MEDICAL MUTUAL®

Drug Policy

Policy:	**201831**	**Initial Effective Date: 09/20/2018**
Code(s):	**HCPCS C9036**	**Annual Review Date: New**
SUBJECT:	**Onpattro ® (Patisiran)**	**Last Revised Date: 12/26/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

Onpattro is a lipid nanoparticle formulated RNA interference (RNAi) therapeutic indicated for treatment of hereditary amyloid transthyretin (hATTR) amyloidosis with polyneuropathy. hATTR amyloidosis is a rare, inherited, rapidly-progressive, debilitating, life-threatening disease. It is a multisystem condition caused by mutation in the transthyretin (TTR) gene that results in misfolded TTR protein accumulation (as amyloid) in the nerves, heart, and other areas of the body. Onpattro targets hepatic production of mutant TTR. By reducing the unstable circulating TTR tetramers, organ deposition of amyloid is prevented, thus, stabilizing or improving symptoms of neuropathy.

POLICY STATEMENT

This policy involves the use of Onpattro. Prior authorization is recommended for medical benefit coverage of Onpattro. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Onpattro as well as the monitoring required for AEs and long-term efficacy, initial approval requires Onpattro be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Polyneuropathy of hereditary transthyretin-mediated amyloidosis**
   Initial Therapy, *Patient must meet all of the following* (a, b, c, d, e, f AND g):

   a. Patient is 18 years of age or older; AND

b. The patient has a documented transthyretin (TTR) mutation verified by genetic testing [documentation required]; AND
c. The patient has tried or is currently receiving at least one systemic agent for symptoms of polyneuropathy from one of the following pharmacologic classes: a gabapentin-type product (e.g., gabapentin [Neurontin], Lyrica [pregabalin capsules]) or a tricyclic antidepressant (e.g., amitriptyline, nortriptyline); AND
d. Presence of clinical signs and symptoms of the disease (e.g., peripheral/autonomic neuropathy, motor disability, cardiovascular dysfunction, renal dysfunction); AND
e. Presence of polyneuropathy characterized by ONE of the following (i or ii); AND
    i. Baseline polyneuropathy disability (PND) score ≤ IIIb
    ii. Baseline FAP Stage 1 or 2
f. Patient will not receive Onpattro in combination with either of the following (i, or ii); AND
    i. Oligonucleotide agents (e.g., inotersen)
    ii. Tetramer stabilizers (e.g., tafamidis, diflunisal)
g. Onpattro is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

***Continuation of therapy**, Patient must meet all of the following* (a, b, c, d, e, f, AND g)*:*

a. Patient has previously received treatment with Onpattro; AND
b. Patient has documented transthyretin (TTR) mutation as confirmed through genetic testing; AND
c. Presence of clinical signs and symptoms of the disease (e.g., peripheral/autonomic neuropathy, motor disability, cardiovascular dysfunction, renal dysfunction); AND
d. Improvement or stability of ONE of the following baseline scores (i or ii); AND
    i. Polyneuropathy disability (PND) score ≤ IIIb
    ii. FAP Stage 1 or 2
e. Patient has experienced a positive clinical response to Onpattro (e.g., improved neurologic impairment, motor function, cardiac function, quality of life assessment, serum TTR levels, etc.); AND
f. Patient will not receive Onpattro in combination with the following agents (i or ii); AND
    i. Oligonucleotide agents (e.g., inotersen)
    ii. Tetramer stabilizers (e.g., tafamidis, diflunisal)
g. Onpattro is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

Dosing in polyneuropathy of hereditary transthyretin-mediated amyloidosis. *Dosing must meet the following:*
For patients weighing less than 100 kg, the recommended dosage of Onpattro is 0.3 mg/kg once every 3 weeks.
For patients weighing 100 kg or more, the recommended dosage of Onpattro is 30 mg once every 3 weeks.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:*6 months

Duration of Therapy: Indefinite

Labs/Diagnostics: Genetic testing is required to confirm TTR mutation

Waste Management for All Indications.
The dose of Onpattro is a 0.3 mg/kg (maximum 30 mg) via intravenous (IV) infusion. The number of vials needed should be calculated.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Onpattro has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.
2. Cardiomyopathy associated with hATTR amyloidosis
3. Primary or leptomeningeal amyloidosis
4. Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Onpattro [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals. August 2018.

2. Adams D, Suhr OB, Dyck PJ, et al. Trial design and rationale for APOLLO, a Phase 3, placebo-controlled study of patisiran in patients with hereditary ATTR amyloidosis with polyneuropathy. BMC Neurol. 2017 Sep 11;17(1):181.

3. Adams D. Recent advances in the treatment of familial amyloid polyneuropathy. Ther Adv Neurol Disord. 2013 Mar; 6(2): 129–139.

4. 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.

5. Alnylam Pharmaceuticals. The Study of an Investigational Drug, Patisiran (ALN-TTR02), for the Treatment of Transthyretin (TTR)-Mediated Amyloidosis in Patients Who Have Already Been Treated With ALN-TTR02 (Patisiran). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National

Library of Medicine (US). 2000- [cited 2018 April 12]. Available from: https://clinicaltrials.gov/show/NCT02510261. NLM Identifier: NCT02510261.

6. Institute for Clinical and Economic Review: Draft Evidence Report - Inotersen and Patisiran for Hereditary Transthyretin Amyloidosis: Effectiveness and Value. July 20, 2018.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes C9036

HCPCS Code(s):	
C9036	Injection, patisiran, 0.1 mg (effective 1/1/2019)