SESLHDMG/115

Medicine Guideline

Patisiran

Areas where Protocol/Guideline applicable	SESLHD inpatient and day-only settings
Authorised Prescribers:	Consultant with experience in the management of amyloid disorders or in consultation with a consultant with experience in the management of amyloid disorders.
Indication for use	Hereditary transthyretin amyloidosis (hTTR)
Clinical condition Patient selection: Inclusion criteria (list investigations necessary and relevant results)	Patient must have Hereditary transthyretin amyloidosis (hTTR) confirmed by genetic testing with either: (i) stage 1 polyneuropathy, (ii) stage 2 polyneuropathy, and be at least 18 years of age. **AND** Patient must have a Polyneuropathy Disability (PND) score description of either I, II, IIIA, IIIB; **OR** Patient must have a Familial Amyloid Polyneuropathy (FAP) stage description of 1 or 2, **AND** Patient must not have previously undergone a liver transplant, **AND** Patient must not exhibit heart failure symptoms (defined as New York Heart Association NYHA class III or IV). **AND** Patient must be undergoing treatment with this drug as a monotherapy (i.e. not in combination with any other disease modifying medicines for amyloidosis disorders). *Patients MUST continue to demonstrate clinical benefit and must not be permanently bedridden or receiving end-of-life care.*
Proposed Place in Therapy	Initial treatment for adult patients with hTTR Amyloidosis with neuropathy.
Adjunctive Therapy	Patient must be undergoing treatment with this drug as a monotherapy (i.e. not in combination with any other disease modifying medicines for amyloidosis disorders). Patients are recommended to take 5000 IU of vitamin A supplement daily for the duration of treatment period
Pre-Medications	To be given 1 hour prior to commencement of patisiran infusion. • Paracetamol PO 500 mg STAT • Cetirizine PO 10 mg • Ranitidine PO 300 mg • Dexamethasone IV 10 mg* **Dexamethasone may be gradually reduced by 2.5mg to a minimum of 5mg after 3 consecutive infusions without infusion reactions*
Rescue Medications	• Dexamethasone IV 10 mg PRN • Cetirizine PO 10 mg PRN

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Contra-indications	History of anaphylaxis or severe hypersensitivity to patisiran or any of the excipients.
Precautions	Hypersensitive reactions including anaphylaxis. **Emergency Resuscitation Equipment MUST be available.** Refer to hospital policy. **Pregnancy** MUST be excluded before initiating treatment and women of childbearing age should practice effective contraception during treatment. If a woman intends to become pregnant, patisiran and Vitamin A should be discontinued, and serum Vitamin A levels should be monitored and return to normal before conception is attempted. Patisiran has been associated with **infusion-related reactions** (IRR). See Adverse Effects.
Important Drug Interactions	No formal drug interaction studies have been performed. Patisiran should be infused on a dedicated intravenous line.
Dosage	Recommended Dose: 0.3 mg/kg intravenously every 3 weeks based on actual body weight. The maximum recommended dose is 30 mg.
Duration of therapy	Depending on clinical outcomes (AE, IRR), can continue lifelong.
Prescribing Instructions	Prescribed by AMO, advanced trainee or registrar from the treating team on the eMR. In the absence of eMM systems, the appropriate paper medication chart may be used. Pre- and Rescue medications MUST also be prescribed. Document the patient's weight in eMR prior to infusion. If changes in weight, adjust dose accordingly. If a dose is missed, patisiran can be infused within three days and then can be continued on patient's normal schedule. If the dose is greater than three days after the missed dose the schedule should continue every 3 weeks thereafter.

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Preparation Instructions

Store patisiran in a refrigerator (2-8 °C). If refrigeration is not available, patisiran can be stored at room temperature up to 25°C for up to 14 days.

Aseptic Preparation in the **POWH** Pharmacy Sterile Suite.

1. Remove Patisiran from the refrigerator. Do not shake or vortex. Discard vial if it has been frozen. Allow to warm to room temperature.
2. Inspect visually for particulate matter and discolouration. Do not use if discolouration or foreign particles are present. *Patisiran 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.*
3. Calculate the required volume of patisiran based on the prescription.
4. Withdraw the entire contents of one or more vials into a single sterile syringe.
5. Filter patisiran through a sterile 0.45 micron polyethersulfone (PES) syringe filter into a sterile container.
6. Withdraw the required volume of filtered patisiran from the sterile container using a sterile syringe and add to an empty DEHP-free infusion bag.
7. Add sodium chloride 0.9% for a total volume of 200mL.

For example:

Patient Weight	Patisiran			**Volume** Sodium Chloride 0.9%	**Total Volume**
	Dose	**Volume**	**Number of Vials**		
75 kg	22.5 mg	11.25 mL	3	188.75 mL	200 mL

8. Gently invert the bag to mix the solution. Do not shake. Do not mix or dilute with other medicinal products.
9. Discard any unused portion of patisiran. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
10. Expiry of prepared infusion bag is up to 16 hours

Administration Instructions	Ensure premedication is given one hour prior to commencement of infusion. • 1.2 micron inline protein binding filter to be primed with dedicated new line. The infusion sets and lines must be free of DEHP. • Connect infusion line aseptically as per hospital policies. • Infuse using a rate-controlled volumetric infusion pump • Via 24 or 22g peripheral cannula **Commence infusion at 1 mL/min (60 mL/hr) for first 15 minutes.** **Increase rate to 3 mL/min (180 mL/hr) for remaining 185 mL of infusion.** Total infusion time approximately 80 minutes. The duration of infusion may be extended in the event of an infusion related reaction. Flush line with 30 mL of Sodium Chloride 0.9% on completion of infusion
Monitoring requirements	Baseline vital observations to be taken prior to commencement of infusion, at sign or symptom of IRR or allergic reaction, and at completion of infusion. Patient to be clinically observed for signs or symptoms of infusion associated or allergic reactions throughout procedure. **Any deterioration in the patient's condition should be escalated via the CERS pathway.**
Adverse Effects	In clinical trials, the most frequently reported adverse reactions that occurred were peripheral oedema (29%) and **infusion-related reactions** IRRs (18%). IRRs are more likely to occur during the first two infusions. IRRs that have been observed during patisiran infusions have included: *Back pain* *Abdominal Pain* *Rash* *Dizziness* *Facial Oedema* *Nausea* *Dyspnoea* *Pruritis* *Fatigue* *Flushing* *Headache* *Chills* *Palpitations* Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of **vitamin A deficiency**, which can include night blindness (difficulty seeing in low light conditions) and xerophthalmia (dry eyes).

Management of Complications	If **infusion-related reaction** occurs, stop the infusion and notify Medical Officer. Give rescue medications as indicated. If symptoms have completely resolved and the patient has been reviewed, the Medical Officer may decide to restart the infusion at a slower rate. Patients that have experienced Infusion reactions should be treated with caution when re-administering subsequent doses of patisiran
Basis of Protocol/Guideline: (including sources of evidence, references)	1. ATTR Hereditary Amyloidosis, Orphanet https://www.orpha.net/en/disease/detail/271861?name=ATTR%20amyloidosis&mode=name, Accessed 25/10/2024 2. *Onpattro TGA https://www.tga.gov.au/resources/auspmd/onpattro, accessed 25/10/2024* 3. *Onpattro Full Prescribing Information TGA https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210922s000lbl.pdf, accessed 25/10/2024* 4. Clinical Emergency Response System (CERS) - Framework for the Recognition and Management of Patients who are Clinically Deteriorating – SESLHD 5. Adult Peripheral Intravenous Cannula Insertion and Management - SESLHD 6. Onpattro Full Prescribing Information eMIMS https://app.emimselite.com.acs.hcn.com.au/medicineview?id=66f04e8c-8183-42fa-a02b-b1aa00fe3667&type=abbpi accessed 25/10/2024 7. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. N Engl J Med. 2018;379(1):11–21.
Groups consulted in development of this guideline	Prince of Wales Hospital Amyloidosis MDT Medison patisiran dosing and preparation guide SESLHD Pharmacy Western Sydney Local Health District Patisiran Intravenous Infusion Policy (draft; created August 2024)

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GOVERNANCE	
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