ONPATTRO®

(patisiran) 2 mg/mL concentrate for solution for infusion

Educational Material for Healthcare Professionals to ensure safe use of Onpattro in the home setting

07 July 2023 (date of HPRA approval)

. Healthcare professionals are asked to report any suspected adverse reactions via one of the following routes:

Alnylam: Alnylam Netherlands B.V. Tel: 0818 882213
or free phone: 1800 924 260
medinfo@alnylam.com

National reporting system: HPRA Pharmacovigilance
Website: www.hpra.ie

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This document concerning the administration of Onpattro® has been created in accordance with ordinance included in the marketing authorisation. Additional risk minimisation measures beyond routine measures have been stipulated in the marketing authorisation of the product, in order to ensure the safe and sustainable administration of Onpattro in the home setting, minimizing the risk of Infusion Related Reactions (IRRs) and to increase the benefit-risk ratio of Onpattro. This document is therefore, an integral and mandatory part of the marketing authorisation to ensure healthcare professionals who prescribe Onpattro and patients are aware of the special safety requirements and that they take these into consideration.

1. Introduction

This guide is intended to supplement the information provided in the Summary of Product Characteristics (SmPC) and in the printed Package Leaflet (PL). Please check that you have read and understood both documents before considering administration of Onpattro to your patient in the home.

2. Suitability of the Patient for Home Infusion

Infusion of Onpattro at home should only be considered for patients who have tolerated at least 3 infusions well in the clinic. Home infusions should be performed by a healthcare professional.

The treating physician should determine the patient's suitability to receive Onpattro infusion in the patient's home setting after evaluating the patient. Outlined below are some of the points that may help the treating physician decide whether the patient is suitable to receive home infusions:

- **Onpattro experience in the clinic**
  - Has the patient received at least 3 Onpattro infusions in a clinical setting and tolerated them well (i.e. without any Infusion Related Reaction (IRRs))?
- **Medical circumstances**
  - Is the patient medically stable?
- **Social and environmental circumstances**
  - Is the patient's residence conducive to home infusion therapy (e.g., appropriate space for infusion preparation, electricity, water and telephone access)?
- **Communication of risks to the patient**
  - Have the risks of delivering Onpattro at home been discussed with the patient?
  - Have the patient educational materials been discussed with the patient?
- **Communication of risks and administration requirements to the HCP responsible for administration of Onpattro in the home setting**
  - Have the educational materials been discussed with, and provided to, the HCP administering Onpattro to the patient at home?

3. Administering Onpattro

The recommended dose of Onpattro is 300 micrograms per kg body weight administered via intravenous (IV) infusion once every 3 weeks. Dosing is based on actual body weight. For patients weighing ≥ 100 kg, the maximum recommended dose is 30 mg.

Supplemental Medications Needed for Administering Onpattro

- Premedications (corticosteroid, paracetamol, H1 and H2 blocker)
- Medication to treat IRRs (epinephrine pen [Epi-pen], IV fluids, corticosteroid, anti-histamines, paracetamol/non-steroidal anti-inflammatory drugs [NSAIDs])

Administration of Premedications

All patients should receive premedication prior to Onpattro administration to reduce the risk of IRRs. Each of the following medicinal products should be given on the day of Onpattro infusion at least 60 minutes prior to the start of infusion:

- IV corticosteroid (dexamethasone 10 mg, or equivalent)
- Oral paracetamol (500 mg)
- IV H1 blocker (diphenhydramine 50 mg, or equivalent)
- IV H2 blocker (ranitidine 50 mg, or equivalent)

For premedications not available or not tolerated intravenously, equivalents may be administered orally.

Method of Preparation

- Inspect visually for particulate matter and discolouration. Onpattro is a white to off-white, opalescent, homogeneous solution. Do not use if discolouration or foreign particles are present.
- Calculate the required volume of Onpattro based on the recommended weight-based dosage (see above and SmPC section 4.2).
- 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 sodium chloride 9 mg/mL (0.9%) solution for a total volume of 200 mL. Use infusion bags that are free of di(2-ethylhexyl)phthalate (DEHP).
- Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other medicinal products.
- Discard any unused portion of Onpattro. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Method of Infusion

- Onpattro must be diluted prior to IV infusion.
- A dedicated line with an infusion set containing a 1.2 micron polyethersulfone (PES) in-line infusion filter must be used. The infusion sets and lines must be free of di(2-ethylhexyl)phthalate (DEHP).

- The diluted solution of Onpattro should be infused intravenously over approximately 80 minutes at an initial infusion rate of approximately 1 mL/min for the first 15 minutes, followed by an increase to approximately 3 mL/min for the remainder of the infusion. The duration of infusion may be extended in the event of an IRR.
- Onpattro must be administered through a free-flowing venous access line. The infusion site should be monitored for possible infiltration during administration. Suspected extravasation should be managed according to local standard practice for non-vesicants.
- The patient should be observed during the infusion and, if clinically indicated, following the infusion.
- After completion of the infusion, the IV administration set should be flushed with sodium chloride 9 mg/mL (0.9%) solution to ensure that all medicinal product has been administered.

Storage Conditions for Onpattro

- Onpattro should be stored in a refrigerator (2-8 °C). If refrigeration is not available, Onpattro can be stored at room temperature (up to 25 °C) for up to 14 days.
- After dilution, it is recommended that Onpattro be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 16 hours at room temperature (up to 30°C), including infusion time.

4. Signs and Symptoms of Infusion Related Reactions (IRRs)

In the double-blind placebo-controlled study, 18.9% of Onpattro-treated patients experienced IRRs, compared to 9.1% of placebo-treated patients. In the Onpattro-treated patients, all IRRs were either mild (95.2%) or moderate (4.8%) in severity.

Among Onpattro-treated patients who experienced an IRR, 78.6% experienced the first IRR within the first 2 infusions. The frequency of IRRs decreased over time. Few IRRs led to infusion interruption. One patient (0.7%) discontinued treatment during clinical studies due to an infusion-related reaction.

The most common symptoms of IRRs were flushing, back pain, nausea, abdominal pain, dyspnea, and headache. Symptoms of IRRs include, but are not limited to:

- arthralgia or pain (including back, neck, or musculoskeletal pain)
- flushing (including erythema of face or warm skin)
- nausea
- abdominal pain
- dyspnea or cough
- dysphonia
- chest discomfort or chest pain
- headache
- rash
- pruritus

- chills
- dizziness
- fatigue
- increased heart rate or palpitations
- hypotension, which may include syncope
- hypertension
- facial oedema

Patients should be informed to tell the health care professional (HCP) administering the infusion if they experience adverse events including IRRs during the infusion.

The HCP should provide the patient with a number to call if the patient experiences an IRR after the HCP has left the patient's house.

Actions in the Event of an IRR

If an IRR occurs, slowing or interrupting the infusion and institution of medical management (e.g., corticosteroids or other symptomatic treatment) should be considered, as clinically indicated. If the infusion is interrupted, resumption of the infusion at a slower infusion rate may be considered after symptoms have resolved. The Onpattro infusion should be discontinued in the case of a severe or life-threatening IRR.

Description of Infusion Related Reactions

Categorization	Description
Mild reaction	Infusion may be continued; if intervention is indicated it is minimal and additional treatment (other than paracetamol for delayed reactions) is not required.
Moderate reaction	Requires treatment including more intensive therapy (e.g., IV fluids, NSAIDs) in addition to infusion interruption but responds promptly to medication. Treatment is indicated for ≤24 hours.
Severe reaction	More than moderate reaction: not rapidly responsive to medication or to interruption of infusion; and/or prolonged (treatment is indicated for >24 hours); recurrence of severe symptoms following initial improvement.

Actions in Case of Emergency

In case of an emergency, discontinue Onpattro infusion and administer rescue medications as needed.

If necessary call 999 immediately.

Steps to Consider to Prevent Further IRRs

Some patients who experience IRRs may benefit from a slower infusion rate or additional or higher doses of one or more of the premedications with subsequent infusions to reduce the risk of IRRs.

Reasons to Consider whether the Patient Should Stop Home Infusions and Return to the Clinic to Receive the Infusions

The treating physician, in collaboration with the HCP responsible for home infusions, should continue to evaluate the patient's suitability to receive Onpattro infusions in the home setting, and whether the patient should return to the clinic to receive their Onpattro infusions.

The corticosteroid premedication dosage must not be altered in the home setting. The patient must be referred back to the clinic for any changes to the corticosteroid premedication. Following any adjustments, the treating physician should decide whether a patient can resume receiving infusions at home; this decision should be made after the patient has been on a stable dose of corticosteroid premedication and has tolerated at least 3 infusions well in the clinic.

5. Reporting Adverse Events

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via their national reporting system or Alnylam, contact details below:

Alnylam:
Alnylam Netherlands B.V. Tel: 0818 882213 or free phone: 1800 924 260
medinfo@alnylam.com

National reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

6. Further Information

Please refer to the Onpattro Summary of Product Characteristic (SmPC) and package leaflet (PL) for further information.

Copies of educational materials, SmPC and Package Leaflet can be found on the following websites:

https://www.hpra.ie/
https://www.medicines.ie/