RXADVANCE
2 Park Central Drive
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Clinical Policy Title:	patisiran
Policy Number:	RxA.619
Drug(s) Applied:	Onpattro®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Patisiran (Onpattro®) is a double-stranded small interfering ribonucleic acid (RNA), formulated as a lipid complex for delivery to hepatocytes.
It is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
patisiran (Onpattro®)	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	See dosing regimen

Dosage Forms

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

Clinical Policy

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

I. Initial Approval Criteria

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

1. Diagnosis of hereditary transthyretin-mediated amyloidosis with polyneuropathy;
2. Documented transthyretin (TTR) mutation (e.g., genetic testing, DNA sequencing);
3. Prescribed by or in consultation with a neurologist;
4. Age ≥ 18 years;
5. Member has not had a prior liver transplant;
6. 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

Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving the medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
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. 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
TTR: Transthyretin
RNA: Ribonucleic Acid

APPENDIX B: Therapeutic Alternatives
- Not applicable

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
    - None
- Boxed Warning(s):
    - None

APPENDIX D: General Information
- All patients should receive premedication prior to ONPATTRO administration to reduce the risk of infusion-related reactions (IRRs). Premedicate with a corticosteroid, acetaminophen, and antihistamines to reduce the risk of infusion-related reactions. Onpattro should be administered by a healthcare professional.
- 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.

References

1. Onpattro Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; February 2020. Available at: https://www.onpattrohcp.com/. Accessed September 14, 2020.
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.
4. Peter D G, Helen J L. Overview of amyloidosis. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2020. Accessed with subscription at: http://uptodate.com. Accessed October 4, 2020

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. Line of Business policy applies to was updated to “All lines of business”. 3. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance”. 4. Appendix A was updated 5. Reference was reviewed and updated.	09/14/2020	12/07/2020