Biosimilars

To provide our members with high quality, cost-effective care, Neighborhood Health Plan of Rhode Island (Neighborhood) has selected biosimilars as preferred agents in comparison to their reference products. If an FDA approved biosimilar is commercially available, Neighborhood will require the trial of the FDA approved biosimilar prior to the use of the reference product for Medicaid and Exchange members. (This will occur for the INTEGRITY (MMP) line of business starting on January 1, 2020.)

Biosimilar Q&A

1. **What is a biosimilar?**
   The U.S Food & Drug Administration (FDA) defines a biosimilar as a biological product that is **highly similar** to, and has **no clinically meaningful differences** from, an existing FDA-approved reference product.

2. **What does "highly similar" and "no clinically meaningful differences" mean?**
   a. **Highly similar:** The manufacturer demonstrated that the biosimilar is highly similar to the reference product by extensively analyzing the structure and function of both products. Comparative tests using state-of-the-art technology are used to compare purity, chemical identity, and bioactivity. Minor differences in clinically inactive components between the two products are acceptable, and any differences are evaluated by the FDA to meet approval standards. Because biological products are derived in a living system (microorganism, plant cell, or animal cell), slight differences between manufactured lots of the same biological product are normal and expected. As part of its review, the FDA assesses the manufacturing process and strategy used to control within-product variations.
   b. **No clinically meaningful differences:** The manufacturer accomplishes this through human pharmacokinetic and pharmacodynamics studies, assessment of immunogenicity, and additional clinical studies (if needed).

3. **What is the approval process for a biosimilar?**
   a. The FDA evaluates each product individually to determine which of the following studies are needed to demonstrate biosimilarity and which studies can be waived if deemed appropriate.
      i. **Analytical studies**: Demonstrates that the biological product is highly similar (with a possibility of minor differences in clinically inactive components) to the reference product.
      ii. **Animal studies**: Demonstrates an assessment of toxicity.
      iii. **Clinical studies:** Demonstrates safety, purity, and potency of the biosimilar. This includes assessing immunogenicity, pharmacokinetics, pharmacodynamics, and may include comparative clinical studies.

4. **What does extrapolation mean?**

Extrapolation is the concept that a biosimilar product may be approved for an indication without direct studies of the biosimilar in that indication. This occurs if the total evidence of the application supports biosimilarity for at least one of the reference product's indications. The manufacturer can use data and information to scientifically justify approval for other indications that were not directly studied.

5. **What does an interchangeable product mean?**
   An interchangeable biosimilar is a product that meets additional requirements outlined by the Biologics Price Competition and Innovation Act. An interchangeable product may be substituted for the reference product without the consultation of the prescriber at the pharmacy level. To meet this requirement, manufactures are required to provide information that shows that a biosimilar is expected to produce the same clinical result as the reference product in any given patient.

   In clinical practice, switching between the interchangeable product and the reference product would not increase or decrease either safety or effectiveness. Currently, there are no interchangeable biosimilars approved in the US.

6. **Have there been studies conducted to evaluate the safety and efficacy of switching stabilized patients from a reference product to a biosimilar?**
   Yes. Before approval, the FDA expects additional safety, efficacy and immunogenicity data for patients who undergo a switch from a reference product to a biosimilar. Switching to a biologic gives the patient access to more affordable products and potentially lowers health care costs through competition.

   A systemic review with meta-analysis was conducted to assess the efficacy and safety of switching patients with Crohn's disease (CD) or ulcerative colitis (UC) from infliximab to the biosimilar, CT-P13. The studies showed no statistically significant difference in sustained clinical response, sustained clinical remission, or adverse events in patients being transitioned from infliximab to CT-P13.

7. **What is the risk of immunogenicity when switching from a reference product to a biosimilar?**
   A biosimilar has an identical amino acid sequence to the reference product. However, subtle differences in post-translational modifications occur during manufacturing in the living organisms, which may be sufficient to trigger an immune response. During development of a biosimilar, the potential for immunogenicity is assessed through analytical studies and in clinical studies by the measurement of anti-drug and neutralizing antibodies. Currently, the majority of clinical trials have not reported a change in immunogenicity.

8. **How to learn more about biosimilars?**
   a. FDA website:
      i. **Biosimilars overview:** https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars

ii. **Biosimilar and Interchangeable Products:** https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products
iii. **Patient and Prescriber Outreach Material:** https://www.fda.gov/drugs/biosimilars/patient-and-prescriber-outreach-materials
iv. **Webinars, Presentations, Articles:** https://www.fda.gov/drugs/biosimilars/webinars-presentations-and-articles

The goal of treatment with a biologic agent is for the patient to achieve remission and maintain remission. Biosimilars allow patients to have access to more affordable products, which lead to decreased health care costs.

References:

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