These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

Vedolizumab (Entyvio) Clinical Guideline for Home Infusion Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: n/a
URAC Standards: n/a
Policy ID: CG005
Effective: 10/20/2022
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Revised: 12/01/2023
Approved by, Title and Date Approved: Kathleen Patrick, President, 12/1/23

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. Vedolizumab is indicated for the treatment of moderate to severe ulcerative colitis and Crohn's disease in adult patients. The induction phase is administered as an intravenous infusion and maintenance dosing can be continued as IV infusions or subcutaneous injections. 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. 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, Management of Allergic/Anaphylactic Reactions (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. Dose (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
3. Following the first two vedolizumab intravenous doses administered at Week 0 and Week 2 in patients with ulcerative colitis, vedolizumab may be switched to subcutaneous injection at Week 6.

**Subcutaneous dosing and administration will not be discussed in the scope of this guideline*

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

D. Duration: Duration of therapy is dependent on patient response and adverse reactions

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

F. Warnings and Precautions

1. **Hypersensitivity Reactions**: reactions including dyspnea, bronchospasm, urticaria, flushing, rash, increased blood pressure, increased heart rate, and anaphylaxis 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. If anaphylaxis or other serious reactions occur, discontinue administration immediately and initiate appropriate emergency treatment.
2. **Infections:** Patients treated with vedolizumab are at an increased risk of developing infections. 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):** 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. Signs and symptoms of PML include progressive weakness on one side of the body, clumsiness of limbs, disturbances of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. 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**: There have been report of elevation of transaminase and/or bilirubin in patients receiving vedolizumab. Patients with jaundice or other evidence of significant liver injury should discontinue vedolizumab.
5. **Live Vaccines:** 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.
6. **Pregnancy and Lactation**: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to vedolizumab during pregnancy. Information about the registry can be obtained by calling 1-877-TAKEDA-7 (1-877-825-3327). Available pharmacovigilance data, data from the ongoing pregnancy registry, and data from published case reports and cohort studies in pregnant women have not identified a vedolizumab associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. There are risks to the mother and the fetus associated with inflammatory bowel disease in pregnancy. Published data suggest that the risk of adverse pregnancy outcomes in women with inflammatory bowel disease (IBD) is associated with increased disease activity. Adverse pregnancy outcomes include preterm delivery (before 37 weeks of gestation), low birth weight (less than 2,500 g) infants, and small for gestational age at birth. No fetal harm was observed in animal reproduction studies with intravenous administration of vedolizumab to rabbits and monkeys at dose levels 20 times the recommended human dosage. Data from a clinical lactation study show the presence of vedolizumab in human milk. The mean calculated daily infant dosage was 0.02 mg/kg/day orally. Systemic exposure in a breastfed infant is expected to be low because monoclonal antibodies are largely degraded in the gastrointestinal tract. There are no data on the effects of vedolizumab on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for vedolizumab and any potential adverse effects on the breastfed infant from vedolizumab or from the underlying maternal condition.

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

H. Adverse Reactions: Nausea (9%), arthralgia (12%), headache (12%), nasopharyngitis (13%), upper respiratory infection (7%), fatigue (6%), fever (9%), infusion reaction (4%)

I. Drug Interactions: Concurrent use with other immunosuppressants and biologics may result in increased immunosuppression and an increased risk of infection.

IV. ADMINISTRATIVE GUIDELINES

A. Administration: IV infusions should be given immediately after reconstitution and dilution. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.

B. Use an **in-line 0.2-micron low protein binding filter** as vedolizumab is a powder that needs reconstituted prior to dilution.

C. Do not co-administer other products in the same infusion IV line.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
1. Alcohol Swabs
2. Gloves
3. Tape
4. Peripheral IV access supplies for patients requiring peripheral IV access:
    a. IV start Kit
    b. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
    c. Extension set 8" with needless connector
5. Port access supplies for patients with a port
    a. Port needle (ex. 22 Gauge x ¾ to 1" safe step)
    b. Extension set 8" needless connector
    c. Central line dressing change kit
6. IV Pole
7. IV injection cap
8. IV administration set (flow regulator [ex: dial-a-flow] or gravity) with in-line or add-on **0.22 micron filter**
9. Syringes (10mL) with needles (20 G x 1")
10. Sharps container

B. Prescription Items:
1. Vedolizumab vial
2. Sterile water for injection vials
3. Bag of sodium chloride 0.9% for dilution 250mL
4. 50mL 0.9% sodium chloride flush bag- (requires 30mL of saline for post-infusion flush)

C. 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.

D. Storage and Handling
Store vials at 36°F to 46°F (2°C to 8°C) in original carton protected from light.

E. 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.

F. Procedures:
1. Explain the reasoning for visit and use of vedolizumab.
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication.
4. Establish venous access prior to preparation of drug.
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to: hypersensitivity reactions, infections, PML, signs and symptoms of liver injury, nausea, arthralgia, and headache.
6. 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 4 hours of preparation.

7. Infusion Rates: Infuse over a period of 30 minutes through a dedicated IV line.
8. Upon completion of the infusion: Flush the infusion set with 30 mL of 0.9% sodium chloride
9. Monitor patient and vital signs periodically during the infusion and for 30 minutes after the completion of the infusion per CarePathRx Nursing Best Practice Administration 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. 2023

United States Pharmacopeia (USP). General Chapter, <797> Pharmaceutical Compounding—Sterile Preparations. (2023) USP-NF. Rockville, MD: United States Pharmacopeia. Accessed November 29, 2023.

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

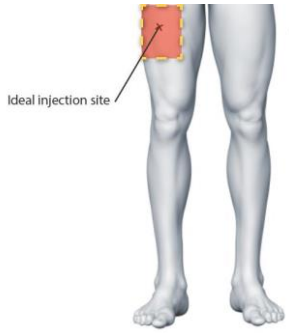
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampul of epinephrine

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 h**old 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.