RENFLEXIS®
(infliximab-abda) for injection, for intravenous use 100 mg

Be confident transitioning patients to RENFLEXIS

DO YOUR PATIENTS HAVE QUESTIONS ABOUT *RENFLEXIS*?

We understand that patients trust you and rely on your recommendations regarding their health care. On renflexis.com, our consumer website, we encourage patients to reach out to you for answers to questions about biosimilars and RENFLEXIS. "Questions to Ask Your Doctor" can be downloaded by patients and may be used to initiate a conversation with you. Please consider the details below about RENFLEXIS, biologics, and biosimilars. This resource is intended to help support discussions with your patients. We hope that you find this information helpful.

What is a biologic? What is a biosimilar? How are they alike or different?

- Biologic medicines are a class of drugs made from living cells. They are large, complex molecules that are produced from a living cell line. Manufacturing biologic medicines requires continual, stringent monitoring to ensure lot-to-lot consistency to control for natural variations that might occur.[1-3]
- A biosimilar is a biologic; it is a licensed copy of an approved biologic medicine (called the originator or reference product). A biosimilar must demonstrate that it is highly similar to the reference biologic product.[3]
- The approval of a biosimilar is based on the FDA's rigorous review of the totality of the evidence supporting that the biosimilar has been shown to be highly similar to the reference product. FDA-approved biosimilars have the same indications, usage, administration, and dosage, and they work the same way in the body (have the same "mechanism of action") as the reference product. Biosimilars are highly similar in safety and effectiveness to the reference product.[1,3]
- Like reference biologics, the manufacturer must monitor output for biosimilars to ensure lot-to-lot consistency.[3]

SELECTED SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with infliximab products. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, tuberculosis [TB], histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. RENFLEXIS is contraindicated in patients with severe hypersensitivity reactions to infliximab products and certain patients with congestive heart failure. Other serious side effects reported include melanoma and Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Selected Safety Information on pages 5-8.

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

RENFLEXIS® (infliximab-abda) demonstrated no clinically meaningful differences in safety, purity, and potency from Remicade (infliximab).[1,4]

If RENFLEXIS is a biosimilar, how does it compare to Remicade, the biologic prescription I was taking?

RENFLEXIS is FDA approved to treat the same health conditions as Remicade, with the same dosing and administration. RENFLEXIS works the same way in the body as Remicade. There are no clinically meaningful differences in safety, purity, and potency.[4]

How does the efficacy and safety of RENFLEXIS compare to the efficacy and safety of Remicade?

RENFLEXIS has been through rigorous testing to show the FDA that it is highly similar in effectiveness and safety to Remicade. The FDA states that there are no clinically meaningful differences in safety, purity, and potency.[3,4]

SELECTED SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with infliximab products. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, tuberculosis [TB], histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. RENFLEXIS is contraindicated in patients with severe hypersensitivity reactions to infliximab products and certain patients with congestive heart failure. Other serious side effects reported include melanoma and Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Selected Safety Information on pages 5-8.

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

RENFLEXIS® (infliximab-abda) and Remicade (infliximab) have the SAME[5]:

INDICATIONS AND USAGE | **DOSAGE AND ADMINISTRATION** | **MECHANISM OF ACTION**

Will treatment and dosing with RENFLEXIS be similar to Remicade treatment?

RENFLEXIS is given the same way as Remicade—an IV infusion with the same dosing schedule—and works in the body the same way as Remicade. RENFLEXIS treats the same health conditions as Remicade.[1,3,5]

How do I know biosimilars have been studied for safety?[3] Are biosimilars approved by the FDA?

- The FDA has strict review standards for biologics, including biosimilars, to ensure that products are assessed for safety and effectiveness.[3]
- FDA approval of a biosimilar is based on data provided by the manufacturer following years of rigorous development, testing, and analysis.[1,3,6,7]
- A biosimilar is approved by the FDA only if the product demonstrates no clinically meaningful differences in safety, purity, and potency in comparison to the reference product.[8]
- After approval, manufacturers are required to conform to Certified Pharmaceutical Good Manufacturing Practices and must provide ongoing reports to the FDA that validate product quality and consistency.[3,9]

BIOSIMILARS OFFER DOCTORS AND PATIENTS MORE TREATMENT OPTIONS.[10]

For more information, you can visit RenflexisHCP.com, or contact your Organon representative.

Patients can go to renflexis.com to learn more.

SELECTED SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with infliximab products. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, tuberculosis [TB], histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. RENFLEXIS is contraindicated in patients with severe hypersensitivity reactions to infliximab products and certain patients with congestive heart failure. Other serious side effects reported include melanoma and Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Selected Safety Information on pages 5-8.

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

INDICATIONS AND USAGE

Crohn's Disease

- RENFLEXIS is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy
- RENFLEXIS is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease

Pediatric Crohn's Disease

- RENFLEXIS is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age or older with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy

Ulcerative Colitis

- RENFLEXIS is indicated for reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to conventional therapy

Pediatric Ulcerative Colitis

- RENFLEXIS is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to conventional therapy

Rheumatoid Arthritis

- RENFLEXIS is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate (MTX)

Psoriatic Arthritis

- RENFLEXIS is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis (PsA)

Ankylosing Spondylitis

- RENFLEXIS is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis (AS)

Plaque Psoriasis

- RENFLEXIS is indicated for the treatment of adult patients with chronic severe (ie, extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. RENFLEXIS should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician

Please see Selected Safety Information on pages 5-8.

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

SELECTED SAFETY INFORMATION (*continued*)

SERIOUS INFECTIONS

Patients treated with infliximab products are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Discontinue RENFLEXIS if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before RENFLEXIS use and during therapy.[11,12] Treatment for latent infection should be initiated prior to RENFLEXIS use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, pneumocystosis, and cryptococcosis. Patients may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella, Listeria, and Salmonella.**

The risks and benefits of treatment with RENFLEXIS should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with RENFLEXIS, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy, who are on treatment for latent TB, or who were previously treated for TB infection.

Risk of infection may be higher in patients greater than 65 years of age, pediatric patients, patients with co-morbid conditions and/or patients taking concomitant immunosuppressant therapy. In clinical trials, other serious infections observed in patients treated with infliximab products included pneumonia, cellulitis, abscess, and skin ulceration.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including infliximab products. Approximately half of these cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of malignancies, including rare malignancies that are usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. The malignancies occurred after a median of 30 months after the first dose of therapy. Most of the patients were receiving concomitant immunosuppressants.

(Continued on page 6)

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

SELECTED SAFETY INFORMATION (*continued*)

MALIGNANCIES (*continued*)

Postmarketing cases of hepatosplenic T-cell lymphoma, a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including infliximab products. These cases have had a very aggressive disease course and have been fatal. The majority of reported cases have occurred in patients with Crohn's disease or ulcerative colitis and most were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF-blocker at or prior to diagnosis. Carefully assess the risks and benefits of treatment with RENFLEXIS, especially in these patient types.

In clinical trials of all TNF inhibitors, more cases of lymphoma were observed compared with controls and the expected rate in the general population. However, patients with Crohn's disease, rheumatoid arthritis, or plaque psoriasis may be at higher risk for developing lymphoma. In clinical trials of some TNF inhibitors, including infliximab products, more cases of other malignancies were observed compared with controls. The rate of these malignancies among patients treated with infliximab products was similar to that expected in the general population whereas the rate in control patients was lower than expected. Cases of acute and chronic leukemia have been reported with postmarketing TNF-blocker use. As the potential role of TNF inhibitors in the development of malignancies is not known, caution should be exercised when considering treatment of patients with a current or a past history of malignancy or other risk factors such as chronic obstructive pulmonary disease (COPD).

Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-blocker therapy, including infliximab products. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.

A population-based retrospective cohort study found a 2- to 3-fold increase in the incidence of invasive cervical cancer in women with rheumatoid arthritis treated with infliximab compared to biologics-naïve patients or the general population, particularly those over 60 years of age. A causal relationship between infliximab products and cervical cancer cannot be excluded. Periodic screening should continue in women treated with infliximab products.

CONTRAINDICATIONS

RENFLEXIS is contraindicated in patients with moderate to severe (NYHA Class III/IV) congestive heart failure (CHF) at doses greater than 5 mg/kg. Higher mortality rates at the 10 mg/kg dose and higher rates of cardiovascular events at the 5 mg/kg dose have been observed in these patients. RENFLEXIS should be used with caution and only after consideration of other treatment options. Patients should be monitored closely. Discontinue RENFLEXIS if new or worsening CHF symptoms appear. RENFLEXIS should not be (re)administered to patients who have experienced a severe hypersensitivity reaction or to patients with hypersensitivity to murine proteins or other components of the product.

HEPATITIS B REACTIVATION

TNF inhibitors, including infliximab products, have been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases were fatal. Patients should be tested for HBV infection before initiating RENFLEXIS. For patients who test positive, consult a physician with expertise in the treatment of hepatitis B. Exercise caution when prescribing RENFLEXIS for patients identified as carriers of HBV and monitor closely for active HBV infection during and following termination of therapy with RENFLEXIS. Discontinue RENFLEXIS in patients who develop HBV reactivation and initiate antiviral therapy with appropriate supportive treatment. Exercise caution when considering resumption of RENFLEXIS and monitor patients closely.

(Continued on page 7)

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

SELECTED SAFETY INFORMATION (*continued*)

HEPATOTOXICITY

Severe hepatic reactions, including acute liver failure, jaundice, hepatitis, and cholestasis have been reported rarely in patients receiving infliximab products postmarketing. Some cases were fatal or required liver transplant. Aminotransferase elevations were not noted prior to discovery of liver injury in many cases. Patients with symptoms or signs of liver dysfunction should be evaluated for evidence of liver injury. If jaundice and/or marked liver enzyme elevations (eg, ≥5 times the upper limit of normal) develop, RENFLEXIS should be discontinued, and a thorough investigation of the abnormality should be undertaken.

HEMATOLOGIC EVENTS

Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia (some fatal) have been reported in patients using infliximab products. The causal relationship to infliximab therapy remains unclear. Exercise caution in patients who have ongoing or a history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs and symptoms of blood dyscrasias or infection. Consider discontinuation of RENFLEXIS in patients who develop significant hematologic abnormalities.

HYPERSENSITIVITY

Infliximab products have been associated with hypersensitivity reactions that differ in their time of onset and required hospitalization in some cases. Most hypersensitivity reactions, which include anaphylaxis, urticaria, dyspnea, and hypotension, have occurred during or within 2 hours of infusion. Serious infusion reactions including anaphylaxis were infrequent. RENFLEXIS should be discontinued for severe hypersensitivity reactions. Medications for the treatment of hypersensitivity reactions should be available.

CARDIOVASCULAR AND CEREBROVASCULAR REACTIONS DURING AND AFTER INFUSION

Serious cerebrovascular accidents, myocardial ischemia/infarction (some fatal), hypotension, hypertension, and arrhythmias have been reported during and within 24 hours of initiation of infliximab infusion. Cases of transient visual loss have been reported during or within 2 hours of infusion of infliximab. Monitor patients during infusion and, if a serious reaction occurs, discontinue infusion. Manage reactions according to signs and symptoms.

NEUROLOGIC EVENTS

TNF inhibitors, including infliximab products, have been associated in rare cases with CNS manifestation of systemic vasculitis, seizure, and new onset or exacerbation of CNS demyelinating disorders, including multiple sclerosis and optic neuritis, and peripheral demyelinating disorders, including Guillain-Barré syndrome. Exercise caution when considering RENFLEXIS in patients with these disorders and consider discontinuation if these disorders develop.

AUTOIMMUNITY

Treatment with infliximab products may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

USE WITH OTHER DRUGS

Concomitant use of RENFLEXIS with anakinra, abatacept, tocilizumab, or other biologics used to treat the same conditions as RENFLEXIS is not recommended because of the possibility of an increased risk of infection. Care should be taken when switching from one biologic to another, since overlapping biological activity may further increase the risk of infection.

(Continued on page 8)

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

SELECTED SAFETY INFORMATION (*continued*)

LIVE VACCINES/THERAPEUTIC INFECTIOUS AGENTS

Live vaccines or therapeutic infectious agents should not be given with RENFLEXIS due to the possibility of clinical infections, including disseminated infections.

Bring pediatric patients up to date with all vaccinations prior to initiating RENFLEXIS. At least a 6-month waiting period following birth is recommended before the administration of any live vaccine to infants exposed *in utero* to infliximab products.

ADVERSE REACTIONS

In clinical trials with infliximab products, the most common adverse reactions occurring in >10% of patients treated with infliximab products included infections (eg, upper respiratory, sinusitis, and pharyngitis), infusion-related reactions, headache, and abdominal pain.

Before prescribing RENFLEXIS, please read the accompanying Prescribing Information, including the Boxed Warning about serious infections and malignancies. The Medication Guide also is available.

EDUCATE YOUR PATIENTS:

- A biosimilar is a medicine that is highly similar to a known biologic product[1]
- RENFLEXIS and Remicade:
  - Have the same approved uses[1,5]
  - Have the same dosing and administration[1,5]
  - Work the same way in the body[1,5]

References: 1. US Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Scientific considerations in demonstrating biosimilarity to a reference product: guidance for industry. Docket Number: FDA-2011-D-0605. Published April 2015. Last revised April 24, 2020. Accessed August 18, 2022. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatory Information/Guidances/UCM291128.pdf **2.** US Food and Drug Administration (FDA). Biological Product Definitions. Accessed August 2, 2022. https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf **3.** US Food and Drug Administration (FDA). Biosimilar and interchangeable biologics: more treatment choices. Updated October 12, 2021. Accessed August 9, 2022. https://www.fda.gov/consumers/consumer-updates/biosimilar-and-interchangeable-biologics-more-treatment-choices **4.** Waheed J. MD. Clinical Review of SB2, a proposed biosimilar to US-licensed Remicade. Samsung Bioepis. 351(k) BLA 761054. January 6, 2017. FDA website. March 21, 2016. Accessed August 2, 2022. https://www.fda.gov/media/104961/download **5.** Remicade. Prescribing Information. Janssen Biotech, Inc.; 2021. **6.** US Food and Drug Administration (FDA). Biosimilar Product Regulatory Review and Approval. Accessed August 18, 2022. https://www.fda.gov/files/drugs/published/Biosimilar-Product-Regulatory-Review-and-Approval.pdf **7.** Blackstone EA, Joseph PF. The economics of biosimilars. *Am Health Drug Benefits.* 2013;6(8):469-478. **8.** Christl L. FDA's overview of the regulatory guidance for the development and approval of biosimilar products in the US. US Food and Drug Administration (FDA). Last updated December 24, 2020. Accessed August 2, 2022. https://www.fda.gov/media/90496/download **9.** Barakat NS. Biological products: manufacturing, handling, packaging and storage. In: Basnet P, ed., *Promising Pharmaceuticals.* IntechOpen; 2012:63–82. doi:10.5772/35760 **10.** US Food and Drug Administration (FDA). Biosimilars action plan: balancing innovation and competition. US Food and Drug Administration (FDA). July 2018. Accessed August 18, 2022. https://www.fda.gov/media/114574/download **11.** American Thoracic Society, Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med.* 2000;161:S221-S247. **12.** See latest Centers for Disease Control and Prevention guidelines and recommendations for tuberculosis testing in immunocompromised patients.

ORGANON

US-SBT-115394 08/22

RENFLEXIS® (infliximab-abda) for injection, for intravenous use 100 mg