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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.

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.

Teprotumumab-trbw (Tepezza) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG019
Effective: 6/1/20
Reviewed: 6/1/20, 7/1/21, 2/10/25
Revised: 7/21, 2/10/25
Approved by, Title and Date Approved: Kathleen Patrick, President, 6/1/20, 7/1/21, 2/10/25

I. BACKGROUND

Teprotumumab is a full human monoclonal antibody used for the treatment of Thyroid Eye Disease (TED). TED is associated with a hyperactive thyroid gland, but it can also be the result of autoimmune disease. Patients with TED can suffer from inflammation, redness, pain, excessive dryness, proptosis, diplopia, vision impairment, corneal ulceration, optic nerve dysfunction, and insecurities with the appearance of bulging eyes. Teprotumumab is currently the only therapy with an FDA indication for the treatment of TED in adult patients and is formulated for IV administration. Teprotumumab targets and inhibits Insulin-like growth factor I receptor (IGF-1). In turn, the inhibition of insulin-like growth factor receptor prevents downregulation of cytokine and hyaluronan production and cellular differentiation. The following outlines the procedures for servicing patients in need of teprotumumab 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
4. Other relevant social and/or medical history

C. Physician orders for teprotumumab must include:

1. Patient weight
2. Drug and dose (including weight-based dosage)
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol
6. Orders for pre-medications

7. Line care protocol
8. Routine lab monitoring, if applicable

D. Baseline lab tests prior to therapy

1. Pregnancy tests are recommended for female patients of childbearing age.

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. PHARMACOLOGY OVERVIEW

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

A. Indications: Treatment of thyroid eye disease in adult patients regardless of disease activity or duration

B. Dosing:

1. Initial infusion: 10mg/kg
2. Infusions #2-8: 20 mg/kg

*Dosing is based off actual body weight. Teprotumumab has not been studied in extremes of body weights.

C. Dose Adjustment

1. No dose adjustments for renal or hepatic impairment
2. Doses should be administered every 3 weeks +/- one day

D. Duration: Treatments occur every 3 weeks for a total of 24 weeks (8 infusions) in one cycle. A subsequent cycle of treatment may be trialed for patients who do not respond to teprotumumab or have relapsing symptoms after the first cycle of 8 infusions. Dosing and duration are at the discretion of the treating physician or may be indicated by the patient's insurance.

E. Contraindications: None

F. Warnings and Precautions

1. **Infusions reactions**: may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with teprotumumab. Signs and symptoms of infusion-related reactions include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain. Infusion reactions may occur during any of the infusions or within 1.5 hours after an infusion. Reported infusion reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an

antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

2. **Exacerbation of Pre-existing Inflammatory Bowel Disease**: Teprotumumab may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of teprotumumab.

3. **Hyperglycemia:** Hyperglycemia or increased blood glucose may occur in patients treated with teprotumumab. In clinical trials, 10% of patients (two thirds of whom had pre-existing diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be controlled with medications for glycemic control, if necessary. Assess patients for elevated blood glucose and symptoms of hyperglycemia prior to infusion and continue to monitor while on treatment with teprotumumab. Ensure patients with hyperglycemia or pre-existing diabetes are under appropriate glycemic control before and while receiving teprotumumab.

4. **Hearing impairment and hearing loss:** may cause severe hearing impairment including hearing loss, which in some cases may be permanent. Assess patients' hearing before, during, and after treatment with teprotumumab and consider the benefit-risk of treatment with patients.

5. **Pregnancy and Lactation:** Based on findings in animals and its mechanism of action inhibiting insulin-like growth factor 1 receptor (IGF-1R), teprotumumab may cause fetal harm when administered to a pregnant woman. Adequate and well-controlled studies with teprotumumab have not been conducted in pregnant women. There is insufficient data with teprotumumab use in pregnant women to inform any drug associated risks for adverse developmental outcomes. In utero teprotumumab exposure in cynomolgus monkeys dosed once weekly with teprotumumab throughout pregnancy resulted in external and skeletal abnormalities. Teprotumumab exposure may lead to an increase in fetal loss. Therefore, teprotumumab should not be used in pregnancy, and appropriate forms of contraception should be implemented prior to initiation, during treatment and for 6 months following the last dose of teprotumumab. If the patient becomes pregnant during treatment, teprotumumab should be discontinued and the patient should be advised of the potential risk to the fetus.

    a. There is no information regarding the presence of teprotumumab in human milk, the effects on the breast-fed infant or the effects on milk production.

G. Pharmacokinetics:

1. Volume of Distribution: 3.6 L
2. Metabolism: Teprotumumab undergoes metabolism through proteolysis.
3. Elimination half-life: 20 days

H. Adverse Reactions

1. Alopecia (13%)
2. Nail disorders- includes nail discoloration, nail disorder and onychoclasis (5%)
3. Xeroderma (8%)
4. Diarrhea (12%)
5. Nausea (17%)

6. Altered sense of taste (8%)
7. Muscle cramps (25%)
8. Headache (8%)
9. Fatigue (12%)
10. Hyperglycemia (10%)
11. Hearing related adverse effects (sensorineural deafness, eustachian tube dysfunction, hyperacusis, hypoacusis, autophony and tinnitus) (10%)
12. Infusion reaction (4%)

I. Drug Interactions: No drug-drug interactions found. Drug-drug interactions may exist. Consult interaction database for patient specific assessment.

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 in-line or add on 0.2-micron low protein-binding filter.**

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

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. IV access supplies as applicable

    a. Peripheral IV access supplies for patients requiring peripheral IV access
        1) IV start Kit
        2) Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
        3) Extension set 8" with needless connector

    b. Port access supplies for patients with a port
        1) Port needle (ex. 22 Gauge x ¾ to 1" safe step)
        2) Extension set 8" needless connector
        3) Central line dressing change kit

5. IV Pole
6. IV injection cap
7. IV administration set (flow regulator [ex: dial-a-flow] or gravity) **with in-line or add-on 0.22 micron filter**
8. Syringes (10-50mL) with needles (20 G x 1")
9. Sharps container

B. Prescription Items:

1. Teprotumumab vial(s)
2. Sterile Water For Injection vial(s) (SWFI)
3. 100 or 250mL 0.9% normal saline stock bag
4. Standard flushes per protocol

C. How Supplied: Teprotumumab-trbw for injection is a sterile, preservative-free, white to off-white lyophilized powder available as follows: Carton containing one 500 mg single-dose vial NDC 75987-130-15.

D. Storage and Handling: Refrigerate at 2°C to 8°C (36°F to 46°F) in original carton until time of use to protect from light. Do not freeze.

E. Compatibility: Compatible with 0.9% normal saline solution

F. Procedures:

1. Explain the reasoning for visit and use of teprotumumab.
2. Don gloves
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication. Notify the ordering physician and pharmacist if signs or symptoms are present.
4. Obtain baseline vital signs and blood glucose level. There is currently no recommendation to hold the infusion based on hyperglycemia. If blood glucose level prior to infusion is > 250mg/dL:

    a. Determine patient's baseline levels (if routinely monitored)
    b. Assess recent oral intake and/or medication use for other causes of hyperglycemia
    c. Proceed with infusion based on clinical judgement and patient's status

5. Establish venous access prior to the preparation of drug.
6. Counsel patient on warnings, precautions, and potential side effects including but not limited to infusions related reactions, hyperglycemia, IBD flares, pregnancy risks, hearing adverse effects, muscles cramps, fatigue, nausea, and diarrhea.
7. Prepare the product

    a. Reconstitute each teprotumumab vial with 10mL of SWFI. Ensure stream of diluent is not directed onto the lyophilized powder. Swirl gently to dissolve powder. **Do not shake**.
    b. The reconstituted solution has a volume of 10.5mL. Visually inspect solution for any particulate matter or discoloration.
    c. Total dose of reconstituted product should be further diluted in 0.9% sodium chloride to a final max concentration of 18mg/mL. Withdraw volume of sodium chloride from the bag equivalent to amount of reconstituted teprotumumab prior to adding drug.
        1) If dose is 1800 mg or less, the total volume will be 100mL
        2) If dose is greater than 1800 mg, the total volume will be 250mL

8. Infusion rates: The first two infusions must be administered over 90 minutes after which the infusion time may be reduced to 60 minutes for infusions 3-8 if well tolerated.
9. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion and 30 minutes after the infusion is complete per CarePathRx Nursing Best Practice Administration Guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy:

1. Baseline labs
2. Counsel female patients of child-bearing age about the risks of getting pregnant during treatment and for 6 months after the last infusion. Assess for birth control, negative pregnancy test, or plans to get pregnant in near future.
3. Assess patients with a history of diabetes
4. Assess patients with a history of inflammatory bowel disease (Crohn's disease or Ulcerative colitis).

B. During Therapy:

1. For female patients of child-bearing age: Assess menstrual cycle, birth control regimen, negative pregnancy test, or chance of pregnancy.
2. For patients with IBD, assess if flare occurs during treatment or any changes with IBD maintenance medications.
3. Assess glucose levels and hyperglycemia specifically in patients with diabetes
4. Assessment of signs and symptoms of disease progression and therapy response (Teprotumumab Citus or Update Call assessment).
5. Assessment of any adverse effects (including changes in hearing, muscle cramps, alopecia, nausea, diarrhea, etc.).
6. For treatment purposes, nurses may request to take photographs of a patient's face to monitor proptosis, eye redness, and related clinical markers. Permission and actions must comply with institutional policy.*

*University of Pittsburgh Medical Center Policy HS-FM0214 provides permission to photograph for treatment purposes. Verify that *Authorization For Video, Audio, Recording, and Photographic Participation* (attachment A) is signed and on file in patient chart.

   a. Explain the reason why we are photographing
   b. Advise the patient that the photograph will be used for treatment purposes only
   c. Assure the patient that the photograph will be scanned and filed in the confidential electronic medical record
   d. Document administration on Teprotumumab Nursing Assessment form and forward with pictures to prescriber.

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

VII. REFERENCES:

Tepezza [package insert]. Lake Forest, IL. Horizon Therapeutics. 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

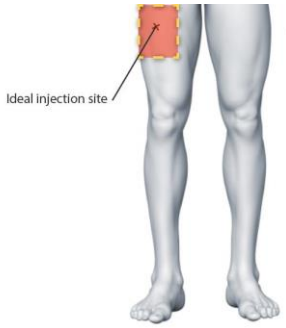
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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 ampul 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 ampul 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 not to 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 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.