



CLINICAL COMMUNICATOR

Cimzia® – New Drug for Crohn's Disease

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SPECIAL POINTS OF INTEREST

Cimzia must be
injected by a health
care professional

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The following is a brief summary of a new drug, and is not a complete discussion of its risks and/or benefits. The complete prescribing information, including all cautions and warnings, as well as current clinical standards of practice should be consulted before use of Cimzia in a specific patient.

Cimzia is the brand name of certolizumab pegol. This new drug was approved by the FDA in April, 2008 for the treatment of Crohn's disease. Cimzia contains a fragment of a humanized antibody that is a potent neutralizer of tumor necrosis factor alpha (TNF-alpha). Like some other injectable drugs, Cimzia's active compound is chemically attached to polyethylene glycol, or PEG (i.e. it is pegylated), to allow for subcutaneous injection with an extended dosing schedule.

Indication: Cimzia has been approved for treatment of moderately to severely active Crohn's disease, in adults who have not responded well to conventional therapy.

Mechanism of Action: Elevated TNF-alpha concentrations have been implicated in the pathology of Crohn's disease, and this chemical is strongly expressed in the bowel wall areas affected by Crohn's. Certolizumab neutralizes both membrane-associated and soluble human TNF-alpha in a dose-dependent manner.

Dose: Administer 400 mg by subcutaneous injection at weeks 0, 2, and 4. If there is a clinical response, continue to administer 400 mg every 4 weeks.

Administration: All doses must be administered by a health care professional. Two 200 mg vials of Cimzia will be needed to provide a dose for Crohn's disease. Each 200 mg is administered as a separate injection; therefore 2 injections are required for each dose. A 23 gauge needle size is recommended for these injections. The drug must be prepared by a health care professional. Like other biologics, the drug should not be shaken during preparation. Complete reconstitution may take up to 30 minutes. The full preparation instructions should be reviewed prior to mixing the drug.

Adverse Effects: As with other TNF blockers, potentially serious adverse drug effects are possible. Prescribers should exercise caution when considering use of Cimzia in patients with preexisting or recent-onset neurological disease, heart failure, or carriers of hepatitis B virus. Cimzia should not be administered to patients who have an active infection; patients should be screened for latent tuberculosis infection prior to treatment. Caution is advised in patients with current or previous significant hematological disorders. Hypersensitivity/anaphylactoid reactions were reported rarely in clinical trials.

Monitoring: Assess for a clinical response at week 6. All patients should be monitored for tuberculosis (TB) infection during treatment, even if an initial TB test is negative. Other serious infections could also develop during therapy. Suggested monitoring includes liver function tests, antinuclear antibody (ANA) titer, CBC, and hepatitis serology.

Drug Interactions: Cimzia should not be used at the same time as abatacept, adalimumab, anakinra, etanercept, infliximab, rilonacept, or live vaccines, among others.

Other Uses: A biologics license application is also under review at the FDA for treatment of active rheumatoid arthritis, and other clinical trials are underway for use of Cimzia in treatment of moderate to severe chronic plaque psoriasis. These uses are not FDA-approved at this time.



FDA Proposes Revised Pregnancy & Lactation Drug Labeling

The FDA requires manufacturers to include information on a drug's label (i.e. the drug's package insert) about potential risks of using that drug during pregnancy or lactation. This information is currently found under the "Pregnancy" section of the label. The "Nursing Mothers" part of the label follows the Pregnancy section, and provides information about excretion of the drug in breast milk and any associated risks to a nursing infant.

The risk of using a drug during pregnancy is currently notated as risk level A, B, C, D, or X. Unless one is very familiar with these categories, it is difficult to remember the meaning assigned to each letter. Some people mistakenly assume that the risk increases for each higher letter, which is not the case. Categories C, D and X are based not just on risk, but on risk weighed against benefit. The current categories also do not always distinguish between risks based on animal and human data, or between differences in frequency, severity, and type of fetal developmental toxicities.

The FDA has recognized a need for better communication about the risk of drug exposure during pregnancy and lactation, and has therefore proposed a new way of providing this vitally important information to health care professionals and patients. The new drug label would still have two separate sections for "Pregnancy" and "Lactation". The difference is that each of these sections would now have three parts:

Pregnancy Section

1. **Fetal Risk Summary** – this section would start with a one-sentence risk conclusion stating the possible risks of structural anomalies, fetal and infant mortality, impaired physiologic function, and alterations to growth. The risk conclusion would state that it is based on animal or human studies. Further discussion would be included when human data is available, such as the seriousness of any observed abnormality, its reversibility, and risks that are related to the gestational timing of exposure.
2. **Clinical Considerations** – included here would be a discussion of the potential risks from inadvertent exposure (where the drug is taken before finding out about a pregnancy). This section would provide specific dosing information applicable to pregnant patients, any suggested monitoring, and information about use of the drug during labor and delivery. Possible effects and suggested interventions applicable to the neonate and/or the later development of the child would also be reviewed.
3. **Data Section** – The purpose of this section would be to provide more details about the available data from human and animal studies related to use of the drug in pregnancy, and its interpretation relative to the fetal risk summary and clinical considerations.

Lactation Section

1. **Risk Summary** – if appropriate, this paragraph would include a statement that the use of the drug is compatible with breast feeding. Information would be provided on the effects of the drug on milk production, how much drug might be present in the milk, and its potential effect on the breast-fed child.
2. **Clinical Considerations** – this section would discuss ways to minimize exposure to the breast-fed child, such as timing or pumping and discarding milk. Potential effects in the child and recommendations for monitoring would be reviewed. Also included here would be any recommended dosing adjustments.
3. **Data** – an overview of the data supporting the risk summary and clinical considerations.

The proposed version of this rule was announced on May 28, 2008. At this time it is only a proposal. The next step is for a period of public comment. The FDA must review and evaluate these comments before the final rule is adopted. This process will take some time. If adopted, the new labeling would be required on drugs approved after the change goes into effect.

According to the FDA's press release, their goal for this change is to "give health care providers better information about the use of prescription drugs during pregnancy and breast-feeding. We believe that better information will help healthcare practitioners, in consultation with their patients, make more informed choices about which drugs to prescribe during pregnancy and breast-feeding. The more detailed information that this labeling will ultimately provide should also help health care providers counsel women who took a drug before they knew they were pregnant."

Reference: FDA, "Summary of Proposed Rule on Pregnancy and Lactation Labeling" dated 5/28/08