Protocol for Transthyretin-mediated Amyloidosis (ATTR) Products
Approved by NJ DURB, October 2019

Onpattro® (patisiran)
Vyndaqel® and Vyndamax® (tafamidis meglumine)
Tegsedi® (inotersen)

Background:
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.

Vyndaqel® (tafamidis meglumine) and **Vyndamax® (tafamidis)** are transthyretin stabilizers indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

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

Criteria for approval:

1. Documentation of diagnosis is confirmed by genotyping, biopsy, immunohistochemical analysis, scintigraphy, or mass spectrometry
2. Medication is prescribed by or in consultation with a neurologist, cardiologist, or a specialist in the treatment of ATTR.
3. Patient has clinical signs and symptoms of the disease (for example, peripheral sensorimotor polyneuropathy, motor disability, cardiovascular dysfunction, carpal tunnel syndrome, etc.)
4. Weight must be received for drugs that have weight-based dosing. Height and weight must be received for drugs that have dosing based on body surface area.
5. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, or national guidelines.
6. The patient will not be receiving the requested drug with any other drugs listed in the policy index

For Onpattro® requests:

a. Patient is 18 years or older
b. Patient has a diagnosis of polyneuropathy of hereditary transthyretin-mediated Amyloidosis

For Vyndaqel® and Vyndamax® requests:

a. Medication is being used to treat cardiomyopathy of wild type or hereditary transthyretinmediated amyloidosis (ATTR-CM) to reduce cardiovascular mortality and cardiovascular-related hospitalization

For Tegsedi® requests:

a. Patient is 18 years or older

b. Patient has a diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis
c. The member must not have any of the following contraindications:
    i. Patient has platelet count < 100,000/mm3
    ii. History of acute glomerulonephritis caused by Tegsedi

Continuation of therapy:

1. Documentation that patient has experienced a positive clinical response to medication (for example, improved neurologic impairment, motor function, quality of life, etc.)
2. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, or national guidelines.
3. For dose increases, weight must be received for drugs that have weight-based dosing. For dose increases, height and weight must be received for drugs that have dosing based on body surface area.

Approval Duration: 6 months

Tegsedi® Boxed Warning

WARNING: THROMBOCYTOPENIA AND GLOMERULONEPHRITIS See full prescribing information for complete boxed warning. Thrombocytopenia • TEGSEDI causes reductions in platelet count that may result in sudden and unpredictable thrombocytopenia, which can be life-threatening. • Testing prior to treatment and monitoring during treatment is required Glomerulonephritis • TEGSEDI can cause glomerulonephritis that may require immunosuppressive treatment and may result in dialysis dependent renal failure. • Testing prior to treatment and monitoring during treatment is required TEGSEDI is available only through a restricted distribution program called the TEGS EDI REMS Program

References:

1. Onpattro [package insert]. Alnylam Pharmaceuticals, Inc. San Diego, CA 92121. August 2018.
2. Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis) [package insert]. Pfizer Labs Inc. NY, NY 10017. May 2019.
3. Tegsedi [package insert]. Ionis Pharmaceuticals, Inc. Carlsbad, CA 92010. October 2018
4. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet Journal of Rare Diseases 2013, 8:31:
5. Maurer MS, Schwartz JH, Gundepaneni B, et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. N Engl J Med 2018; 379:1007-1016.
6. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically
7. Donnelly JP, et al. Cardiac amyloidosis: An update on diagnosis and treatment. Cleve Clin J Med. 2017;84(12 suppl
8. 3):12-26. Available at https://mdedge-files-live.s3.us-east-2.amazonaws.com/files/s3fspublic/issues/articles/hanna_.cardiacamyloidosis.pdf. Accessed September 12, 2019.
9. Nativi-Nicolau J, Maurer MS. Amyloidosis cardiomyopathy: update in the diagnosis and treatment of the most common types. Curr Opin Cardiol. 2018;33(5):571-579
10. Rigopoulos AG, et al. Advances in the diagnosis and treatment of transthyretin amyloidosis with cardiac involvement. Heart Fail Rev. 2019 Jul;24(4):521-533.

11. Gertz, MA. Hereditary ATTR Amyloidosis: Burden of Illness and Diagnostic Challenges. Am J Manag Care. 2017;23:S107-S112.
12. Adams D, Gonzales-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Thransthyretin Amyloidosis. N Engl J Med 2018;379:11-21.
13. Benson MD, Waddington-Cruz M, Berk JL. Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. N Engl J Med 2018;379:22-31