Onpattro® (Patisiran)

Policy Number: CS2021D0072H
Effective Date: September 1, 2021

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

<table>
<thead>
<tr>
<th>State</th>
<th>Policy/Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indiana</td>
<td>Onpattro® (Patisiran) (for Indiana Only)</td>
</tr>
<tr>
<td>Kansas</td>
<td>None</td>
</tr>
<tr>
<td>Kentucky</td>
<td>Onpattro® (Patisiran) (for Kentucky Only)</td>
</tr>
<tr>
<td>Louisiana</td>
<td>Onpattro® (Patisiran) (for Louisiana Only)</td>
</tr>
<tr>
<td>North Carolina</td>
<td>None</td>
</tr>
</tbody>
</table>

Coverage Rationale

Onpattro® (patisiran) is proven and medically necessary for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in patients who meet all of the following criteria:1,8

- For initial therapy, all of the following:
  - Both of the following:
    - Diagnosis of hATTR amyloidosis with polyneuropathy
    - Documentation that the patient has a pathogenic TTR mutation (e.g., V30M) and
  - Prescribed by or in consultation with a neurologist; and
  - Documentation of one of the following:
    - Patient has a baseline polyneuropathy disability (PND) score ≤ IIIb
    - Patient has a baseline FAP Stage 1 or 2 and
  - Patient has not had a liver transplant; and
  - Presence of clinical signs and symptoms of the disease (e.g., peripheral sensorimotor polyneuropathy, autonomic neuropathy, motor disability, etc.); and
Patient is not receiving Onpattro in combination with either of the following:

- Oligonucleotide agents [e.g., Tegsedi (inotersen)]
- Vyndaqel (tafamidis meglumine) or Vyndamax (tafamidis)

Patisiran dosing is in accordance with the U.S. Food and Drug Administration prescribing information; and

Initial authorization is for no more than 12 months

- For continuation of therapy, all of the following:
  - Patient has previously received treatment with Onpattro; and
  - Prescribed by or in consultation with a neurologist; and
  - Documentation of one of the following:
    - Patient continues to have a polyneuropathy disability (PND) score ≤ IIIb
    - Patient continues to have a FAP Stage 1 or 2
  - Documentation that the patient has experienced a positive clinical response to Onpattro (e.g., improved neurologic impairment, motor function, quality of life, slowing of disease progression, etc.); and
  - Patient is not receiving Onpattro in combination with either of the following:
    - Oligonucleotide agents [e.g., Tegsedi (inotersen)]
    - Vyndaqel (tafamidis meglumine) or Vyndamax (tafamidis)
  - Patisiran dosing is in accordance with the U.S. Food and Drug Administration prescribing information; and
  - Authorization is for no more than 12 months

Onpattro® (patisiran) is unproven and not medically necessary for the treatment of:

- Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis
- Primary or leptomeningeal amyloidosis

**Applicable Codes**

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J0222</td>
<td>Injection, patisiran, 0.1 mg</td>
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<table>
<thead>
<tr>
<th>Diagnosis Code</th>
<th>Description</th>
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<tr>
<td>E85.1</td>
<td>Neuropathic heredofamilial amyloidosis</td>
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**Background**

Hereditary ATTR (hATTR) amyloidosis, formerly known as familial amyloid polyneuropathy, is a progressive, disabling and life-threatening polyneuropathy affecting the peripheral and autonomic nervous system. This disease is an autosomal transmission disorder which is usually due to a point mutation of the transthyretin (TTR) gene. The disease is caused by misfolded transthyretin (TTR) protein that accumulates as amyloid fibrils in multiple organs, including the nerves, heart, and gastrointestinal tract.

Onpattro (patisiran) is a double-stranded small interfering RNA (siRNA) that targets a sequence of mRNA conserved across wild-type and all TTR variants and can thereby degrade and reduce serum levels and protein deposits in tissues of both wild-type and mutated protein. It is formulated as lipid nanoparticles which direct it to the liver, the primary source of circulating TTR. Patisiran therapy is associated with observed lowering of TTR levels in both wild-type and mutant (V30M) forms of TTR.
A genetic testing service is available in the United States and Canada and a genetic counseling service is available in the United States. Medical professionals and patients may access information on the Alnylam Pharmaceuticals website.

Clinical Evidence

A randomized, double-blind, placebo-controlled, phase III, global study (APOLLO) evaluated the efficacy and safety of patisiran in patients with hATTR amyloidosis with polyneuropathy. Adult patients 18 to 85 years of age were eligible for the study if the investigatory estimated survival to be ≥ 2 years, Neuropathy Impairment Score (NIS) of 5 to 130, and polyneuropathy disability score ≤ IIIb. Patients were randomized 2:1 (N=148:77) to receive either intravenous (IV) patisiran 0.3 mg/kg or placebo every 3 weeks. The primary endpoint was to determine the efficacy of patisiran at 18 months based on the difference in the change in modified NIS+7 (a composite measure of motor strength, sensation, reflexes, nerve conduction, and autonomic function) between the patisiran and placebo groups. Secondary endpoints evaluated the effect of patisiran on Norfish-Diabetic Neuropathy quality of life questionnaire score, nutritional status (as evaluated by modified body mass index), motor function (as measured by NIS-weakness and timed 10-m walk test), and autonomic symptoms (as measured by the Composite Autonomic Symptom Score-31 questionnaire). Exploratory objectives include assessment of cardiac function and pathologic evaluation to assess nerve fiber innervation and amyloid burden. Safety of patisiran was also assessed throughout the study. Overall patisiran reduced mean left ventricular wall thickness (least-squares basal region (overall least-squares mean [SE] difference, 2.1% [0.8%]; 95% CI, 0.6%-3.6%; P = .006) and no significant differences in the mid and apical regions among groups. Patisiran reduced mean left ventricular wall thickness (least-squares mean change ± SEM: –0.9±0.4 mm, P=0.017), interventricular septal wall thickness, posterior wall thickness, and relative wall thickness at month 18 compared with placebo. Patisiran also led to increased end-diastolic volume (8.3±3.9 mL, P=0.036), decreased global longitudinal strain (–1.4±0.6%, P=0.015), and increased cardiac output (0.38±0.19 L/min, P=0.044) compared with placebo at month 18. Patisiran lowered N-terminal prohormone of brain natriuretic peptide at 9 and 18 months (at 18 months, ratio of fold-change patisiran/placebo 0.45, P<0.001). A consistent effect on N-terminal prohormone of brain natriuretic peptide at 18 months was observed in the overall APOLLO patient population (n=225). Median follow-up duration was 18.7 months. The exposure-adjusted rates of cardiac hospitalizations and all-cause death were 18.7 and 10.1 per 100 patient-years in the placebo and patisiran groups, respectively (Andersen–Gill hazard ratio, 0.54; 95% CI, 0.28–1.01). The authors concluded that patisiran prevented the deterioration of LV GLS and decreased mean LV wall thickness over 18 months, suggesting that patisiran may halt or reverse the progression of the cardiac manifestations of hATTR amyloidosis.

Institute for Clinical and Economic Review (ICER)

On October 4, 2018, ICER released a clinical report entitled, “Inotersen and Patisiran for Hereditary Transthyretin Amyloidosis: Effectiveness and Value”. ICER recommendations are as follows:13

- ICER judges the clinical evidence for patisiran to be “incremental” or “better”.

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On average, patients on patisiran demonstrated improvement in neuropathy symptoms, as measured by the mNIS+7. Based on the current body of evidence, there is moderate certainty of a substantial net health benefit with high certainty of at least a small net health benefit compared to best supportive care.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Onpattro® (patisiran) contains a transthyretin-directed small interfering RNA and is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

References

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as Interqual criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.