

ONPATTRO™ (PATISIRAN)

Policy Number: 2019D0072D

Effective Date: March 1, 2019

[Instructions for Use](#) ⓘ

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Related Commercial Policy

- [Provider Administered Drugs – Site of Care Review Guidelines](#)

COVERAGE RATIONALE

See [Benefit Considerations](#) ⓘ

Onpattro (patisiran) is proven for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis.

Onpattro (patisiran) is medically necessary for the treatment of the polyneuropathy of hATTR amyloidosis in patients who meet ALL of the following criteria:^{1,8}

- I. For **initial therapy, all** of the following:
 - A. **Both** of the following:
 1. Diagnosis of hATTR amyloidosis with polyneuropathy
 2. Documentation that the patient has a pathogenic TTR mutation (e.g., V30M)**and**
 - B. Prescribed by or in consultation with a neurologist; **and**
 - C. Documentation of **one** of the following:
 1. Patient has a baseline polyneuropathy disability (PND) score ≤ IIIb
 2. Patient has a baseline FAP Stage 1 or 2**and**
 - D. Patient has not had a liver transplant; **and**
 - E. Presence of clinical signs and symptoms of the disease (e.g., peripheral sensorimotor polyneuropathy, autonomic neuropathy, motor disability, etc.); **and**
 - F. Patient is not receiving Onpattro in combination with either of the following:
 1. Oligonucleotide agents [e.g., Tegsedi (inotersen)]
 2. Tafamidis meglumine**and**
 - G. Patisiran dosing is in accordance with the US Food and Drug Administration prescribing information (0.3 mg/kg up to a maximum of 30mg, every 3 weeks); **and**
 - H. Initial authorization is for no more than 12 months.
- II. For **continuation therapy, all** of the following:
 - A. Patient has previously received treatment with Onpattro; **and**
 - B. Prescribed by or in consultation with a neurologist; **and**
 - C. Documentation of **one** of the following:
 1. Patient continues to have a polyneuropathy disability (PND) score ≤ IIIb
 2. Patient continues to have a FAP Stage 1 or 2**and**
 - D. 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**

- E. Patient is not receiving Onpattro in combination with either of the following:
 1. Oligonucleotide agents [e.g., Tegsedi (inotersen)]
 2. Tafamidis meglumine**and**
- F. Patisiran dosing is in accordance with the US Food and Drug Administration prescribing information (0.3 mg/kg up to a maximum of 30mg, every 3 weeks); **and**
- G. 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

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

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.

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](#).

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 the member specific benefit plan document 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 Coverage Determination Guidelines may apply.

HCPCS Code	Description
C9036	Injection, patisiran, 0.1 mg
J3490	Unclassified drugs

ICD-10 Diagnosis Code	Description
E85.1	Neuropathic heredofamilial amyloidosis

BENEFIT CONSIDERATIONS

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

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 \leq 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 Norfolk-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 the mean max serum TTR reduction by 87.8% from baseline in the patisiran treated group over 18 months. The LS mean change in the mNIS+7 from baseline at 18 months was -33.99 ($p = 9.26 \times 10^{-24}$); (Patisiran - 6.03; placebo +27.96). The LS mean change in the Norfolk QOL-DN from baseline at 18 months was -21.1 ($p = 1.10 \times 10^{-10}$); (Patisiran -6.7; placebo +14.4). All secondary endpoints (e.g., NIS-W, R-ODS, COMPASS-31, etc.) also achieved statistical significance at 18 months. The investigators also concluded that patisiran therapy was relatively safe and well tolerated with no increases in the frequency of events for patisiran compared to placebo group by system organ class. Overall, 13 deaths occurred in the APOLLO study, however, none of these were considered related to the study drugs and were consistent with natural history. The majority of infusion-related reactions were mild in severity, with no severe or life-threatening, or serious reactions. These reactions decreased over time and led to treatment discontinuation in only 1 patient. The investigators concluded that patisiran treatment resulted in significant improvement in polyneuropathy relative to placebo while significantly reducing disease symptoms and disability, improvement in quality of life, nutritional status, strength, and ambulation seen with patisiran relative to placebo.^{1,8}

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Patisiran. Local Coverage Determinations (LCDs) do not exist at this time.

In general, Medicare may cover outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the [Medicare Benefit Policy Manual \(Pub. 100-2\), Chapter 15, section 50 Drugs and Biologicals](#). (Accessed April 13, 2018)

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
04/01/2019	<ul style="list-style-type: none"> Updated list of related policies; removed reference link to the policy titled <i>Review at Launch for New to Market Medications</i> Removed language pertaining to Review at Launch program (prior authorization effective Jan. 1, 2019)
03/01/2019	Reorganized policy template; simplified and relocated <i>Instructions for Use and Benefit Considerations</i> section. Archived previous policy version 2019D0072C.
01/01/2019	Updated list of applicable HCPCS codes to reflect annual code edits; replaced C9399 with C9036. Policy 2018D0072B archived.
12/01/2018	Off cycle review. Revised coverage rationale. Approved by National Pharmacy & Therapeutics Committee on 11/16/2018. Policy 2018D0072A archived.
09/01/2018	New policy 2018D0072A. Approved by National Pharmacy & Therapeutics Committee on 08/17/2018.

INSTRUCTIONS FOR USE

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. 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.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence ([Medicare IOM Pub. No. 100-16, Ch. 4, §90.5](#)).

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. 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.