

## Patisiran: Filters for Preparation and Infusion

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### SUMMARY

- The protocol for preparation of patisiran includes filtering the drug through a 0.45 micron 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.<sup>1</sup>
  - If 0.45 micron PES filters are unavailable, a 0.2 micron PES filter can be used; however, each vial of patisiran will require filtration through a separate 0.2 micron filter due to the smaller pore size.
- In the APOLLO study, 0.2 micron syringe filters were used to prepare patisiran. Study drug was then administered with a non-DEHP extension set with a PES 1.2 micron in-line infusion filter.<sup>2</sup>
- In the APOLLO-B, HELIOS-A, and Global OLE studies, sites were allowed the choice to use 0.2 micron or 0.45 micron PES syringe filters for preparation of patisiran.<sup>3-5</sup>

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### ONPATTRO PRESCRIBING INFORMATION – RELEVANT CONTENT

The **DOSAGE AND ADMINISTRATION** section provides the following information<sup>1</sup>:

#### **Preparation Instructions**

- *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).*

### **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.

## **RELEVANT DOSING AND PREPARATION INFORMATION**

Patisiran may form small amounts of aggregated particles if stored at room temperature and if subjected to mechanical stress, such as in conditions of shipping, shaking, or vibrations. During the time of exposure of patisiran to room temperature, excessive shaking or vibrations may create aggregated particles that can clog the 1.2 micron in-line infusion filter, which may require replacement.<sup>6</sup>

The protocol for preparation of patisiran includes filtering the drug through a 0.45 micron 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.<sup>1</sup> The 1.2 micron PES in-line infusion filter removes any particles potentially present in the infusion bag. The use of the 0.45 micron syringe filter prior to dilution of patisiran in the infusion bag minimizes the particle load the 1.2 micron filter must address in order to minimize back pressure that can trigger infusion pump shutdown.<sup>6</sup> If 0.45 micron PES filters are unavailable, a 0.2 micron PES filter can be used; however, each vial of patisiran will require filtration through a separate 0.2 micron filter due to the smaller pore size.

An additional vial of patisiran may be required to prepare the full recommended dose, depending on the type of filter used and the amount of product that remains in the filter (hold-up volume). Consult the dispensing pharmacy or filter manufacturer to determine the expected hold-up volume for the filter used to prepare each patisiran dose.

## **CLINICAL TRIALS EXPERIENCE**

In the APOLLO study, 0.2 micron syringe filters were used to prepare patisiran. Study drug was then administered with a non-DEHP extension set with a PES 1.2 micron in-line infusion filter.<sup>2</sup>

In the APOLLO-B, HELIOS-A, and Global OLE studies, sites were allowed the choice to use 0.2 micron or 0.45 micron PES syringe filters for preparation of patisiran.<sup>3-5</sup> If the site chose to use a 0.45 micron syringe, the entire contents of one or more vials could be drawn up into the syringe and filtered through the single, sterile 0.45 micron PES syringe filter into a sterile container. If a 0.2 micron syringe was used, the entire contents of one vial would be withdrawn into the sterile syringe and filtered through the 0.2 micron filter into a sterile container. This was repeated for each additional vial, as needed, using a new syringe filter for each vial.<sup>2</sup>

## **LABORATORY EXPERIENCE**

### **Filtration Study**

A study was conducted to determine the differences between the 0.2 micron pore size syringe filters and 0.45 and 1.2 micron pore size syringe filters. This study aimed to evaluate the filters' effect on quality attributes and filterability. In an attempt to simplify the dose preparation procedure, alternative methods of filtration, and alternative filters, were evaluated.<sup>7</sup>

Filterability was significantly improved by increasing the pore size to the 0.45 micron filter. Additionally, a 0.45 micron filter produced the same desirable effects as a 0.2 micron filter when filtering the maximum clinically relevant dose through a single filter, but without the risk of incomplete filtration as seen with the 0.2 micron syringe filter. Lipid content and assay results with the 1.2 micron pore size syringe filter indicated a difference between the 0.2 and 1.2 micron filters that specifically affected the lipid nanoparticles.<sup>7</sup>

### Hold-up Volume Study

An evaluation of clinical syringe filters and vial hold-up volume for patisiran was conducted. The objectives were to determine average volume loss and assess the potential product loss when various types of syringe filters were used to prepare the product.<sup>8</sup>

During an internal laboratory simulation, 20 vials of patisiran were filtered through five different syringe filters<sup>8</sup>:

- Millipore Millex-GP 0.22-micron 33 mm PES Syringe Filters, Ref# SLGP033RS
- Pall PharmAssure 0.2-micron 25 mm PES Syringe Filters, Part# HP1002
- Millipore Millex-HP 0.45-micron 33 mm PES Syringe Filters, Part# SLHPM33RS
- Pall PharmAssure 0.45-micron 32 mm PES Syringe Filters, Part# HP4644
- Pall PharmAssure 1.2-micron 25 mm PES Syringe Filters, Part# HP1012

Product loss ranged from 0.5 mL to 1.1 mL amongst the filters; results were consistent with the product inserts provided by the manufacturer of each filter. Average syringe filter hold-up volumes for all filters tested are in **Table 1**.

**Table 1. Average Syringe Filter Hold-up Volume.**<sup>9–13</sup>

Syringe Filter	Average Filter Hold-up Volume (mL)
Millipore Millex-GP 0.22-micron 33 mm PES Syringe Filter	0.5
Pall PharmAssure 0.2-micron 25 mm PES Syringe Filter	0.6
Millipore Millex-HP 0.45-micron 33 mm PES Syringe Filter	0.6
Pall PharmAssure 0.45-micron 32 mm PES Syringe Filter	1.1
Pall PharmAssure 1.2-micron 25 mm PES Syringe Filter	0.7

Abbreviations: PES = polyethersulfone.

For additional information regarding the filters above, please contact the respective manufacturers.

### Compatibility Study

#### PES Syringe Filters

Results from a compatibility and stability evaluation of the patisiran admixture with commonly used IV administration devices demonstrated that PES filters were compatible with LNPs. The IV administration devices were tested in four different configurations, and all the filters used in each configuration were PES filters. Other types of filters were not tested, thus PES filters are recommended.<sup>14</sup>

#### In-line Filters

The IV administration devices were tested in four different configurations, and all the in-line filters used in each configuration were 1.2 µm filters. Other sizes of filters were not tested, thus 1.2 µm in-line filters are recommended.<sup>14</sup>

## ABBREVIATIONS

DEHP = di(2-ethylhexyl)phthalate; IV = intravenous; LNP = lipid nanoparticle; OLE = open label extension; PES = polyethersulfone; Ref = reference.

*Updated 5 November 2025*

## REFERENCES

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