Reference number(s)
4731-A

Standard Medicare Part B Management Tegsedi

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Tegsedi	inotersen

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 Indications[1]

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 listed in this document should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

- Initial requests:
  - Testing or analysis confirming a pathogenic variant in the TTR gene.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

  - Medical record documentation demonstrating clinical manifestations of transthyretin-type familial amyloid polyneuropathy [ATTR-FAP] (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
  - Medical record documentation confirming that the member demonstrates signs and symptoms of polyneuropathy.
- Continuation requests: Chart notes or medical record documentation supporting clinical benefit of therapy compared to baseline.

Coverage Criteria

Polyneuropathy of Hereditary Transthyretin-mediated Amyloidosis[1-4]

Authorization of 12 months may be granted for the 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:

- Member is 18 years of age or older.
- The diagnosis is confirmed by detection of a pathogenic variant in the TTR gene.
- Member exhibits clinical manifestations of ATTR-FAP (e.g., amyloid deposition in biopsy specimens, TTR protein variants in serum, progressive peripheral sensory-motor polyneuropathy).
- The requested medication will not be used in combination with vutrisiran (Amvuttra), patisiran (Onpattro), eplontersen (Wainua), tafamidis meglumine (Vyndaqel), tafamidis (Vyndamax), or acoramidis (Attruby).

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:

- The member is currently receiving treatment with the requested medication.
- The requested medication is being used to treat an indication listed in the coverage criteria section.
- There is a clinical benefit from therapy with the requested medication compared to baseline (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).

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Tegsedi.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- Guideline of transthyretin-related hereditary amyloidosis for clinicians.
- Hereditary Transthyretin Amyloidosis. In: GeneReviews.
- Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis.

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

Explanation of Rationale

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

Support for using the above initial criteria can be found in a guideline from Ando and colleagues and a Gene Reviews chapter 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 shows amyloid deposits that bind to anti-TTR antibodies, and there is identification of pathogenic variants in 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.

Pharmacologic treatment approaches for hereditary TTR amyloidosis (ATTR) include ribonucleic acid (RNA)-targeted therapies (e.g., Amvuttra, Onpattro, Tegsedi, Wainua) that interfere with hepatic TTR synthesis, and transthyretin tetramer stabilizers (e.g., Vyndaqel, Vyndamax) that reduce formation of TTR amyloid through stabilization of the tetramer configuration and subsequently prevent the release of amyloidogenic monomers. These therapies work to decrease TTR production. Currently, there is no literature supporting the combination use of any therapies approved for ATTR.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.

References

1. Tegsedi [package insert]. Waltham, MA: Sobi, Inc.; January 2024.
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, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.
4. Sekijima Y. Hereditary Transthyretin Amyloidosis. 2001 Nov 5 [Updated 2021 May 30]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1194/. Accessed March 18, 2025.

© 2025 CVS Caremark. All rights reserved.

This document contains confidential and proprietary information of CVS Caremark and cannot be reproduced, distributed or printed without written permission from CVS Caremark. This document contains prescription brand name drugs that are trademarks or registered trademarks of pharmaceutical manufacturers that are not affiliated with CVS Caremark.