

Pharmacy Policy Bulletin

Title: Amyloidogenic 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™)** as provided under the member's prescription drug benefit.

▸ Description:

Hereditary transthyretin amyloidosis (hATTR) is a rare autosomal dominant, progressively debilitating, and often fatal generic 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 leptomeningeal 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.

▸ 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
 - b. Score I, II, IIIa, or IIIb on the Polyneuropathy Disability (PND) scoring tool
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
4. Documentation confirming the member has not had a liver transplant
5. Prescribed by or in consultation with a neurologist

CONTINUATION CRITERIA

Tegsedi™ (inotersen) is approved when there is documentation of BOTH of the following

1. Documentation of one of the following
 - a. Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the Familial Amyloid Polyneuropathy (FAP) staging tool
 - b. Score I, II, IIIa, or IIIb on the Polyneuropathy Disability (PND) scoring tool
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.

AUTHORIZATION DURATION: 16 months for initial and indefinite for continuation

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:

Gorevic PD. Genetic factors in the amyloid diseases. UpToDate Web site. Updated June 26, 2018. www.uptodate.com. Accessed January 30, 2019.

Sekijima Y. Transthyretin (ATTR) amyloidosis: clinical spectrum, molecular pathogenesis and disease-modifying treatments. *J Neurol Neurosurg Psychiatry*. 2015;86:1036-1043.

Tegsedi™ (inotersen) [prescribing information]. Boston MA. Akcea Therapeutics, Inc. October 2018. Available at: <https://tegsedi.com/wp-content/uploads/2018/10/prescribing-information.pdf>. Accessed January 30, 2019

Applicable Drugs:

i 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

Cross References:

N/A

Policy Version Number:	1.00
P&T Approval Date:	January 10, 2019
Policy Effective Date:	April 01, 2019
Next Required Review Date:	January 10, 2020

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and 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.