Clinical Policy: Inotersen (Tegsedi)

Reference Number: ERX.SPA.318
Effective Date: 03.01.19
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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. Member has not had a prior liver transplant;
5. Tegsedi is not prescribed concurrently with Amvuttra or Onpattro;
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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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

VI. Product Availability

Single-dose, prefilled syringe: 284 mg

VII. References

1. Tegsedi Prescribing Information. Boston, MA: Akcea Therapeutics, Inc.; May 2021. Available at: https://tegsedi.com/prescribing-information.pdf. Accessed September 30, 2021.
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
1Q 2020 annual review: 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 reviewed and updated.	11.03.20	02.21
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.	07.19.22	11.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.