VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Amyloidosis – Tegsedi Utilization Management Medical Policy

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

REVIEW DATE: 11/29/2023

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 sensiomotor 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 atment 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® (patisiran intravenous infusion) 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 ATTR.[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 x 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 x 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 medical benefit coverage of Tegsedi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tegsedi is recommended in those who meet the following criteria:

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 ≥ 18 years of age; AND
   - **B)** Patient has a transthyretin mutation 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.

   Dosing. Approve 284 mg subcutaneously once weekly.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Tegsedi is not recommended in the following situations:

1. **Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran lipid complex intravenous infusion), or a Tafamidis Product.** Note: Examples of tafamidis products are Vyndaqel and Vyndamax. There are insufficient data supporting the safety and efficacy of concurrent use of these agents for hATTR with polyneuropathy. The Vyndaqel/Vyndamax pivotal trial, which took place prior to when Onpattro and Tegsedi were under investigation for amyloidosis, did not include patients who were taking investigational drugs. The pivotal trials for Onpattro and Tegsedi did not allow concurrent use of tetramer stabilizers (e.g., tafamidis, diflunisal). A scientific statement from the American Heart Association notes that there is little data to support combination therapy for these products.[3]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Tegsedi® injection [prescribing information]. Waltham, MA: Sobi/Akcea; June 2022.
2. Alcantara M, Mezi MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. *Can J Nero 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
Selected Revision	**Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR):** Criteria requiring the patient to have tried or is currently receiving at least one systemic agent for symptoms of polyneuropathy from one of the following pharmacologic classes: a gabapentin-type product, duloxetine, or a tricyclic antidepressant was removed. **Concomitant Use With Amvuttra (vutrisiran subcutaneous injection), Onpattro (patisiran lipid complex intravenous infusion), or a Tafamidis Product.** Amvuttra was added to this condition not recommended for coverage.	06/29/2022
Annual Revision	No criteria changes.	11/16/2022
Annual Revision	No criteria changes.	11/29/2023