Clinical Criteria

Subject:	Onpattro (patisiran)		
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Status:	~~New~~Revised	**Last Review Date**:	~~08/17/2018~~08/16/2019

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Overview

This document addresses the use of Onpattro (patisiran), an RNA interference (RNAi) therapeutic agent approved by the Food and Drug Administration (FDA) for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis was formerly known as familial amyloid polyneuropathy (FAP).

Hereditary transthyretin (hATTR) amyloidosis is a multisystemic, progressive, life-threatening disease characterized by extracellular deposition of amyloid fibrils composed of misfolded transthyretin (TTR), a plasma transport protein produced predominantly by the liver. Amyloid fibrils accumulate in various organs and tissues such as the heart, kidney, gastrointestinal tract, and peripheral nerves, resulting in clinical manifestations such as polyneuropathy and cardiomyopathy. Potential symptoms associated with hATTR amyloidosis include but are not limited to muscle weakness, difficulty ambulating, impaired balance, orthostatic hypotension, disturbances in GI mobility, heart failure, arrhythmias, and sudden death due to severe conduction disorders.

Due to the constellation of symptoms and multisystemic nature of the disease, various assessments need to be utilized in an effort to quantify the overall disease burden for each individual with hATTR amyloidosis. Examples of clinical tests include the Neuropathy Impairment Score (NIS) and Polyneuropathy Disability (PND) Score. Clinical trials evaluated the use of Onpattro in individuals with hATTR amyloidosis and mild to moderate polyneuropathy. An example of mild to moderate polyneuropathy status is an individual who is able to ambulate with or without the use of assistance.

The efficacy of Onpattro was demonstrated in a randomized, double-blind, placebo-controlled trial in 225 adults with hereditary transthyretin amyloidosis with polyneuropathy. Study participants had a Neuropathy Impairment Score (NIS) of 5-130 (NIS scale ranges from 0-244), a polyneuropathy disability score of IIIb or lower and a TTR mutation confirmed by genotyping. Key exclusion criteria were previous liver transplant, New York Heart Association (NYHA) class III or IV heart failure, severe renal impairment or end-stage renal disease, moderate or severe hepatic impairment and other causes of polyneuropathy unrelated to hATTR amyloidosis. The primary efficacy assessment favored Onpattro over placebo. The difference in least-squares mean change from baseline to 18 months between groups was -34.0 points (95% CI -39.9 to -28.1) for the standardized modified Neuropathy Impairment Score+7 (mNIS+7) composite score.

Treatment with Onpattro leads to a decrease in serum vitamin A levels. Individuals should be advised to take vitamin A supplementation at the recommended daily allowance while receiving Onpattro therapy.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Onpattro (patisiran)

Requests for Onpattro (patisiran) may be approved if the following criteria are met:

I. Individual has a diagnosis of hereditary transthyretin (hATTR) amyloidosis or familial amyloid polyneuropathy (FAP); **AND**
II. Individual has a TTR mutation confirmed by genotyping (Adams, 2018); **AND**
III. Individual has associated mild to moderate polyneuropathy (Adams, 2018).

Requests for Onpattro (patisiran) may not be approved for the following:

I. All other indications not included above; **OR**
~~I.~~II. Individual has a history of liver transplantation; **OR**
~~II.~~III. Individual has severe renal impairment or end-stage renal disease; **OR**
~~III.~~IV. Individual has moderate or severe hepatic impairment; **OR**
~~IV.~~V. Individual has New York Heart Association (NYHA) class III or IV heart failure (Adams, 2018); **OR**
VI. Individual has sensorimotor or autonomic neuropathy not related to hATTR amyloidosis (monoclonal gammopathy, autoimmune disease, etc.) (Adams, 2017); **OR**
~~V.~~VII. Individual is using in combination with Tegsedi, Vyndaqel or Vyndamax.

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Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9036	Injection, patisiran, 0.1 mg [Onpattro] (Delete 10/1/19)
J3490	Injection, unclassified drugs when specified as Onpattro (Delete 10/1/19)
J0222	Injection, Patisiran, 0.1 mg [Onpattro] (Effective 10/1/19)

ICD-10 Diagnosis

E85.1-E85.9	Neuropathic heredofamilial amyloidosis
G62.9	Polyneuropathy unspeciifed

Document History

Revised: 08/16/2019
Document History:

- 08/16/2019 – Annual Review: Add may not approve criteria for combination use with other agents for amyloidosis. Wording and formatting changes. Coding Reviewed: Added J0222 for Onpattro Effective (10/1/19), Delete HCPCS J3490, C9036 (Effective 10/1/19) Added ICD-10 codes G62.9 and extended code range E85.1-E85.9 to include TTR mutation.
- 11/21/2018 – Deleted HCPCS codes C9399. Added HCPCS codes: C9036.
- 11/8/2018 – Added ICD-10 E85.1.
- 11/2/2018 – Added HCPCS codes: C9399 and J3490.
- 08/17/2018 – Annual Review: Add new clinical criteria for Onpattro.

References

1. Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. *N Engl J Med*. 2018;379(1):11-21.
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;17(1):181.
3. Ando Y, Coelho T, Berk JL, et. al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis*. 2013;8(31).
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: June 14, 2018.
5. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
6. Gertz MA, Benson MD, Dyck PJ, et. al. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. *J Am Coll Cardiol*. 2015;66(21):2451-2466.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2019; Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.