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CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

CLINICAL GUIDELINES FOR INTRAVENOUS PATISIRAN (ONPATTRO)

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: NUR254
Effective: 1/3/23
Reviewed:
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Approved by: Kathleen Patrick, President, 1/3/23

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 (intravenous) in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. 19% of patients in clinical trials experienced an infusion related reaction with 79% experienced with the first two infusions. The following criteria will be evaluated:
   1. Prescriber preference
   2. Allergy profile
   3. Age > 18 years old
   4. Ability to secure contracted nursing for subsequent infusions
   5. Other relevant social and/or medical history

C. Physician orders must include:
   1. Patient weight

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

D. Recommended baseline serum vitamin A level

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

III. PHARMACOLOGIC OVERVIEW

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

A. Indications
    1. Treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

B. Dosing
    1. IV dosing is based on actual body weight:
        a. <100kg: 0.3mg/kg once every 3 weeks
        b. ≥100kg: 30mg once every 3 weeks
        c. No renal or hepatic dose adjustments

C. Contraindications
    1. Severe hypersensitivity to patisiran or any component of the formulation.

D. Precautions
    1. Reduced vitamin A levels
        a. A decrease in serum vitamin A has been reported with treatment. Supplement at recommended daily allowance (RDA) of vitamin A during treatment. Higher than RDA doses are not recommended.
        b. Monitor for ocular symptoms associated with vitamin A deficiency (e.g., night blindness)

c. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of a Vitamin A deficiency

2. Pregnancy/lactation:
    a. 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.
    b. 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.
    c. It is unknown if patisiran passes into breast milk.

3. Infusion reactions:
    a. Majority are occurring 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.

E. 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

F. Drug Interactions
1. No known drug interactions

G. Pharmacokinetics
1. Onset of action: 10 to 14 days (mean serum TTR reduced by 80%)
2. Volume of distribution: 0.26 ± 0.2L/kg
3. Half-life elimination: 3.2 ± 1.8 days
4. Excretion: urine: <1% as unchanged drug

IV. ADMINISTRATIVE GUIDELINES

A. Required Pre-medications: Pre-medicate 60 minutes prior to infusion:
   1. Intravenous corticosteroid. Dexamethasone 10mg 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 500mg by mouth
   3. Intravenous H1 blocker. Diphenhydramine 50mg IV or equivalent
   4. Intravenous H2 blocker. Famotidine 20mg 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.

B. Intravenous Administration
   1. **Use 1.2-micron polyethersulfone (PES) in-line filter. Infusion sets and lines should be DEHP-free.**
   2. 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. May increase duration to manage or prevent infusion related reactions.
   3. Do not co-administer other IV medications during infusion
   4. Diluted solution must be used within one hour of preparation per current USP Immediate-Use Guidelines.

C. Missed Doses
   1. If a dose is missed, administer patisiran as soon as possible.
      i. If patisiran is administered within 3 days of the missed dose, continue dosing according to the patient's original schedule.
      ii. If patisiran is administered more than 3 days after the missed dose, continue dosing every 3 weeks thereafter.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
   1. Supplies (use infusion sets and lines that are DEHP-free)
   2. Alcohol swabs
   3. Vials of patisiran
   4. Syringes (10-20mL) with needles (ex: 20G x1")
   5. 0.45-micron PES syringe filter
   6. Sterile container (ex: glass vial or syringe)
   7. Saline stock bag (250mL) or prefilled saline bag
   8. Gloves
   9. Tape
   10. IV start kit
   11. Peripheral IV catheter
   12. Central IV-line kit if patient has a central line

13. Port access needles if patient has a port
14. 8” extension set
15. IV injection cap
16. Infusion pump tubing with **1.2-micron filter**
17. Pole mounted infusion pump
18. Batteries for infusion pump (9 Volt Duracell battery or 4 Double A batteries)
19. Battery change procedure teaching sheet
20. Pump delivery mode teaching sheet
21. Pump return box
22. IV pole and pole clamp
23. Saline flush bag (50mL)

B. 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 not available, patisiran can be stored at room temperature up to 25°C (up to 77°F) for up to 14 days.

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.
    2. Dispensing pharmacy will provide prefilled bags, or the nurse will need to remove saline from a stock bag for total volume of 200mL.

D. Compatibility
    1. Compatible with 0.9% normal saline.

E. Procedure
    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 vial 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 of more vials into a single syringe.
        d. Filter patisiran via a 0.45-micron PES syringe filter into sterile container.

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.
    i. 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.
        a. May increase duration to manager or prevent infusion related reactions
    c. After completion of infusion, flush the administration set with 0.9% normal saline to ensure all drug has been administered.
    d. Do not co-administer other IV medications during infusion.
9. Monitoring
    a. Monitor the infusion site for possible infiltration during drug administration.
    b. Monitor patient for infusion reactions or anaphylaxis during administration.
    c. Follow Protocol for Management of Adult Infusion Reactions & have anaphylaxis kit for infusion or anaphylaxis reactions (Appendix A).
    d. Patients with history of severe infusion reactions should only be considered for home infusion after a thorough discussion of safety for the patient and risk vs. benefit with physician. If home infusion continues, a slower infusion rate will be utilized.
    e. The nurse should remain with the patient for at least 30 minutes following medication administration to monitor vital signs and response to therapy.

VI. CLINICAL MONITORING

A. Monitor for signs and symptoms of infusion reactions and anaphylaxis during administration of medication.
    1. Slowing the infusion rate can mitigate adverse effects and decrease infusion related reactions.

B. During administration, monitor IV site for extravasation.

C. Monitor for any adverse effects. Most commonly upper respiratory infections, musculoskeletal pain, headache, hypotension, nausea, or pruritis.

D. Patient should be monitored for signs of vitamin A deficiency such as changes in vision, especially night blindness.

E. If vitamin A levels are low, consult with a physician for possible supplementation.

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.

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

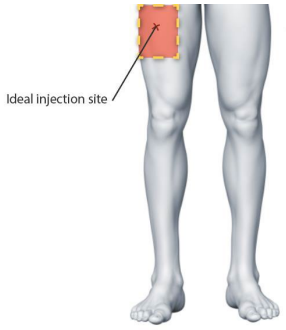
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampul of epinephrine

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.