Clinical Policy: Inotersen (Tegsedi)

Reference Number: PA.CP.PHAR.405
Effective Date: 01/2019
Last Review Date: 04/2024

Description
Inotersen (Tegsedi®) is a transthyretin-directed antisense oligonucleotide.

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

***Akcea Therapeutics, Inc., the manufacturer of Tegsedi, will discontinue commercial availability of Tegsedi effective September 27, 2024 based on low utilization of the product** *(see Appendix D).*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Tegsedi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Diagnosis of hATTR with polyneuropathy;
2. Documentation confirms presence of a transthyretin (TTR) mutation;
3. Biopsy is positive for amyloid deposits or medical justification is provided as to why treatment should be initiated despite a negative biopsy or no biopsy;
4. Prescribed by or in consultation with a neurologist;
5. Age ≥ 18 years;
6. Member has not had a prior liver transplant;
7. Recent (dated within the last month) platelet count ≥ 100 x 10^9/L;
8. Member has not received prior treatment with Amvuttra™,Onpattro®™ or Wainua™
9. Tegsedi is not prescribed concurrently with Amvuttra, Onpattro or Wainua;
10. Dose does not exceed 284 mg (1 syringe) per week.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Hereditary Transthyretin-Mediated Amyloidosis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Recent (dated within the last month) platelet count ≥ 100 x 10^9/L;
3. Member is responding positively to therapy – including but not limited to improvement in any of the following parameters:
   a. Neuropathy (motor function, sensation, reflexes, walking ability);
   b. Nutrition (body mass index);
   c. Cardiac parameters (Holter monitoring, echocardiography, electrocardiogram, plasma BNP or NT-proBNP, serum troponin);
   d. Renal parameters (creatinine clearance, urine albumin);
   e. Ophthalmic parameters (eye exam);
4. Member has not had a prior liver transplant;
5. Tegsedi is not prescribed concurrently with Amvuttra, Onpattro or Wainua;
6. If request is for a dose increase, new dose does not exceed 284 mg (1 syringe) per week.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BNP: B-type natriuretic peptide
FDA: Food and Drug Administration
hATTR: hereditary transthyretin-mediated amyloidosis
NT-proBNP: N-terminal pro-B-type natriuretic peptide
TTR: transthyretin

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Platelet count below 100 x 10^9/L
  - History of acute glomerulonephritis caused by Tegsedi

  - History of a hypersensitivity reaction to Tegsedi
- Boxed warning(s): Thrombocytopenia and glomerulonephritis
- Tegsedi is available only through a restricted distribution program called the Tegsedi REMS Program.

Appendix D: Discontinuation from market

- Akcea Therapeutics, Inc., the manufacturer of Tegsedi, will discontinue the commercial availability of the product in the United States effective September 27, 2024. The decision is based on low utilization of the product and is not related to quality, manufacturing, or safety measures.
  - Healthcare providers should transition all patients who have been prescribed Tegsedi to any of the commercially available treatment alternatives indicated for hATTR with polyneuropathy.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
hATTR with polyneuropathy	284 mg SC once weekly	284 mg/week

VI. Product Availability

Single-dose, prefilled syringe: 284 mg

VII. References

1. Tegsedi Prescribing Information. Boston, MA: Akcea Therapeutics, Inc.; January 2024. Available at:https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/211172s014lbl.pdf. Accessed February 12, 2024.
2. Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis*. 2013 Feb 20;8:31.
3. Benson MD, Waddington-Cruz M, Berk JL, et al. Inotersen treatment for patients wth hereditary transthyretin amyloidosis. *N Engl J Med.* 2018;379:22-31. DOI: 10.1056/NEJMoa1716793.
4. Adams D, Gonzalez-Duarte A, O'Riordan WD, Yang CC, Ueda M, Kristen AV, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. *N Engl J Med*. 2018 Jul 5;379(1):11-21.
5. Luigetti M, Romano A, Di Paolantonio A, et al. Diagnosis and treatment of hereditary transthyretin amyloidosis (hATTR) polyneuropathy: current perspectives on improving patient care. *Therapeutics and Clinical Risk Management.* 2020;16:109–23.
6. Adams D, Ando Y, Beirao HM, et al. Expert consensus recommendations to improve diagnosis of ATTR amyloidosis with polyneuropathy. J Neurology. 2021;268:2109-22.
7. Carroll A, Dyck PJ, de Carvalho M, et al. Novel approaches to diagnosis and management of hereditary transthyretin amyloidosis. J Neurol Neurosurg Psychiatry. 2022;93:668–78.
8. Tegsedi Healthcare Providers. Tegsedi [homepage]. Boston, MA: Akcea Therapeutics, Inc.; 2024. Available at: https://tegsedihcp.com/. Accessed February 29, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-

to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3490	Unclassified drugs
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created.	01/2019
1Q 2020 annual review: references reviewed and updated.	01/2020
1Q 2021 annual review: references reviewed and updated.	01/2021
Added requirement that Tegesedi is not prescribed concurrently with Onpattro; Added REMS requirement for platelet count $\geq 100 \times 10^9$/L	10/2021
1Q 2022 annual review: no significant changes; references reviewed and updated.	07/2022
Added requirement that member has not received prior treatment with Amvuttra or Onpattro as a result of the recent Amvuttra FDA approval and for consistency across this therapeutic area; applied to continued therapy requirement that member has not had a prior liver transplant; added Amvuttra should not be prescribed concurrently with Tegsedi.	10/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024
2Q 2024 annual review: added Wainua to list of drugs that should not have been previously received or prescribed concurrently; added active HCPCS codes [C9399] and [J3490]; added disclaimer regarding manufacturer discontinuing commercial avilaiblity of Tegsedi and added Appendix D; references reviewed and updated.	04/2024