Clinical Policy: Inotersen (Tegsedi)

Reference Number: LA.PHAR.405
Effective Date: 12.21.23
Last Review Date: ~~06.14.23~~05.02.24
Line of Business: Medicaid

Revision Log

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

****Please note: This policy is for medical benefit****

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 Louisiana Healthcare Connections® 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™ or Onpattro®;
9. Tegsedi is not prescribed concurrently with Amvuttra or Onpattro;
10. Dose does not exceed 284 mg (1 syringe) per week.

Approval duration: 6 months

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 LA.PMN.255
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 LA.PMN.53

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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;
1. Recent (dated within the last month) platelet count ≥ 100 x 10^9/L;
2. 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);
3. Member has not had a prior liver transplant;
4. Tegsedi is not prescribed concurrently with Amvuttra or Onpattro;
5. 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. 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 LA.PMN.255
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 LA.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 – LA.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.

V. Dosage and Administration

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

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VI. Product Availability

Single-dose, prefilled syringe: 284 mg

VII. References

1. Tegsedi Prescribing Information. Boston, MA: Akcea Therapeutics, Inc.; June 2022. Available at: https://tegsedi.com/pdf/prescribing-information.pdf. Accessed ~~November 22, 2022~~October 13, 2023.
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.*~~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.*~~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.

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Converted from corporate to local policy	06.14.23	10.24.23

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Annual review: no significant changes; references reviewed and updated.	05.02.24	

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

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.