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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.

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Bezlotoxumab (Zinplava) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: CG015
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Revised: N/A
Approved by: Kathleen Patrick, President, 10/01/2024

I. BACKGROUND

Zinplava (Bezlotoxumab) is a human monoclonal antibody that binds to C. difficile toxin B and neutralizes its effects. It is indicated to reduce recurrence of Clostridium difficile infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment for CDI and are at high risk for CDI recurrence. Bezlotoxumab is not indicated for the treatment of CDI and is not an antibacterial drug. It should only be used in conjunction with antibacterial drug treatment of CDI. The following outlines the procedures for servicing patients in need of outpatient bezlotoxumab 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
4. Other relevant social and/or medical history

C. Physician orders for Bezlotoxumab must include:

1. Patient weight
2. Drug
3. Dose (including weight-based dosage)
4. Route of administration
5. Frequency of administration
6. Emergency medications per protocol
7. Orders for pre-medications
8. Line care protocol
9. Routine lab monitoring, if applicable

D. Patient should have confirmed diagnosis of CDI and completing standard of care therapy (vancomycin, metronidazole, or fidaxomicin) for the baseline CDI episode.

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*)

III. PHARMACOLOGIC OVERVIEW

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

A. Indications

1. Reduction of recurrence of Clostridium difficile infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence.

B. Dosing

1. 10 mg/kg administered as single IV infusion
2. Dosing is based off actual body weight. Infliximab has not been studied in extremes of body weights

C. Dose Adjustments: No dose adjustments

D. Duration: One-time single dose

E. Contraindications: None

F. Warning/Precautions

1. Heart failure

a. Heart failure was reported more commonly in the two Phase 3 clinical trials in Bezlotoxumab -treated patients compared to placebo-treated patients. These adverse reactions occurred primarily in patients with underlying congestive heart failure (CHF). Additionally, in patients with a history of CHF, there were more deaths in Bezlotoxumab -treated patients than in placebo-treated patient during the 12-week study period. The causes of death varied and included cardiac failure, infections, and respiratory failure.
b. In patients with a history of CHF, Bezlotoxumab should be reserved for use when the benefit outweighs the risk.

2. Pregnancy and Lactation

a. Adequate and well controlled studies with ZINPLAVA have not been conducted in pregnant women. No animal reproductive and developmental studies have been conducted with bezlotoxumab.
b. There is no information regarding the presence of bezlotoxumab in human milk, the effects on the breast-fed infant, or the effects on milk production.

G. Pharmacokinetics

1. Vd ~ 7.33 L
2. Half-life ~ 19 days
3. Metabolism: catabolism into smaller peptides and amino acids

H. Adverse Reactions

1. >10% of patients
    a. Cardiovascular: Heart failure 2%; worsening of heart failure:13%), <5%

2. 1% to 10% patients
    a. Gastrointestinal: Nausea (7%)
    b. Hypersensitivity: Infusion-related reaction (10%)
    c. Nervous system: Headache (4%)
    d. Miscellaneous: Fever (5%)
    e. Cardiovascular: Heart failure 2%
    f. pyrexia (1%),
    g. dizziness (1%),
    h. dyspnea (1%)

3. <1% patients
    a. Ventricular tachyarrhythmia (<1%)

I. Drug Interactions

1. Since Bezlotoxumab is eliminated by catabolism, no metabolic drug-drug interactions are expected
2. Caution when using Fc receptor-binding agents (efgartigimod alfa and rozanolixizumab); monitor therapy

IV. ADMIMISTRATIVE 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. Infuse over 60 minutes through a sterile, nonpyrogenic, low-protein binding **0.2 to 5 micron** in-line or add-on filter. Do not administer as an IV push or bolus. May be infused via a central or peripheral line.

C. The safety and efficacy of repeat administration of bezlotoxumab in patients with CDI have not been studied

D. Do not co-administer other drugs simultaneously through the same infusion line.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol swabs
2. Gloves
3. Shoe covers
4. Face shield
5. Protective gown
6. Mask
7. Tape
8. Peripheral start kit
9. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾" for patients needing peripheral access)
    a. Extension set 8"
    b. Needless connector
    c. IV start kit
10. Non-coring needle for port access (ex. 22 Gauge x ¾ to 1" safe step for patients with a port)
    a. Dressing change kit
    b. Needless connector
11. 20-60 mL Luer Lock Syringe (size dependent on volume of drug needed)
12. Needles (ex: 18 gauge x 1")
13. IV administration set (dial-a-flow or gravity) with an in-line or add-on **0.2 to 5 micron filter**
14. IV pole
15. Sharps container

B. Prescription items:

1. Bezlotoxumab vial(s)
2. 0.9% Sodium Chloride Injection or 5% Dextrose Injection bag for dilution – appropriate volume to allow for a final concentration ranging from 1 mg/mL to 10 mg/mL
3. Standard flushes per protocol

C. How Supplied

Bezlotoxumab is a sterile, preservative-free, clear to moderately opalescent, colorless to pale yellow solution and is supplied as a 1,000 mg/40 mL vial. [Solution contains polysorbate 80]

D. Storage and Handling

Store in a refrigerator, 2ºC to 8ºC (36ºF to 46ºF) in original carton to protect from light. Do Not Freeze. Do Not Shake.

E. Compatibility

Dilute with either 0.9% Sodium Chloride Injection or 5% Dextrose Injection prior to use

F. Procedures:

1. Explain the reasoning for visit and use of bezlotoxumab.
2. Don shoe covers, gown, face/mask cover, and gloves prior to entering the patient's home. Wash hands with soap and water (not alcohol) before donning face mask with shield and a new pair of clean gloves
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing

medication. Notify ordering physician and pharmacist if signs or symptoms are present.

4. Establish venous access prior to preparation of drug.
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to heart failure, nausea, headache, and hypersensitivity reactions.
6. Prepare Product
    a. Remove bezlotoxumab from the refrigerator and allow to come to room temperature.
    b. Inspect vial contents for discoloration and particulate matter prior to dilution. Bezlotoxumab is a clear to moderately opalescent, colorless to pale yellow solution. Do not use the vial if the solution is discolored or contains visible particles.
    c. Withdraw the required volume from the vial(s) based on the patient's weight (in kg) and transfer into an intravenous bag containing either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to prepare a diluted solution with a final concentration ranging from 1 mg/mL to 10 mg/mL. Mix diluted solution by gentle inversion. Do not shake.
    d. Discard vial(s) and all unused contents and was hands with soap and water (not alcohol).
7. Infusion Rates
    a. Infuse over 60 minutes via a flow-regulated administration set.
8. Monitor patient and vitals periodically throughout the infusion and for at least 30 minutes after end of infusion per CarepathRx Nursing Best Practice Administration Guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy

1. Pregnancy status
2. Heart failure history
3. Confirmed diagnosis of CDI and receiving appropriate standard of care therapy

B. During therapy

1. Monitor for signs of clinical cure of the presenting CDI episode
2. Monitor for signs/symptoms of CDI recurrence
3. Monitor for adverse reactions
    a. Heart failure, Arrythmias
    b. Hypersensitivity reactions
    c. Dyspnea
    d. Headache
    e. Dizziness
    f. Fever

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

VII. REFRENCES

1. Zinplava (bezlotoxumab) [prescribing information]. Whitehouse Station, NJ; Merck & Co Inc: October 2016.

2. 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

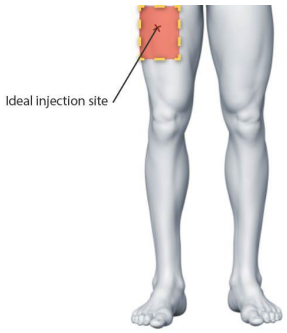
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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 ampule.**
3. Holding the ampule upright, **swirl and flick the ampule 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 ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **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 ampule 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 ampule.
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.