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Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Neuromuscular Drugs	**Original Policy Date:**	August 24, 2018
Subject:	Onpattro	**Page:**	1 of 6

Last Review Date: June 13, 2024

Onpattro

Description

Onpattro (patisiran)

Background

Onpattro (patisiran) is a double-stranded siRNA that causes degradation of mutant and wild-type TTR mRNA through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults (1).

Regulatory Status

FDA-approved indication: Onpattro contains a transthyretin-directed small interfering RNA and is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults (1).

Infusion-related reactions may occur with Onpattro. Patients should premedicate with a corticosteroid, acetaminophen and antihistamines on the day of Onpattro infusion, at least 60 minutes prior to the start of infusion. Monitor patients during the infusion for signs and symptoms of infusion-related reactions. If one occurs, consider slowing or interrupting the Onpattro infusion and instituting medical management, as clinically indicated. Some patients who experience these reactions 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 reactions (1).

The safety and effectiveness of Onpattro in pediatric patients have not been established (1).

Related policies
Amvuttra, Tegsedi, Wainua

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Onpattro may be considered **medically necessary** if the conditions indicated below are met.

Onpattro may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis

AND ALL of the following:

1. Diagnosis of hATTR confirmed by a genetic test **OR** tissue biopsy showing amyloid deposition
2. Patient must have **ONE** of the following baseline scores:
    a. Polyneuropathy disability (PND) score ≤ IIIb (see Appendix 1)
    b. FAP Stage 1 or 2 (see Appendix 2)
3. Will be administered by a healthcare professional
4. Patient will receive premedication to reduce the risk of infusion-related reactions
5. Prescriber agrees to supplement the patient with the recommended daily allowance of Vitamin A if indicated
6. Patient has **NONE** of the following:
    a. New York Heart Association (NYHA) class III or IV heart failure
    b. Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.)
    c. Prior liver transplantation
7. Prescribed by or in consultation with a neurologist, or a specialist in the treatment of the patient's diagnosis
8. **NO** dual therapy with another Prior Authorization (PA) medication for polyneuropathy caused by hATTR amyloidosis (see Appendix 3)

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis

AND ALL of the following:

1. Patient condition has improved or stabilized
2. Will be administered by a healthcare professional
3. Patient will receive premedication to reduce the risk of infusion-related reactions
4. Prescriber agrees to supplement the patient with the recommended daily allowance of Vitamin A if indicated
5. **NO** dual therapy with another Prior Authorization (PA) medication for polyneuropathy caused by hATTR amyloidosis (see Appendix 3)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 12 vials per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Onpattro (patisiran) is a double-stranded siRNA that causes degradation of mutant and wild-type TTR mRNA through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. The safety and effectiveness of Onpattro in pediatric patients have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Onpattro while maintaining optimal therapeutic outcomes.

References

1. Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; January 2023.

Policy History

Date	Action
August 2018	Addition to PA
October 2018	Addition of no dual therapy with Tegsedi
November 2018	Annual review. Addition of Vitamin A supplementation requirement per SME
May 2019	Addition of renewal requirement: Patient has been assessed for improvement and has experienced a clinical benefit from therapy. Addition of quantity limit of 12 vials per 84 days
June 2019	Annual review
September 2019	Annual review
September 2020	Annual review and reference update
September 2021	Annual review and reference update
July 2022	Addition of Appendix 1, 2, and 3 and modification of dual therapy requirement to no dual therapy with a PA medication for hATTR amyloidosis. Per FEP: to align with BCBS association criteria: added requirement of 1. Diagnosis of hATTR confirmed by a genetic test OR documentation of tissue biopsy showing amyloid deposition; 3. Patient must have ONE of the following baseline scores:a.Polyneuropathy disability (PND) score ≤ IIIb (see appendix 1) b. FAP Stage 1 or 2 (see appendix 2);4.Patient has NONE of the following:a.New York Heart Association (NYHA) class III or IV heart failure b. Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.) c. Prior liver transplantation; 8. Prescribed by or in consultation with a neurologist, or a specialist in the treatment of the patient's diagnosis; revised continuation requirement to improvement or stabilization of condition

September 2022	Annual review and reference update
September 2023	Annual review and reference update
December 2023	Annual review
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.

Appendix 1 - Polyneuropathy Disability (PND) Severity Scoring System

Polyneuropathy Disability (PND) Score	
Stage 0	No impairment
Stage I	Sensory disturbances but preserved walking capability
Stage II	Impaired walking capability but ability to walk without a stick or crutches
Stage IIIA	Walking only with the help of one stick or crutches
Stage IIIB	Walking only with the help of two sticks or crutches
Stage IV	Confined to a wheelchair or bedridden

Appendix 2 - FAP Stage Severity Scoring System

FAP Stage	
Stage 0	No symptoms
Stage I	Unimpaired ambulation; mostly mild sensory, motor, and autonomic neuropathy in the lower limbs
Stage II	Assistance with ambulation required; mostly moderate impairment progression to the lower limbs, upper limbs, and trunk
Stage III	Wheelchair bound or bedridden; severe sensory, motor, and autonomic involvement of all limbs

Appendix 3 - List of PA Medications for Polyneuropathy caused by hATTR Amyloidosis

Generic Name	Brand Name
eplontersen	Wainua
inotersen	Tegsedi
patisiran	Onpattro
vutrisiran	Amvuttra