The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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EMEA PUBLIC STATEMENT ON INFLIXIMAB (REMICADE)
Increased incidence of mortality and hospitalisation for worsening Congestive Heart Failure

The EMEA's scientific committee CPMP has been made aware of preliminary findings from a study in congestive heart failure patients (CHF), showing higher incidences of mortality and hospitalisations for worsening heart failure in patients treated with infliximab (Remicade).

Infliximab is a monoclonal antibody that inhibits the biological activity of tumour necrosis factor alpha (TNFα). Remicade was authorised in the European Union in August 1999. It is indicated for the treatment of severe, active Crohn's disease or of fistulising Crohn's disease, as well as the treatment of active rheumatoid arthritis.

Remicade is not indicated for the treatment of CHF. In a study designed to evaluate Remicade in CHF, 150 patients with moderate to severe (NYHA class III-IV) CHF were treated with 3 infusions of Remicade 5 mg/ kg, 10 mg/ kg, or placebo over 6 weeks. Higher incidences of mortality and hospitalisation for worsening heart failure were seen in those patients treated with Remicade, especially those treated with the higher dose of 10 mg/ kg. At present 7 of 101 patients treated with Remicade have died compared to no deaths among the 49 patients on placebo.

To date, there are insufficient data regarding the pathological mechanism behind these findings and regarding any dose relationship. Additional information has been requested and the evaluation is currently ongoing.

In view of the seriousness of the preliminary findings, and pending additional data, the EMEA draws attention to the following precautionary measures.

For physicians considering therapy of patients with rheumatoid arthritis or Crohn's disease with Remicade:

- Do not initiate therapy in patients with congestive heart failure.

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Physicians should reevaluate patients with congestive heart failure currently receiving Remicade treatment with respect to their cardiac status:

- Treatment should be discontinued in patients whose congestive heart failure is worsening.

- Treatment discontinuation should be considered in patients with stable concomitant congestive heart failure. If a decision is made to continue treatment, cardiac status should be closely monitored.

Information for Patients

- Patients currently under Remicade treatment for Crohn's disease or active rheumatoid arthritis, and without congestive heart failure, should continue treatment. In case of doubt, patients should contact their treating physician for advice.

- Patients treated with Remicade who suffer from congestive heart failure should contact their treating physician, who will reassess their treatment and may decide to monitor their cardiac status.

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