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.

CLINICAL GUIDELINES FOR INTRAVENOUS PATISIRAN (ONPATTRO)

Section: Clinical Guidelines
Policy ID: CG044
Effective: 1/3/2023
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Revised: 12/1/2025
Approved by: Kathleen Patrick, President, 1/3/23, 12/1/25

I. BACKGROUND

Patisiran (Onpattro) is a double-stranded siRNA that causes degradation of mutant and wild-type TTR mRNA through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. Patisiran is indicated for use in the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults. The following outlines guidelines for servicing patients in need of outpatient intravenous patisiran.

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 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 must include:

1. Patient weight
2. Drug
3. Dose including weight-based dose
4. Route of administration
5. Frequency of administration
6. Emergency medications per protocol
7. Orders for required pre-medications:
    a. Intravenous corticosteroid (ex: dexamethasone 10 mg or equivalent
    b. Oral acetaminophen (500 mg)
    c. Intravenous H1 blocker (ex: diphenhydramine 50 mg or equivalent)
    d. Intravenous H2 blocker (ex: Famotidine 20mg IV or equivalent)
8. Line care protocol
9. Routine lab monitoring, if applicable

D. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless more comprehensive patient-specific orders are provided by the 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 polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

B. Dosing:

1. <100kg: 0.3mg/kg IV once every 3 weeks
2. ≥100kg: 30 mg IV once every 3 weeks

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

C. Dose adjustments:

1. No renal or hepatic dosing adjustments.
2. Missed dose: If a dose is missed, administer patisiran as soon as possible. If therapy is administered within 3 days of the missed dose, continue dosing according to the patient's original schedule. If patisiran is administered more than 3 days after the missed dose, continue dosing every 3 weeks thereafter.

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

E. Contraindications: None.

F. Warnings and Precautions:

1. **Infusion reactions**: Majority occurs within the first two infusions and frequency decreases with additional infusion. Common symptoms include abdominal, back, or chest pain, dyspnea, facial edema, flushing, headache, nausea, rash, and tachycardia. Monitor closely following the start of infusion. Consider slowing or interrupting infusion for infusion reactions. Patients should receive pre-medications with each infusion. Pre- medicate 60 minutes prior to patisiran administration.
2. **Reduced Vitamin A levels**: a decrease in serum Vitamin A has been reported with treatment of patisiran. Supplement Vitamin A at recommended daily allowance (RDA) during treatment. Higher than RDA doses are not recommended. Monitor for ocular symptoms associated with vitamin A deficiency (e.g., night blindness). Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of a Vitamin A deficiency
3. **Pregnancy/lactation:** Patisiran decreases vitamin A levels required for normal fetal development. Effects to the fetus are unknown for maternal vitamin A supplementation. Effects to the fetus of reducing maternal serum transthyretin are also unknown. There is a pregnancy exposure registry that monitors pregnancy

outcomes in women exposed to patisiran during pregnancy. Physicians are encouraged to enroll patients at alnylampregnancyprogram@iqvia.com. It is unknown if patisiran passes into breast milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for patisiran and any potential adverse effects on the breastfed infant from patisiran or from the underlying maternal condition.

G. Pharmacokinetics:

1. Onset of action: 10 to 14 days (mean serum TTR reduced by 80%)
2. Volume of distribution: 0.26 L/kg
3. Metabolism: patisiran is primarily metabolized in the liver by nucleases to nucleotides.
4. Half-life elimination: 3.2 ± 1.8 days
5. Excretion: urine: <1% as unchanged drug

H. Adverse Reactions:

1. Upper respiratory infection (29%)
2. Miscellaneous infusion reactions (19%): abdominal or back pain, flushing, headache, hypotension, nausea, pruritus, and syncope
3. Cardiovascular (3%): atrioventricular block
4. Dermatological (7%): erythema of skin
5. Gastrointestinal (8%): dyspepsia
6. Nervous System (5%): vertigo
7. Neuromuscular & skeletal: arthralgia (7%), muscle spasm (8%)
8. Ophthalmic: blurred vision (3%), dry eye syndrome (5%), vitreous opacity (2%)
9. Respiratory: bronchitis (7%), dyspnea (8%)
10. Miscellaneous: vitamin A deficiency, antibody development

I. Drug Interactions:

1. No Known Drug Interactions
2. 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. Required Pre-medications: Pre-medicate 60 minutes prior to infusion:

1. Intravenous corticosteroid. Dexamethasone 10 mg IV or equivalent. In patients who tolerate infusions but experience adverse reactions from the corticosteroid, the corticosteroid dose may be reduced by 2.5 mg increments to a minimum dose of 5mg IV dexamethasone, or equivalent.
2. Acetaminophen 500 mg by mouth
3. Intravenous H1 blocker: Diphenhydramine 50mg IV or equivalent
4. Intravenous H2 blocker. Famotidine 20 mg IV or equivalent

5. Some patients may require additional or higher doses of one or more of the pre-medications listed above to reduce the risk of infusion-related reactions.
6. For premedication not available or not tolerated IV, equivalents may be administered orally.

C. A sterile **0.45-micron polyethersulfone (PES) syringe filter** is required to filter drug product prior to administration.

D. A **1.2-micron polyethersulfone (PES) in-line filter** is required for administration**.** Infusion sets and lines should be DEHP-free.

E. Do not co-administer patisiran with other IV therapies in the same IV 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) Needless connector
        3) Central line dressing change kit

5. IV Pole
6. Syringes (10-20 mL) with needles (20 G x 1")
7. 0.45-micron PES syringe filter
8. Sterile container (ex: glass vial or syringe)
9. Sharps container
10. Supplies if utilizing a pole mounted ambulatory infusion pump:

    a. Ambulatory pump tubing with **1.2-micron filter**
    b. Pole mounted ambulatory pump
    c. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
    d. Battery change procedure teaching sheet
    e. Continuous delivery mode teaching sheet
    f. Pump return box

B. Prescription items:

1. Vials of patisiran

2. 0.9% sodium chloride diluent bag (supplied as either a 250 mL stock bag or prefilled saline bag)
3. 0.9% sodium chloride 50 mL post infusion flush bag
4. Standard flushes per protocol
5. Required pre-medications including:

    a. Dexamethasone 10 mg IV or equivalent
    b. Acetaminophen 500 mg
    c. Diphenhydramine 50mg IV or equivalent
    d. Famotidine 20 mg IV or equivalent

6. Anaphylaxis kit per protocol

C. How Supplied:

1. Patisiran is a sterile, preservative-free, and white to off-white, opalescent, homogeneous solution for supplied as a 10 mg/5 mL solution in a single-dose glass vial. A white to off-white coating may be observed on the inner surface of the vial, typically at the liquid-headspace interface. The vial stopper is not made with natural rubber latex.

D. Storage and Handling:

1. Store undiluted vial at 2°C to 8°C (36°F to 46°F). Do not freeze. Discard vial if has been frozen.
2. If refrigeration is not available, patisiran can be stored at room temperature up to 25°C (up to 77°F) for up to 14 days.

E. Compatibility: Compatible with 0.9% normal saline

F. Procedures

1. Explain reason for visit and use of patisiran
2. Don gloves
3. Obtain baseline vital signs
4. Establish venous access prior to preparing medication
5. Counsel patient on warnings, precautions and potential side effects including but not limited to infusion reactions, abdominal or back pain, flushing, headache, nausea, anaphylactic reaction.
6. Administer ordered pre-infusion medications (corticosteroids, antihistamines, and acetaminophen) one hour prior to administration of patisiran.
7. Prepare product:

    a. Allow vials to warm to room temperature. Do not shake or vortex
    b. Calculate the dose based on recommended weight-based dosage.
    c. Withdraw entire contents of one or more vials into a single syringe.
    d. Filter patisiran through a 0.45-micron PES syringe filter into sterile container (ex: sterile vial or syringe)
    e. After filtering into a sterile container (vial or syringe), discard syringe with filter needle.

f. Withdraw the required volume of filtered patisiran from the sterile container using a new sterile syringe with regular needle.
g. Dilute the required volume of filtered patisiran into a DEHP-free infusion bag containing 0.9% sodium chloride solution for a total volume of 200mL.
    1) If stock bag is being used, the appropriate volume of NS will need to be removed prior to adding patisiran to NSS bag.

h. Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other drugs.
i. Discard any unused portion of patisiran.

8. Administer product:

    a. Use a dedicated line containing a **1.2-micron PES in-line filter.** Use infusion sets and lines that are DEHP-free.
    b. Infuse via an ambulatory infusion pump, over 80 minutes, at an initial infusion rate of approximately 1 mL/min for the first 15 minutes, then increase to 3 mL/min for the remainder of the infusion
    c. May increase the duration of the infusion to manage or prevent infusion related reactions.

9. After completion of infusion, flush the entire administration tubing with 0.9% sodium chloride to ensure all of the medication is administered. Spike the 50mL 0.9% Sodium chloride flush bag and administer the flush at the same rate as the infusion of patisiran to ensure all drug has been administered.
10. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion including the ramp up period. Continue to monitor the patient and vital signs 30 minutes after the infusion is complete per CarePathRx Nursing Best Practice Administration Guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy:

1. Vitamin A level
2. Confirm patient is taking Vitamin A supplementation

B. During therapy:

1. Monitor for signs and symptoms of Vitamin A deficiency such as changes in vision, especially night blindness. Continued Vitamin A supplementation
2. Monitor for any adverse effects. Most commonly upper respiratory infections, musculoskeletal pain, headache, hypotension, nausea, or pruritis.
3. Monitor for signs and symptoms of infusion reactions and anaphylaxis during administration.
4. Monitor for disease progression and symptoms including peripheral neuropathy, carpal tunnel syndrome, heart palpitations, edema, shortness of breath, wheezing, nausea, and vomiting.

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

REFERENCES

Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; 2022

Onpattro: New Drug Approval. Miami, FL. IPD Analytics; August 2022.

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

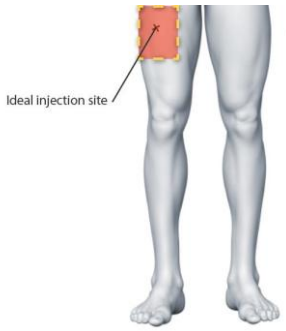
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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 ampul. **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 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.