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May 2017

Drug of the Month

Renflexis™ (infliximab-abda)

The second biosimilar drug for Remicade® was approved by the Food and Drug Administration (FDA) on April 21, 2017. Renflexis (infliximab-abda) is made by Samsung Bioepis and joins Inflectra® (infliximab-dyyb), the first Remicade biosimilar, which was approved for Celltrion in April of last year. Both biosimilar drugs are based on the reference product from Janssen Biotech Inc., Remicade (infliximab), which is a biologic medication indicated in the treatment of various inflammatory conditions including Crohn's Disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. The biosimilar, Renflexis, was FDA-approved for all of Remicade's indications with the exception of pediatric ulcerative colitis.

Renflexis is an injectable product available as 100 mg infliximab-abda in a 20 mL vial for intravenous use. The approved dosing for Renflexis varies based on the condition being treated, but in general the drug is injected on a specific regimen usually involving an intravenous induction period with administration at 0, 2, and 6 weeks followed by a regular maintenance dose given every 8 weeks (every 6 weeks in the case of ankylosing spondylitis). Renflexis is immunosuppressive in nature as it works by blocking tumor necrosis factor (TNF) within the body, a regulator of immune cells. Patients should be monitored for the occurrence of opportunistic infections during therapy as they may be at an increased risk of hospitalization or death from serious infections such as tuberculosis (TB), bacterial sepsis, and invasive fungal infections (e.g., histoplasmosis). Due to these risks, it is recommended that the patient undergo a test for latent TB before starting Renflexis, and the patient should continue to be evaluated for active TB periodically throughout Renflexis treatment. Patients with any active infection should not be started on Renflexis, and live vaccines or therapeutic infectious agents should not be given with Renflexis.

Adverse effects reported during administration of Renflexis infusion include flu-like symptoms, headaches, shortness of breath, low blood pressure, fever, chills, gastrointestinal symptoms, and skin rashes. A severe allergic reaction known as anaphylaxis may also occur at any time during Renflexis infusion. The medical provider may choose to premedicate the patient with antihistamines, acetaminophen, and/or corticosteroids before Renflexis administration in an effort to mitigate these effects. Along with infusion-related reactions, the other most common adverse reactions associated with Renflexis use include infections (e.g., upper respiratory, sinusitis, pharyngitis), headache, and abdominal pain.

Biosimilar products are often less costly than their biologic reference product counterparts. According to Medispan, the cost comparison (based on AWP) between the reference biologic (Remicade) and the first available biosimilar is as follows: Remicade $1,401.38/vial vs. Inflectra $1,135.54/vial. Pricing is not yet available for the newest biosimilar product, Renflexis; however, it can be reasonably expected to follow the lower comparative price point typical of biosimilar drugs. If an injured worker is currently receiving a work comp-approved prescription for Remicade, this may be an opportunity to engage in a discussion with the provider regarding a switch to one of the available biosimilar medications. The prescriber would need to contact the pharmacy to expressly authorize a change from Remicade to the biosimilar product, or they may simply write the prescription for the specific biosimilar medication going forward.

In any case, biosimilar medications like Renflexis fall in the "specialty" drug category, and additional oversight is recommended due to the complex or costly nature of these types of drugs. Furthermore, the conditions treated by Renflexis are not typically considered to be work-related as a person is genetically predisposed to have these diagnoses. The appropriateness for use of Renflexis in relation to the work injury should be determined prior to coverage consideration.

Reference: https://www.accessdata.fda.gov/scripts/cder/daf/

What does "biosimilar" drug mean?

Biologics

To adequately address this question, we must first define "biologics" as a "biosimilar" which is simply a version of the former. FDA defines a biologic product as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound)." So for example, products such as the Tdap vaccine and insulin would fall under the category of biologics. In general, biologics are similar to chemical drugs but typically represent larger, more complex molecules that are derived from living cells or organisms. These properties contribute to added concerns for administration, storage, manufacturing, and immunogenicity.

Biologics have been shown to improve patient outcomes in various diseases and are being researched today for the management of difficult-to-treat conditions such as cancer, rheumatoid arthritis, hepatitis C, H.I.V., and even chronic pain; however, they also represent a significant cost. The IMS Institute for Healthcare Informatics predicts global spending on biologics will exceed $390 billion by 2020.[1] It also predicts biologic agents will continue to outpace overall pharmaceutical spending growth.

Biosimilars

A biosimilar is a biologic product that is approved by the FDA based on a showing that it is highly similar to an already-existing biological product that serves as the "reference product" and that it has no clinically meaningful differences in terms of safety, purity, or potency compared to that reference product. The advantage, similar to the case with generics subbed in for brand medications, is that there is typically a lower cost associated with the use of a biosimilar product. The FDA approved the nation's first biosimilar in March 2015, and we now have a handful available on the market. A full list of currently licensed biological and biosimilar products can be found here.

Biosimilars can be identified by looking at their product information as well as through their labeling. Essentially, the FDA indicates that a statement recognizing the biosimilar and reference product should be included in the "Highlights" section of the product label that follows this format:

> "[BIOSIMILAR PRODUCT'S PROPRIETARY NAME (biosimilar product's proper name)] is biosimilar to [REFERENCE PRODUCT'S PROPRIETARY NAME (reference product's proper name)] for the indications listed."

Here is an example illustrating the product labeling and the differences in naming using the reference biologic product Neupogen® and its biosimilar Zarxio®:

> "Zarxio (filgrastim-sndz) is biosimilar to Neupogen (filgrastim) for the indications listed."

In general, biosimilar products can be easily identified by looking at the proper name and noting whether or not it contains a dash followed by four letters designating the manufacturer after the therapeutic molecule. Other examples include infliximab-abda, infliximab-dyyb, etanercept-szzs, and adalimumab-atto.

Challenges in Workers' Comp

For workers' compensation, specialty drugs are prescribed to treat conditions either directly or indirectly related to workplace injuries or illnesses. Directly related conditions, such as H.I.V. and hepatitis, might occur when individuals working in health care settings or emergency services are exposed to contaminated material. Indirectly related conditions, such as inflammatory arthritis, are common. The subsequent work disability and/or potential of being linked to this group of illnesses is significant. Other indirectly related conditions that could be compensable in workers' compensation are those aggravated by a workplace injury, including multiple sclerosis. How much of an effect specialty drugs will have on workers' compensation claims will largely depend on the demographics of the insured population. Injured workers taking biologics would benefit from close oversight and guidance because of the complicated nature of these medications and the importance of dosing compliance.

Specialty and biologic medications pose other challenges. About half of these medications are dispensed in doctors' offices, clinics, and hospitals[2] and not through traditional pharmacies. Many are billed with J-Codes. The medications can generate significant revenue for entities that dispense them. In addition, not all biosimilars receive interchangeability status. This means the provider's approval is required before a pharmacy can swap the brand biologic for the biosimilar version of the drug. That being said, there is a discussion around interchangeable biosimilar products where the biologic substitution could occur without express prescriber permission, but we do not currently have any products on the market today for which this is the case.

While costs and other challenges are likely to remain a concern, specialty drugs such as biologics and biosimilars may provide relief that traditional therapies cannot. This can result in better quality of life, as well as fewer hospital admissions, emergency room visits, and laboratory tests. In other cases, less expensive but equally effective alternative therapies might offer a better choice. For more information related to methods for managing these types of medications, please contact your account manager. You can also send your client-specific questions to our team of clinical pharmacists at askthepharmacist@cvty.com.

References:
1. http://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/Documents/IMS_Institute_Biosimilar_Brief_March_2016.pdf

2. https://coventrywcs.com/content/dam/pdf_assets/archive/c142815.pdf