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Information Exchange System

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Infliximab (Remicade) – reports of tuberculosis infections

European Union. The Committee for Proprietary Medicinal Products (CPMP) of the European Medicines Evaluation Agency (EMEA) has been made aware of 28 post-marketing reports of tuberculosis (TB) in patients treated with infliximab (Remicade: Centocor).

Infliximab is a chimeric human-murine monoclonal antibody that binds to and thereby inhibits the biological activity of TNF- . Remicade was first approved in the USA in August 1998. Within the European Union, a marketing authorization was issued in August 1999 for the treatment of severe, active Crohn's disease or of fistulising Crohn's disease, in patients who have not responded despite a full and adequate course of therapy with conventional treatment such as a corticosteroid and/or an immunosuppressant. In June 2000, Remicade received additional approval for reducing the signs and symptoms of active rheumatoid arthritis in patients whose response to disease-modifying drugs, including methotrexate, has been inadequate.

Since its first marketing in the USA in August 1998, an estimated 100,000 patients have been treated with the product worldwide.

To date, 28 cases of TB have been reported (9 cases in North America and 19 cases in Europe), of which one had a fatal outcome. Some of these have been miliary tuberculosis and some have been of unusual extrapulmonary location. The majority of patients had a prior history of treatment with immunosuppressants and corticosteroids and in a significant proportion, the onset of active TB occurred after three or less infusions of infliximab, thus supporting a possible relationship with initiation of infliximab therapy. As clinical experience with infliximab is still limited, the onset (or re-activation) of TB or of other opportunistic infections after a longer period of treatment cannot be ruled out.

The approved Summary of Product Characteristics (SPC) currently contraindicates the use of infliximab in clinically serious infections. It also warns of the known risks of exacerbating infections through the inhibition of TNF- , which is an important mediator of inflammation and cellular immune responses.

In view of the seriousness of these reports, the EMEA also wishes to draw attention to the following recommendations:

If active tuberculosis is suspected, infliximab treatment should be stopped until the diagnosis is ruled out or the infection has been treated in accordance with current guidelines.

Before starting treatment with infliximab, patients should be evaluated for both active and inactive ('latent') tuberculosis, by way of a detailed medical history that includes personal history of tuberculosis or possible previous contact with tuberculosis and consideration of appropriate screening tests (chest x-ray, tuberculin test). Prescribers are reminded that false negative tuberculin test results may be obtained in patients who are severely ill or immunosuppressed. If inactive ('latent') tuberculosis is diagnosed, measures should be taken to prevent the activation of

tuberculosis and the risk/benefit for the patient should be considered before starting infliximab therapy.

Patients should also be instructed to seek medical advice if signs and/or symptoms suggestive of tuberculosis (e.g. persistent cough, wasting/weight loss, low-grade fever) appear.

As an urgent measure, the patient and prescribing information has been amended accordingly through a rapid procedure at the request of the marketing authorization holder. The EMEA thought it necessary to provide this new information to the public.

The revised sections of the Summary of Product Characteristics and of the patient leaflet are available in the European Public Assessment Report of infliximab (Remicade) published on the EMEA Website.

Further information may be obtained from Mr Noel Wathion, Head, Evaluation of Medicines for Human Use (Tel: +44 20 7418 8592, Fax: +44 20 7418 8668).

Reference:

EMEA Public statement on infliximab (Remicade) - reports of tuberculosis infections. London 20 December 2000 (EMEA/CPMP/4445/00).
http://www.eudra.org/humandocs/PDFs/PS/444500en.pdf]