Paediatric patients

In children and adolescents aged 6 to 17 years, Remsima is indicated for:

- Severe, active Crohn's disease in patients who have not responded to conventional therapy including a corticosteroid, an immunomodulator and primary nutrition therapy; or who are intolerant to or have contraindications for such therapies.
- Severely active ulcerative colitis in patients who have had an inadequate response to conventional therapy including corticosteroids and 6-MP or AZA, or who are intolerant to or have medical contraindications for such therapies.

Paediatric malignancy

- The risk of developing cancer cannot be excluded in children and adolescents treated with anti-TNFs, including infliximab. Approximately half the cancers reported in children, adolescents and young adults were lymphomas.
- Rare cases of HSTCL have been reported with anti-TNFs, including infliximab. The vast majority of cases in patients receiving infliximab were in patients with Crohn's disease or ulcerative colitis; most of these were in adolescent or young adult males who received AZA or 6-MP concomitantly with, or immediately before, infliximab.
- Patients who are at increased risk should be closely monitored. If cancer develops, discontinuation of infliximab should be considered.

Infection

- In clinical studies, infections have been reported in a higher proportion of paediatric patients than adult patients.

Vaccinations

- There are limited data on the response to live vaccines in patients treated with infliximab. The concurrent administration of live vaccines with Remsima is not recommended.
- There is an increased risk of infection in paediatric patients. It is therefore important that they are up-to-date with their vaccinations before starting infliximab.
- In infants exposed in utero to infliximab, fatal outcome due to disseminated Bacillus Calmette-Guerin (BCG) infection has been reported following administration of BCG vaccine after birth.
- Administration of live vaccines to children who were potentially exposed to infliximab during pregnancy should be performed with caution. At least a six month waiting period following birth is recommended before the administration of live vaccines to infants exposed in utero to infliximab.
- Cases of agranulocytosis, in infants exposed in utero to infliximab, have also been reported. A mother should inform her infant's doctors and other health care professionals of her use of Remsima during pregnancy.

Reference

1. Remsima® (Infliximab), Summary of Product Characteristics.

Important Safety Information for Infliximab for Healthcare Professionals

Remsima® Infliximab

HEALTHCARE CELLTRION

Infliximab may be associated with serious potentially life-threatening adverse reactions that need to be either prevented or identified and treated as early as possible.

This brochure includes details on the risk of potentially life-threatening adverse reactions including tuberculosis (TB) and other serious infections.

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, Celltrion Healthcare has included a Patient Alert Card with each pack of Remsima®. This should be read in conjunction with the Package Information Leaflet. It is advisable to go through the Patient Alert Card with the patient or carer to ensure their understanding.
It is important to record the batch number of the pack of Remsima administered to the patient.
In the event of an adverse drug reaction, include the batch number and brand name of the product administered in the report.
The information in this brochure does not replace the full prescribing information in the Summary of Product Characteristics, which should be read and understood before prescribing infliximab.

These aides and further information can be requested from the local representative:
Medical Logistics Ltd.
¾, Cantrija Complex, Triq it-Targa,
Il-Maghtab, Naxxar NXR6613 Malta
Tel: +356 2755 9990
Email: safety@medicallogisticsltd.com

Reporting of side effects
ADR reporting
Sir Temi Zammit Buildings, Malta Life Sciences Park,
San Gwann SGN 3000, Malta
Email: postlicensing.medicinesauthority@gov.mt

Tuberculosis

- Infliximab is contra-indicated in patients with TB.
- Before starting treatment, patients must be screened for active and latent TB. Screening should include appropriate tests (e.g. tuberculin skin test, chest X-ray or interferon gamma release assay) and a detailed medical history.
- If screening reveals active TB, infliximab therapy must not be started.
- If screening reveals latent TB, anti-TB therapy must be started before initiation of infliximab. Anti-TB therapy should also be considered in patients with a history of active or latent TB, but in whom adequate treatment cannot be confirmed.
- Patients should be monitored for TB during and after treatment with infliximab. Elimination of infliximab can take up to six months, so monitoring should continue during this time.
- Patients should be advised to seek medical advice if they develop symptoms suggestive of TB (e.g. night sweats, persistent cough, wasting/weight loss, low-grade fever) during or after treatment. If such symptoms develop, patients should be given appropriate treatment (tuberculostatic agents, immune stimulants, etc.).

Other serious infections (including sepsis and opportunistic infections)

- Infliximab is contra-indicated in patients with severe infections (e.g. sepsis, abscesses) or opportunistic infections (e.g. pneumocystosis, candidiasis, listeriosis and aspergillosis).
- Patients taking an anti-TNF (including infliximab) are more susceptible to serious infection.
- Caution should be exercised when considering infliximab therapy in patients with a chronic infection or a history of recurrent infections. Patients should be advised of, and avoid exposure to, potential risk factors for infection (as appropriate).
- Patients should be monitored for infection during and after treatment with infliximab. Elimination of infliximab can take up to six months, so monitoring should continue during this time.
- If patients develop a serious systemic illness, an invasive fungal infection (e.g. aspergillosis, candidiasis, pneumocystosis, histoplasmosis, coccidioidomycosis or blastomycosis) should be suspected. These infections may present as disseminated rather than localised, and antigen and antibody testing may be negative in patients with active infection.
- Infliximab should be discontinued if a patient develops a new serious infection or sepsis. Appropriate antimicrobial or antifungal therapy should be initiated until the infection is controlled.

Serious infusion reaction

- Infliximab has been associated with acute infusion-related reactions (including anaphylactic shock) and delayed hypersensitivity reactions (see below). Acute infusion reactions may develop during the infusion, or within a few hours afterwards. Patients may be pre-treated with anti-histamines, hydrocortisone, and/or paracetamol to prevent mild and transient effects.
- Antibodies to infliximab have been associated with an increased frequency of infusion reactions. Concomitant administration of immunomodulators is associated with a lower incidence of antibodies and a reduced frequency of infusion reactions. This effect is more profound in episodically-treated patients than in patients receiving maintenance therapy.
- Limited data in psoriasis patients show that the risk of infusion reactions (including serious ones) is greater following re-administration compared with maintenance therapy.
- Patients should be monitored for signs of anaphylactic and anaphylactic-like symptoms. Symptoms of infusion reaction include dyspnoea, urticaria, facial oedema and hypotension.
- The infliximab infusion should be stopped immediately if an acute infusion reaction occurs. Emergency equipment (adrenaline, corticosteroids, antihistamines, artificial airway) must be available.
- If an infusion reaction occurs during a shortened infusion, a slower infusion rate may be considered for future infusions (if treatment is to continue).

Serum sickness (delayed hypersensitivity reaction)

- Infliximab is contra-indicated in patients with a history of hypersensitivity to infliximab.
- Available data suggest an increased risk for delayed hypersensitivity with increasing infliximab-free interval. If patients are re-treated after a prolonged period, they must be closely monitored for signs and symptoms of delayed hypersensitivity.
- Signs and symptoms of delayed hypersensitivity include: myalgia and/or arthralgia with fever and/or rash; pruritus; facial, hand, or lip oedema; dysphagia; urticaria; sore throat; headache.
- Patients should be advised to seek immediate medical advice if they experience any delayed adverse event.
- If a serious reaction occurs, patients should be given symptomatic treatment. Further infliximab infusions should not be administered.

Leukaemia and lymphoma (excluding hepatosplenic T-cell lymphoma)

- The risk of developing lymphomas or other cancers cannot be excluded in patients treated with anti-TNFs. In the post-marketing setting, cases of leukaemia have been reported in patients treated with an anti-TNF. Patients taking infliximab may have an increased risk of developing lymphomas or other cancers. Patients with long-standing, highly active inflammatory rheumatoid arthritis have an increased background risk for leukaemia and lymphoma.
- Caution should be exercised when considering infliximab for patients with a history of cancer, and when considering continued treatment in patients who develop cancer.
- Patients who are at increased risk should be closely monitored. If cancer develops, discontinuation of infliximab should be considered.

Hepatosplenic T-cell lymphoma (HSTCL)

- The risk of developing HSTCL cannot be excluded in patients treated with anti-TNFs.
- The potential risk associated with the combination of azathioprine (AZA) or 6-mercaptopurine (6-MP) and infliximab should be carefully considered in patients with Crohn's disease or ulcerative colitis (particularly adolescent or young adult males).
- Patients who are at increased risk should be closely monitored. If HSTCL develops, discontinuation of infliximab should be considered.

Congestive heart failure

- Infliximab is contra-indicated in patients with moderate or severe heart failure [New York Heart Association (NYHA) class III/IV].
- There have been post-marketing reports of worsening heart failure, with and without identifiable precipitating factors, in patients taking infliximab. There have also been rare post-marketing reports of new onset heart failure, including heart failure in patients without known pre-existing cardiovascular disease. Some of these patients have been under 50 years of age.
- Infliximab should be used with caution in patients with mild heart failure (NYHA class I/II) and patients should be closely monitored.
- Infliximab must be discontinued if new or worsening symptoms of heart failure occur. Patients should receive treatment according to current medical standards.

Hepatitis B virus (HBV) reactivation

- Treatment with anti-TNFs, including infliximab, may cause HBV reactivation in patients who carry this virus. In some cases, this can be life-threatening.
- Patients should be tested for HBV before starting treatment.
- HBV carriers should be closely monitored for signs and symptoms of reactivation during therapy, and for several months afterwards.
- Signs and symptoms of HBV reactivation include a sequential increase in HBV replication and the appearance of hepatic injury.
- Infliximab should be discontinued if HBV reactivation develops. Anti-viral therapy with appropriate supportive treatment should be initiated.

Malignancy

- Test for history (patient and/or family) of malignancy.
- Melanoma, Merkel cell carcinoma and rare post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL) have been reported in patients treated with TNF-blocking agents including infliximab.
- Caution should be exercised in patients with psoriasis and a medical history of extensive immunosuppressant therapy or prolonged PUVA treatment.
- Periodic skin examination is recommended, particularly for patients with risk factors for skin cancer. Periodic cervical cancer screening is recommended in women, including those above 60 years of age.
- All patients with ulcerative colitis who are at increased risk for dysplasia or colon carcinoma (e.g. patients with a long-standing ulcerative colitis or primary sclerosing cholangitis), or who had a prior history of dysplasia or colon carcinoma should be screened for dysplasia at regular intervals before therapy and throughout their disease course. This evaluation should include colonoscopy and biopsies per local recommendations.

Cervical Cancer

- Women taking Remsima may have an increased risk of developing cervical cancer.
- Women who do not have a regular cervical cancer screening test may have a higher risk of developing cervical cancer with Remsima treatment.
- Periodic cervical cancer screening should continue in women treated with Remsima, including those over 60 years of age.
- Patients who are at increased risk should be closely monitored. If cancer develops, discontinuation of infliximab should be considered.

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