UNC INFLAMMATORY BOWEL DISEASE DRUG PROTOCOL

ADALIMUMAB (HUMIRA)

TREATMENT PROTOCOL:

Adalimumab is a **humanized** IgG1 monoclonal antibody that binds tumor necrosis factor alpha (TNF α) with high affinity and neutralize its effect in promoting inflammatory response. It has a bioavailability of 64% and terminal half-life of 2 weeks (range: 10 to 20 days)

- **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. Induction and maintenance of clinical remission in patients who have lost response to or are intolerant to infliximab*
  3. Induction and maintenance of clinical remission in **pediatric patients** 6 years of age and older with moderately to severely active Crohn’s disease who have had an inadequate response to conventional therapy*
  4. Post-operative prophylaxis for high risk patients.
  5. Can be considered for severe, refractory extraintestinal manifestations (arthritis, pyoderma gangrenosum, Hidradenitis suppurativa, and iritis/uveitis)

- **Ulcerative Colitis:**
  1. Induction and maintenance therapy for patients with moderate to severe disease who have had an inadequate response to conventional therapy*
  2. Can be considered for severe, refractory extraintestinal manifestations (arthritis, pyoderma gangrenosum, Hidradenitis suppurativa, and iritis/uveitis)

### Current IBD indications for adalimumab at UNC

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### Dosage and Route of Administration

- **Route of administration:** Subcutaneous Injection

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* FDA-approved indications
• **Dosage forms and strength:** 40 mg/0.8 ml in a single-use **prefilled pen** (HUMIRA PEN) OR single-use **prefilled glass syringe**

• **Dose and intervals:**
  
  o **Adult Crohn's Disease and Ulcerative Colitis:**
    
    ▪ Induction: 160 mg (four 40 mg injections) on week 0, 80 mg (two 40 mg injections) on week 2, 40 mg (one injection) on week 4
    
    ▪ Maintenance: 40 mg (one injection) every 2 weeks
  
  o **Pediatric Crohn's disease:**
    
    ▪ 17 kg (37 lbs) to < 40 kg (88 lbs):
      
      • Induction: 80 mg on day 1, 40 mg on day 15, and 20 mg on day 29
      
      • Maintenance: 20 mg every other week
    
    ▪ ≥ 40 kg (88 lbs) → Same dose as adults

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

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**Time for Response**

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

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**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
  - Anthea Darling, RN (Dr. Isaacs, Dr. Sartor, and Dr. Jain)
  - 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)§

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† 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.

§ 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.
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:**

- The Humira prefilled pen or prefilled syringe 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.
- The Humira prefilled pen or prefilled syringe should be brought to room temperature before injection (this can be achieved by taking the dose out of the refrigerator 15-30 minutes before the injection).
- Applying ice pack at the site of injection before injecting the Humira can reduce burning sensation and improve tolerance.
- 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.

**Other considerations related to drug administration:**
1. Humira should NOT be used if frozen, even if it has been thawed.
2. The prefilled pen or prefilled syringe should NOT be used if the liquid is cloudy, discolored, or has flakes or particle in it.
3. If needed for traveling, the Humira dose can be stored at room temperature-with protection from light in the original carton for a maximum of 14 days. If not used within 14 days, it should be discarded.
4. Patients sensitive to latex should be instructed not to handle the gray needle cover of the 27 gauge HUMIRA Pen and prefilled syringe because it contains natural rubber latex.

**Laboratory monitoring while on therapy:**

- CBC with differential, ALT, and creatinine every 3 months.
- CRP if clinically indicated.
- Periodic TB testing**
- Adalimumab trough level/antibodies if clinically indicated.

**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](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.**

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**January 9, 2016**
Special Considerations

- Adalimumab is pregnancy Category B and should be continued during pregnancy. It can cross the placenta during the third trimester and therefore live or live-attenuated vaccines should not be given to infants born to mothers 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:


