Clinical Policy: Patisiran (Onpattro)

Reference Number: ERX.SPA.290
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Patisiran (Onpattro™) is a double-stranded small interfering ribonucleic acid, formulated as a lipid complex for delivery to hepatocytes.

FDA Approved Indication(s)
Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Onpattro is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy;
2. Documentation confirms presence of a transthyretin (TTR) mutation;
3. Biopsy is positive for amyloid deposits or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy;
4. Prescribed by or in consultation with a neurologist;
5. Age ≥ 18 years;
6. Member has not had a prior liver transplant;
7. Onpattro is not prescribed concurrently with Tegsedi®;
8. Dose does not exceed the following (based on actual body weight):
   a. Weight < 100 kg: 0.3 mg/kg once every 3 weeks;
   b. Weight ≥ 100 kg: 30 mg once every 3 weeks.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy [e.g., improved measures of polyneuropathy (e.g., motor strength, sensation, and reflexes), improvement in quality of life, motor function, walking ability (e.g., as measured by timed 10-m walk test), and nutritional status (e.g., as evaluated by modified mass index)];
3. Onpattro is not prescribed concurrently with Tegsedi;

4. If request is for a dose increase, new dose does not exceed the following (based on actual body weight):
   a. Weight < 100 kg: 0.3 mg/kg once every 3 weeks;
   b. Weight ≥ 100 kg: 30 mg once every 3 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
TTR: transthyretin

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- To confirm amyloidosis, the demonstration of amyloid deposits via tissue biopsy is essential. Deposition of amyloid in the tissue can be demonstrated by Congo red staining of biopsy specimens. With Congo red staining, amyloid deposits show a characteristic green birefringence under polarized light; however, negative biopsy results should not be interpreted as excluding the disease.
- DNA sequencing is usually required for genetic confirmation. Current techniques for performing sequence analysis of TTR, the only gene known to be associated with TTR amyloidosis, detect > 99% of disease-causing mutations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hereditary transthyretin-mediated amyloidosis-associated polyneuropathy	• Adults weighing < 100 kg: 0.3 mg/kg IV every 3 weeks • Adults weighing ≥ 100 kg: 30 mg IV every 3 weeks • Pre-medicate with a corticosteroid, acetaminophen, and antihistamines to reduce the risk of infusion-related reactions. • Onpattro should be administered by a healthcare professional.	See dosing regimen

VI. Product Availability

Lipid complex injection (single-dose vial): 10 mg/5 mL (2 mg/mL)

VII. References

1. Onpattro Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; May 2021. Available at: https://www.alnylam.com/wp-content/uploads/pdfs/ONPATTRO-Prescribing-Information.pdf. Accessed August 16, 2021.
2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013 Feb 20;8:31.
3. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5;379(1):11-21.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.11.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.05.19	11.19
4Q 2020 annual review: no significant changes; genetic testing methodology examples removed from criteria with deference to appendix; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: added requirement that Onpattro is not prescribed concurrently with Tegsedi; added biopsy requirement to align with previously P&T-approved approach for this class of medications; references reviewed and updated.	08.16.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.