Clinical Policy: Inotersen (Tegsedi)

Reference Number: CP.PHAR.405
Effective Date: 11.20.18
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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. Tegsedi is not prescribed concurrently with Amvuttra, Onpattro, or Wainua;
9. Dose does not exceed 284 mg (1 syringe) per week.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Recent (dated within the last month) platelet count $\geq 100 \times 10^9$/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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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 January 17, 2025.
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 13, 2025.

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	P&T Approval Date
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154 references reviewed and updated.	11.03.20	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added requirement that Tegesedi is not prescribed concurrently with Onpattro.	08.05.21	11.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.30.21	02.22
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. Template changes applied to other diagnoses/indications and continued therapy section.	07.19.22	11.22
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.22.22	02.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.13.23	02.24
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.	02.12.24	05.24
2Q 2025 annual review: removed criteria "member has not received prior treatment with Amvuttra, Onpattro, or Wainua" per competitor analysis; references reviewed and updated.	01.17.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.