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Mandated Payor Switching with Infliximab (IFX) Biosimilars

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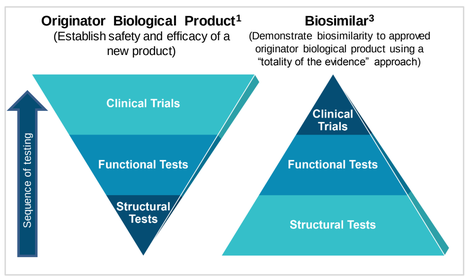
Introduction

- The Biologics Price Competition and Innovation Act (BPCIA) was established in 2009 to create an abbreviated licensure pathway for biological products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-licensed biological product.[1]
- Goals of the new pathway are to:
  - Reduce healthcare costs
  - Increase treatment options[2]
- Biosimilars are biological products that are FDA approved as being (1) "highly similar to the reference products notwithstanding minor differences in clinically inactive components" and that (2) "there are no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency of the product."
- Although there are distinct approval requirements for reference products, biosimilars, and interchangeable products, the approval standards that apply to each type of biological product assure prescribers of the safety and effectiveness of each type of product. All biological products are approved only after they meet FDA's rigorous approval standards as noted in the diagram below. This leads to extrapolation with biosimilar approval for all indications of the originator product based on supporting evidence of similarity in at least 1 indication.[3]



Infliximab biosimilars were studied in:

- ankylosing spondylitis
- rheumatoid arthritis

Approved for:

- ankylosing spondylitis
- Crohn's disease
- psoriatic arthritis
- psoriasis
- ulcerative colitis

- The FDA evaluates each biosimilar product on a case-specific basis to determine what data are needs to demonstrate biosimilarity and which data element can be waived if deemed scientifically appropriate. This determination may be informed by what is already publicly known about the reference product.
- Many factors can help tailor the data requirements for each biosimilar application. Some examples include:
  - Strength and robustness of the comparative analytical studies showing similar structure and function between the proposed biosimilar and the reference product.
  - Similarity of he PK and PD profiles between the biosimilar and reference product.
  - Pre-existing information about the safety profile of the reference product.
- In April 2016 the FDA approved **infliximab-dyyb (Inflectra®)** as the first biosimilar agent to infliximab (Remicade®), and this was followed in April 2017 with the approval of **infliximab-abda (Renflexis®).**

Medical clinical practice must address the following with the use of biosimilars:

Extrapolation (particularly applicable to pediatrics)	Switching/transitioning	Interchangeability

- The medical practice of changing one medicine for another that is expected to achieve the same clinical result in a given clinical setting and in any patient should be on the initiative or with the agreement of the prescriber.

Interchangeability

- No US biosimilar agents are currently deemed interchangeable.
- Nonetheless, insurance coverage payor policies may require clinicians to interchange these agents.

- Biosimilars are now being selected by hospitals for formulary inclusion to reduce healthcare costs, but the outpatient uses of either the reference product or biosimilar may be mandated by insurance payors for reasons not obvious to prescribers.
- The Rand report estimates a potential cost savings of $54 billion over 10 years in the US with the use of biosimilars.[4] The physician office site of care was noted by the report to provide cost savings to insurers and to patients, assuming access to biosimilars unrestricted by payors.

Case Information

A 60-year-old white female with a history of ulcerative pancolitis was hospitalized for a deteriorating clinical course evidenced by diffuse abdominal pain and up to 6 episodes per day of bloody diarrhea. Intravenous methylprednisolone was given upon admission. She had been receiving mesalamine which was initially administered and then discontinued to give a first dose of IFX (Remicade®). Remicade® was formulary substituted in the hospital with infliximab-dyyb (Inflectra®) at 5 mg/kg/dose. Over the next 48 hrs, the patient had significant clinical improvement associated with resolution of her abdominal pain and rectal bleeding. On day 4, the patient was discharged to continue high dose oral prednisone and complete Inflectra® induction as outpatient. The commercial insurance payor, Cigna, refused to approve the use and reimbursement of the IFX biosimilar. Repeated attempts by the provider to allow the same biosimilar that was initiated were refused and the physician's order was changed to Remicade® for continued treatment. Subsequent Remicade® infusions were generally well tolerated.

Discussion

- This case is an example in where a biosimilar was initiated in the hospital setting with a mandated drug switch to the reference product by the insurance payor for outpatient therapy.
- The ECCO position statement notes "Switching from originator to a biosimilar should be performed following appropriate discussion between physicians, nurses, pharmacists and patients, and according to national recommendation."[5]

The payor selection of biosimilars eliminates physician and patient therapy options.

- The variations noted below in payor policies for non-substantiated preferred use of originator infliximab limits the use of a lower cost biosimilar and potentially increases patient and provider costs.
- This unregulated area of payor policy merits future oversight.

References

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4. Mulcahy AW, et al. Biosimilar cost savings in the United States: initial experience and future potential. RAND Corporation Website. https://www.rand.org/pubs/perspectives/PE264.html. Accessed September 10, 2018.
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Payor Specific Criteria for Use of Infliximab and Infliximab Biosimilars*

Payor	Infliximab (Remicade®)	Infliximab Biosimilars	Detailed Criteria for Use
Aetna	**Allowed**	Allowed	**Crohn's Disease:** Patient must have failed 6-mercaptopurine/azathioprine OR corticosteroids **Fistulizing Crohn's Disease:** No criteria for treatment failure; fistula must be present for at least three (3) months **Ulcerative Colitis:** Patient must have failed ALL continuous immunosuppression with corticosteroids for 30 days for oral therapy or 7 to 10 days for IV therapy, 5-aminosalicylic acid agents, AND immunosuppressants
Anthem	**Preferred**	Allowed only upon failure or contraindication to Remicade®	**Crohn's Disease:** Patient must have failed conventional therapy or previously responded to therapy with infliximab **Fistulizing Crohn's Disease:** No criteria for treatment failure; fistula must be present for at least three (3) months **Ulcerative Colitis:** Patient must have failed conventional therapy
Blue Cross Blue Shield of Texas	**Allowed**	Allowed	**Crohn's Disease; Ulcerative Colitis:** Patient must have failed conventional therapy **Fistulizing Crohn's Disease:** No criteria for treatment failure
Cigna	**Preferred**	Allowed only with intolerance to Remicade®	**Crohn's Disease:** No criteria for treatment failure **Fistulizing Crohn's Disease:** No criteria for treatment failure; fistula must be present for at least three (3) months **Ulcerative Colitis:** Patient must have failed conventional therapy
Humana	**Preferred**	Allowed only upon failure with Remicade®	**Crohn's Disease; Fistulizing Crohn's Disease; Ulcerative Colitis:** Patient must have failed conventional therapy
Scott and White Health Plan	**Preferred**	Allowed only with failure and/or intolerance to Remicade®	**Crohn's Disease; Fistulizing Crohn's Disease; Ulcerative Colitis:** Patient must have failed conventional therapy
United Healthcare	**Preferred/Required**	Allowed only with failure and/or intolerance to Remicade® (If started on biosimilar, switch will be required to Remicade® if above not met)	**Crohn's Disease; Ulcerative Colitis:** Patient must have failed conventional therapy **Fistulizing Crohn's Disease:** No criteria for treatment failure

*Respective medical and pharmacy coverage policies were accessed April 30, 2018