RXADVANCE
2 Park Central Drive
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Clinical Policy Title:	inotersen
Policy Number:	RxA.506
Drug(s) Applied:	Tegsedi®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Inotersen (Tegsedi®) is a transthyretin-directed antisense oligonucleotide. It is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
inotersen (Tegsedi®)	Hereditary transthyretin-mediated amyloidosis with polyneuropathy	284 mg SC once weekly	284 mg/week

Dosage Forms

- Single-dose, prefilled syringe: 1.5 mL of solution containing 284 mg of inotersen.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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 or older;
6. ALT, AST, and total bilirubin should be in normal range (monitored within last month);
7. Recent (dated within the last month) platelet count is 100 x 10^9 /L or more;
8. Member's UPCR is less than 1,000 mg/g;
9. Dose does not exceed 284 mg (1 syringe) per week.

Approval Duration

Commercial: 6 months

Medicaid: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy.
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. If request is for a dose increase, new dose does not exceed 284 mg (1 syringe) per week.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
BNP: B-type natriuretic peptide
NT-proBNP: N-terminal pro B-type natriuretic peptide
hATTR: hereditary transthyretin- mediated amyloidosis
TTR: transthyretin
UPCR: urine protein to creatinine ratio
ALT: alanine transaminase
AST: aspartate transaminase

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

APPENDIX D: General Information

- Tegsedi® is an antisense oligonucleotide that causes degradation of mutant and wild-type TTR mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.
- In a clinical study, cases of liver transplant rejection were reported 2-4 months after starting Tegsedi® in patients whose liver allografts had previously been clinically stable (for over 10 years) prior to starting Tegsedi®. In these cases, the patients clinically improved and transaminase levels normalized after

glucocorticoid administration and cessation of Tegsedi®. In patients with a history of liver transplant, monitor ALT, AST, and total bilirubin monthly. Discontinue Tegsedi® in patients who develop signs of liver transplant rejection.

- Measure platelet count, serum creatinine, estimated glomerular filtration rate (eGFR), urine protein to creatinine ratio (UPCR), ALT, AST, and total bilirubin, and perform urinalysis before treatment with Tegsedi®.

References

1. Tegsedi® Prescribing Information. Boston, MA: Akcea Therapeutics, Inc.; September 2020. Available at: www.tegsedi.com. Accessed September 30, 2020.
2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013; 8:31. Accessed September 24, 2020.
3. Benson MD, Waddington-cruz M, Berk JL, et al. Inotersen treatment for patients with hereditary transthyretin amyloidosis. N Engl J Med 2018;379 (1):22-31. Accessed September 24, 2020.
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;379(1):11-21. Accessed September 24, 2020.
5. Inotersen, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed September 24, 2020.
6. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed September 24, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Line of business policy applies was updated to All lines of business. 2. Initial approval criteria were updated: "Recent (dated within the last month) platelet count is 100 x 10^9 /L or more" and "Member's UPCR is less than 1,000 mg/g" were added. "Member has not had a liver transplant" was updated to "ALT, AST, and total bilirubin should be in normal range (monitored within last month)". 3. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 4. Commercial approval duration was updated from Length of benefit to 6 months for Initial and to 12 months for continued approval criteria. 5. Appendix A was updated: UPCR, ALT, AST were added.	9/24/2020	12/7/2020

6. Appendix D was added. 7. References were updated.		