Clinical Policy: Inotersen (Tegsedi)

Reference Number: PA.CP.PHAR.405
Effective Date: 01/2019
Last Review Date: 01/2023

Coding Implications
Revision Log

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 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™ 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 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 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 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.

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.; June 2022. Available at: https://tegsedi.com/prescribing-information.pdf. Accessed November 22, 2022.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval 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 ≥ 100 x 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	