Familial Amyloid Polyneuropathy

**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.

Other applications are considered investigational and are not a covered benefit.

**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. Patient is receiving Vitamin A supplementation prior to initiating therapy with the requested drug and will continue to receive for duration of treatment.

6. Member will not be receiving the requested medication in combination with another TTR stabilizer (tafamidis, inotersen, diflunisal).

**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. Member has a baseline platelet count ≥100 x 10⁹/L prior to starting therapy.
6. Member has a baseline urinary protein to creatinine ratio (UPCR) <1000mg/g prior to starting therapy.
7. Member will not be receiving the requested medication in combination with another TTR stabilizer (tafamidis, patisiran, diflunisal).

**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. Polyneuropathy 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

**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 transthyretin proteins misfold, resulting in amyloid deposition to organs and tissues. Clinical 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.

- J3490 Drugs unclassified injection

**REFERENCES**

POLICY HISTORY

Policy #: 05.02.54
Policy Creation: October 2018
Reviewed:
Revised:
Current Effective Date: January 31, 2019