Pharmacy Policy Bulletin

Title: Transthyretin Amyloidosis Agents

Policy #: Rx.01.215

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **inotersen (Tegsedi™)**), **tafamidis meglumine (Vyndamax®, Vyndaqel®)** as provided under the member's prescription drug benefit.

Description:

Hereditary transthyretin amyloidosis (hATTR) is a rare autosomal dominant, progressively debilitating, and often fatal genetic disease characterized by the accumulation of abnormal amyloid protein in tissues. Transthyretin (TTR) is produced primarily by the liver and is responsible for the transport of thyroxine and retinol binding protein-vitamin A complex. The hATTR genetic mutations lead to mutated TTR protein which results in destabilization from the TTR tetramer into monomers and oligomers, protein misfolding, and aggregation resulting in formation of TTR amyloid fibrils. hATTR can present with peripheral and/or autonomic neuropathy, infiltrative cardiomyopathy, vitreous amyloid, or leptomenigeal disease.

Inotersen (Tegsedi™) is an antisense oligonucleotide that causes degradation of mutant and wild-type TTR mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

Inotersen (Tegsedi™) is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Transthyretin-mediated amyloidosis with cardiomyopathy (ATTR-CM) occurs when amyloidosis occurs in the cardiac tissue. Wild type ATTR-CM typically presents in men aged 65 years and older, but it can occur in women and in younger patients. Amyloid accumulates in the cardiac tissue leading to atrial and ventricular wall thickening and diastolic dysfunction, arrhythmias, and preserved ejection fraction heart failure. For wild type ATTR-CM, the median survival is reported to be 3.6 years.

Patients with wild type ATTR may also present with bilateral carpal tunnel syndrome as an initial symptom years before the onset of cardiac symptoms (Sekijima 2015).

Due to the lack of effective therapy, testing for ATTR-CM has been underutilized. Testing may include echocardiogram, cardiac magnetic resonance imaging (MRI), and nuclear scintigraphy. Tissue biopsy, either endomyocardial tissue or other locations such as abdominal fat pad, is the gold standard for diagnosis of amyloidosis. A non-invasive test to identify those with ATTR-CM is radiotracer 99mtechnetium pyrophosphate scan (99mTc-PYP). The FDA-has not yet approved 99mTc-PYP test for the diagnosis of ATTR-CM, but it is being used in clinical practice (Vyndaqel Dossier 2019).

Tafamidis meglumine (Vyndaqel®, Vyndamax ®) is a selective transthyretin (TTR) stabilizer, limiting the dissociation of the native TTR tetramer into monomers, which reduces TTR amyloid fibril formation.

Tafamidis meglumine (Vyndaqel®, Vyndamax ®) is indicated for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related

hospitalization.

Policy:

INITIAL CRITERIA Tegsedi™ (inotersen) is approved when ALL of the following are met:

1. Diagnosis of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis with transthyretin mutation (e.g., V30M) confirmed by molecular genetic testing; and
2. Documentation of ONE of the following baseline ambulation parameters in either the Familial Amyloid Polyneuropathy (FAP) Stage or Polyneuropathy Disability (PND) Score:
    a. Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the Familial Amyloid Polyneuropathy (FAP) staging tool; or
    b. Score I, II, IIIa, or IIIb on the Polyneuropathy Disability (PND) scoring tool; AND
3. Documented presence of cardiac or renal manifestations, or motor, sensory, or autonomic neuropathy related to the hATTR amyloidosis with polyneuropathy (e.g., neuropathic pain, muscle weakness that affects daily living, orthostatic hypotension, diarrhea, nausea, vomiting, heart failure, arrhythmias, proteinuria, renal failure; vision disorders, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or scalloped appearance; and
4. Documentation confirming the member has not had a liver transplant; and
5. Prescribed by or in consultation with a neurologist

Initial authorization duration: 16 months

CONTINUATION CRITERIA Tegsedi™ (inotersen) is re-approved when BOTH of the following are met:

1. Documentation of one of the following:
    a. Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the Familial Amyloid Polyneuropathy (FAP) staging tool; or
    b. Score I, II, IIIa, or IIIb on the Polyneuropathy Disability (PND) scoring tool; AND
2. Documented improvement or stability in the signs and symptoms hATTR amyloidosis with polyneuropathy (e.g., neuropathic pain, muscle weakness that affects daily living, orthostatic hypotension, diarrhea, nausea, vomiting, heart failure, arrhythmias, proteinuria, renal failure; vision disorders, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or scalloped appearance), based on objective or standard evaluation scales.

Continuation authorization duration: 2 years

INITIAL CRITERIA Tafamidis meglumine (Vyndamax®, Vyndaqel®) is approved when ALL of the following are met:

1. Member is 18 years of age or older; AND
2. Diagnosis of transthyretin-mediated amyloidosis with cardiomyopathy (ATTR-CM) confirmed by ONE of the following:
    A. Member has a transthyretin (TTR) mutation (e.g., V122I), or
    B. Cardiac or noncardiac tissue biopsy demonstrating histologic confirmation of TTR amyloid deposits, or
    C. All of the following: echocardiogram or cardiac magnetic resonance image suggestive of amyloidosis, scintigraphy scan suggestive of cardiac TTR amyloidosis, and absence of light-chain amyloidosis; AND
3. Prescribed by or in consultation with a cardiologist; and
4. One of the following:
    A. History of heart failure (HF), with at least one prior hospitalization for HF, or
    B. Presence of clinical signs and symptoms of HF (e.g., dyspnea, edema); or
5. Member has New York Heart Association (NYHA) Functional Class I, II, or III heart failure.

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Tafamidis meglumine (Vyndamax®, Vyndaqel®) is re-approved when ALL of the following are met:

1. Positive clinical response to therapy; and
2. Member continues to have NYHA Functional Class I, II, or III heart failure; and
3. Prescribed by or in consultation with a cardiologist.

Reauthorization duration: 12 months

Black Box Warning as shown in the drug Prescribing Information:

WARNING: THROMBOCYTOPENIA AND GLOMERULONEPHRITIS

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

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

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Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Tegsedi™	Inotersen
Vyndamax®, Vyndaqel®	Tafamidis meglumine

Cross References:

Off-Label Use Rx.01.33

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P&T Approval Date:	June 09, 2022
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professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.