Onpattro® (patisiran) Abbreviated Prescribing Information

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard

Adverse events should also be reported to Alnylam Pharmaceuticals at 08001412569 (+44 1628 878592) or medinfo@alnylam.com

Please refer to the Summary of Product Characteristics for further information.

Name of the Medicinal Product

Onpattro ▼ 2 mg/mL concentrate for solution for infusion.

Qualitative and quantitative composition

Each vial contains patisiran sodium equivalent to 10 mg patisiran formulated as lipid nanoparticles.

Therapeutic Indication

Onpattro is indicated for the treatment of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) in adult patients with stage 1 or stage 2 polyneuropathy.

Posology

The recommended dose of Onpattro is 300 micrograms per kg body weight administered via intravenous (IV) infusion once every 3 weeks. Vitamin A supplementation at approximately 2500 IU vitamin A per day is advised for patients treated with Onpattro.

All patients should receive premedication prior to Onpattro administration to reduce the risk of infusion-related reactions (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:

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

For premedications not available or not tolerated intravenously, equivalents may be administered orally. If clinically indicated, the corticosteroid may be tapered in decrements no greater than 2.5 mg to a minimum dose of 5 mg of dexamethasone (intravenous, IV), or equivalent. The patient should receive at least 3 consecutive infusions of Onpattro without experiencing IRRs before each reduction in corticosteroid premedication.

Therapy should be initiated under the supervision of a physician knowledgeable in the management of amyloidosis.

Contraindications

Severe hypersensitivity (e.g., anaphylaxis) to the active substance or any of the excipients.

Special warnings and precautions for use

IRRs have been observed in patients treated with Onpattro. In patients experiencing an IRR, the majority experienced the first IRR within the first 2 infusions. Across clinical studies, the most common symptoms

(reported in ≥ 2% of patients) of IRRs were flushing, back pain, nausea, abdominal pain, dyspnoea, and headache. IRRs may also include hypotension and syncope.

To reduce the risk of IRRs, patients should receive premedications on the day of Onpattro infusion, at least 60 minutes prior to the start of infusion. 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 serious or life-threatening IRR.

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.

By reducing serum TTR protein, Onpattro treatment leads to a decrease in serum vitamin A (retinol) levels. Serum vitamin A levels below the lower limit of normal should be corrected and any ocular symptoms or signs due to vitamin A deficiency should be evaluated prior to initiation of treatment with Onpattro.

Patients receiving Onpattro should take oral supplementation of approximately 2500 IU vitamin A per day to reduce the potential risk of ocular toxicity due to vitamin A deficiency. Referral for ophthalmological assessment is recommended if patients develop ocular symptoms suggestive of vitamin A deficiency, including reduced night vision or night blindness, persistent dry eyes, eye inflammation, corneal inflammation or ulceration, corneal thickening or corneal perforation.

Fertility, pregnancy and lactation
There are no data on the effects of Onpattro on human fertility. No impact on male or female fertility was detected in animal studies.

There are no data on the use of Onpattro in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Due to the potential teratogenic risk arising from unbalanced vitamin A levels, Onpattro should not be used during pregnancy, unless the clinical condition of the woman requires treatment. As a precautionary measure, vitamin A and thyroid stimulating hormone (TSH) levels should be obtained early in pregnancy. Close monitoring of the foetus should be carried out in the event of an unplanned pregnancy, especially during the first trimester. Women of childbearing potential have to use effective contraception during treatment with Onpattro.

It is unknown whether Onpattro is excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Onpattro, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Undesirable effects
The most frequently occurring adverse reactions reported in Onpattro-treated patients were peripheral oedema (29.7%) and infusion-related reactions (18.9%). The most common adverse reaction resulting in the discontinuation of Onpattro was an infusion-related reaction (0.7%).

The adverse reactions are presented below as MedDRA preferred terms under the MedDRA System Organ Class (SOC) by frequency. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The frequency of the adverse reactions is expressed according to the following categories:

- Very common (≥ 1/10)
- Common (≥ 1/100 to < 1/10)
- Uncommon (≥ 1/1,000 to < 1/100)

Table 1: Adverse reactions reported for Onpattro 300 micrograms per kg

System Organ Class	Adverse Reaction	Frequency
Infections and infestations	Bronchitis	Common
	Sinusitis	Common
	Rhinitis	Common
Immune system disorders	Infusion-related reaction	Very common
Ear and labyrinth disorders	Vertigo	Common
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Common
Gastrointestinal disorders	Dyspepsia	Common
Skin and subcutaneous tissue disorders	Erythema	Common
Musculoskeletal and connective tissue disorders	Arthralgia	Common
	Muscle spasms	Common
General disorders and administration site conditions	Peripheral oedema	Very common
	Extravasation	Uncommon

Prescribers should consult the Summary of Product Characteristics for further details of the above and for details of other adverse reactions.

Marketing Authorisation Number
EU/1/18/1320/001

Marketing Authorisation Holder
Alnylam Netherlands B.V. Strawinskylaan 3051 1077 ZX Amsterdam Netherlands

Local Representative
Alnylam UK Ltd Braywick Gate Braywick Road Maidenhead Berkshire SL6 1DA

Legal Classification
Medicinal product subject to restricted medical prescription.

NHS List Price
£7,676.47 per vial (10mg/5ml) of Onpattro (patisiran) concentrate for solution for infusion

Date of last revision
20 May 2020

Revisions history

Version	Effective date	Type of revisions (Creation, update, administrative change)	Revision description
1.0	2018-10-12	Creation	Creation of the abbreviated product information based on the SmPC dated 2018-08-27
2.0	2019-05-02	Update	Update further to grouped variations type IA (batch release site, ATC code, typos corrections)
3.0	2019-08-30	Update	Update further to variation type IB (shelf-life extension)
4.0	2020-05-20	Update	Updated following EMA approval PSUSA variation hypotension and syncope, approved 20-May-2020