Clinical Policy: Inotersen (Tegsedi)

Reference Number: CP.PHAR.405
Effective Date: 11.20.18
Last Review Date: 02.21
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.

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 liver transplant;
7. Recent (dated within the last month) platelet count ≥ 100 x 10^9/L;
8. 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

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): 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. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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. 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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   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): 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 100,000/µL
  - 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hereditary transthyretin-mediated amyloidosis 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.; September 2020. Available at: https://tegsedi.com/prescribing-information.pdf. Accessed November 3, 2020.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	11.20.18	02.19
No significant changes; finalized line of business to apply to HIM.	04.22.19	
1Q 2020 annual review: removed HIM disclaimer for HIM NF drugs; no significant clinical changes; references reviewed and updated.	11.19.19	02.20
Added REMS requirement for platelet count ≥ 100 x 10^9/L while REMS is not strictly enforced.	04.17.20	05.20
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

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.

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.