Merck Announces U.S. Launch of RENFLEXIS™ (infliximab-abda), a Biosimilar of Remicade, for All Eligible Indications

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KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced the U.S. launch of RENFLEXIS™ (infliximab-abda), a biosimilar of the originator biologic medicine Remicade (infliximab). RENFLEXIS was approved by the U.S. Food and Drug Administration (FDA) on April 21 for all eligible indications. RENFLEXIS is the first medicine available in the U.S. under a global biosimilars development and commercialization agreement between Merck and Samsung Bioepis Co., Ltd.

“Merck looks forward to launching RENFLEXIS in the United States to help meet the needs of patients, physicians and payers,” said Dora Bibila, general manager, Merck Biosimilars. “As a global health care leader, Merck believes that biosimilars have the potential to help increase access to these important medicines while also providing savings for the health care system.”

RENFLEXIS will be introduced in the U.S. at a list price (wholesaler acquisition cost) of $753.39, representing a 35 percent discount to the current list price of Remicade, its reference product. Wholesaler acquisition costs do not include discounts that may be paid on the products.

Serious and sometimes fatal side effects have been reported with infliximab products. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (e.g., 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, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, neurological events, and lupus-like syndrome.

Launch resources will include comprehensive education and support services for health care professionals, patients and their caregivers, including biosimilars education, disease education, and reimbursement and access support.

The FDA approval of RENFLEXIS (infliximab-abda) was based on Samsung Bioepis’ comprehensive data package, including analytical, nonclinical and clinical pharmacokinetic, safety and effectiveness data demonstrating that RENFLEXIS is highly similar to its reference product Remicade, in terms of the safety, purity and potency of the product.

**Indications for RENFLEXIS (infliximab-abda) for Injection, 100 mg**

RENFLEXIS is a tumor necrosis factor (TNF) blocker approved in the U.S. for the following indications.

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 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 and older with moderately to severely active Crohn's disease 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 who have had an inadequate response to conventional therapy.

Rheumatoid Arthritis – RENFLEXIS, in combination with methotrexate, 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.

Ankylosing Spondylitis – RENFLEXIS is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.
Plaque Psoriasis — RENFLEXIS is indicated for the treatment of adult patients with chronic severe (i.e., 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.

**Selected Safety Information about RENFLEXIS (infliximab-abda)**

**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. 1, 2 Treatment for latent infection should be initiated prior to RENFLEXIS use.

- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis and pneumocystosis.** Patients may present with disseminated, rather than localized, disease. 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 and Listeria.**

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 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.

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 (infliximab-abda), 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.

**CONTRAINDICATIONS**

RENFLEXIS (infliximab-abda) 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.

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 (e.g., ≥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 (infliximab-abda) in patients who develop significant hematologic abnormalities.

HYPERSENSITIVITY

Infliximab products have been associated with hypersensitivity reactions that differ in their time of onset. Acute urticaria, dyspnea, and hypotension have occurred in association with infusions of infliximab products. Serious infusion reactions including anaphylaxis were infrequent. Medications for the treatment of hypersensitivity reactions should be available.

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.

ADVERSE REACTIONS

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

USE WITH OTHER DRUGS

Concomitant use of RENFLEXIS (infliximab-abda) 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.

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.

About the Merck and Samsung Bioepis collaboration

Merck and Samsung Bioepis announced in February 2013 a development and commercialization agreement under which Merck will commercialize multiple biosimilar candidates in certain partnered territories. Under terms of the agreement, Samsung Bioepis is responsible for preclinical and clinical development, process development and manufacturing, clinical trials and regulatory registration. Merck will be responsible for all commercialization activities for products approved in its partnered territories.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world’s most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with
customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company’s 2016 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).


REFERENCES


2. See latest Centers for Disease Control guidelines and recommendations for tuberculosis testing in immunocompromised patients.

Language:

English

Contact:

Merck
Media:
Pamela Eisele, 267-305-3558
or
Robert Consalvo, 908-740-6518
or
Investors:
Teri Loxam, 908-740-1986
or
Amy Klug, 908-740-1898

Ticker Slug:
Ticker: MRK
Exchange: NYSE
@Merck