

UNC INFLAMMATORY BOWEL DISEASE DRUG PROTOCOL

CERTOLIZUMAB PEGOL)CIMZIA(

TREATMENT PROTOCOL:

Certolizumab is pegylated humanized antibody Fab' fragment of tumor necrosis factor alpha (TNF-alpha) monoclonal antibody. Certolizumab pegol binds to and selectively neutralizes human TNF-alpha activity. It has a bioavailability of 80% and half-life of 14 days

Current IBD indications for certolizumab at UNC

- **Crohn's disease:**
 1. Induction and maintenance of clinical remission in adult patients with moderate to severe active Crohn's disease who have had an inadequate response to conventional therapy*
 2. Post-operative prophylaxis for high risk patients.
 3. Can be considered for severe, refractory extraintestinal manifestations (arthritis, pyoderma gangrenosum, and iritis/uveitis)

Dosage and Route of Administration

- **Route of administration:** Subcutaneous Injection
- **Dosage forms and strength:** if comes in 200 mg/mL solution in a single-use **prefilled syringes** for self-injection or in 200 mg **lyophilized powder** for reconstitution in a single-use vial with 1 mL of sterile water for injection, which is administered by nurse[†]
- **Dose and intervals:**
 - Induction: 400 mg (two 200 mg injections) at weeks 0, 2, and 4
 - Maintenance: 400 mg (two 200 mg injections) every 4 weeks

* FDA-approved indications

[†] The company that makes the medication has nurses who will come to your home for the monthly injections

Higher dose or shorter intervals can be used based on the clinical situation

Time for Response

- Patients may feel better by the time they receive the second injection. It may take up to 6 weeks for a definitive clinical response.

Contraindications

- **Absolute:**
 1. Moderate or severe HF (New York Heart Association [NYHA] class III/IV)
 2. Active solid or hematological malignancies
 3. Active systemic infection
 4. Untreated latent TB
- **Relative/may use with caution:**
 1. Mild heart failure (NYHA functional class I or II)[‡]
 2. History of demyelinating disease (MS, optic neuritis)[§]
 3. Family history of demyelinating disease (MS, optic neuritis)
 4. History of solid or hematological malignancy within the past 5 years
 5. History of malignant melanoma
 6. Patients with multiple comorbid conditions that may increase risk of infections (tobacco use, DM, COPD)

Administration and Safety Monitoring

Before initiation of therapy:

- Careful medical history to assess for any absolute and relative contraindications
- Evaluate immunization status and provide any indicated vaccines (influenza, pneumonia, hepatitis B, HPV)
- Prior authorization: Email IBD nurse the patient's information

[‡] Baseline echocardiogram with ejection fraction documentation and cardiology consultation are needed prior to initiation of anti-TNF therapy. In this situation, should avoid high doses of anti-TNF therapy and provide close follow-up with prompt discontinuation of anti-TNF-alpha therapy if HF worsens

[§] Can only be used under the discretion of treating neurologist.

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 - Laurie Powers, RN (Dr. Herfarth, Dr. Hansen)
 - Christina Womble, RN (Dr. Long, Dr. Sheikh)
- Patient's teaching/training in subcutaneous injection technique
 - Pre-treatment laboratory evaluation:
 1. Screen for latent Tuberculosis (Quantiferon gold TB test or Tuberculin skin test + chest X-ray)**
 2. Screen for chronic infections (HBs-Ag, HBs-Ab, HBc-Ab, HCV Ab, HIV testing)
 3. Baseline LFTs, albumin, CBC, renal function and CRP

Therapy administration:

- Cimzia prefilled syringe:
 - Prefilled syringes should be stored in a refrigerator at 36°F to 46°F (2°C to 8°C) in the original container until it is used. It should also be protected from light
 - Cimiza prefilled syringes should be brought to room temperature before injection, this can help reducing injection site reactions
 - Injections should occur at separate sites in the thigh or abdomen. Patient should be instructed to rotate injection sites and not to give injections into areas where the skin is tender, bruised, red or hard
- CIMZIA Lyophilized powder:††
 - CIMZIA should be brought to room temperature before reconstituting.
 - Use appropriate aseptic technique when preparing and administering CIMZIA.
 - Reconstitute the vial(s) of CIMZIA with 1 mL of Sterile Water for Injection, USP using the 20-gauge needle provided.

** Tuberculosis testing and anti-TNF therapy:

- Tuberculin skin test (TST) can be falsely negative in patients with (1) severe malnutrition and (2) receiving immunosuppressive drug (corticosteroids, anti-TNF therapy, and chemotherapy).
- Neither Quantiferon gold TB test nor TST can provide 100% sensitivity for detecting latent TB.
- **In patients at high risk for TB, both tests should be considered with treatment if either one is positive.**
- In patients with latent TB, anti-TNF therapy can be started after 4 weeks of TB therapy. In patients with active TB, anti-TNF therapy should be delayed until completion of TB therapy is possible.

†† This form is given by a nurse from the drug company. It can be used for patients who are unable to self-administer the injection or when there are concerns about compliance

- Gently swirl each vial of CIMZIA without shaking, assuring that all of the powder comes in contact with the Sterile Water for Injection.
 - Leave the vial(s) undisturbed to fully reconstitute, which may take approximately 30 minutes.
 - The final reconstituted solution contains 200 mg/mL and should be clear to opalescent, colorless to pale yellow liquid essentially free from particulates.
 - Once reconstituted, CIMZIA can be stored in the vials for up to 24 hours between 2° to 8° C (36° to 46° F) prior to injection. Do not freeze
 - Prior to injecting, reconstituted CIMZIA should be at room temperature but do not leave reconstituted CIMZIA at room temperature for more than two hours prior to administration.
 - Withdraw the reconstituted solution into a separate syringe for each vial using a new 20 gauge needle for each vial so that each syringe contains 1 mL of CIMZIA (200 mg of certolizumab pegol).
 - Replace the 20-gauge needle(s) on the syringes with a 23-gauge(s) for administration.
 - Inject the full contents of the syringe(s) subcutaneously into thigh or abdomen. Where a 400 mg dose is required, two injections are required, therefore, separate sites should be used for each 200 mg injection.
- Cimzia prefilled syringe components do NOT contain any latex or dry natural rubber.

Laboratory monitoring while on therapy:

- CBC with differential, ALT, and creatinine every 3 months
- CRP is clinically indicated
- Periodic TB testing^{‡‡}

Special Considerations

^{‡‡} Patients should be assessed for risk of TB exposure at each clinic visit with repeat testing based on the risk. Patients at high risk include: 1. Exposure to patients with active TB, 2. History of travel to high-risk countries- Mexico, Philippines, Vietnam, India, China, Haiti, and Guatemala. For complete list of high risk countries visit: <http://www.stoptb.org/countries/tbdata.asp> .3. Patients who live or work in a high-risk environment- homeless shelter, prison or jail, or long-term care facility, and 4. Health-care workers.

- Certolizumab is pregnancy Category B and should be continued during pregnancy. Compared to the other anti-TNF agents, it has the lowest potential to cross the placenta. However, live or live-attenuated vaccines should not be given to the infant born to mother receiving adalimumab within the first 6 months of life.
- The limited data available suggests that anti-TNF therapies are compatible with breastfeeding and therefore the anti-TNF therapy should not influence the decision to breast-feed, and breast-feeding should not influence the decision to use these medications
- Live vaccines are contraindicated if patient receiving anti-TNF agents or planning to initiate therapy within 4-6 weeks
- Patients should be advised to comply with general cancer screening protocols: mammograms, annual pap smears, CRC/dysplasia surveillance
- Protect against UV radiation (sunscreen) and annual dermatological screening

References:

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