Implementation of Biosimilars: The Good, the Bad, the Ugly
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Learning Objectives

1. Discuss how to effectively assess individual biosimilars for formulary addition
2. Review approaches for building biosimilars into an electronic health record
3. Discuss approaches to securing appropriate insurance approval and reimbursement
4. List effective education methods for nursing, pharmacy, physician staff on implementation of biosimilars

Audience Response

What is the adoption rate of available biosimilar agents at your institution?
A. NA, biosimilar agents are not used
B. Less than 10%
C. 10 - 25%
D. 25 - 50%
E. 50 - 75%
F. Greater than 75%
The Biologics Price Competition & Innovation Act of 2009 (BPCI Act)
- Passed as part of health reform (Affordable Care Act)
- President Obama signed into law on March 23, 2010

BPCI Act creates an abbreviated licensure pathway for biological products shown to be:
- Biosimilar (highly similar) to
- Interchangeable with an FDA-licensed reference product
Biosimilar Background

- A biosimilar medication is highly similar, but not identical, to a biologic innovator product.
- There is no clinically meaningful difference between the biosimilar and innovator product and recognizes that the two molecules are in fact different, but exert highly similar effects.
- Pre-clinical / clinical data must be submitted to provide justification for each indication sought.

Structural and Physicochemical Biosimilarity Studies

Totality of Evidence

- Analytical Studies
- Additional Clinical Studies
- Clinical Pharmacology
- Non-Clinical
- Functional & Biological
- Structural & Physicochemical

Primary Structure: Peptide Mapping by HPLC1

AU

Minutes

US Remicade
Inflectra
EU Remicade

*High Performance Liquid Chromatography
In Vitro TNF-α Neutralization

16 lots 13 lots 13 lots

CT-P13 (Infelctra®) Infliximab-dyyb). Inflectra Manufacturer Overview Slides. Hospira UK, a Pfizer Company.

Single-Dose 3-Way PK Study:
Showed Similar PK over 8 Weeks

Biosimilar Background

<table>
<thead>
<tr>
<th>Requirement</th>
<th>CT-P13 BLA Fulfillment of Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference Product</td>
<td>US Remicade® (Infliximab)</td>
</tr>
<tr>
<td>Analytical Data</td>
<td>Demonstrated highly similar structure and function</td>
</tr>
<tr>
<td>Non-Clinical Studies</td>
<td>Confirmed similar pharmacology and toxicology</td>
</tr>
<tr>
<td>Clinical Studies</td>
<td>Compared PK/FO, immunogenicity, efficacy, safety</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>Principally mediated by binding and neutralization of soluble and transmembrane TNFα</td>
</tr>
<tr>
<td>Conditions of Use</td>
<td>Same as reference product¹</td>
</tr>
<tr>
<td>Route of Administration, Dosage Form &amp; Strength</td>
<td>Same as reference product</td>
</tr>
<tr>
<td>“Biosimilar” Definition</td>
<td>High structural and functional similarity with no clinically meaningful differences</td>
</tr>
<tr>
<td>Fulfillment of Bridging Criteria</td>
<td>3-way PK similarity data</td>
</tr>
</tbody>
</table>

### Biosimilar Indication Comparison

<table>
<thead>
<tr>
<th><strong>Biosimilar</strong></th>
<th><strong>Product (Brand)</strong></th>
<th><strong>FDA Approval Date</strong></th>
<th><strong>Current Status</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>infliximab-dyyb (Inflectra)</td>
<td>Infliximab (Remicade)</td>
<td>04/05/2016</td>
<td>Launch Date 11/2016</td>
</tr>
<tr>
<td>infliximab-abda (Remisma)</td>
<td>Infliximab (Remicade)</td>
<td>04/21/2017</td>
<td>Launch Date 07/2017</td>
</tr>
<tr>
<td>infliximab-qbtx (ixli)</td>
<td>Infliximab (Remicade)</td>
<td>12/13/2017</td>
<td>Not Launched</td>
</tr>
</tbody>
</table>

### Audience Response

**Biosimilars have the same indication listed in their package insert as the reference product?**

A. True  
B. False

### Biosimilar Indication Comparison

<table>
<thead>
<tr>
<th>Disease State</th>
<th>Infliximab (Remicade)</th>
<th>Infliximab-dyyb (Inflectra)</th>
<th>Infliximab-abda (Remisma)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn's Disease</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
</tr>
<tr>
<td>Pediatric Crohn's Disease</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
</tr>
<tr>
<td>Pediatric Ulcerative Colitis</td>
<td>✔ ✔ ✔</td>
<td>X ✗ X</td>
<td>✔ ✔ ✔</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
</tr>
<tr>
<td>Plaque psoriasis</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
</tr>
</tbody>
</table>
### Biosimilar Clinical Trial Comparison: Infliximab

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Infliximab (Remicade)</th>
<th>Infliximab-dyyb (Inflectra)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>Rheumatoid arthritis (RA)</td>
<td>Rheumatoid arthritis (RA)</td>
</tr>
<tr>
<td>Study Design</td>
<td>Phase III, multi-center, randomized, double-blind</td>
<td>Phase III, multi-center, multi-national, randomized, double-blind, parallel-group trial</td>
</tr>
<tr>
<td>Patients</td>
<td>N = 428</td>
<td>N = 606</td>
</tr>
<tr>
<td>Results</td>
<td>Clinically and statistically significant improvement in signs and symptoms of RA per ACR20*</td>
<td>Clinically similar efficacy with similar adverse events to reference product</td>
</tr>
</tbody>
</table>

*American College of Rheumatology response criteria = ACR 20


**Audience Response**

What factors are important to consider when placing a biosimilar on formulary?
Biosimilar Formulary Checklist

- Marketplace availability
- Distribution channel supports effective workflow
- Available on contract at a favorable discount (including 340B)
- Favorable reimbursement
- Favorable 340B contract pricing
- Insurance/PBM coverage for the biosimilar supports use
- Equivalent patient assistance program(s) available

Biosimilar Pipeline

<table>
<thead>
<tr>
<th>Earliest Possible Launch</th>
<th>Biosimilar Name</th>
<th>Reference Drug</th>
<th>Brand Companies</th>
<th>Status</th>
<th>Triggering Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2022</td>
<td>Amjevita</td>
<td>Humira</td>
<td>Amgen</td>
<td>Approved (09/23/16)</td>
<td>Settlement</td>
</tr>
<tr>
<td>2019</td>
<td>Cyltezo</td>
<td>Enbrel</td>
<td>Sandoz</td>
<td>Approved (09/13/16)</td>
<td>Court decision</td>
</tr>
<tr>
<td>2019</td>
<td>Filgrastim</td>
<td>Neupogen</td>
<td>Adello Biologics; Amneal; AE Companies</td>
<td>Pending (05/2018)</td>
<td>FDA approval</td>
</tr>
<tr>
<td>2020</td>
<td>GP2017</td>
<td>Humira</td>
<td>Sandoz</td>
<td>Pending (11/2018)</td>
<td>FDA approval</td>
</tr>
<tr>
<td>2017</td>
<td>Ixifi</td>
<td>Remicade</td>
<td>Pfizer</td>
<td>Approved (12/13/17)</td>
<td>Launch</td>
</tr>
<tr>
<td>2018</td>
<td>Lapelga</td>
<td>Neulasta</td>
<td>Apotex; Accord; Intas</td>
<td>Pending (11/03/18)</td>
<td>FDA approval</td>
</tr>
<tr>
<td>2018</td>
<td>Mvasi</td>
<td>Avastin</td>
<td>Amgen; Allergan</td>
<td>Approved (09/14/17)</td>
<td>Patent expiration</td>
</tr>
<tr>
<td>2018</td>
<td>Nivestym</td>
<td>Neupogen</td>
<td>Hospira; Pfizer</td>
<td>Approved (07/20/18)</td>
<td>Launch</td>
</tr>
<tr>
<td>2018</td>
<td>Ogivri</td>
<td>Herceptin</td>
<td>Mylan; Biocon</td>
<td>Approved (12/01/17)</td>
<td>Settlement</td>
</tr>
<tr>
<td>2018</td>
<td>SB3</td>
<td>Herceptin</td>
<td>Samsung Bioepis; Merck &amp; Co</td>
<td>Pending (10/20/18)</td>
<td>Patent Office decision</td>
</tr>
<tr>
<td>2018</td>
<td>Truxima</td>
<td>Rituxan</td>
<td>Celltrion; Teva</td>
<td>Pending (11/2018)</td>
<td>FDA approval</td>
</tr>
<tr>
<td>2018</td>
<td>Udenyca</td>
<td>Neulasta</td>
<td>Coherus</td>
<td>Pending (11/03/18)</td>
<td>FDA approval</td>
</tr>
</tbody>
</table>

Electronic Health Record (EHR) Build

- **Strategy #1**
  - Build out all formulations (reference products and all biosimilars) in order sets
  - Wait until insurance approval to determine product dispensed
  - Remove orders for other formulations not covered by insurance

- **Strategy #2**
  - Build out separate ordersets
  - Review insurance formulary for covered product, then provider enters the order
Insurance Reimbursement

• Increase in biosimilars being preferred product on insurance formularies
• Many insurance providers still require precertification/prior authorization prior to use
• Ensure precertification approval for determined formulary agent (institutional or insurance)
Insurance Reimbursement

- Ideal to have dedicated staff member or well established process to complete precertifications
  - Automate precertification requests via EHR
  - Manually request precertifications and track manually
- Pharmacy staff to ensure precertification approval obtained prior to dispensing

Pharmacy Logistics

- Storage of multiple formulations for product
  - Example Infliximab
    - Reference product:
      - Infliximab (Remicade)
    - Biosimilars
      - Infliximab-dyyb (Inflectra)
      - Infliximab-abda (Renflexis)
- Medication Safety Concerns
  - Ordering correct product covered by insurance
  - Dispensing correct product ordered

Biosimilar Policy

- Institutional policy on Biosimilars
  - Ensure your institution has a policy to address stance on biosimilars
    - Are they considered interchangeable?
    - Does physician have to be notified prior to interchanging?
    - Discuss patient notification of biosimilar use vs reference product
Resources

- Biosimilar Policy Components
  - Background
    - Robust FDA approval process
      - Disease state specific Drug Advisory Committee approvals
      - Many times phase III efficacy trials
    - Definitions: reference product vs biosimilar
    - Highly similar vs interchangeable
    - Stance of interchangeability at institution
    - Outline physician and/or patient notification of biosimilar use

Audience Response

Who are the important stakeholders to engage when introducing a biosimilar?

Successful Implementation

- Identify Key Stakeholders:
  - Senior Leadership
    - Chief Medical Officer
    - Chief Nursing Officer
    - Chief Pharmacy Officer
    - Director of Pharmacy
    - Pharmacy & Therapeutics Chair
  - Clinicians
    - Pharmacy Team (Supervisors and Front line staff)
    - Nursing Team (Manager, Educators, Front line staff)
  - Patients
Stakeholder Resources

Evidence based SBAR, White Paper
Executive Summary Slides
Elevator Speech
Internal Talking Points for Managers
Frequently Asked Questions (FAQs)
Key patient stories
Executive Memo
Letter to Referring Clinicians
Letter to Patients

Implementation Education

• Clinical Staff Education
  – Physicians
  – Pharmacists
  – Nurses and Nurse Practitioners
• Handout
  – Biosimilar background
  – Clinical trial comparisons
  – Dosing, admixture, and administration comparisons
  – Cost savings data

Key Takeaways

1. Use a biosimilar checklist when reviewing a new agent for formulary addition
2. Plan your approach to building biosimilars into the EHR
3. Establish a formal process for biosimilar precertification and insurance approval
4. Develop effective education methods for nursing, pharmacy, physicians, and patients
Key References