

Invasive fungal infections - TNF α blockers, including Cimzia[®] (certolizumab pegol)

- TNF α blockers, including Cimzia[®] (certolizumab pegol), have a REMS program because there is a risk of developing serious fungal infections, including histoplasmosis and other invasive fungal infections, which are not consistently recognized in patients taking TNF α blockers .
- Delays in antifungal treatment may result in increased morbidity and mortality. In addition, patients treated with Cimzia[®] (certolizumab pegol) are at increased risk for developing serious infections, including histoplasmosis and other invasive fungal infections, that may lead to hospitalization or death.
- Cimzia[®] (certolizumab pegol) is indicated for reducing signs and symptoms of Crohn's Disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.

Please Note: *These slides do not include a comprehensive description of the serious and significant risks associated with the use of Cimzia[®] (certolizumab pegol). Please read the accompanying Prescribing Information and Medication Guide for a complete description of the serious and significant risks associated with the use of Cimzia[®] (certolizumab pegol), including the Boxed Warning regarding the risk of serious infections, Contradictions, Warnings, Precautions and Adverse Events.*

Serious Fungal infections and TNF α blocker therapy, including Cimzia[®] (certolizumab pegol)

- Tsiodras, et al. reported¹:
 - **281 cases in PubMed and MEDLINE through June 2007**
 - **Pneumonia most common presentation**
 - **Most common organisms: histoplasmosis, candidiasis, aspergillosis**
- FDA safety alert²:
 - **240 cases of histoplasmosis associated with TNF α blockers**
 - **85% from Ohio and Mississippi River valleys**
 - **21 cases unrecognized/delayed diagnosis**
 - **12 deaths with 5 diagnoses made at autopsy**
 - **Additionally, cases of coccidioidomycosis, blastomycosis were reported**
- **Cases of serious fungal infections, including histoplasmosis, have been reported in patients treated with Cimzia[®] (certolizumab pegol)³**

1. *Mayo Clinic Proc* 2008;83:181-194.

2. *Information for Healthcare Professional Cimzia[®] (certolizumab pegol), Enbrel (etanercept), Humira (adalimumab), and Remicade (infliximab)*. http://www.fda.gov/cder/drug/InfoSheets/HCP/TNF_blockersHCP.htm. Accessed September 25, 2008.

3. *Data on file, UCB Inc.*

Selected fungal infections: endemic areas

- Histoplasmosis
 - *Histoplasma capsulatum*
 - Mississippi and Ohio River Valleys (Midwest USA) and areas in Central and South America, Africa, India, and Southeast Asia
- Coccidioidomycosis
 - *Coccidioides immitis*
 - Southwestern US, Mexico, Central and South America
- Blastomycosis
 - *Blastomyces dermatitidis*
 - South Central, Southeastern and Midwestern United States and areas in Central and South America and parts of Africa
- Aspergillosis
 - *Aspergillus sp.*
 - Present diffusely in the environment

Recommendations for health care providers in patients using TNF α blockers, including Cimzia[®] (certolizumab pegol)

- Invasive fungal infections should be suspected in patients who reside or travel in regions where mycoses are endemic (e.g. Ohio and Mississippi River Valleys) and who develop signs and symptoms of possible serious systemic illness.
- Empiric antifungal therapy in these patients should be considered until the pathogen(s) are identified and in consultation with an infectious disease specialist when feasible.
- Patients should report and be closely monitored during and after treatment with TNF blockers for the development of any signs and symptoms of invasive fungal infection including fever, malaise, weight loss, sweats, cough, dyspnea, pulmonary infiltrates on x-ray, or serious systemic illness.
- Patients who develop an infection, including any persistent or recurring infections should have their TNF α blocker, including Cimzia[®] (certolizumab pegol), discontinued and undergo a complete diagnostic workup.
- TNF α blockers , including Cimzia[®] (certolizumab pegol), may be restarted after recovery from the infection based on a reevaluation of risks and benefits. The decision to restart TNF α blocker therapy and the duration of the antifungal therapy should be made in consultation with an infectious disease specialist when feasible.