KANSAS DRUG UTILIZATION REVIEW NEWSLETTER

Health Information Designs, LLC ***2nd Quarter 2020***

Welcome to the Quarterly edition of the "Kansas Drug Utilization Review Newsletter", published by Health Information Designs, LLC (HID). This newsletter is part of a continuing effort to keep the Medicaid provider community informed of important changes in the Kansas Medical Assistance Program (KMAP).

Helpful Web Sites

KMAP Web Site
https://www.kmap-state-ks.us/

KDHE-DHCF Web Site
http://www.kdheks.gov/hcf/

KanCare Web Site
http://www.kancare.ks.gov/

Fee-For-Service (FFS) Helpful Numbers

Provider Customer Service (Provider Use Only)
1-800-933-6593

Beneficiary Customer Service
1-800-766-9012

KMAP PA Help Desk
1-800-285-4978

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Biosimilar Products

Biological Products

Rather than being synthesized by a series of chemical reactions, like traditional small molecule drugs, biological products are generally made from living material (e.g., bacteria, plant cells, animal cells) and are larger and more complex in structure.[1] Biological products are large molecule drugs, most of which are composed of proteins ("alpha amino acid polymer that is greater than 40 amino acids in size") and chemically synthesized polypeptides ("alpha amino acid polymer that is made entirely by chemical synthesis and is greater than 40 amino acids but less than 100 amino acids in size"), as the target of a biologic is a protein or a gene.[6,7] They require certain conditions (e.g., light, temperature, production equipment) to be controlled throughout the manufacturing process. This ensures consistent quality and prevention of microbial and/or viral contamination. Because of their labile nature (sensitivity to light and temperature), biological products are often lyophilized (freeze-dried), which requires refrigeration for storage. A reference product is a single biological product that has undergone full nonclinical and clinical testing and been approved by the US Food and Drug Administration (FDA), both of which are required of all medications.[1]

Biosimilar Products

Biosimilars were created under the Biologics Price Competition and Innovation (BPCI) Act of 2009. This act was signed into law through The Patient Protection and Affordable Care Act on March 23, 2010.[2] The BPCI Act created an abbreviated approval pathway for biological products that demonstrate to be biosimilar to or interchangeable with an FDA-approved biological product, known as a reference product. (The difference between interchangeability and biosimilarity is discussed below.) Biosimilarity can be demonstrated if data show the product is both highly similar to an already approved biological product and the biosimilar product has no clinically meaningful differences. For a biosimilar to be highly similar to a reference product, approval requires that the structure and function were compared to the biologic, looking at purity, molecular structure, and bioactivity. The studies of the biosimilar must show there are no clinically meaningful differences compared to the reference product in safety, purity, and potency (i.e., safety and effectiveness). Studies to assess meaningful differences can include pharmacokinetic studies, immunogenicity assessments, and any additional clinical studies (e.g., pharmacodynamic studies) deemed necessary.[1]

Biosimilar Products, cont.

The introduction of an abbreviated approval pathway for biosimilars has ushered in a new way to drive down costs and expand the reach of biologics through increased competition. The abbreviated pathway could potentially offer a shorter timeline to product approval. Biosimilar products must still meet the same high standards for manufacturing, which involves supplying data to support the product is as safe and effective for the requested indications as all other biological products approved by the FDA. Biosimilars are approved through abbreviated pathways that avoid duplicating costly clinical trials. Biosimilar products are permitted to have differences from the reference product because of the complexity and variability of biological products. Minor differences in clinically inactive properties (e.g., stabilizers, buffers) and lot-to-lot differences (i.e., acceptable within-product differences) are acceptable.[1]

A manufacturer interested in marketing a biosimilar product submits an application under the Public Health Service Act. Within the application, manufacturers are required to show the product demonstrates biosimilarity based on:[1]

- Analytical studies, which serve as the foundation of a biosimilar development program. These demonstrate high similarity to the reference product, minus any minor differences in clinically inactive components. This includes understanding the reference product's mechanism of action, structure-function relationships, clinically active components, critical quality attributes, functional characterizations, and biochemical characterizations.
- Animal studies assess toxicity and further support biosimilarity. These also assess immunogenicity, which is the tendency of a product to generate an immune response. Similar immunogenicity between the two products is an important element to demonstrate biosimilarity.
- Clinical studies demonstrate safety, purity, and potency compared to the reference product. Comparative human pharmacokinetic and pharmacodynamic studies are done to demonstrate no clinically meaningful differences between the biosimilar product and reference product. Additional clinical studies may be required if there is residual uncertainty about biosimilarity.

Additional steps required are:[1]

- A thorough chemistry, manufacturing, and control plan, which applies to all biological products.
- Follow the current Good Manufacturing Practice regulations, which apply to all drug products.

Interchangeable Products

Although a type of biological product, an interchangeable product also meets the standards in the BPCI Act for interchangeability. For example, the product must be biosimilar and produce the same clinical result in any given patient and the risk, in terms of safety and reduced efficacy, of switching back and forth between a reference product and interchangeable product has been evaluated during the application process. If the product does not meet the additional requirements to become an interchangeable product, the biologic would continue as a biosimilar without interchangeability. Like a generic drug, an interchangeable product can be substituted by a pharmacist without any intervention of the prescriber, as long as the prescription does not specify Dispense as Written (DAW).[1] As of June 2020, there are no currently approved interchangeable biological products.

Future of the Biosimilar Market

The FDA is responsible for implementing laws that increase access of biosimilars to the market. In July 2018, the FDA unveiled a Biosimilars Action Plan (BAP). The agency is taking steps to modernize policies to make the development of biosimilars more efficient and accommodate scientific tools better able to compare biosimilars and reference products, which may decrease the need for clinical studies.[3] The FDA's full action plan can be found at https://www.fda.gov/media/114574/download.

The FDA and Federal Trade Commission (FTC) released a joint statement on February 3, 2020, that includes several new actions as part of the BAP and ways they collaboratively intend to promote a competitive market for biological products. The FDA and FTC will work to identify and deter manufacturer behaviors that delay a prospective applicant from accessing samples of the reference product. There have been false or misleading communications by biological product manufacturers that misrepresent the efficacy of a biosimilar in order to deceive customers or deter competition. The FDA and FTC intend to take appropriate steps to address communications that potentially impact public health. These agencies will educate health care professionals and patients about the safety and efficacy of any FDA-approved biosimilar.[4,5]

Biosimilar Products, cont.

As of June 2020, there are currently 27 approved biosimilar products.[1]

Biosimilar Product	Approval Date	Reference Product	Market Availability*
Zarxio (filgrastim-sndz)	March 2015	Neupogen (filgrastim)	Yes
Inflectra (infliximab-dyyb)	April 2016	Remicade (infliximab)	Yes
Erelzi (etanercept-szzs)	August 2016	Enbrel (etanercept)	No
Amjevita (adalimumab-atto)	September 2016	Humira (adalimumab)	No
Renflexis (infliximab-abda)	May 2017	Remicade (infliximab)	Yes
Cyltezo (adalimumab-adbm)	August 2017	Humira (adalimumab)	No
Mvasi (bevacizumab-awwb)	September 2017	Avastin (bevacizumab)	Yes
Ogivri (trastuzumab-dkst)	December 2017	Herceptin (trastuzumab)	Yes
Ixifi (infliximab-qbtx)	December 2017	Remicade (infliximab)	No
Retacrit (epoetin alfa-epbx)	May 2018	Epogen (epoetin-alfa)	Yes
Fulphila (pegfilgrastim-jmdb)	June 2018	Neulasta (pegfilgrastim)	Yes
Nivestym (filgrastim-aafi)	July 2018	Neupogen (filgrastim)	Yes
Hyrimoz (adalimumab-adaz)	October 2018	Humira (adalimumab)	No
Udenyca (pegfilgrastim-cbqv)	November 2018	Neulasta (pegfilgrastim)	Yes
Truxima (rituximab-abbs)	November 2018	Rituxan (rituximab)	Yes
Herzuma (trastuzumab-pkrb)	December 2018	Herceptin (trastuzumab)	No
Ontruzant (trastuzumab-dttb)	January 2019	Herceptin (trastuzumab)	No
Trazimera (trastuzumab-qyyp)	March 2019	Herceptin (trastuzumab)	Yes
Eticovo (etanercept-ykro)	April 2019	Enbrel (etanercept)	No
Kanjinti (trastuzumab-anns)	June 2019	Herceptin (trastuzumab)	Yes
Zirabev (bevacizumab-bvzr)	June 2019	Avastin (bevacizumab)	Yes
Ruxience (rituximab-pvvr)	July 2019	Rituxan (rituximab)	No
Hadlima (adalimumab-bwwd)	July 2019	Humira (adalimumab)	No
Ziextenzo (pegfilgrastim-bmez)	November 2019	Neulasta (pegfilgrastim)	Yes
Abrilada (adalimumab-afzb)	November 2019	Humira (adalimumab)	No (anticipated 2023)
Avsola (infliximab-axxq)	December 2019	Remicade (infliximab)	No
Nyvepria (pegfilgrastim-apgf)	June 2020	Neulasta (pegfilgrastim)	No

***If no, the anticipated availability is currently unknown unless otherwise stated.**

References:

1. U.S. Food and Drug Administration. Biosimilars. February 3, 2019. Accessed May 14, 2020. Available at https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/biosimilars.
2. Patient Protection and Affordable Care Act, H.R. 3590, 111th Cong. (2009-2010).
3. U.S. Food and Drug Administration. FDA's Biosimilar Action Plan (BAP). July 2018. Accessed May 15, 2020. Available at https://www.fda.gov/media/114574/download.
4. Federal Trade Commission. Joint Statement of the Food & Drug Administration and the Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace. February 3, 2020. Accessed May 15, 2020. Available at https://www.ftc.gov/system/files/documents/public_statements/1565273/v190003fdaftcbiologicsstatement.pdf.
5. U.S. Food and Drug Administration. Joint Statement of the Food & Drug Administration and the Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace. February 3, 2020. Accessed May 15, 2020. Available at https://www.fda.gov/media/134864/download.
6. Definition of the Term "Biological Product". Vol. 83, No. 238. Fed. Reg. (December 12, 2018) (to be codified at 21 C.F.R. pt 600).
7. Defining the difference: What Makes Biologics Unique. Biotechnol Healthc. 2004;1(4):24-29. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3564302/.

Generic Medications

Recently Approved Generic Drugs:

February 2020	March 2020	April 2020
Naproxen/esomeprazole tablets (Vimovo®) Olopatadine ophth solution (Pazeo®) Albuterol inhaler (ProAir HFA®) Pyrimethamine tablets (Daraprim®) Dihydroergotamine nasal spray (Migranal®)	Metformin solution (Riomet®) Dabigatran capsules (Pradaxa®)	Albuterol inhaler (Proventil HFA®)

Upcoming Generic Drugs:

Generic Name	Brand Name	Anticipated Launch
Tolvaptan	Samsca®	2020
Icosapent ethyl	Vascepa®	2020

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