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

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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%

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Biosimilar Background

- 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 **or**
  - Interchangeable with an FDA- licensed reference product

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Implementation of the Biologics Price Competition and Innovation Act of 2009. United States Food and Drug Administration. Compliance and Regulatory Information. Page Last Updated: 03/10/2011.

351 (k) Application

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

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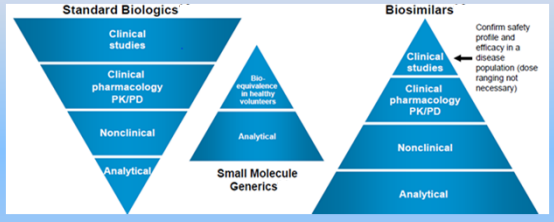
Implementation of the Biologics Price Competition and Innovation Act of 2009. United States Food and Drug Administration. Compliance and Regulatory Information. Page Last Updated: 03/10/2011.

Development Pathways



CT-P13 (Infelctra®) Infliximab-dyyb). Inflectra Manufacturer Overview Slides. Hospira UK, a Pfizer Company. McCamish M. Presented at EMA Workshop on Biosimilars; London; October 2013.

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

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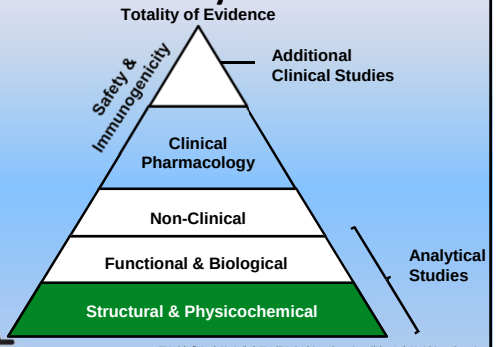
Structural and Physicochemical Biosimilarity Studies



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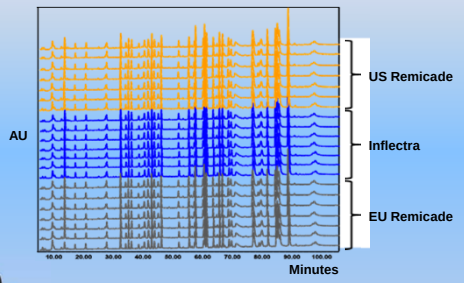
CT-P13 (Infliximab Biosimilar). FDA CT-P13 Advisory Committee Slides. Arthritis Advisory Committee February 9, 2016. CELLTRION, Inc.

Primary Structure: Peptide Mapping by HPLC1



[1] High-Performance Liquid Chromatography

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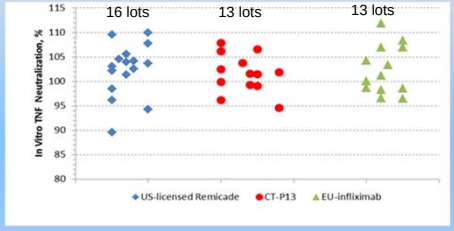
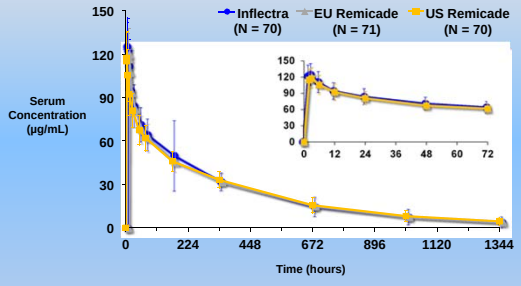
CT-P13 (Infliximab Biosimilar). FDA CT-P13 Advisory Committee Slides. Arthritis Advisory Committee February 9, 2016. CELLTRION, Inc.

In Vitro TNF-α Neutralization



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

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



CT-P13 (Infliximab Biosimilar). FDA CT-P13 Advisory Committee Slides. Arthritis Advisory Committee. February 9, 2016. CELLTRION, Inc.

Biosimilar Background

Requirement	CT-P13 BLA Fulfillment of Requirement
Reference Product	US Remicade® (infliximab)
Analytical Data	Demonstrated highly similar structure and function
Non-Clinical Studies	Confirmed similar pharmacology and toxicology
Clinical Studies	Compared PK/PD, immunogenicity, efficacy, safety
Mechanism of Action	Principally mediated by binding and neutralization of soluble and transmembrane TNFα
Conditions of Use	Same as reference product[1]
Route of Administration, Dosage Form & Strength	Same as reference product
Fulfillment of "Biosimilar" Definition	High structural and functional similarity with no clinically meaningful differences
Fulfillment of Bridging Criteria	3-way analytical data 3-way PK similarity data

U.S. Food and Drug Administration, FDA Briefing Document: CT-P13, A Proposed Biosimilar to Remicade (Infliximab), BLA 125544, February 9, 2016, https://www.fda.gov/downloads/%E2%80%A6/UCM484859.pdf

Biosimilar Indication Comparison

Biosimilar	Product (Brand)	FDA Approval Date	Current Status
Infliximab-dyyb (Inflectra)	Infliximab (Remicade)	04/05/2016	Launch Date 11/2016
Infliximab-abda (Renflexis)	Infliximab (Remicade)	04/21/2017	Launch Date 07/2017
Infliximab-qbtx (Ixifi)	Infliximab (Remicade)	12/13/2017	Not Launched

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Audience Response

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

A. True
B. False

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Biosimilar Indication Comparison

Disease State Indication	Infliximab (Remicade)	Infliximab-dyyb (Inflectra)	Infliximab-abda (Renflexis)
Crohn's Disease	✔	✔	✔
Pediatric Crohn's Disease	✔	✔	✔
Ulcerative Colitis	✔	✔	✔
Pediatric Ulcerative Colitis	✔	x	x
Rheumatoid Arthritis	✔	✔	✔
Psoriatic Arthritis	✔	✔	✔
Plaque psoriasis	✔	✔	✔

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Remicade. [package insert]. Horsham, PA. Janssen Biotech, Inc. 2018.
Inflectra. [package insert], New York, NY. Pfizer, Inc. 2018
Renflexia. [package insert]. Station, NJ. Merck & Co, Inc. 2018

Biosimilar Clinical Trial Comparison: Infliximab

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

*American College of Rheumatology response criteria = ACR 20

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Yoo DH et al. *Ann Rheum Dis* 2013;72:1613-1620.
Remicade. (package insert). Horsham, PA. Janssen Biotech, Inc.2018.

Biosimilar vs Reference Product Cost

Product	Vial Size	AWP Cost Per 100mg Vial	AWP Cost per 600mg Dose
Infliximab (Remicade)	100mg	$1,401.38	$8,408.28
Infliximab-dyyb (Inflectra)	100mg	$1,135.54	$6,813.24
Infliximab-abda (Renflexis)	100mg	$904.07	$5,424.42

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Remicade®. Lexi-Drugs Online. Accessed July 1, 2018.
Inflectra®. Lexi-Drugs Online. Accessed July 1, 2018
Renflexis®. Lexi-Drugs Online. Accessed July 1, 2018

Audience Response

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

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Picture provided from: www. http://realtybiznews.com

Biosimilar Formulary Checklist

- Marketplace availability
- Distribution channel supports effective work flow
- 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

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Biosimilar Pipeline

Earliest Possible Launch	Biosimilar Name	Reference Drug Name	Brand Companies	Status	Triggering Event
2022	Amjevita Cyltezo	Humira	Amgen	Approved (09/23/16)	Settlement
2019	Erelzi	Enbrel	Sandoz	Approved (08/30/16)	Court decision
2018	Filgrastim Adello	Neupogen	Adello Biologics; Amneal; AE Companies	Pending (05/2018)	FDA approval
2020	GP2017	Humira	Sandoz	Pending (11/2018)	Patent Office decision
TBD	Grastofil	Neupogen	Apotex; Accord; Intas	Pending	FDA approval
2018	Herzuma	Herceptin	Celltrion; Teva; Nippon Kayaku	Pending (12/2018)	Patent Office decision
TBD	Ixifi	Remicade	Pfizer	Approved (12/13/17)	Launch
TBD	Lapelga	Neulasta	Apotex; Accord; Intas	Pending	FDA approval
2019	Mvasi	Avastin	Amgen; Allergan	Approved (09/14/17)	Patent expiration
2018	Nivestym	Neupogen	Hospira; Pfizer	Approved (07/20/18)	Launch
2018	Ogivri	Herceptin	Mylan; Biocon	Approved (12/01/17)	Settlement
2018	SB3	Herceptin	Samsung Bioepis; Merck & Co	Pending (10/2018)	Patent Office decision
2018	Truxima	Rituxan	Celltrion; Teva	Pending (11/2018)	FDA approval
2018	Udenyca	Neulasta	Coherus	Pending (11/03/18)	FDA approval

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

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EHR Strategy #1

EHR Strategy #1

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

- Biosmilar 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

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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

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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

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Key References

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Questions?

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