

PRIOR AUTHORIZATION POLICY

POLICY: Amyloidosis – Onpattro Prior Authorization Policy

- Onpattro® (patisiran intravenous infusion – Alnylam)

REVIEW DATE: 11/30/2022

OVERVIEW

Onpattro, a lipid nanoparticle formulated RNA interference therapeutic, is indicated for treatment of adults with **polyneuropathy of hereditary amyloid transthyretin amyloidosis (hATTR)**.¹ hATTR is a progressive disease caused by mutations in the transthyretin (TTR) gene leading to multisystem organ dysfunction.² Common neurologic manifestations include sensorimotor polyneuropathy, autonomic neuropathy, small-fiber polyneuropathy, and carpal tunnel syndrome.

The pivotal trial for Onpattro did not include patients with liver transplantation, which has historically been a treatment modality for hATTR.^{1,6} A Phase IIIb, open-label trial evaluated the efficacy of Onpattro in adults with hATTR polyneuropathy progression post liver transplant (n = 23).⁶ Patients received Onpattro at the FDA-approved dose for 12 months. The average of Month 6 and Month 12 serum TTR reduction was 91%. In addition, improvements in neuropathy, quality of life, autonomic symptoms from baseline to Month 12, and stabilized disability and nutritional status was noted.

Guidelines

A scientific statement from the American Heart Association (AHA) on the treatment of cardiomyopathy of hATTR amyloidosis (July 2020) includes recommendations related to polyneuropathy.³ Canadian guidelines for the treatment of patients with polyneuropathy (February 2021) and recommendations from the European Society of Cardiology (ESC) [2021] include treatment recommendations for hATTR polyneuropathy as well.^{2,4} In general, Onpattro and Tegsedi® (inotersen subcutaneous injection) are recommended for patients with hATTR polyneuropathy.

For patients with hATTR amyloidosis with polyneuropathy, the AHA recommends treatment with Onpattro or Tegsedi.³ For patients with hATTR with polyneuropathy and cardiomyopathy, Onpattro, Tegsedi, or Vyndamax™ (tafamidis capsules)/Vyndaqel® (tafamidis meglumine capsules) are recommended. Use of combination therapy is discussed; however, it is noted that there is little data to support combination therapy.

The Canadian guidelines recommend Onpattro and Tegsedi as first-line treatment to stop the progression of neuropathy and improve polyneuropathy in early and late stage hATTR amyloidosis with polyneuropathy.²

The ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure note that TTR stabilization and reduction are the recommended basis of treatment for cardiomyopathy of ATTR.⁴ Onpattro and Tegsedi may be considered for patients with hATTR polyneuropathy and cardiomyopathy.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Onpattro. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Onpattro as well as the monitoring required for adverse events and long-

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term efficacy, approval requires Onpattro to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Onpattro is recommended in those who meet the following criteria:

FDA-Approved Indication

- 1. Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR).** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
 - A) Patient is ≥ 18 years of age; AND**
 - B) Patient has a transthyretin mutation as confirmed by genetic testing; AND**
 - C) Patient has symptomatic polyneuropathy; AND**

Note: Examples of symptomatic polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch). Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.
 - D) The medication is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.**

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Onpattro is not recommended in the following situations:

- 1. Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Tegsedi, or a Tafamidis Product.** Note: Examples of tafamidis products are Vyndaqel and Vyndamax. There are insufficient data supporting the safety and efficacy of concurrent use of these agents for hATTR with polyneuropathy. The Vyndaqel/Vyndamax pivotal trial, which took place prior to when Onpattro and Tegsedi were under investigation for amyloidosis, did not include patients who were taking investigational drugs. The pivotal trials for Amvuttra, Onpattro and Tegsedi did not allow concurrent use of tetramer stabilizers (e.g., tafamidis, diflunisal). A Phase II open-label extension study (n = 27) included 13 patients who were treated concomitantly with Onpattro and tafamidis.⁵ Following 24 months of treatment, there was no significant difference in the median serum TTR percent change from baseline with concomitant Onpattro and tafamidis (-80%) vs. Onpattro monotherapy (-88%). A scientific statement from the American Heart Association notes that there is little data to support combination therapy for these products.³
- 2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.**

REFERENCES

1. Onpattro® [prescribing information]. Cambridge, MA: Alnylam; July 2022.
2. Alcantara M, Mezi MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. *Can J Neuro Sci.* 2022;49:7-18.
3. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation.* 2020;142:e7-e22.
4. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42:3599-3726.
5. Lin H, Merkel M, Hale C, Marantz JL. Experience of patisiran with transthyretin stabilizers in patients with hereditary transthyretin-mediated amyloidosis. *Neurodegener Dis Manag.* 2020;10(5):289-300.
6. Schmidt HH, Wixner J, Plante-Bordeneuve V; on behalf of the Patisiran Post-LT Study Group. Patisiran treatment in patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy after liver transplantation. *Am J Transplant.* 2022;22:1646-1657.