clearly defined regulatory term\(^1\)

• Biobetter
  • Essentially a marketing term with no universally accepted definition\(^2\)
  • Different from the existing product and evaluated as a new drug\(^2\)
  • Biologic that seeks to establish superiority in one or more aspects of its clinical profile, compared with the originator product
  • Strategy against the use of less expensive biosimilars

Follow-On

• Biosimilars sometimes referred to as follow-on or copy versions of the reference biologic

• Follow-on biologics:
  • Application Process: 505(b)(2)
  • Omnitrope (somatropin): (May 06); Model product: Genotropin (somatropin)
  • Basaglar Kwikpen (insulin glargine) (Aug 14); Lantus Solostar (insulin glargine)

Summary

A reference product is a single biological product, already FDA approved against which a proposed biosimilar product is compared.

A biosimilar is a biologic that is “highly similar” to an approved biologic (or reference product) already being used to treat patients; No clinically meaningful differences in terms of safety and effectiveness from the original product (reference product).

Regarding drug development, biosimilars are lower in scientific difficulty, take less time and cost less than reference biologics.

Biosimilars are not generics or biobetters or follow-on medications.
FDA
Background: U.S. and World View

• All FDA-approved biological products (reference and biosimilar) undergo rigorous evaluation
  • Patients assured of efficacy, safety and quality¹

• European Medicines Agency (EMA) first body to develop an overarching framework for approving biosimilars
  • Approved for use in the European Union since 2006²

• Japan, Canada, India, China, Australia, Latin America and other countries³

Amgen. 2017 Trends in biosimilars report: Navigating the path to biosimilars.
The Law

• Mar 23, 2010 President Obama signed into law the Patient Protection and Affordable Care Act (Affordable Care Act)

• Contained the Biologics Price Competition and Innovation Act of 2009 (BPCIA)

• Includes the new biosimilar abbreviated approval pathway under Public Health Service Act (PHS Act)
Biologics Price Competition and Innovation Act (BPCIA)

- 351(k) abbreviated pathway for licensure of biosimilars
- 12-year period of exclusivity for initial reference product; Zero for biosimilar
- Exclusivity period first biosimilar determined to be interchangeable with a particular reference product
- Litigation process for patent issues
351(k) Application Requirements

Demonstration that biological product:

- Is biosimilar to a reference product
- same mechanism(s) of action for the proposed condition(s) of use -- but only to the extent the mechanism(s) are known for the reference product
- Condition(s) of use proposed in labeling have been previously approved for the reference product
- Has the same route of administration, dosage form, and strength as the reference product
- Is manufactured, processed, packed, or held in a facility that meets standards designed to assure that the biological product continues to be safe, pure, and potent.

FDA Approval Process: Stepwise Approach

• Totality of evidence to establish that a biosimilar essentially same drug as reference product

• Greater emphasis on biological and physicochemical characterizations of biosimilar molecule

• Array of comparative data
Stepwise Approach: Advantages

- No need to conduct as many expensive and lengthy clinical and nonclinical trials
- Potentially shorter and less costly drug development program
- Potentially leading to greater access to additional therapeutic options
- Potentially lowering health care costs through competition

Product Naming System

• Biologics given both a brand name (e.g., Neupogen) and a nonproprietary (proper) name (e.g., filgrastim)

• Two-part nonproprietary name consisting of:
  1. Core name - same for biosimilar and reference products
  2. Distinguishing suffix devoid of meaning and composed of four lowercase letters, separated from the core name by a hyphen

• Rules not fully established when first products approved

• Applied retrospectively

  *Biosimilar: Zarxio (filgrastim-sndz); Reference Product: Neupogen (filgrastim)*

Product Naming System: Stakeholder Views

**Biologics Prescribers Collaborative**
- “…concerned with "random" suffixes”
- “…memorable suffix [so] manufacturer immediately recognizable for AE reporting

*Aims to ensure that sound policies are in place to promote the safest possible use of all biologics, including biosimilars, for all patients; Member groups include gastroenterology, rheumatology*

**Biosimilars Forum**
- “…disappointed in meaningless suffixes”
- Difficult to remember
- AE tracking

*nonprofit organization to advance biosimilars in the United States with the intent of expanding access and availability of biological medicines, and improving health care; Companies*

**PharmD, Clinical Pharmacy Specialist**
- Nonproprietary core name: Recognize reference product
- A suffix useful:
  - Address interchangeability
  - Recognize indications
  - Computer order systems
  - AE tracking/reporting

Summary

- Biologics Price Competition and Innovation Act (BPCIA) includes new biosimilar abbreviated approval pathway under Public Health Service Act (PHS Act)
- The Stepwise Approach focuses on biological and physiochemical characterizations (analytical studies, animal studies if needed, clinical PK/PD studies, clinical immunogenicity assessment and additional clinical studies as needed)
- Potential advantages to the Stepwise Approach: greater access to additional therapeutic options and lowering healthcare costs
- Two-part nonproprietary name consists of: 1) Core name that will be the same for biosimilar product and reference product and 2) Distinguishing suffix devoid of meaning
Medications
Biologics: Therapeutic Applications

• Diagnose
• Prevent
• Mitigate
• Treat
• Cure
• Wide range of diseases and medical conditions
• Vastly improve:
  • Rheumatoid arthritis, anemia, leukopenia, inflammatory bowel disease, psoriasis and various forms of cancer

Approvals: Litigation

• Biosimilars > importance/presence as more regulatory and litigation hurdles eliminated

• BPCIA: Procedure for patent litigation (“patent dance”)

• Remains a key offensive/defensive strategy for the reference product company

• Biosimilar company: launch-at-risk ramifications
  • Product withdrawals
  • Royalties

<table>
<thead>
<tr>
<th>Biosimilar/Nonproprietary Name/ Indications</th>
<th>Applicant/ Manufacturer</th>
<th>Reference Drug/ Nonproprietary Name/Indications</th>
<th>Approval Date</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inflectra (infliximab-dyyb)</strong> Crohn’s Dis (CD), Ped CD, Ulcer Col (UC), Rheum Arth (RA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Plaque Psoriasis (Ps)</td>
<td>Celltrion/Hospira/Pfizer</td>
<td>Remicade (infliximab) (Janssen Biotech, Inc.) Same + Pediatric UC</td>
<td>April 5, 2016</td>
<td>Launched in US November 2016; ongoing patent litigation</td>
</tr>
<tr>
<td>Erelzi (etanercept-szsz) RA, Juvenile Idiopathic Arthritis (JIA), PsA, AS, Ps</td>
<td>Sandoz</td>
<td>Enbrel (etanercept) (Amgen) Same</td>
<td>August 30, 2016</td>
<td>No launch until 2018 at earliest pending outcome of litigation</td>
</tr>
<tr>
<td><strong>Amjevita (adalimumab-atto)</strong> RA, JIA, PsA, AS, CD, UC, Ps</td>
<td>Amgen</td>
<td>Humira (adalimumab) (AbbVie) Same + Pediatric CD, Hidradenitis Suppurativa</td>
<td>September 23, 2016</td>
<td>Launch in US on January 31, 2023 pursuant to global settlement agreement</td>
</tr>
<tr>
<td><strong>Cyltezo (adalimumab-adbm)</strong> RA, JIA, PsA, AS, CD, UC, Ps</td>
<td>Boehringer Ingelheim</td>
<td>Humira (adalimumab) (AbbVie) Same + Pediatric CD, Hidradenitis Suppurativa</td>
<td>August 25, 2017</td>
<td>No launch date announced; litigation pending</td>
</tr>
<tr>
<td>Mvasi (bevacizumab-awwb) Cancers: colorectal, lung, brain/spine, renal, cervical</td>
<td>Amgen/Allergan</td>
<td>Avastin (bevacizumab) (Genentech) Same + ovarian</td>
<td>September 14, 2017</td>
<td>No launch date announced; litigation pending</td>
</tr>
<tr>
<td>Ogivri (trastuzumab-dkst) Cancers: breast, gastric</td>
<td>Mylan/Biocon</td>
<td>Herceptin (trastuzumab) (Genentech) Same</td>
<td>December 1, 2017</td>
<td>Launch date undisclosed under settlement agreement</td>
</tr>
<tr>
<td><strong>Ixifi (infliximab-qbtx)</strong> CD, Ped CD, UC, RA, AS, PsA, Ps</td>
<td>Pfizer</td>
<td>Remicade (infliximab) (Janssen) Same + Pediatric UC</td>
<td>December 13, 2017</td>
<td>No current plans for US launch</td>
</tr>
</tbody>
</table>
The Purple Book

- Lists of licensed biological products
  - Reference product exclusivity
  - Biosimilarity
  - Interchangeability evaluations
Summary

- Help patients with a wide range of conditions including autoimmune diseases and types of cancer
- Indicated for all or a subset of the same indications as the reference product dependent upon unexpired exclusivity
- Common occurrence for biosimilar applicants to have pending lawsuits involving conflicting interpretation of the “patent dance” process
Perspectives
Outline

Concerns
Barriers
Solutions

CMS
Payer
MD
Patient
P & T
Pharmacist
Concerns/Barriers with Biosimilar Use

[Inflectra (infliximab)]

Oskouei S. Following the biosimilar breadcrumbs: When health systems and manufacturers approach forks in the road. JMCP. 2017;23(12):1245-1248.
Payer: Benefit & Challenges

1. **Potential Cost Savings**
   “With the prediction that 80% of top-selling drugs in 2016 will be biologicals, biosimilars could be a saving grace for the economy.” (CVS Health Payor Solutions)

2. **Greater patient accessibility**

1. **Reimbursement**
   - **Switching:** Clinical assurance to inspire confidence in patient benefit
   - **Formulary Acceptance:**
     - Key evidence
     - Hands-on, Real-world experience

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3. Oskouei S. Following the biosimilar breadcrumbs: When health systems and manufacturers approach forks in the road. JMCP. 2017;23(12):1245-1248.
Biosimilar Acceptance: Zarxio (filgrastim-sndz)

Kaiser Permanente (Kaiser Foundation Hospitals, Kaiser Health Plan and the Permanente Medical Groups): 96% uptake of Zarxio

Organizations saw increase in provider willingness to prescribe throughout 2016

Will replace reference product on UnitedHealth formulary in 2017

Follows similar such exclusions released by Express Scripts and CVS Health

As of November 2016, market share of [reference product] reduced by about one-third

End of 2016, approximately 30% of prescriptions were for the biosimilar product

Biosimilar product would be given preferred status on the formulary in 2017

Health System/Payer: Solution

Published a policy to address biosimilars before release

To remove roadblocks

Results:

1. The two approved biosimilar products were added to formulary

2. Preferred product use leading to greater reimbursement for providers and less cost for the patient

3. Ultimate reduction in overall costs to the health care system

Health system-owned third-party administrator, with a fully insured business

MD: Main Concerns

- Safety Issues
- Efficacy
- Substitution
- Switching
- Evaluation Biosimilar vs. Reference Rx
- Patient Type
- Type of Care
- Patient Access
- Experience
- Education
MD: Main Concerns

Switching

• 1,201/150 specialists: More comfortable prescribing biosimilars for treatment-naïve patients rather than switching stable patients to biosimilars

Type of Care: Supportive Care (CD, RA) vs. Curative Treatment (Cancer)

• “I’m more willing to let economics drive supportive care instead of therapeutic medications. I’d like a higher standard of data in a therapeutic [curative] indication.” (Oncologist)

Pharmacist: Key Role

Positive effect on biosimilar market uptake\(^1\)
Managing introduction of biosimilars into healthcare systems\(^2\)
Educating
Communicating
Collaborating \(^1\)
Medication Experts\(^1\)
Pharmacist

Pharmacist: Key Role

Biosimilarity

Abbreviated Pathway

Evaluate with a different lens

Analytical and physiochemical data

Indication extrapolation

Oskouei S. Following the biosimilar breadcrumbs: When health systems and manufacturers approach forks in the road. JMCP. 2017;23(12):1245-1248.
Patients

• Majority not familiar with biosimilars¹

• By 2025, an additional 1.2 million patients could gain access to biologic therapies²

• “…knowledgeable about/fiercely loyal to the brands that are keeping them well” (Patient Advocate, Editorial Council Member)³

• Intense emotional connection with biologics for the profound impact they have on their lives³

Center for Medicare and Medicaid Services (CMS): Medicaid

“State Medicaid programs should view the launch of biosimilar biological products as a unique opportunity to achieve measurable cost savings and greater beneficiary access to expensive therapeutic treatments for chronic conditions”

• Not qualify as authorized generic drugs for the purpose of the Medicaid Drug Rebate program (no NDA)

• Subject to brand level rebates

• “Best price of the reference biologic and the biosimilar biologic should be determined separately as the lowest price available from each manufacturer.”

Medicare Part D

• From 2009 to 2012, spending on biologic drugs under Medicare Part D grew:
  • 32% (prescription volume)
  • 45% (prices)

• Gross spending on biologics by high-cost enrollees went from $1.9 billion to $3.5 billion nearly doubling during that same period

• Biosimilars treated in a manner similar to generics:
  • They are not subject to the 50% discount required for brand drugs when the Medicare Part D beneficiary is in the coverage gap

• Costs for Medicare Part D patients may not always favor biosimilars
  • Patients facing the coverage gap may experience higher out-of-pocket costs for biosimilars than for the branded reference product

Summary

- Health systems succeed by developing a policy to address biosimilars before market release in order to facilitate adoption.

- Payers are responsible for evaluating a number of factors: clinical (biosimilarity), humanistic (clinician/patient accessibility), economic (significant cost savings, e.g., reimbursement).

- Pharmacists have a key role in supporting acceptance and appropriate utilization of biosimilars by serving as experts: educating/communicating/collaborating with healthcare teams and patients.

- Medicaid does not treat biosimilars as generics (are subject to brand level rebates); Medicare Part D treats biosimilars as generics (even though may be more costly to patients).
Challenges
Outline

• Timing
• Interchangeability
• State Laws
• Pharmacovigilance
Timing

• Process for getting biosimilars to market slower than expected

• 351(k) pathway established in 2010¹

• First biosimilar approved five years after²

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2. Tharaldson A. Dr. Aimee Tharaldson expects the biosimilar approval process to pick up speed. AJMC.com Interviews. June 10, 2016.
Interchangeability: FDA Draft Guidance

• Definition:
  • Practice where one product can be interchanged for another equivalent product in a clinical setting without the risk of a negative health outcome\(^1\)

• Guidance:
  • “Considerations in Demonstrating Interchangeability with a Reference Product. Draft Guidance: Guidance for Industry”\(^2\)

• Clinical switching studies required to support determination\(^2\)

• Remicade (infliximab) to Inflectra (infliximab-dyyb)
  • NOR-SWITCH trial (52 week, Phase 4)
  • Met primary endpoint of non-inferiority\(^3\)

• AMCP: non-U.S. based switching studies should be accepted as supporting evidence\(^4\)

State Laws: Substitution

• FDA determines interchangeability but state boards of pharmacy control substitution (biosimilar for reference)\(^1\)

• At least 45 states have considered legislation establishing state standards for substitution of a “biosimilar” prescription product\(^1\)

• Nine biosimilars FDA approved (Dec 2017)
  • Not currently designated as interchangeable, so none of the state laws can be applied to dispensing decision\(^2\)

• Managed Care Organizations:
  • National plan: how communicate biosimilar strategy across state lines with all of the variability of state rulings

State Law: Georgia Law

• GA Senate Bill (SB) 51
  • 2015-2016 Regular Session

• Substitutions of interchangeable biological products

• May substitute a biological product with an interchangeable biological product

• Rx written by its nonproprietary name
  • Dispense lowest retail priced interchangeable biological in stock
Pharmacovigilance: Long-term Track Record

• Pharmacovigilance: the monitoring and tracking of drug safety over time

• Biosimilars lack a long-term track record in the U.S.

• Until more data is compiled, questions about performance in the real-world setting will remain

Amgen. 2017 Trends in biosimilars report: Navigating the path to biosimilars.
Summary

Major challenges to the adoption and effective utilization of biosimilars include: timing, interchangeability, state laws and pharmacovigilance.

The BCPIA specifies that interchangeable biosimilars may be substituted for the reference product; however, no biosimilars have this designation.

Robust postmarketing safety monitoring is essential yet lacking.
Exploring Potential Benefits
Outline

Potential Biosimilar Benefits
Advantages: Other

Additional therapeutic options/choices for healthcare providers and patients\textsuperscript{1-3}

Abbreviated but rigorous development programs may provide cost savings without compromising quality\textsuperscript{3,4}

Competition/Innovation may increase access to biologic products for appropriate patients\textsuperscript{3}

The Cost Factor

R & D

• Biosimilars: approximately $100 million to $200 million
  • [Reference] Biologic approximately $800 million or >
  1
• Biosimilar: 8 to 10 years to develop (50/50 chance)

Price

• Biosimilar compared to biologic price:
  • 10% to 40% less than reference biologic

Savings

• 2014 and 2024 if 11 reach the market savings of $250 billion
• 2014 and 2024, $44.2 billion reduction in direct spending on biologic drugs

<table>
<thead>
<tr>
<th>The Clinical Picture&lt;sup&gt;1,2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Though the biosimilar is a little bit cheaper, I wonder if that discount will equate to any savings for patients in general?”</td>
</tr>
<tr>
<td>“What happens should the biosimilar not work and they end up in a hospital, which ultimately accrues more healthcare costs?”</td>
</tr>
<tr>
<td>“What if they’re then switched back to [the reference product], and they’ve developed antibodies?”</td>
</tr>
</tbody>
</table>
CMS: Change in Codes

• CMS previously grouped all biosimilars of a reference biologic under a single billing code and payment rate (Jan 2016)¹

• U.S. government could save $11.4 billion over the next 10 years if CMS were to revise its current reimbursement policy for biosimilar medicines²

• CMS changed to present policy on biosimilar reimbursement³

• Begin issuing unique Healthcare Common Procedure Coding System (HCPCS) codes to each individual biosimilar product (effective Jan 1 2018)³

• Reduce concerns and confusion around biosimilar pharmacovigilance⁴

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Resources
Resources: Education

- Awareness levels in the U.S. remain low; educational efforts are improving\(^1\)
- No stone left unturned in educating key stakeholders about biosimilars
- Important to target the “four P’s”: providers, pharmacists, patients and payors\(^2\)
- Allow for informed decision when evaluating products\(^2\)

2. Oskouei S. Following the biosimilar breadcrumbs: When health systems and manufacturers approach forks in the road. JMCP. 2017;23(12):1245-1248.
Resources

Biosimilars Resource Center (BRC)

• AMCP

  • “Educational resources and information on biosimilars to healthcare providers and other stakeholders in a policy-neutral and non-promotional manner”
  
  • Provides access to educational tools and training materials for biosimilars, including one-pagers, web-based educational seminars, continuing education and journal articles
  
  • Launched in 2016 by the AMCP in partnership with the American Association of Colleges of Pharmacy, America’s Health Insurance Plans, the American Pharmacists Association, the American Society of Consultant Pharmacists, the Hematology/Oncology Pharmacists Association, the National Alliance of State Pharmacy Associations and the National Community Pharmacists Association

  • info@BiosimilarsResourceCenter.org

Continuing Education for Pharmacists, Physicians, Nurses and other Healthcare Professionals

• AMCPLearn (Academy of Managed Care Pharmacy)
  
  • Biosimilars Basics and Beyond: The Science of Biosimilars (available until Jul 6, 2018)
  
  • Biosimilars Basics and Beyond: Regulating Biosimilars (available until Sept 20, 2018)

• CDERLearn (FDA)
  
  • FDA Overview of Biosimilar Products (available until Feb 17, 2019)

• APhA Home Study Library (American Pharmacists Association)
  
  • The Emerging Role of Biosimilars (available until Mar 14, 2018)
  
  • Biosimilars: What Every Pharmacists Needs to Know (available Mar 4, 2019)

• PowerPak C.E.
  
  • Basic Concepts and Evolution of Biosimilars in Patient Therapy - Implications for Pharmacy Management (available until Jan 31, 2019)
  
  • But How Similar Is It? – What You Need to Know and What to Tell Your Patients about Biosimilars (available until Dec 2018)

• Pharmacy Times Continuing Education (PTCE)
  
  • Adoption of Biosimilars: Prescribers, Pharmacy and Payer Perspectives (April 12, 2016 – April 12, 2017)
  
  • Clinical and Managed Care Implications of Biosimilars: Evaluating the Science and Challenges to Update (expired Dec 12, 2016)
Resources

**AMCP Webinar Recordings (non-CE)**

**JMCP (Journal of Managed Care & Specialty Pharmacy)**
- Theme: “Biosimilars: The First 2 Years”
- Dec 2017

**FDA:**
- Biosimilar Education Campaign (Oct 2017)
  - Educational campaign to help healthcare providers gain a better understanding of biosimilars and the approval process
- Consumer Update
  - “Biosimilars: More Treatment Options Are on the Way” (April 7, 2016)
- FDA Biosimilars Drop-In Articles
  - Newsletter Article: Prescribers
  - Newsletter Article: Patients
Post-Test
1. A biosimilar product is:
   a. A generic version of the reference (innovator) biologic product
   b. Interchangeable with the reference biologic product and other biosimilars in the same category
   c. Highly similar to and has no clinically meaningful differences in terms of purity and potency (safety and effectiveness) from the reference product
   d. Relatively simple to manufacture using established chemical and production processes
   e. Identical or bioequivalent to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use

2. Benefits of biosimilar medications include:
   a. Increasing competition
   b. Decreasing cost of care
   c. Maintaining optimal patient outcomes
   d. Greater access to safe, effective, lifesaving biological products
   e. More treatment options
   f. All of the above

3. Biosimilars differ from generics in the following way(s):
   a. Easier to produce
   b. Less expensive
   c. Require additional clinical studies
   d. None of the above
   e. All of the above
4. Which of the following is true about all physicians:
   a. Knowledgeable about biosimilars
   b. Require education about biosimilars
   c. Indicate they will embrace the use of biosimilars in practice
   d. Are aware that biosimilars are not the same as generics
   e. All of the above

5. Strategies to address issues associated with biosimilar uptake include:
   a. Passage of state laws and regulations that do not impede the use of biosimilars (e.g., interchangeable biosimilars)
   b. Use of non-product-specific tracking information in electronic health records and surveillance systems
   c. Uni-directional communication among pharmacists, prescribers and other members of the care team

6. Medicaid considers biosimilars to be subject to brand level rebates and are not treated as generics; yet Medicare Part D does treat biosimilars as generics
   a. True
   b. False
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   b. False
Concluding Observations
Questions??

What does the future hold for biosimilars in the U.S.? Is it a case that biosimilars need to succeed in order to support a more sustainable healthcare system, or will the biosimilars market crumble under the weight of its own expectations?
Concluding Observations

As the U.S. continues to gain experience with biosimilars and as more products enter the market, health systems, payers, physicians, pharmacists, patients and manufacturers will be able to reflect on early successes and challenges to further develop biosimilar strategies1

APhA (American Pharmacists Association): Convened Biologics and Biosimilars Stakeholder Conference (Nov 2016)2

ASHP (American Society of Health-System Pharmacists) 2017 Mid-Year Meeting: “Pharmacists are in a key position...we are at the forefront of making sure that patients understand the differences and education is such a key point with biosimilars...”3

1. Oskouei S. Following the biosimilar breadcrumbs: When health systems and manufacturers approach forks in the road. JMCP. 2017;23(12):1245-1248.
Thank You!
Appendix Slides
### FDA Approval: Comparison

Get footnote from AMGEN, Biosimilars: Clinical......

<table>
<thead>
<tr>
<th></th>
<th>Originator(^{1-3})</th>
<th>Biosimilar(^{1,4})</th>
<th>Generic(^{5})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Studies</strong></td>
<td>Establish clinical benefit and risks</td>
<td>Demonstrate no clinically meaningful differences</td>
<td>Not required</td>
</tr>
<tr>
<td>(safety, efficacy,</td>
<td></td>
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<td>immunogenicity)</td>
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<td><strong>Clinical Pharm.</strong></td>
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<td>(PK/PD)</td>
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<td><strong>In Vivo Studies</strong></td>
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<td>(nonclinical)</td>
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<tr>
<td><strong>In Vitro Studies</strong></td>
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<td>(analytical</td>
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<td>characterization)</td>
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<tr>
<td>PK and dose finding</td>
<td>PK equivalence</td>
<td>Demonstrate bioequivalence</td>
<td></td>
</tr>
<tr>
<td>In vivo safety and</td>
<td>Toxicology similarity</td>
<td>Not required</td>
<td></td>
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<tr>
<td>efficacy</td>
<td></td>
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<tr>
<td>Quality profile</td>
<td>Quality profile and analytical similarity</td>
<td>Quality profile</td>
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</table>
### Summary:
**Important Considerations in Evaluating Biosimilars**

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical data</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Has the totality of evidence demonstrated biosimilarity between the proposed biosimilar and reference biologic product?</td>
</tr>
<tr>
<td><strong>Immunogenicity</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Are there any differences from reference biologic product in incidence and severity of immune responses, such as development of antibody titer and neutralizing antibodies?</td>
</tr>
<tr>
<td><strong>Product characteristics</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Are there any differences from reference biologic product in formulation and excipients?</td>
</tr>
<tr>
<td><strong>Product stability/administration</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Are there any differences from reference biologic product in storage and shelf life?</td>
</tr>
<tr>
<td><strong>Extrapolation</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Is appropriate scientific justification provided to support use in other indications?</td>
</tr>
<tr>
<td><strong>Variety of indications</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Has the biosimilar been evaluated to support use in all of the reference biologic product indications?</td>
</tr>
<tr>
<td><strong>Product naming</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Will the name ensure traceability of adverse events?</td>
</tr>
</tbody>
</table>

1. FDA. *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. Guidance for Industry.* Published April 2015.
2. FDA. *Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product. Guidance for Industry* Published April 2015.
3. FDA. *Nonproprietary Naming of Biological Products: Guidance for Industry.* Published August 2015.
Biosimilar Timeline

Figure 1: Biosimilar Timeline

- Biologics Price Competition and Innovation Act of 2009 (BPCI Act)
- 2014 Purple Book
- April 2015 FDA Finalizes Initial Guidance
- March 2016 FDA Draft Guidance (Labeling)
- 2012–2013 Draft FDA Guidance
- March 2015 First Biosimilar Approved
- August 2015 FDA Draft Guidance (Naming)
- April 2016 Second Biosimilar Approved
Litigation

- Biosimilars even greater importance/presence as more regulatory and litigation hurdles are eliminated  
  Mattina, Looking Ahead: AJMC

- BPCI Act:
  - FDA: reference biologics are given 12 years of patent protection Joszt (2)
  - Patent litigation procedure
  - Commonly referred to as “the patent dance”
    Runmore

- Remains a key offensive/defensive strategy for the reference product company

- Results: 34 35
  - Single infringement could delay product launch
  - Biosimilar applicant may decide to launch at risk
  - Could result in withdrawal of the product from the market and/or royalties for the reference product sponsor at the end of the lawsuit


An Overall Picture (Crespi-Lofton)

- American Pharmacists Association (APhA): convened the Biologics and Biosimilars Stakeholder Conference (Nov 2016)

- Objectives:
  1. To determine key issues/challenges for biologics, follow-on biologics (FOBs) and biosimilars
  2. To identify potential roles/responsibilities of pharmacists
  3. To identify actions/activities for pharmacists to optimize safe and cost-effective use

- National thought leaders and stakeholder representatives
  - FDA
  - Centers for Medicare and Medicaid Services (CMS)
  - A private third-party payer
  - Manufacturers
  - Several national organizations of healthcare professionals

- Not all stakeholders were represented
  - Patient advocacy organizations
  - Wholesalers that distribute biological products
  - Data compendia which deliver product information
An Overall Picture (Crespi-Lofton)

• Despite the potential benefits of biosimilars, certain factors may limit their uptake:
  • Technology
  • Prescriber-pharmacist communication
  • Legislation/regulations
  • Limited patient and healthcare practitioner knowledge of products
  • Patient and healthcare practitioner perceptions of biosimilars
  • Evolving science or lack of long-term data

• Strategies to address issues:
  • Need to enhance the education of pharmacists, prescribers and patients
  • Passage of state laws and regulations that do not impede the use of biosimilars (e.g., interchangeable biosimilars)
  • Use of product-specific tracking information in electronic health records and surveillance systems
  • Bidirectional communication among pharmacists, prescribers and other members of the care team
    • To support pharmacovigilance and the maintenance of accurate patient records
  • Development of evidence-based third-party payer policies

• Extent of such growth is, in part, dependent on various stakeholder decisions to provide, pay for or use these products in a safe and thoughtful manner
Health System: Challenges

• Ensure that the most cost-effective therapies are used

• Properly evaluating biosimilar products from Standpoints:
  • Clinical
    • Then it comes to clinically evaluating a biosimilar, health systems are faced with making clinical recommendations without typical resources, such as extensive clinical trials. Oskouei
  • Operational standpoint to Oskouei
  • Financial
    • Potential cost savings with the infliximab biosimilar, 76% perceived a cost savings opportunity compared with the reference product Oskouei

• Variables to consider when analyzing the overall financial effect
  • Type of biosimilar since biosimilars indicated for supportive care versus curative/disease management have varied impact and payer implications
  • Provider setting since acquisition costs and reimbursement models vary depending on sites of care
  • Reimbursement - the greater financial focus in the cost-savings equation Oskouei
  • Additional steps required to ensure appropriate management of the products (e.g., stocking multiple products)
Payers: Unanswered Questions

Do payers agree with the current regulatory pathway for biosimilars in the US, and how do they perceive it changing moving forward, particularly in relation to interchangeability? Report Buyer

How have payer views in relation to the key market-shaping issues of switching, automatic substitution, extrapolation of indications, and biosimilar naming changed over the past year, and how have key events in these areas shaped and changed thinking? Report Buyer

What does the future hold for biosimilars in the US; it is a case that biosimilars need to succeed in order to support a more sustainable healthcare system, or will the biosimilars market crumble under the weight of its own expectations? Report Buyer

How do payors expect pricing dynamics within the US biosimilars market to evolve, and what are their expectations in relation to the pricing of originator biologics in response to biosimilar competition? Report Buyer
MD: Concerns

• **Biosimilar Experience**
  • Alliance for Safe Biologic Medicines 2015 survey of U.S. prescribers
    • Suggests adoption of biosimilars may initially be slow/incremental due to lack of familiarity
    • Only 20% of 400 prescribers were “very familiar” with biosimilars
  • InCrowd, Inc. Feb 2016 survey of U.S. physicians (n=150)
    • Routinely treat patients with biologics and are familiar with biosimilars
    • Only 17% expect biosimilars to “become the norm or replace biologics” in the next few years

• **Biosimilar Education**
  • Lack specific detailed information that would help them readily use these products in their practice
  • 94% believed biosimilars would provide value to healthcare yet only 17% of those who prescribed biologicals said they were very likely to prescribe biosimilars
MD: Main Concerns

Switching

• 150 specialists: More comfortable prescribing biosimilars for treatment-naïve patients rather than switching stable patients to biosimilars 37 INCROWD Survey

• 1,201 specialists (high prescribers): 44.8% believed biosimilars would be safe and appropriate for use in existing patients as well as treatment-naïve patients Cohen Biosimilars Forum survey 2015-2016

Type of Care (Supportive Care (disease) vs. Curative Treatment (diseases))

• “I’m more willing to let economics drive supportive care instead of therapeutic medications. I’d like a higher standard of data in a therapeutic [curative] indication.” (Oncologist)38

Patient Access

• 91% would consider switching from an originator biologic to a biosimilar if it would help the patient have better access to medications Cohen biosimilars forum survey
Pharmacist: Key Role

• **Medication experts on the health care team:**
  - Beyond patient education and counseling during dispensing
  - Specialty pharmacy
  - Health plans
  - P & T committees Crespi-Lofton
  - Determining whether a patient receives an interchangeable biosimilar product, Crespi lofton

• **Prepared to lead evaluation of comparability regarding:**
  - Safe prescribing and use
  - Manufacturing differences
  - Pharmacokinetics
  - Immunogenicity
  - Storage
  - Indications
  - Interchangeability Runmore
  - Substitutions
  - Principles of biosimilar development and evolving regulatory guidelines Stevenson
Pharmacist: Key Role

- Abbreviated pathway
- Heavy focus on analytical and physiochemical data
- Healthcare providers to clinically evaluate biosimilars with a different lens
- Oskouei ALL
- Biosimilarity: Comparative data & reference product data
- Indication extrapolation
P & T: Formulary Considerations

- Additional impact factors:
  - Efficacy
  - Interchangeability
  - Product and administration issues
    - Dosage form, routes of administration, stability, history of recalls
  - Market penetration
  - Packaging and labeling
  - Delivery system
  - Practitioner preferences
  - Cost
  - Reimbursement

Runmore
Interchangeability

Practice where one product can be interchanged for another equivalent product in a clinical setting without the risk of a negative health outcome 2

BPCIA: interchangeable biosimilars may be substituted for reference product Runmore

None of the biosimilar products approved so far designated as interchangeable

BRC What are Interchangeable Biologic Products?
Interchangeability: FDA Draft Guidance


• Currently reviewing public comments

• Clinical switching studies required to support this determination | FDA Biosimilar Development, Review and Approval
  • Raise provider optimism | Runmore
    • Major concern is switching patients to a biosimilar and then back to the original biologic
    • Several recent studies have shown that this can be safely achieved | Dangi-Garimella 3

• **Switching studies:**
  • Infliximab (Remicade) to Inflectra (infliximab-dyyb)
    • NOR-SWITCH trial
    • 52-week, Phase 4 study
    • Crohn’s disease, ulcerative colitis, spondyloarthropathy, RA, psoriatic arthritis, plaque psoriasis
    • Met primary endpoint of non-inferiority in patients switched from the reference infliximab to biosimilar infliximab-dyyb | Davio
  
  • Remicade to Inflectra
    • New single-center prospective cohort study
    • Switching both safe and feasible | Dangi-Garimella 3

• **AMCP:** non-U.S. based switching studies to be accepted as supporting | Mattina
State and Federal Law: Issues

**Benefit:** State laws that facilitate biosimilar use can stimulate more competitive marketplace.

**Barriers to U.S. market entry of biosimilars:**

**Drawbacks:**
- Unnecessarily restrictive, burdensome
- Hinder use/uptake of biosimilar and interchangeable products
- Undermine patient and prescriber confidence

- **MD: FDA draft guidance**
  - Physicians from several organizations have submitted their comments to the FDA draft guidance
  - Concerns: extrapolation of indications, switching, labeling, naming, postmarketing studies

- **Managed Care Organizations:**
  - National plan: how communicate biosimilar strategy across state lines with all of the variability of state rulings
  - Upon interchangeability, designation strategies to ensure effective interchangeability
Pharmacovigilance

Rigorous pharmacovigilance is essential for all biologics to protect patients and ensure any adverse events are quickly detected, reported, and attributed to the correct product and manufacturer\(^1,2\).

Safety monitoring should take into account the safety or effectiveness concerns associated with the reference biologic product\(^1\).

Safety monitoring should have the ability to differentiate between adverse events associated with the proposed biosimilar product vs those associated with the reference drug or other biosimilars\(^1\).

### Product Considerations

#### Implications
- Payers, healthcare providers, pharmacists, nurses, patients and caregivers 67 Amgen 2017 Trends

#### Competition
- Biosimilars likely to face competition from new biologics in the same therapeutic class
- Incremental improvements to existing reference products12 Stevenson

#### Clinical Differences
- **Indications**
  - Example: biosimilar received all the available indications of the reference product but does not, as of January 2017, have a dose formulation for all patient populations67
- **Doses**
- **Dosage forms Amgen 2017**

#### Nonclinical Differences
- **Delivery device**
  - Example: first FDA approved biosimilar only available as a prefilled syringe (as of January 2017), while the reference product is available as a prefilled syringe and a vial65,66
- **Packaging**
- **Distribution channels**
Extrapolation

**Extrapolation**: process by which a proposed biosimilar product may be licensed in one or more additional conditions for which the reference product is licensed

**Biosimilar:**
- If appropriate scientific justification is provided
- If patent landscape allows for it
- If totality of evidence addresses any identified differences between the biosimilar and reference product

**The Unknown**: (patients and physicians)
- Whether a biosimilar can be used in all the same indications as the reference product
  - First four approved biosimilars in the U.S. received approval for all available (i.e., non-orphan) indications
  - Some indications may be initially excluded from an approved biosimilar label due to FDA established exclusivity periods
- Specialty physicians survey (2016) (n=1,201)

**Postmarketing Surveillance and Data**: from observational studies may help address concerns around extrapolation

---

Manufacturer: Future Sustainability

• Concerns:
  • Stability of the market and where it may go in the future
  • Reimbursement and policy and coverage Forys

• Biosimilars market different from generics market
  • Pathway for approval can take a lot longer and be a lot more expensive
    • Generics: 3-5 year time development with a $1 million to $2 million investment
    • Biosimilars: 8-10 year development time with a $100 million to $200 million investment

• Slow down pipeline 5, 10, 15 years from now Forys
Summary

Even though there are factors that need to be balanced, potential reduction in cost to patients, families, caregivers, payers and the healthcare system Stevenson.

The CMS change in coding policy will have a positive effect on competition, innovation, pharmacovigilance and patient access Syrop.

Ultimate benefit: Improving access to expensive therapies Stevenson and creating a more sustainable healthcare system AMGEN 2017 Trends.
P & T: Formulary Considerations

Figure 3 Formulary Considerations for Biosimilars

- Off-label use; All indications?
- Restrict to treatment-naïve patients?
- Transitions of care
- Medication use policies/guidelines
- Supply chain reliability
- Handling conditions, shelf life, storage
- CPOE, eMAR

CPOE = computerized provider order entry; eMAR = electronic medication administration records.