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HEALTHCARE
CELLTRION

Educational Brochure for Healthcare Professionals:

Management of Children with Inflammatory Bowel Disease

Remsima®
Infliximab

Indication

Remsima® (infliximab) is a biosimilar monoclonal antibody for the treatment of severely active pediatric Crohn's disease (PCD) and pediatric ulcerative colitis (PUC) in patients aged 6 years and older (age 6–17).

PCD and PUC are associated with excessive levels of tumor necrosis factor alpha (TNF-α) in the body, which cause an inflammatory response. Remsima® is a TNF-α inhibitor that works by blocking excess TNF-α, thereby reducing the inflammation.

This brochure is intended to support the medical approach to the management of pediatric patients with inflammatory bowel diseases treated with Remsima®. It outlines the key risks associated with infliximab use. More information, including a list of contraindications, is available in the SmPC or upon request.

Key risks:

- **The risk of opportunistic infections and tuberculosis (TB) in patients treated with infliximab.**
  - Assess the risk of TB in patients prior to treating with infliximab
  - A patient alert card is provided with every pack of Remsima®. This card highlights the risks of infections and TB, and encourages the recording of TB screening. It is recommended that this card is discussed with the patient and/or caregiver.
- **The risk of acute infusion-related reactions and delayed hypersensitivity reactions.**
- **The risk of lymphoma and other malignancies.**
- **Younger patients may be at increased risk of developing infections and there is a need for immunizations to be up-to-date.**

To help mitigate the risk, a Patient Alert Card has been provided with each Pack of Remsima®. This should be read in conjunction with the Package Information Leaflet.

In the event of a patient experiencing any suspected adverse drug reaction (ADR), it is important to record both the **brand name** and **batch number** of the product received by the patient. The events should be reported via the national ADR reporting system.

IMPORTANT SAFETY INFORMATION

Serious Infections

Treatment with infliximab increases the patients' risk of developing serious infections. Some of these infections have resulted in hospitalization and have been fatal. The majority of patients who developed these serious infections were receiving concomitant immunosupressants (eg, corticosteroids or methotrexate). Infliximab should be discontinued if a patient develops a serious infection or sepsis.

Reported serious infections include:

- Active TB with patients presenting with disseminated or extrapulmonary disease and reactivation of latent TB. Patients should be tested for latent TB before and during treatment. Treatment for latent infection should be initiated prior to treatment with Remsima®.
- Bacterial, fungal, and viral infections. Other infections caused by opportunistic pathogens such as Listeria and Legionella have been reported.
- Rarely, invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis have been reported. Patients may present with disseminated, rather than localized, disease. Empiric antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.

Healthcare providers should carefully consider the risks and benefits of treatment with Remsima® before initiating treatment in patients with either reoccurring or chronic infection. During and after treatment with Remsima®, patients should be closely monitored for the signs and symptoms of the development of infection, and this includes the development of TB in patients negative for latent TB infection before starting treatment.

Risk of infection may be higher in pediatric patients, patients with comorbid conditions and/or patients taking concomitant immunosuppressant therapy.

Hypersensitivity

Acute and delayed hypersensitivity reactions have occurred after treatment with infusions of infliximab; acute urticaria, dyspnea, and hypotension have been reported, while serious reactions such as anaphylaxis are uncommon. Acute infusion reactions including anaphylactic reactions may develop during, within seconds, or within a few hours following infusion. If acute infusion reactions occur, the infusion must be interrupted immediately. Emergency equipment, such as adrenaline, antihistamines, corticosteroids, and an artificial airway must be available. Patients may be pretreated with eg, an antihistamine, hydrocortisone, and/or paracetamol to prevent mild and transient effects. Available data suggest an increased risk for delayed hypersensitivity with increasing infliximab-free interval. If patients are retreated after a prolonged period, they must be closely monitored for signs and symptoms of delayed hypersensitivity.

Malignancies

Malignancies, which in some cases were fatal have been reported in children, adolescents, and young adults (up to 22 years old) treated with TNF-blocker therapy. Approximately half of the reported cases were lymphomas, while the other cases were various malignancies including rare malignancies more usually linked to immunosuppression. 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. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer. 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.

Vaccinations

There are limited date on the response to live vaccines in patients treated with infliximab. The concurrent administration of live vaccines with Remsima® is not recommended. Due to increased risk of infection in pediatric patients, it is important that they are up to date with all vaccinations prior to initiating Remsima®. The administration of live vaccines to children who are potentially exposed to infliximab during pregnancy should be performed with caution. It is recommended that these children should not receive "live vaccines" such as BCG within 6 months after birth. Cases of agranulocytosis, in infants exposed in utero to infliximab, have also been reported. A mother should inform her infant's doctors and other healthcare professionals of her use of Remsima® during pregnancy.

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