



PRIOR AUTHORIZATION POLICY

- POLICY:** Amyloidosis – Tegsedi Prior Authorization Policy
- Tegsedi® (inotersen subcutaneous injection – Ionis/Akcea Therapeutics)

REVIEW DATE: 12/04/2024

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna National Formulary Coverage:

Overview

Tegsedi, an antisense oligonucleotide, is indicated for treatment of adults with **polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR)**.¹ Tegsedi has not been studied in patients with a history of liver transplantation. hATTR is a progressive disease caused by mutations in the transthyretin (TTR) gene leading to multisystem organ dysfunction.² Common neurologic manifestations include sensorimotor polyneuropathy, autonomic neuropathy, small-fiber polyneuropathy, and carpal tunnel syndrome.

Guidelines

A scientific statement from the American Heart Association (AHA) on the treatment of cardiomyopathy of hATTR (July 2020) includes recommendations related to polyneuropathy.³ Canadian guidelines for the treatment of patients with polyneuropathy (February 2021) and recommendations from the European Society of Cardiology (ESC) [2021] include treatment recommendations for hATTR polyneuropathy as well.^{2,4} The American College of Cardiology (ACC) expert consensus decision pathway on comprehensive multidisciplinary care for patients

with cardiac amyloidosis (2023) mention Tegsedi for polyneuropathy of hATTR.⁵ In general, Onpattro and Tegsedi are recommended for patients with hATTR polyneuropathy.

For patients with hATTR with polyneuropathy, the AHA recommends treatment with Onpattro or Tegsedi.³ For patients with hATTR with polyneuropathy and cardiomyopathy, Onpattro, Tegsedi, or Vyndamax/Vyndaqel are recommended. Use of combination therapy is discussed; however, it is noted that there is little data to support combination therapy.

The Canadian guidelines recommend Onpattro and Tegsedi as first-line treatment to stop the progression of neuropathy and improve polyneuropathy in early and late stage hATTR with polyneuropathy.²

The ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure note that TTR stabilization and reduction are the recommended basis of treatment for cardiomyopathy of hATTR.⁴ Onpattro and Tegsedi may be considered for patients with hATTR polyneuropathy and cardiomyopathy.

Safety

Tegsedi has a Boxed Warning regarding sudden and unpredictable thrombocytopenia which may be life-threatening.¹ It is contraindicated in patients with a platelet count less than $100 \times 10^9/L$. Based on monitoring, Tegsedi may need to be interrupted or discontinued. Following discontinuation, continue to monitor platelet counts for 8 weeks (or longer if platelet count is less than $100 \times 10^9/L$). Tegsedi also has a Boxed Warning regarding glomerulonephritis, which may require immunosuppressive treatment and may lead to dialysis-dependent renal failure. Due to the risks and frequent monitoring for both serious bleeding caused by severe thrombocytopenia and because of glomerulonephritis, Tegsedi is only available through a restricted distribution program under the Tegsedi REMS (Risk Evaluation and Mitigation Strategy).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Tegsedi. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Tegsedi as well as the monitoring required for adverse events and long-term efficacy, approval requires Tegsedi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Tegsedi® (inotersen subcutaneous injection – Ionis/Akcea Therapeutics)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR). Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):

A) Patient is \geq 18 years of age; AND

B) Patient has a transthyretin pathogenic variant as confirmed by genetic testing; AND

C) Patient has symptomatic polyneuropathy; AND

Note: Examples of polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch). Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.

D) Patient does not have a history of liver transplantation; AND

E) The medication is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

CONDITIONS NOT COVERED

- **Tegsedi® (inotersen subcutaneous injection – Ionis/Akcea Therapeutics)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra [vutrisiran subcutaneous injection], Attruby [acoramidis tablets], Onpattro [patisiran lipid complex intravenous infusion], Wainua [eplontersen subcutaneous injection], or a tafamidis product).

The requested medication should not be administered in combination with other medications indicated for polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

REFERENCES

1. Tegsedi® injection [prescribing information]. Carlsbad, CA: Ionis/Akcea Therapeutics; January 2024.
2. Alcantara M, Mezi MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. *Can J Neuro Sci.* 2022;49:7-18.
3. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific

statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation*. 2020;142:e7-e22.

4. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42:3599-3726.
5. Kittleson M, Ruberg FL, Ambardekar AV, et al. A report of the American College of Cardiology Solution Set Oversight Committee. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis. *JACC*. 2023;81(11):1076-1126.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/29/2023
Selected Revision	Conditions Not Covered Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran lipid complex intravenous infusion), Wainua (eplontersen subcutaneous injection), or a Tafamidis Product. Wainua was added to this condition not recommended for approval.	01/03/2024
Annual Revision	Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR): For diagnosis confirmed by genetic testing, rephrased the term "mutation" to "pathogenic variant." Conditions Not Covered: Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Amvuttra (vutrisiran subcutaneous injection), Attruby (acoramidis tablets), Onpattro (patisiran lipid complex intravenous infusion), Wainua (eplontersen subcutaneous injection), or a Tafamidis Product.) was changed to as listed (previously, concomitant use with Amvuttra [vutrisiran subcutaneous injection], Onpattro [patisiran lipid complex intravenous infusion], Wainua [eplontersen subcutaneous injection], or a Tafamidis product was listed).	12/04/2024

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