

**IMPORTANT
DRUG
WARNING**

December 2009

Dear Healthcare Professional:

Centocor Ortho Biotech Inc., the makers of REMICADE® (infliximab), would like to inform you of important safety information regarding risk of serious fungal infections associated with Tumor Necrosis Factor-alpha (TNF α) blockers.

On 04 September 2008, the U.S. Food and Drug Administration (FDA) issued an Alert on invasive fungal infections reported in association with TNF blockers. The FDA reported histoplasmosis and other invasive fungal infections not consistently recognized in patients taking the Tumor Necrosis Factor- α blockers: REMICADE®, Cimzia® (certolizumab pegol), Enbrel® (etanercept), and Humira® (adalimumab).¹ This has resulted in delays in appropriate antifungal treatment, sometimes resulting in death.

REMICADE® is indicated for the treatment of adults with rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, and ulcerative colitis and for children with Crohn's disease.

Important information about the risk of invasive fungal infections, such as histoplasmosis, is listed in the *Boxed Warning* and *Warnings* sections of REMICADE's prescribing information and the Medication Guide for patients.

The following should be considered by REMICADE® prescribers and by healthcare professionals providing supportive care to patients receiving REMICADE®:

- TNF blockers are immunosuppressants. Patients receiving TNF blockers, including REMICADE®, are at risk for developing infections including invasive fungal infections such as histoplasmosis, coccidioidomycosis, blastomycosis, aspergillosis, candidiasis, and other opportunistic infections.
- Healthcare professionals should be alert to this risk in REMICADE®-treated patients, particularly if they reside in or travel to regions endemic for histoplasmosis, coccidioidomycosis, or blastomycosis (eg, Ohio and Mississippi River valleys or the Southwestern United States). Invasive fungal infections should be suspected if they develop a serious systemic illness.
- Patients should be encouraged to report signs of infection and be closely monitored during and after treatment with REMICADE® for the development of signs or symptoms of possible systemic fungal infection including fever, malaise, weight loss, sweats, cough, dyspnea, pulmonary infiltrates on x-ray, or serious systemic illness, including shock.
- Patients who develop an infection, including any persistent or reoccurring infections, should be discontinued from REMICADE® therapy and undergo a complete diagnostic workup, which may include fungal cultures, histopathological or cytological evaluations, antigen detection and serum antibody titers. Empiric antifungal therapy should be considered until the pathogen(s) are identified and in consultation with an infectious diseases specialist when feasible.
- REMICADE®, or other TNF α blocker, may be restarted after recovery from the infection. The decision to restart REMICADE® should include a reevaluation of the benefits and risks of TNF blocker therapy, especially in patients who live in regions of endemic mycoses. Both the decision to restart REMICADE® and the duration of antifungal therapy should be made in consultation with an infectious diseases specialist, when feasible.

For further information please refer to the following FDA links:

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124185.htm>

<http://www.accessdata.fda.gov/psn/printer.cfm?id=878>

PLEASE NOTE: This letter does not include a comprehensive description of the serious and significant risks associated with the use of REMICADE® (infliximab). Please read the accompanying full prescribing information and Medication Guide for a complete description of the serious and significant risks associated with the use of REMICADE®, including Boxed Warning regarding the risk of serious infections, Contraindications, Warnings, Precautions, and Adverse Events.

Healthcare professionals should report cases of serious fungal infections or any serious adverse events suspected to be associated with the use of REMICADE® to Centocor Ortho Biotech Services, LLC Medical Affairs Department 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 <http://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 Ortho Biotech Services, LLC Medical Affairs Department at 1-800-457- 6399.

Sincerely,



Peter Callegari, MD
Vice President, Medical Group
Immunology Medical Affairs
Centocor Ortho Biotech Services, LLC

References:

Information for Healthcare Professional REMICADE (infliximab), Cimzia® (certolizumab pegol), Enbrel® (etanercept), and Humira® (adalimumab).
<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124185.htm>.
Accessed 16 June 2009.