CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

GUIDELINES FOR OUTPATIENT INTRAVENOUS VEDOLIZUMAB (ENTYVIO) THERAPY

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: NUR245
Effective: 10/20/22
Reviewed:
Revised:
Approved by: Kathleen Patrick, President 10/20/22

I. BACKGROUND

Vedolizumab (Entyvio) is a humanized monoclonal antibody utilized for the treatment of Crohn's disease and ulcerative colitis in adult patients. Vedolizumab binds to alpha-4-beta-7 integrin and blocks the interaction of alpha-4-beta-7 integrin with the mucosal addressin cell adhesion molecule-1 (MAdCAM-1). This in turn inhibits the migration of memory T-lymphocytes across the endothelium into the inflamed gastrointestinal parenchymal tissue. The interaction of alpha-4-beta-7 integrin with MAdCAM-1 has been implicated as an important contributor o the chronic inflammation that is a hallmark to ulcerative colitis and Crohn's disease. The following outlines the procedures for servicing patients in need of outpatient vedolizumab home infusions

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:
   1. Prescriber preference
   2. Allergy profile
   3. Age ≥18 years
   4. Ability to secure contracted nursing for ongoing infusions
   5. Other relevant social and/or medical history

C. Physician orders for vedolizumab must include:
   1. Drug and dose
   2. Route of administration
   3. Frequency of administration
   4. Emergency medications per protocol

5. Any orders for pre-medications
6. Line care protocol
7. Routine lab monitoring, if applicable

D. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGY OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information

A. Indications: Adult Ulcerative Colitis and Adult Crohn's disease

B. Dosage (for both Ulcerative Colitis and Crohn's disease):
   1. Induction dosing: 300 mg IV at weeks 0, 2, 6
   2. Maintenance dosing: 300 mg IV every 8 weeks thereafter

C. Contraindications: Patients who have had a known serious or severe hypersensitivity reaction to vedolizumab or any of its excipients

D. Warnings and Precautions
   1. Hypersensitivity Reactions
      a. Dyspnea
      b. Bronchospasm
      c. Urticaria
      d. Flushing
      e. Rash
      f. Increased blood pressure
      g. Increased heart rate
      h. Anaphylaxis
         i. These reactions have been reported with vedolizumab. Reactions may vary in their time of onset from during the infusion or immediately post infusion to occurring up to several hours post infusion.
         ii. If anaphylaxis or other serious reactions occur, discontinue administration immediately and initiate appropriate emergency treatment.
   2. Infections
      a. Patients treated with vedolizumab are at an increased risk of developing infections.
      b. Vedolizumab is not recommended in patients with active, severe infections. Consider postponing treatment with vedolizumab in patients who develop a severe infection and exercise caution in patients with recurring infections. Consider screening for tuberculosis according to local practice.
   3. Progressive Multifocal Leukoencephalopathy (PML)
      a. There were zero cases of PML in vedolizumab clinical trials. However, another integrin receptor antagonist has been associated with PML, a rare opportunistic infection that is fatal to the central nervous system. Monitor patients for any new or worsening neurological symptoms.
      b. Signs and symptoms of PML include:
         i. Progressive weakness on one side of the body
         ii. Clumsiness of limbs
         iii. Disturbances of vision

iv. Changes in thinking, memory, and orientation leading to confusion and personality changes

c. Signs and symptoms progress over days to weeks, and progression of deficits leads to death or severe disability in weeks to months. If PML is suspected, withhold vedolizumab treatment and refer patient to a neurologist. If PML is confirmed, discontinue vedolizumab.

4. Liver injury
    a. There has been report of elevation of transaminase and/or bilirubin in patients receiving vedolizumab.
    b. Patients with jaundice or other evidence of significant liver injury should discontinue vedolizumab.
5. Live Vaccines
    a. Prior to starting with vedolizumab, patients should be up to date with all immunizations according to current immunization guidelines. Patients receiving vedolizumab may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.

E. Pharmacokinetics:
1. Volume of distribution: 5 L
2. Excretion: 0.157 L/day
3. Elimination half-life: 18.3 days; 25 days

F. Adverse Reactions
1. Nausea (9%)
2. Arthralgia (12%)
3. Headache (12%)
4. Nasopharyngitis (13%)
5. Upper respiratory infection (7%)
6. Fatigue (6%)
7. Fever (9%)
8. Infusion reaction (4%)

G. Drug Interactions
1. Concurrent use with other immunosuppressants including tofacitinib, infliximab, and anifrolumab-fnia may result in increased immunosuppression and an increased risk of infection.

IV. ADMINISTRATIVE GUIDELINES

A. Administration
1. IV infusions should be given immediately after reconstitution and dilution. Reconstituted and diluted solution must be used within 1 hour of preparation per current USP Immediate-Use Guidelines.
2. Use an **in-line 0.2-micron low protein binding filter** as vedolizumab is a powder that needs reconstituted prior to dilution
3. Do not co-administer other products in the same infusion line

B. Duration
1. Duration of therapy is dependent on patient response and adverse reactions

C. Dose Adjustments
    1. Discontinue therapy in patients with hepatic injury or jaundice. No dose adjustments for renal impairment.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
    1. Alcohol Swabs
    2. Gloves
    3. Vedolizumab vial
    4. Sterile water for injection vials
    5. Bag of sodium chloride 0.9% for dilution 250mL.
    6. Dressing change kit
    7. IV Pole
    8. IV Start Kit
    9. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾" for patients needing peripheral access)
    10. Port access needle (ex. 22 Gauge x ¾ to 1" safe step for patients with a port)
    11. Tape
    12. Extension set 8"
    13. IV injection cap
    14. IV administration set (dial-a-flow or gravity) with in-line or add-on 0.22-micron filter
    15. Syringes (10mL) with needles (20 G x 1")
    16. Normal Saline (0.9%) syringes for flushing
    17. Sharps container

B. How Supplied: Vedolizumab is supplied in a sterile 20 mL single use glass vial, containing 300mg of vedolizumab as a white to off-white powder.

C. Storage and Handling
    1. Store vials at 36°F to 46°F (2°C to 8°C) in original carton protected from light
    2. Diluted product must be used within 1 hour of preparation. Protect from light.
    3. Refer to specific product packing and prescribing information for storage, stability, and excursion information.

D. Compatibility
    1. Stable in Normal saline and Lactated Ringer's solution
    2. Do not infuse with other agents
    3. Do not dilute with dextrose solutions or 0.45% saline solution

E. Procedures
    1. Explain the reasoning for visit and use of vedolizumab
    2. Don gloves.
    3. Establish venous access prior to preparation of drug.
    4. Counsel patient on warnings, precautions, and potential side effects including but not limited to:
        a. Hypersensitivity reactions
        b. Infections
        c. PML
        d. Signs and symptoms of liver injury

e. Nausea
f. Arthralgia
g. Headache.

5. Prepare Product
    a. Remove vial from the refrigerator and inspect vial for particulate matter and discoloration.
    b. Reconstitute vedolizumab vial with 4.8mL of sterile water for injection.
    c. Gently swirl for at least 15 seconds to dissolve the lyophilized power. Do not vigorously shake
    d. Visually inspect reconstituted solution for particulate matter and discoloration prior to administration. Solution should be clear or opalescent, colorless to light brownish yellow and free of visible particulates.
    e. Prior to withdrawing the reconstituted vedolizumab, gently invert the vial three times
    f. Withdraw 5mL (300mg) of the reconstituted vedolizumab solution using a syringe and add to a 250mL 0.9% sodium chloride bag.
    g. Reconstituted and diluted solution must be infused with 1 hour of preparation.
6. Infusion Rates
    a. Infuse over a period of 30 minutes through a dedicated IV line.
7. Upon completion of the infusion:
    a. Flush the infusion set with 30 mL of 0.9% sodium chloride
8. Monitor patient and vital signs periodically during the infusion and for 30 minutes after the completion of the infusion per INS guidelines

VI. CLINICAL MONITORING

A. Prior to therapy:
    1. TB screening
    2. CBC, Liver function panel, and renal function
    3. Ensure patient is up to date on vaccines
B. During therapy:
    1. Monitor for signs and symptoms of infection. Therapy may need interrupted during an active infection
    2. Signs and symptoms of a hypersensitivity reaction
    3. Monitor for PML including new or worsening neurological symptoms
    4. Monitor for liver injury including liver function tests and jaundice
    5. CBC, LFTs, and renal function periodically throughout therapy
C. Disease progression and therapy efficacy
    1. Assess for worsening symptoms including abdominal pain, cramps, changes in stool, changes in weight, and frequency of flares

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

Entyvio [package insert]. Deerfield, IL. Takeda Pharmaceuticals America, Inc. 2014

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

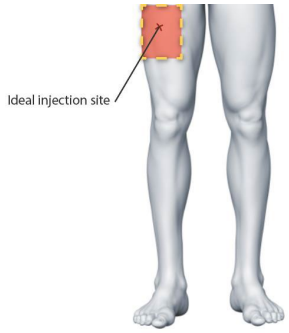
Open the IM Epinephrine Bag

1. Remove 1 of each item
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1")
    d. 1 ampul of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. Attach the brown filtered needle to syringe
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an alcohol swab, wipe the neck of the epinephrine ampul.
3. Holding the ampul upright, swirl and flick the ampul until all fluid flows to the bottom chamber (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampul and with your other hand grasp the bottom chamber of the ampul. Quickly snap the top of the ampul off, directing the snap way from you.
5. Place the tip of the brown filter needle inside the ampul. Tilting the ampul, withdraw dose of medication into the syringe by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampul and hold the syringe upright with the needle pointing upward. Gently tap the side of the syringe to bring any air to the top of the syringe.
7. Push the air out of the syringe by gently pushing on the plunger.
8. Replace the cap on the brown filter needle. Discard remainder in ampul.
9. Remove the brown filter needle and place the black safety needle onto the syringe.

Give your IM Epinephrine injection



1. Grasp your leg muscle at the outer mid-thigh and cleanse the area with a new alcohol wipe.
2. Push the needle into your leg muscle straight in at a 90-degree angle.
3. Inject the medication by depressing the plunger in a slow and steady motion.
4. Remove the needle and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (maximum 3 doses) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. Give the bag to the nurse or EMT, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
Call 911 or have someone drive you to the emergency department.