Patisiran: Preparation and Administration

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SUMMARY

- The protocol for preparation of patisiran includes filtering the drug through a 0.45 micron PES filter into a sterile container (i.e., glass container, vial, or sterile syringe) prior to diluting in a DEHP-free infusion bag containing 0.9% Sodium Chloride Injection, USP (normal saline). The prepared drug is then infused from the bag through an in-line 1.2 micron PES filter.[1]
- The final total volume of the prepared patisiran dose is 200 mL.[1]
  - If using a 250 mL infusion bag, it is necessary to remove the calculated volume of patisiran plus 50 mL of normal saline to ensure that the final total volume is 200 mL.[2]

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ONPATTRO PRESCRIBING INFORMATION – RELEVANT CONTENT

The DOSAGE AND ADMINISTRATION section provides the following information[1]:

Preparation Instructions

ONPATTRO must be filtered and diluted prior to intravenous infusion. The diluted solution for infusion should be prepared by a healthcare professional using aseptic technique as follows:

- *Remove ONPATTRO from the refrigerator and allow to warm to room temperature. Do not shake or vortex.*
- *Inspect visually for particulate matter and discoloration. Do not use if discoloration or foreign particles are present. ONPATTRO is a white to off-white, opalescent, homogeneous solution. A white to off-white coating may be observed on the inner surface of the vial, typically at the liquid-headspace interface. Product quality is not impacted by presence of the white to off-white coating.*
- *Calculate the required dose of ONPATTRO based on the recommended weight-based dosage [see Dosing Information below].*
- *Withdraw the entire contents of one or more vials into a single sterile syringe.*
- *Filter ONPATTRO through a sterile 0.45 micron polyethersulfone (PES) syringe filter into a sterile container.*
- *Withdraw the required volume of filtered ONPATTRO from the sterile container using a sterile syringe.*

- *Dilute the required volume of filtered ONPATTRO into an infusion bag containing 0.9% Sodium Chloride Injection, USP for a total volume of 200 mL. Use infusion bags that are di(2-ethylhexyl)phthalate-free (DEHP-free).*
- *Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other drugs.*
- *Discard any unused portion of ONPATTRO.*
- *ONPATTRO does not contain preservatives. The diluted solution should be administered immediately after preparation. If not used immediately, store in the infusion bag at room temperature (up to 30°C [86°F]) for up to 16 hours (including infusion time). Do not freeze.*

Infusion Instructions

- *Use a dedicated line with an infusion set containing a 1.2 micron polyethersulfone (PES) in-line infusion filter. Use infusion sets and lines that are DEHP-free.*
- *Infuse the diluted solution of ONPATTRO intravenously, via an ambulatory infusion pump, over approximately 80 minutes, at an initial infusion rate of approximately 1 mL/min for the first 15 minutes, then increase to approximately 3 mL/min for the remainder of the infusion. The duration of infusion may be extended in the event of an infusion-related reaction (IRR).*
- *Administer only through a free-flowing venous access line. Monitor the infusion site for possible infiltration during drug administration. Suspected extravasation should be managed according to local standard practice for non-vesicants.*
- *Observe the patient during the infusion and, if clinically indicated, following the infusion.*
- *After completion of the infusion, flush the intravenous administration set with 0.9% Sodium Chloride Injection, USP to ensure that all ONPATTRO has been administered.*

Dosing Information

ONPATTRO should be administered by a healthcare professional.

ONPATTRO is administered via intravenous (IV) infusion. Dosing is based on actual body weight.

For patients weighing less than 100 kg, the recommended dosage is 0.3 mg/kg once every 3 weeks.

For patients weighing 100 kg or more, the recommended dosage is 30 mg once every 3 weeks.

RELEVANT INFORMATION

Filling Volume of the Patisiran Vial

Patisiran is supplied as a 10 mg/5mL solution in a single-dose glass vial. Patisiran is filled into vials to a nominal volume of 5.0 mL with a specification for the extractable volume of "not less than 5.0 mL." The process is designed to have a target weight of 5.5 g (5.4 mL) with a range of 5.2 g to 5.8 g (5.1 mL to 5.7 mL).[3]

Sterile Containers

Patisiran must be withdrawn into a sterile syringe from the vial and then filtered through a 0.45 micron PES syringe filter into a sterile container.[1] Options for sterile containers include glass containers, vials, or sterile syringes.

Filtering Directly from Vial to Infusion Bag

Patisiran must be withdrawn into a sterile syringe from the vial and then filtered through a 0.45 micron PES syringe filter into a sterile container.[1] Filtering patisiran directly out of the vial could cause shearing of the lipid nanoparticles due to increased pressure and prevent the active drug from being delivered to the hepatocytes, therefore this is not recommended.

Final Total Volume of Patisiran Infusion Bag

The final total volume of the prepared patisiran dose is 200 mL.[1] If using a 250 mL infusion bag, it is necessary to remove the calculated volume of patisiran plus 50 mL of normal saline to ensure that the final total volume is 200 mL.[2]

Preparation - Filtration

The protocol for preparation of patisiran includes filtering the drug through a PES filter prior to diluting in an infusion bag of normal saline. The prepared drug is then infused from the bag through a second in-line PES filter of 1.2 micron pore size.[1] These 2 filtration steps ensure delivery of patisiran without residual particles that could cause filter-clogging events during the infusion.

Administration - Extravasation Prevention

Per the APOLLO study manual for patisiran administration, the infusion was administered via a peripheral catheter using an IV cannula or catheter between 18-22 G, or via a central line.[2]

The following recommendations were provided to minimize the risk of extravasation if patisiran was administered via a peripheral line[2]:

- Select a large vein away from joints or tendons, if possible, such as in the forearm. Warming with water may help to dilate veins.
- Do not use a pre-existing IV of questionable placement, function, or unknown size.
- Make a clean venipuncture. Leave the needle entry site visible for observation during the infusion.
- Have IV flowing freely at all times with normal saline. Ensure good IV flow prior to patisiran drug administration.
- Ensure infusion pump is set at the appropriate rate and that the drug infusion tubing is connected to the 3-way stopcock. Initiate patisiran and watch the infusion site to ensure good flow. Check the infusion site every 2-3 minutes for any evidence of extravasation (swelling or erythema). If there is increased pain during the infusion, check for any evidence of extravasation.
- Flush with normal saline.
- Elevate limb and maintain gentle pressure over the venipuncture site for 5 minutes after needle withdrawn.

The following recommendations were provided to minimize the risk of extravasation if patisiran was administered via a central venous catheter[2]:

- Prior to administration of patisiran, blood should first be aspirated to ensure location in the vein.
- A bolus of normal saline (approximately 25 mL) should be infused to ensure free flow without local discomfort or swelling. Patisiran can then be administered.
- Following infusion of patisiran, the device should be flushed with at least 25 mL of normal saline.

Compatibility Studies

Patisiran is formulated as lipid nanoparticles for delivery to hepatocytes.[1] Due to the hydrophobic nature of the lipid nanoparticles, and an increased propensity for leaching of the plasticizer DEHP from PVC contact surfaces that contain this plasticizer, only DEHP-free PVC, or non-PVC DEHP-free infusion components have been assessed for compatibility. These data support the infusion of patisiran using infusion sets and lines that are DEHP-free.[4]

ABBREVIATIONS

DEHP = di(2-ethylhexyl)phthalate; IRR = infusion-related reaction; IV = intravenous; PES = polyethersulfone; PVC = polyvinyl chloride; USP = United States Pharmacopeia.

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REFERENCES

1. ONPATTRO (patisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.
2. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTR02-1800579.
3. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTR02-1900006.
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTR02-1900027.