Centocor

11 August 2004

IMPORTANT DRUG WARNING

Dear Healthcare Professional:

Centocor would like to inform you of important safety information concerning hematologic and neurologic events for REMICADE® (infliximab), a biological therapeutic product indicated for the treatment of rheumatoid arthritis and Crohn's disease.

In postmarketing experience worldwide, hematologic events including leukopenia, neutropenia, thrombocytopenia and pancytopenia, some with a fatal outcome, have been reported in patients receiving REMICADE. Accordingly, Centocor has added a Warning on Hematologic Events to the labeling for the product as follows:

> **Hematologic Events**
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> Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia, some with a fatal outcome, have been reported in patients receiving REMICADE. The causal relationship to REMICADE therapy remains unclear. Although no high-risk group(s) has been identified, caution should be exercised in patients being treated with REMICADE who have ongoing or a history of significant hematologic abnormalities. 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) while on REMICADE. Discontinuation of REMICADE therapy should be considered in patients who develop significant hematologic abnormalities.

In addition, the Warning on Neurologic Events has been updated (see Warnings in the enclosed prescribing information) to:

- describe rare cases of CNS manifestation of systemic vasculitis; and
- warn that discontinuation of REMICADE should be considered in patients who develop significant central nervous system adverse reactions.

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Finally, the Adverse Reaction sections of the REMICADE prescribing information has been updated to add the following adverse events that have been reported during post-approval use of REMICADE: neutropenia, pericardial effusion and systemic and cutaneous vasculitis.

Since August 24, 1998, when REMICADE was approved in the US, approximately 509,000 patients have been treated with REMICADE worldwide.

Enclosed please find the updated prescribing information as well as the patient information sheet.

Centocor is committed to ensuring that REMICADE is used safely and effectively and is committed to providing you with the most current product information for REMICADE. You can assist us with monitoring the safety of REMICADE by reporting adverse events to Centocor at 1-800-457-6399. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), facsimile (1-800-FDA-0178), the MedWatch website at www.fda.gov/medwatch, or mailed to MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852-9787. Both healthcare professionals and consumers should use Form 3500 for reporting adverse events.

Should you have any questions or require further information regarding the use of REMICADE, please contact Centocor's Medical Affairs Department at 1-800-457-6399.

Sincerely,

Daniel Everitt

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