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# STANDARD MEDICARE PART B MANAGEMENT

## TEGSEDI (inotersen)

## POLICY

### I. INDICATIONS

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

FDA-Approved Indication
Tegsedi is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

### II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
A. For initial requests:
   1. Testing or analysis confirming a mutation of the TTR gene
   2. Medical record documentation confirming that the member demonstrates signs and symptoms of polyneuropathy (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy)
B. For continuation requests: medical record documentation confirming the member demonstrates clinical benefit compared to baseline

### III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a neurologist, geneticist, or physician specializing in the treatment of amyloidosis.

### IV. CRITERIA FOR INITIAL APPROVAL

**Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis**
Authorization of 12 months may be granted for treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis (also called transthyretin-type familial amyloid polyneuropathy [ATTR-FAP]) when all of the following criteria are met:
A. The diagnosis is confirmed by detection of a mutation of the TTR gene.

B. Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
C. The member is not a liver transplant recipient.
D. The requested medication will not be used in combination with patisiran (Onpattro), tafamidis (Vyndaqel, Vyndamax) or vutrisiran (Amvuttra)

## V. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving treatment with the requested medication.
B. The requested medication is being used for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis.
C. There is a clinical benefit from therapy with the requested medication (e.g., improvement of neuropathy severity and rate of disease progression as demonstrated by the modified Neuropathy Impairment Scale+7 (mNIS+7) composite score, the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) total score, polyneuropathy disability (PND) score, FAP disease stage, manual grip strength).

## VI. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Tegsedi.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. Guideline of transthyretin-related hereditary amyloidosis for clinicians

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Tegsedi are covered.

## VII. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Tegsedi and the above initial criteria can be found in the guideline from Ando and colleagues discussing hereditary transthyretin amyloidosis. The diagnosis of ATTR should be suspected in patients with progressive sensorimotor and/or autonomic neuropathy. The diagnosis of hereditary ATTR is established when characteristic clinical features are present, a biopsy showing amyloid deposits that bind to anti-TTR antibodies, and identification of mutations of the TTR gene.
The treatment for peripheral and autonomic neuropathy is orthotopic liver transplantation, TTR tetramer stabilizers and gene-silencing therapies. Liver transplantation provides a wild type gene expressing normal TTR in the liver. Successful liver transplantation results in the disappearance of the variant TTR protein and thus halts the progression of peripheral and/or autonomic neuropathy.

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## VIII.REFERENCES


1. Tegsedi [package insert]. Waltham, MA: Sobi, Inc.; June 2022.
2. Benson MD, et. al., Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5; 379(1):22-31.
3. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.