Prior Authorization Criteria

Onpattro (patisiran)
Policy Number: Pending Number

CRITERIA EFFECTIVE DATES:

<table>
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<tr>
<th>ORIGINAL EFFECTIVE DATE</th>
<th>LAST REVIEWED DATE</th>
<th>NEXT REVIEW DATE</th>
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<tr>
<td>11/01/2019</td>
<td>09/18/2019</td>
<td>09/2020</td>
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J CODE: J0222- Injection, patisiran, 0.1 mg

TYPE OF CRITERIA: RxPA

LAST P&T APPROVAL/VERSION: Q4 2019 20191030

PRODUCTS AFFECTED:
Onpattro (patisiran)

DRUG CLASS:
small interfering ribonucleic acid (siRNA)

ROUTE OF ADMINISTRATION:
Intravenous solution
Related Administration Codes 96365: Ther/proph/diag iv inf init, 96366: Ther/proph/diag iv inf addon

PLACE OF SERVICE:
Specialty Pharmacy or Buy and Bill
The recommendation is that medications in this policy will be for medical benefit coverage and the IV infusion products administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider’s office, free-standing ambulatory infusion center)

AVAILABLE DOSAGE FORMS:
Lipid Complex Injection: 10 mg/5 mL (2 mg/mL) in a single-dose vial

FDA-APPROVED USES:
Polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults

COMPELLING APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults
E85.1 Neuropathic heredofamilial amyloidosis

REQUIRED MEDICAL INFORMATION:
A. HEREDITARY TRANSTHYRETIN-MEDIATEDAMYLOIDOSIS ASSOCIATED POLYNEUROPATHY (hATTR-PN):
   1. Documented pathogenic transthyretin (TTR) mutation verified by genetic testing
      [DOCUMENTATION REQUIRED]
      Note: More than 120 different transthyretin (TTR) gene mutations have been identified, with predominant symptom presentation varying by genotype. The most common mutations in the US are V122I, T60A, and V30M3
AND
2. Documentation of one of the following: Polyneuropathy disability (PND) score ≤ IIIb, Familial amyloidotic polyneuropathy (FAP) stage 1 or 2 OR Neuropathy impairment score (NIS) between 10 and 130
AND
2. Documentation of presence of clinical signs and symptoms of the disease such as: (a) Peripheral sensory-motor neuropathy (e.g., neuropathic pain, paresthesia, weakness, bilateral carpal tunnel syndrome, difficulty walking), Autonomic neuropathy (e.g., orthostatic hypotension, recurrent urinary tract infections, sexual dysfunction, sweating abnormalities, urinary retention), Gastrointestinal manifestations (e.g., diarrhea, nausea, vomiting, unintentional weight loss), Cardiovascular manifestations (e.g., arrhythmias, conduction abnormalities, heart failure)
AND
3. 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
4. Patient will not receive Onpattro in combination with Oligonucleotide agents (e.g., inotersen) OR Tetramer stabilizers (e.g., tafamidis, diflunisal)
AND
5. Prescriber attests that patient has not had a liver transplant

DURATION OF APPROVAL: Initial authorization: 6 months, Continuation of Therapy: 6 months

QUANTITY: 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.

PRESCRIBER REQUIREMENTS: Prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

AGE RESTRICTIONS: 18 years of age and older

GENDER: Male and Female

CONTINUATION OF THERAPY:
A. HEREDITARY TRANSTHYRETIN-MEDIATED AMYLOIDOSIS ASSOCIATED POLYNEUROPATHY (hATTR-PN):
   1. Improvement or stability of ONE of the following baseline scores: Polyneuropathy disability (PND) score < IIIb OR FAP Stage 1 or 2
      AND
   2. Adherence to therapy at least 85% of the time as verified by the prescriber or member’s medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation required)
      AND
   3. Documentation of no intolerable adverse effects or drug toxicity
CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION: All other uses of Onpattro (patisiran) are considered experimental/investigational and therefore, will follow Molina’s Off-Label policy. Contraindications include hypersensitivity to any component of the product.

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. Coverage is not recommended for the following circumstances: Cardiomyopathy associated with hATTR amyloidosis, Primary or leptomeningeal amyloidosis, Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis or Concurrent use with Tegsedi (inotersen) injections

OTHER SPECIAL CONSIDERATIONS:
A. Infusion-related reactions:
   a. Monitor for signs and symptoms during infusion
   b. Slow or interrupt the infusion if clinically indicated
   c. Discontinue if a serious or life-threatening infusion-related reaction occurs
B. Patisiran can lead to reduced serum vitamin A levels, vitamin A supplementation is advised if patient is taking patisiran.
   a. Refer to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur
C. Patisiran has not been studied in patients with severe renal or hepatic impairment

BACKGROUND:
Hereditary transthyretin-mediated amyloidosis (hATTR) is a rare condition affecting about 50,000 people worldwide. It manifests as abnormal buildup of amyloids which are protein fibers that deposit in organs and tissues in consequence interfering with normal functioning. The amyloid deposits usually occur in the peripheral nervous system, which can result in a loss of sensation, pain, or immobility in the arms, legs, hands and feet. They can also deposit in heart, kidneys, eyes and gastrointestinal tract and affect their functioning. The focus of the hATTR treatment is generally symptom management.3

Patisiran is a small interfering ribonucleic acid (siRNA) which works by silencing a portion of RNA involved in causing polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults. More specifically, patisiran prevents production of transthyretin (TTR) which leads to reduction in accumulation of amyloid deposits in peripheral nerves, improving symptoms and helping patients better manage the condition.3

The FDA approved Onpattro in August 2018 based on data from “Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis” study. It was multicenter, international, randomized, double-blind, placebo-controlled, phase 3 trial of patisiran in patients with hATTR polyneuropathy. The primary end point was the change from baseline in the modified Neuropathy Impairment Score+7 (mNIS+7) at 18 months. Participants were adult patients (aged 18 to 85 years) with a documented pathogenic variant in TTR; a diagnosis of hereditary transthyretin amyloidosis with peripheral neuropathy, with a NIS of 5 to 130 and a polyneuropathy disability score of IIIb or lower. A total of 225 patients underwent randomization (148 to the patisiran group and 77 to the placebo group). The mean (±SD) mNIS+7 at baseline was 80.9±41.5 in the patisiran group and 74.6±37.0 in the placebo group; the least-squares mean (±SE) change from baseline was −6.0±1.7 versus 28.0±2.6 (difference, −34.0 points; P<0.001) at 18 months. The effect on gait speed and modified
BMI was also observed at 18 months. The least-squares mean change from baseline in gait speed was 0.08±0.02 m per second with patisiran versus −0.24±0.04 m per second with placebo (difference, 0.31 m per second; P<0.001). The least-squares mean change from baseline in the modified BMI was −3.7±9.6 versus −119.4±14.5 (difference, 115.7; P<0.001). Patisiran improved multiple clinical manifestations of hereditary transthyretin amyloidosis in this trial.4

APPENDIX:
The polyneuropathy disability score is an additional assessment tool with ranking based on different classes I-IV. Higher scores are indicative of more impaired walking ability. The varying classes are defined as follows:
I: preserved walking, sensory disturbances
II: impaired walking without need for a stick or crutches
IIIa: walking with one stick or crutch
IIIb: walking with two sticks or crutches

Familial Amyloid Polyneuropathy (FAP) clinical staging:
Stage 0: no symptoms
Stage 1: unimpaired ambulation; mostly mild sensory, motor, and autonomic neuropathy in the lower limbs
Stage 2: assistance with ambulation required; mostly moderate impairment progression to the lower limbs, upper limbs, and trunk
Stage 3: wheelchair-bound or bedridden; severe sensory, motor, and autonomic involvement of all limbs

REFERENCES:
3. Commissioner, Office of the. FDA Approves First-of-Its Kind Targeted RNA-Based Therapy to Treat a Rare Disease. U.S. Food and Drug Administration, FDA [online].
