Familial Amyloid Polyneuropathy

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

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.

Tegsedi (inotersen) is a transthyretin-directed antisense oligonucleotide indicated for treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

POLICY

Required Documentation

The following information is necessary to initiate the prior authorization review:

1. TTR gene mutation confirmed by genetic testing
2. Medical records documenting polyneuropathy disability (PND) score and neuropathy impairment score (NIMS)

Criteria for Initial Approval

A. Onpattro may be considered **medically necessary** when ALL of the following criteria are met:

1. Member is 18 years of age or older.
2. Member has a diagnosis of hereditary ATTR amyloidosis with polyneuropathy confirmed by the presence of a TTR gene mutation (e.g. V30M)

3. Member has a polyneuropathy disability (PND) score ≤ IIIb (see Appendix A)
4. Member has clinical signs and symptoms of polyneuropathy (i.e. weakness, sensory loss, decreased motor strength, decreased gait speed)
5. Other causes of peripheral neuropathy have been assessed and ruled out (see Appendix B)
6. Patient is receiving Vitamin A supplementation prior to initiating therapy with the requested drug and will continue to receive for duration of treatment
7. Member will not be receiving the requested medication in combination with another TTR stabilizer (tafamidis, inotersen, diflunisal)
8. Medication is being prescribed by or in consultation with a neurologist or a specialist in the treatment of amyloidosis

Initial approval will be for **9 months**

B. Tegsedi may be considered **medically necessary** when ALL of the following criteria are met:
1. Member is 18 years of age or older.
2. Member has a diagnosis of hereditary ATTR amyloidosis with polyneuropathy confirmed by the presence of a TTR gene mutation (e.g. V30M)
3. Member has a polyneuropathy disability (PND) score ≤ IIIb
4. Member has clinical signs and symptoms of polyneuropathy (i.e. weakness, sensory loss, decreased motor strength, decreased gait speed)
5. Other causes of peripheral neuropathy have been assessed and ruled out (see Appendix B)
6. Member has a baseline platelet count ≥100 x 10^9/L prior to starting therapy
7. Member has a baseline urinary protein to creatinine ratio (UPCR) <1000mg/g prior to starting therapy
8. Member will not be receiving the requested medication in combination with another TTR stabilizer (tafamidis, patisiran, diflunisal)
9. Medication is being prescribed by or in consultation with a neurologist or a specialist in the treatment of amyloidosis

Initial approval will be for **9 months**

Continuation of Therapy

Continuation of therapy may be granted for members that meet all initial criteria and have achieved a therapeutic response as evidenced by stabilization or improvement from baseline in polyneuropathy disability (PND) or neuropathy impairment score (NIS).

Approval will be for **12 months**

Quantity Limits Apply

Onpattro
- 3 vials per 21 days

Tegsedi
- 4 pre-filled syringes per 28 days

Dosing

Onpattro
- For patients weighing less than 100 kg, the recommended dosage is 0.3 mg/kg every 3 weeks. For patients weighing 100 kg or more, the recommended dosage is 30 mg every 3 weeks.
- Patients should receive pre-medication with a corticosteroid, acetaminophen, and antihistamines prior to infusion to prevent infusion-related reactions.

Tegsedi
- The recommended dosage is 284 mg administered by subcutaneous injection once weekly.

APPENDIX

A. Polyneuoropathy Disability Score (PND)

Stage 0: no impairment
Stage I: sensory disturbances but preserved walking capability
Stage II: impaired walking capability but ability to walk without a stick or crutches
Stage IIIa: walking only with the help of one stick or crutch
Stage IIIb: walking with the help of two sticks or crutches
Stage IV: confined to a wheelchair or bedridden

B. Other Causes of Peripheral Neuropathy

a. Diabetes
b. Glucose Intolerance
c. Vitamin B_{12} deficiency
d. Charcot-Marie-Tooth disease
e. Chemotherapeutic agents (e.g. platins,vincristine, taxanes, lenalidomide, thalidomide)
f. Trauma
g. Vasculitis
h. Autoimmune diseases (e.g. Sjögren's syndrome, lupus, rheumatoid arthritis)
i. Chronic kidney disease
j. Vitamin B_6 toxicity
k. Paraneoplastic syndrome
l. Viral infections (e.g. varicella-zoster, herpes simplex, Lyme disease, West Nile, cytomegalovirus, HIV)

CLINICAL RATIONALE

Hereditary transthyretin amyloidosis (hATTR) is an autosomal dominant disease caused by mutations in transthyretin encoding genes. Affecting multiple organ systems, the disease is progressive and fatal, as circulating tranthyretin proteins misfold, resulting in amyloid deposition to organs and tissues. Clincial manifestations include cardiomyopathies and neuropathies.

Onpattro is the first FDA-approved agent for the treatment of polyneuropathy of hATTR amyloidosis in adults. Onpattro is a small interfering RNA (siRNA), targeting transthyretin synthesis within the liver. In a phase III trial, Onpattro treatment every 3 weeks for 18 months was found to be superior to placebo in achieving a decrease from baseline in mNIS+7, demonstrating improvement in neuropathy impairment. Clinical benefit was assessed with change from baseline in Norfolk QoL-DN, favoring the Onpattro treatment group. Infusion related reactions occurred more frequently in patients receiving Onpattro. Labeling requirements include instructions for pre-medication and monitoring during infusion. Onpattro has also been found to decrease serum Vitamin A levels. Supplementation of Vitamin A during treatment is recommended. An extension study following completion of the phase III trial is ongoing.

Tegsedi is the second agent to be FDA-approved for the treatment of polyneuropathy of hATTR amyloidosis in adults, just two months following the approval of Onpattro. Tegsedi is an oligonucleotide. Although Tegsedi and Onpattro have unique mechanisms, they both target hepatic synthesis of transthyretin. A phase III trial evaluated the safety and efficacy of Tegsedi. The primary endpoints were achieved, with significant differences from placebo in the change in the mNIS+7 and Norfolk QOL-DN scores following 15 months of treatment. Adverse events including glomerulonephritis and thrombocytopenia were reported, resulting in one death. As a result, Tegsedi will only be available through a REMS program and requires

ongoing lab monitoring of platelets, serum creatinine, estimated glomerular filtration rate, and urinary protein to creatinine ratio.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J0222 Injection, Patisiran, 0.1 mg (effective 10/1/2019)

REFERENCES

- Onpattro [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc; January 2020..
- Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018;379:11-21.
- Tegsedi [package insert]. Boston, MA: Akcea Therapeutics, Inc. September 2020.
- Benson MD, Waddington-Cruz M, Berk JL, et al. Inotersen Treatment for Patients with Hereditary Tranthyretin Amyloidosis. N Engl J Med. 2018;379:22-31.

POLICY HISTORY

Policy #: 05.02.54
Policy Creation: October 2018
Reviewed: January 2021
Revised: January 2020
Current Effective Date: March 6, 2020