APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in the CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Links of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND

According to the National Institute of Health, transthyretin amyloidosis is a slowly progressive condition characterized by the buildup of abnormal deposits of a protein called amyloid (amyloidosis) in the body’s organs and tissues. These protein deposits most frequently occur in the peripheral nervous system, which is made up of nerves connecting the brain and spinal cord to muscles and sensory cells that detect sensations such as touch, pain, heat, and sound. Protein deposits in these nerves result in a loss of sensation in the extremities. The autonomic nervous system, which controls involuntary body functions such as blood pressure, heart rate, and digestion, may also be affected by amyloidosis. In some cases, the brain and spinal cord (central nervous system) are affected. Other areas of amyloidosis include the heart, kidneys, eyes, and gastrointestinal tract. The age at which symptoms begin to develop varies widely among individuals with this condition, and is typically between ages 20 and 70.1

Transthyretin amyloidosis is an inherited autosomal dominant condition caused by a mutation in the TTR gene. The TTR gene provides instructions for producing a protein called transthyretin. Transthyretin transports vitamin A and the hormone, thyroxine, throughout the body. In order to transport retinol and thyroxine, four transthyretin proteins must be attached to each other to form a four-protein unit. TTR gene mutations are thought to alter the structure of transthyretin, impairing its ability to bind to other transthyretin proteins and altering its normal function. Abnormally structured transthyretin can lead to amyloid deposits in the nervous system and heart.1,2

There are three major forms of transthyretin amyloidosis which are distinguished by their symptoms and the body systems they affect. The first form, neuropathic, primarily affects the peripheral and autonomic nervous systems. The leptomeningeal form affects the central nervous system and the cardiac form affects the heart.1

Because the neuropathic form of transthyretin amyloidosis primarily affects the peripheral and autonomic nervous systems, patients with the disease may experience peripheral neuropathy and difficulty controlling bodily functions. Impairments in bodily functions can include sexual impotence, diarrhea, constipation, problems with urination, and orthostatic hypotension. Some people experience heart and kidney problems as well. Various eye problems may...
occur, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or "scalloped" appearance. Some people with this form of transthyretin amyloidosis develop carpal tunnel syndrome. Patients with cardiac transthyretin amyloidosis may experience arrhythmia, cardiomegaly, orthostatic hypotension, and eventually congestive heart failure.\(^1,2\)

Onpattro™ (patisiran) lipid complex injection contains a transthyretin-directed small interfering RNA and is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. It was approved for use in the United States in 2018. Dosing is as follows: For patients weighing less than 100 kg, the recommended dosage is 0.3 mg/kg every 3 weeks by intravenous infusion and for patients weighing 100 kg or more, the recommended dosage is 30 mg. It is recommended that patients be premedicated with a corticosteroid, acetaminophen, and antihistamines. Onpattro™ should be infused over approximately 80 minutes. The most frequently reported adverse reactions were upper respiratory tract infections and infusion-related reactions.\(^3\)

**POSITION STATEMENT**

**Applicable To:**
- Medicaid – KY

**Exclusions**

Onpattro™ is **not considered medically necessary and not a covered benefit** when any of the following apply:
1. Diagnosis of any disorder other than polyneuropathy of hereditary transthyretin-mediated amyloidosis; OR,
2. Members under the age of 18 years old.

**Coverage**

Onpattro™ is **considered medically necessary and a covered benefit** for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis when ALL of the following apply:
1. Member is age 18 years or older; **AND,**
2. Member has a documented pathogenic variant in TTR, **AND,**
3. Member has a documented peripheral neuropathy, **AND,**
4. Attestation that the member will receive all required premedication at least 60 minutes prior to the start of Onpattro infusion including (intravenous premedication can be given orally if not available or not tolerated):
   A. Intravenous corticosteroid (e.g., dexamethasone 10 mg, or equivalent); **AND,**
   B. Oral acetaminophen (500 mg); **AND,**
   C. Intravenous H1 blocker (e.g., diphenhydramine 50 mg, or equivalent); **AND,**
   D. Intravenous H2 blocker (e.g., ranitidine 50 mg, or equivalent); **AND,**
5. Dose is 0.3 mg/kg IV every 3 weeks, maximum of 30 mg; **AND,**
6. Prescribed by or in consultation with a neurologist, cardiologist, or gastroenterologist.

**CODING**

**Covered CPT Codes**

- 96365 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
- 96366 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hr.
- 96367 Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour
- 96379 Unlisted therapeutic, prophylactic, or diagnostic intravenous or intra-arterial injection or infusion
- 96413 Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
- 96415 Chemotherapy administration, intravenous infusion technique; each additional hour

**Covered HCPCS Codes**

- C9036 Injection, patisiran, 0.1mg

Clinical Coverage Guideline
J3490 Unclassified drugs

Covered ICD-10 Code

E85.1 Neuropathic heredofamilial amyloidosis

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal/state laws.

REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/1/2018</td>
<td>• Approved by MPC. New.</td>
</tr>
</tbody>
</table>