Update on Biosimilars in the United States: Impacts of Biosimilar Approval for Managed Care, Hospital, and Specialty Pharmacy

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be better able to:

1. Discuss the differences between small-molecule drugs and generics and between biologic drugs and biosimilars;
2. Describe current regulations and standards associated with biosimilar development and approval in the United States (U.S.);
3. Analyze issues related to the substitution, interchangeability, and indication extrapolation of current biosimilars;
4. Review biosimilars currently approved or under development in the U.S.;
5. Assess issues relating to the clinical safety and efficacy of biologics and biosimilar agents; and
6. Analyze pharmacoeconomic issues related to biosimilar use in the U.S.

Post-Test/Rationale:

1. Which of the following is best described as a drug product that may consist of proteins, sugars, nucleic acids, or cells/tissues that has the purpose of preventing, treating, or curing a disease in humans?

   A. A biologic***
   B. A small-molecule drug
   C. A generic
   D. None of the above

Correct answer: A
Rationale (Objective #1): A biologic is a drug product that may consist of proteins, sugars, nucleic acids, or cells/tissues; its purpose is preventing, treating, or curing a disease in humans.

2. Which of the following is NOT a characteristic of biological drug products?

   A. They have a high potential for immunogenicity
   B. They are manufactured using recombinant DNA technology
   C. They are generally small in size with a low molecular weight***
   D. All of the above are characteristics of biological drugs

Correct answer: C
Rationale (Objective #1): Biological drugs are large in size, complex in structure, manufactured using recombinant DNA technology, sensitive to external conditions, and have a relatively high potential for immunogenicity.
3. Which of the following approval pathways can be used for biosimilars to expedite their approval by the United States Food and Drug Administration?

A. New Drug Application defined in section 505(b) of the Food, Drug, and Cosmetic Act (FD&C Act)
B. Abbreviated New Drug Application defined in section 505(j) of the FD&C Act
C. Biologics License Application defined in section 351(a) of the Public Health Service (PHS) Act
D. Biosimilar Biologics License Application defined in section 351(k) of the PHS Act

Correct answer: D

Rationale: An approval process for biosimilars, section 351(k) Biosimilar Biologics License Application, was created as an amendment to the PHS Act by the Biologics Price Competition and Innovation Act when the Patient Protection and Affordable Care Act was passed in 2010.

4. Which of the following best describes the first step required to generate evidence in support of United States Food and Drug Administration approval for a biosimilar?

A. Animal studies to assess pharmacokinetics/pharmacodynamics and immunogenicity
B. An analysis of structure and function of the biosimilar
C. Clinical studies to assess efficacy and safety
D. Pharmacovigilance

Correct answer: B

Rationale: The foundation of evidence for biosimilar development is analytical data presenting how similar the biosimilar is to the originator product in terms of structure and function. On the basis of results of structure and function analyses, the biosimilar is categorized as not similar, similar, highly similar, or highly similar with fingerprint-like similarity. Those classified as highly similar or highly similar with fingerprint-like similarity meet the biosimilar standard, which allows the manufacturer to continue on to the next step of biosimilarity investigation.

5. Which of the following references provides a list of all approved biologics and classifies medications as originators, biosimilars, or interchangeables?

A. The Orange Book
B. The Purple Book
C. Micromedex
D. The Red Book

Correct answer: B

Rationale: The Purple Book provides a list of all approved biologic drug products and classifies the medications are originators, biosimilars, or interchangeables.
6. Which of the following is the originator for the biosimilar product Zarxio?

A. Neupogen (filgrastim)***
B. Lantus (insulin glargine)
C. Remicade (infliximab)
D. Enbrel (etanercept)

Correct answer: A

Rationale (Objective #4): Zarxio (filgrastim-sndz) is biosimilar to Neupogen. It was approved by the United States Food and Drug Administration on March 6, 2015.

7. Which of the following is a potential advantage of using a naming convention for biosimilars that uses a different 4-letter suffix than the originator product?

A. Less resistance to substitution and easier acceptance of designated status of interchangeability
B. Lower costs incurred due to marketing competition of different products
C. Easier to track and associate adverse events and/or change in disease with the correct product
D. All of the above are potential advantages***

Correct answer: D

Rationale (Objective #3): Potential advantages of using a naming convention for biosimilars that uses a different 4-letter suffix (as opposed to using the same 4-letter suffix as the originator product) include ease of tracking and associating adverse events and/or change in disease with the correct product, facilitation of accurate records of automatic substitutions (e.g., insurance-mediated switches), and lower costs due to marketing competition between different biologic products.

8. Which of the following is the originator for the biosimilar product Inflectra?

A. Neupogen (filgrastim)
B. Lantus (insulin glargine)
C. Remicade (infliximab)***
D. Enbrel (etanercept)

Correct answer: C

Rationale (Objective #4): The FDA announced the approval of Inflectra, a biosimilar to the tumor necrosis factor inhibitor Remicade, in April 2016.
9. Which of the following is considered a key factor that can contribute to the immunogenic profile of a biologic drug?

   A. Product-specific characteristics
   B. The underlying disease process
   C. Patient-specific factors
   D. All of the above***

Correct answer: D
Rationale (Objective #5): Factors that can contribute to the immunogenic profile of a biologic include the product’s characteristics, the underlying disease process, and patient-specific factors.

10. Which of the following is NOT considered a key reason why biosimilar agents will never reach levels of price discounting achieved by small-molecule generics?

   A. Biosimilar development costs are considerably lower than costs for small-molecule drugs due to the requirement for only pre-clinical and clinical studies for biosimilars***
   B. Biological drug manufacturing costs are higher than small-molecule drug manufacturing costs
   C. Few biosimilar competitors are expected to enter the market due to the challenges of biosimilar development and marketing, resulting in less intense price competition
   D. Clinician concerns about comparability may need to be addressed in post-launch studies, which will require additional resources and investment

Correct answer: A
Rationale (Objective #6): Biosimilar development costs are considerably higher than those for small-molecule drugs due to the requirement for pre-clinical and clinical studies of biosimilars.