Ixifi
infliximab

Pfizer Breakthroughs that change patients' lives®

Healthcare Professional Brochure

This document has been reviewed and approved by the Saudi Food and Drug Authority (SFDA).

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Pfizer Breakthroughs that change patients' lives®

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Reference:

1. Ixifi Summary of Product Characteristics, Saudi Arabia, December 2023.

Important Safety Information
Ixifi/Infliximab

- Infliximab may be associated with serious infections that may lead to hospitalization or death.[1]
- This brochure includes details on the risk of potentially life-threatening adverse reactions including tuberculosis (TB) and other serious infections.[1]
- A patient screening sheet to provide guidance on appropriate screening and selection of patients is distributed together with this brochure.
- To help mitigate the risk of TB in patients, a Patient Alert Card is provided.
- This should be read in conjunction with the Package Information Leaflet.
- It is advised to go through the Patient Alert Card with the patient or caregiver to ensure their understanding.

Ixifi/Infliximab Approved Indications:

- Rheumatoid Arthritis[1]
- Ankylosing Spondylitis[1]
- Psoriatic Arthritis[1]
- Plaque Psoriasis[1]
- Adult and Pediatric Crohn's Disease[1]
- Adult and Pediatric Ulcerative Colitis[1]

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Summary of Safety Concerns and Precautions

Infusion Reactions and Hypersensitivity

- Infliximab has been linked to infusion-related reactions, including anaphylactic and hypersensitivity reactions, which can vary in onset time and have occasionally required hospitalization.[1]
- Most hypersensitivity reactions, which include anaphylaxis, urticaria, dyspnea, and/or hypotension, have occurred during or within 2 hours of infusion.[1]
- Infliximab should be discontinued for severe hypersensitivity reactions. Medications for the treatment of hypersensitivity reactions (e.g., acetaminophen, antihistamines, corticosteroids, and/or epinephrine) should be available for immediate use in the event of a reaction.[1]
- Treatment with infliximab products can be associated with the development of antibodies to infliximab products. Patients who were antibody-positive were more likely to have higher rates of clearance, reduced efficacy and to experience an infusion reaction than were patients who were antibody negative.[1]
- Concomitant immunosuppressant agents seem to lower the occurrence of antibodies to infliximab and infusion reactions.[1]
- In some cases, serum sickness-like reactions have been observed in patients after initial infliximab products therapy (i.e., as early as after the second dose), and when infliximab product therapy was reinstituted following an extended period without treatment.[1]
- These reactions were associated with a marked increase in antibodies to infliximab products, loss of detectable serum concentrations of infliximab products, and possible loss of drug efficacy.[1]
- In rheumatoid arthritis, Crohn's disease, and plaque psoriasis clinical trials, re-administration of infliximab after a period of no treatment resulted in a higher incidence of infusion reactions relative to regular maintenance treatment.[1]
- If serious reactions occur, symptomatic treatment must be given, and further infliximab infusions must be discontinued.[1]
- In clinical studies, delayed hypersensitivity reactions have been reported.[1]

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- Infliximab infusion should be discontinued in case of severe hypersensitivity reactions.[1]
- Before treatment, ensure that the appropriate personnel and medication are available to manage any reactions (e.g., hypersensitivity or other reactions) that may occur during and immediately after the infusion.[1]

Infections

- Patients receiving infliximab treatment should be closely monitored for signs and symptoms of infection both during and after therapy. This includes monitoring for tuberculosis, even in patients who tested negative for latent tuberculosis infection before starting treatment.[1]
- Infliximab should be discontinued if a patient develops a serious infection or sepsis.[1]
- Caution should be exercised when considering the use of infliximab in patients with chronic infection or a history of recurrent infections, including concomitant immunosuppressive therapy.[1]
- Infliximab should not be used in patients with serious or active infections, including significant localized infections. Documented infections associated with infliximab include active tuberculosis, reactivation of latent tuberculosis, invasive fungal infections, and opportunistic infections such as pneumocystosis, candidiasis, listeriosis, and aspergillosis.[1]
- Patients treated with infliximab are at increased risk for developing serious infections.[1]
- Tuberculosis, bacterial infections, including sepsis and pneumonia, invasive fungal, viral, and other opportunistic infections have been observed in patients treated with infliximab. Some of these infections have been fatal.[1]
- Opportunistic infections due to bacterial, mycobacterial, invasive fungal, viral, or parasitic organisms including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, legionellosis, listeriosis, pneumocystosis, salmonellosis, and tuberculosis have been reported with TNF-blockers.[1]
- A patient who develops a new infection during treatment with infliximab should be closely monitored, undergo a prompt and complete diagnostic workup appropriate for an immunocompromised patient, and appropriate antimicrobial therapy should be initiated.[1]

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- The risks and benefits of treatment with infliximab should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.[1]

Tuberculosis

- There have been reports of active tuberculosis in patients receiving infliximab.
  It should be noted that patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease.[1]
- Before starting treatment with infliximab, all patients must be evaluated for both active and latent tuberculosis.[1]
- Induration of 5 mm or greater with tuberculin skin testing should be considered a positive test result when assessing if treatment for latent tuberculosis is needed prior to initiating infliximab, even for patients previously vaccinated with Bacille Calmette-Guérin (BCG).[1]
- Tests for latent tuberculosis infection may also be falsely negative while on therapy with infliximab.[1]
- If active tuberculosis is diagnosed, infliximab therapy must not be initiated.[1]
- For patients who test negative for latent tuberculosis but have risk factors for tuberculosis infection, it is advisable to consult a physician specializing in tuberculosis treatment.[1]
- The risks and benefits of treatment should be considered prior to initiating therapy in patients:[1]
  - with chronic or recurrent infection;
  - who have been exposed to tuberculosis;
  - with a history of an opportunistic infection;
  - who have resided or traveled in areas of endemic tuberculosis or endemic mycoses, such as histoplasmosis, coccidioidomycosis, or blastomycosis; or
  - with underlying conditions that may predispose them to infection.

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Tuberculosis (cont.)

- If latent tuberculosis is diagnosed, treatment for latent tuberculosis must be started with anti-tuberculosis therapy before the initiation of infliximab.[1]
- Consultation with a physician with expertise in the treatment of tuberculosis is recommended to aid in the decision whether initiating anti-tuberculosis therapy is appropriate for an individual patient.[1]
- Anti-tuberculosis therapy should also be considered prior to initiation of infliximab in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection.[1]
- Patients should be tested for latent tuberculosis before infliximab use and during therapy.[1]

Hepatotoxicity

- In the post-marketing setting, there have been cases of acute liver failure, jaundice, hepatitis, and cholestasis (some with features of autoimmune hepatitis) with infliximab.
  This should be taken into consideration when starting infliximab treatment.[1]
- Patients receiving infliximab who show signs and symptoms of liver dysfunction should be evaluated for evidence of liver injury.[1]
- In general, patients who developed alanine transaminase (ALT) and aspartate transaminase (AST) elevation were asymptomatic, and the abnormalities decreased or resolved with either continuation or discontinuation of infliximab or modified concomitant therapy.[1]
- Infliximab should be discontinued if jaundice and/or marked liver enzyme elevations ≥5 times the upper limit of normal develop, and a thorough investigation of the abnormality should be undertaken.[1]
- Severe hepatic reactions have been observed between 2 weeks and over 1 year after starting infliximab products. In many cases, elevations in hepatic aminotransferase levels were not detected before the liver injury was identified.

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Hepatitis B (HBV) Reactivation

- Reactivation of hepatitis B has occurred in patients receiving a TNF-antagonist including infliximab, who are chronic carriers of this virus. Some cases have had fatal outcome.[1]
- Patients should be tested for HBV infection before initiating treatment with infliximab.[1]
  For patients who test positive for hepatitis B surface antigen, consultation with a physician with expertise in the treatment of hepatitis B is recommended.[1]
- Carriers of HBV who require treatment with infliximab should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for several months following termination of therapy.[1]
- In patients who develop HBV reactivation, infliximab should be stopped and effective antiviral therapy with appropriate supportive treatment should be initiated.[1]

Vaccinations

- It is recommended that all pediatric and adult patients update vaccinations in accordance with current vaccination guidelines, prior to initiating infliximab.[1]
- Therapeutic infectious agents should not be given concurrently with infliximab.[1]
- There are limited data on the response to live vaccines or on the secondary transmission of infection by live vaccines in patients treated with infliximab.[1]
- The concurrent administration of live vaccines with infliximab is not recommended.[1]
- Infliximab crosses the placenta and has been detected up to 6 months following birth.[1]
- Administration of live vaccines (e.g., BCG vaccine) to infants exposed to infliximab *in utero* during the latter parts of pregnancy is not recommended for at least 12 months after birth.[1]
- There is an increased risk of infection in pediatric patients. It is therefore important that they are up to date with their vaccinations before starting infliximab.[1]

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Lupus-Like Syndrome

- Treatment with infliximab products may result in the formation of autoantibodies and in the development of a lupus-like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome following treatment with infliximab, treatment should be discontinued.[1]

Neurologic Reactions

- Anti-TNF treatment has been associated with CNS manifestation of systemic vasculitis, seizure and new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disorders (including multiple sclerosis and optic neuritis), and peripheral demyelinating disorders (including Guillain-Barré syndrome).[1]
- Caution should be exercised in considering the use of infliximab in patients with these neurologic disorders.[1]
- Discontinuation of infliximab should be considered if these disorders develop.[1]

Heart Failure

- Administering infliximab at doses exceeding 5 mg/kg is contraindicated for patients with moderate-to-severe heart failure (NYHA class III/IV).[1]
- Patients should be closely monitored during therapy, and infliximab should be discontinued in patients who develop new or worsening symptoms of heart failure.[1]

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Malignancies (Excluding Hepatosplenic T-cell Lymphoma)

- The risk of developing lymphoma, melanoma, Merkel cell carcinoma or other cancers cannot be excluded in patients treated with anti-TNFs. In the post-marketing setting.[1]
- Cases of acute and chronic leukemia have been reported in patients treated with an anti-TNF. Patients taking infliximab may have an increased risk of developing lymphoma, melanoma, Merkel cell carcinoma or other cancers.[1]
- Patients with long-standing, highly active inflammatory rheumatoid arthritis have an increased background risk for leukemia and lymphoma.[1]
- Caution should be exercised in considering infliximab treatment in patients with a history of malignancy or in continuing treatment in patients who develop malignancy while receiving infliximab.[1]
- Caution should be exercised in considering treatment of patients with increased risk for malignancy due to heavy smoking and in patients with plaque psoriasis and a medical history of chronic exposure immunosuppressant therapy or prolonged phototherapy treatment.[1]

Hepatosplenic T-cell Lymphoma (HSTCL)

- Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), 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.[1]
- Almost all patients had received treatment with the immunosuppressants AZA or 6-MP concomitantly with a TNF-blocker or prior to diagnosis. The majority of cases have occurred in patients with Crohn's disease or ulcerative colitis and most were reported in adolescent or young adult males.[1]

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Haematologic Reactions

- Pancytopenia, leucopenia, neutropenia, and thrombocytopenia have been reported in patients receiving anti-TNFs, including infliximab.[1]
- Caution should be exercised in patients being treated with infliximab who have ongoing or a history of significant hematologic abnormalities.[1]
- All patients should be advised to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever).[1]
- Discontinuation of infliximab should be considered in patients who develop significant hematologic abnormalities.[1]

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Report Side Effects

- The National Pharmacovigilance Center (NPC) at Saudi Food and Drug Authority (SFDA):

SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

- Pharmacovigilance Department in the Company

E-mail: SAU.AEReporting@pfizer.com

For extra copies, please send an email with your contact details and the required amount to SAU.AEReporting@pfizer.com

- For Further Information Check IXIFI SPC.

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