Department:	Pharmacy	**Original Approval:**	01/10/2019
Policy #:	PM568	**Last Approval:**	01/10/2019
Title:	Patisiran (Onpattro) intravenous injection		
Approved By:	UM Pharmacy Subcommittee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Patisiran (Onpattro) for subcutaneous use: History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Age -Prescribed by or in consultation with a Aneurologist, geneticist, or a physician who specializes in the treatment of amyloidosis. - Labs/diagnostics - Medication list (current and past) to include start and end dates of previous trials for amyloid cardiomyopathy.

BACKGROUND

Onpattro is a lipid nanoparticle formulated RNA interference (RNAi) therapeutic indicated for treatment of hereditary amyloid transthyretin amyloidosis (hATTR) with polyneuropathy.[1] hATTR is a rare, inherited, rapidly-progressive, debilitating, life-threatening disease.[2-4] It is a multisystem condition caused by mutation in the transthyretin (TTR) gene that results in misfolded TTR protein accumulation (as amyloid) in the nerves, heart, and other areas of the body. Onpattro targets hepatic production of mutant TTR. By reducing the unstable circulating TTR tetramers, organ deposition of amyloid is prevented, thus, stabilizing or improving symptoms of neuropathy.

Guidelines

There are no other approved therapies in the US for treatment of hATTR.[3] There is a European consensus for diagnosis, management, and treatment of transthyretin familial amyloid polyneuropathy (2016). Symptomatic management associated with sensory-motor neuropathy and autonomic dysfunction should be started at diagnosis. This may include painkillers, antidiarrheal drugs, treatment of symptomatic orthostatic hypotension, diuretics for heart failure, prophylactic pacemaker implantation for conduction disorders, and/or vitrectomy/trabeculectomy for ocular amyloidosis or glaucoma. Tetramer stabilizers (tafamidis and diflunisal) are mentioned as treatment options that slow the rate of amyloidogenesis by preventing the dissociation, misfolding, and misassembly of mutated TTR. Tafamidis is recommended for use in patients with Stage 1 disease. Those presenting with Stage 2 disease are recommended for a clinical trial with an antisense oligonucleotide, small interfering RNA, doxycycline-tauroursodeoxycholic acid, or off-label use of diflunisal. Onpattro is mentioned as an emerging therapy for hATTR.

DEFINITIONS

None

INDICATIONS/CRITERIA

Medicaid Members	***Continue to criteria for approval below.***
Medicare Members	***Step-utilization of Part D drugs not required.***

FDA-Approved Indication

1. **Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR).** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** The patient has a documented transthyretin (TTR) mutation verified by genetic testing; AND
   - **B)** The patient has symptomatic peripheral neuropathy (e.g., reduced motor strength/ coordination, impaired sensation [e.g., pain, temperature, vibration, touch]); AND
   - **C)** 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
   - **D)** The patient is 18 years of age or older; AND
   - **E)** Onpattro is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

   Dosing: Onpattro 0.3 mg/kg IV is administered as an IV infusion once every 3 weeks (maximum dose 30 mg).

   Initial Approval/Extended Approval: 1 year

   Duration of Therapy: Indefinite

Waste Management for All Indications.
The dose of Onpattro is a 0.3 mg/kg (maximum 30 mg) via intravenous (IV) infusion. The number of vials needed should be calculated.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
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. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances *not* listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS

None

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

CFR		
WAC	WAC 284-43-2050	
RCW		
Contract Citation	☒ WAH	
	☒ IMC	
	☒ MA	
Other Requirements		
NCQA Elements		
References	1. Onpattro lipid complex injection, for intravenous use [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; August 2018. 2. Rizk M, Tüzmen Ş. Update on the clinical utility of an RNA interference-based treatment: focus on patisiran. *Pharmgenomics Pers Med*. 2017;10:267-278. 3. Adams D, Suhr OB, Hund E, et al. First European consensus for diagnosis, management, and treatment of transthyretin familial amyloid polyneuropathy. *Curr Opin Neurol*. 2016;29 Suppl 1:S14-26.	

	4. Gertz MA, Benson MD, Dyck PJ, et al. Diagnosis, prognosis, and therapy of transthyretin amyloidosis. *J Am Coll Cardiol.* 2015;66(21):2451-2466.

Revision History

Revision Date	Revision Description	Revision Made By
01/02/2019	New policy	Jennifer Farley, PharmD
01/10/2019	Approval	UM Pharmacy Subcommittee