MEDICAL MUTUAL®

Drug Policy

Policy:	**201836**	**Initial Effective Date: 11/10/2018**
Code(s):	**HCPCS C9399, J3490**	**Annual Review Date: 10/17/2024**
SUBJECT:	**Tegsedi ® (inotersen)**	**Last Revised Date: 10/17/2024**

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

OVERVIEW

Tegsedi is a self-administered, once weekly, subcutaneous injection for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis is a rare, inherited, rapidly-progressive, debilitating, life-threatening disease. It is a multisystem condition caused by mutation in the transthyretin (TTR) gene that results in misfolded TTR protein accumulation (as amyloid) in the nerves, heart, and other areas of the body. The clinical presentation of hATTR includes a predominately neurologic phenotype, a predominately cardiac phenotype, or a combination of both. Tegsedi is not indicated to treat the cardiac manifestations of hATTR amyloidosis.

Tegsedi is an antisense oligonucleotide that works by targeting RNA to reduce the production of TTR protein. Tegsedi's FDA label includes two black box warnings related to potential for life-threatening thrombocytopenia and glomerulonephritis that may require immunosuppressive treatment and may result in dialysis. Tegsedi is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) program because of these risks.

The Site of Care Medical Necessity Criteria applies to initial therapy and reauthorizations.

POLICY STATEMENT

This policy involves the use of Tegsedi. Prior authorization is recommended for medical benefit coverage of Tegsedi. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are

listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Tegsedi as well as the monitoring required for AEs and long-term efficacy, initial approval requires Tegsedi be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

The requested medication will not be used concurrently with Onpattro (patisiran) injections, Amvuttra (vutrisiran) injections, or tafamadis products (Vynaqel and Vyndamax); AND

The requested medication will not be used for the treatment of any of the following: Cardiomyopathy associated with hATTR amyloidosis, Primary or leptomeningeal amyloidosis or Sensorimotor or autonomic neuropathy not related to hATTR amyloidosis; AND

1. <u>Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR)</u>
Criteria.

Initial therapy: *Patient must meet the following criteria* (A, B, C, D, E, F, G, H, I <u>and</u> J)

A. Patient is ≥ 18 years of age; AND
B. Patient has documented transthyretin (TTR) mutation as confirmed through genetic testing [documentation required]; AND
C. Presence of polyneuropathy characterized by ONE of the following (i or ii) [documentation requirement]; AND
    i. Baseline polyneuropathy disability (PND) score ≤ IIIb
    ii. Baseline FAP Stage 1 or 2
D. Patient will not receive Tegsedi in combination with either of the following (i, or ii); AND
    i. Anti-transthyretin small interfering ribonucleic acid agents (e.g., Onpattro, Amvuttra)
    ii. Tetramer stabilizers (e.g., tafamidis, diflunisal)
E. The patient has 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 (e.g., gabapentin [Neurontin], Lyrica [pregabalin capsules]) duloxetine, or a tricyclic antidepressant (e.g., amitriptyline, nortriptyline); AND
F. Patient has a platelet count ≥ 100 x 10^9/L; AND
G. Patient does not have a history of acute glomerulonephritis caused by Tegsedi; AND
H. Tegsedi is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis; AND
I. Both patient and physician will be enrolled in and follow the conditions of the Tegsedi REMS program: AND
J. Site of care medical necessity is met*

***Continuation of therapy**, Patient must meet all of the following* (A, B, C, D, E, F, G, H, I <u>and</u> J)*:*

A. Patient has previously received treatment with Tegsedi; AND
B. Patient has documented transthyretin (TTR) mutation as confirmed through genetic testing; AND
C. Patient has experienced a positive clinical response to Tegsedi (e.g., improved neurologic impairment, motor function, cardiac function, quality of life assessment, serum TTR levels, etc.); AND
D. Improvement from baseline or stabilization of ONE of the following (i or ii); AND
    i. Baseline polyneuropathy disability (PND) score < IIIb
    ii. Baseline FAP Stage 1 or 2
E. Patient will not receive Tesedi in combination with the following agents (i or ii); AND
    i. Anti-transthyretin small interfering ribonucleic acid agents (e.g., Onpattro)
    ii. Tetramer stabilizers (e.g., tafamidis, diflunisal)
F. Patient has a platelet count $\geq$ 100 x 10^9/L; AND
G. Patient does not have a history of acute glomerulonephritis caused by Tegsedi; AND
H. Tegsedi is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis; AND
I. Both patient and physician will be enrolled in and follow the conditions of the Tegsedi REMS program; AND
J. Site of care medical necessity is met*

Dosing in polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR). *Dosing must meet the following:* Tegsedi recommended dosing is 284 mg administered by subcutaneous injection once weekly.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months (180 days)
B) *Extended Approval:* 12 months (365 days)

Duration of Therapy in polyneuropathy of hATTR amyloidosis: indefinite

Labs/Diagnostics:
- Genetic testing is required to confirm TTR mutation.
- Kidney function is assessed by eGFR, urinalysis, and UPCR as part of the Tegsedi REMS program
- Platelet count is assessed weekly as part of the Tegsedi REMS program

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Waste Management for All Indications.
Tegsedi is supplied in a prefilled syringe. Each syringe contains 1.5 ml of solution containing 284 mg of inotersen (equivalent to 300 mg inotersen sodium salt).

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not

medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Tegsedi injection [prescribing information]. Carlsbad, CA: Ionis/Akcea Therapeutics; June 2022.
2. Tegsedi REMS [prescriber Training]. Carlsbad, CA: Ionis/Ackea Therapeutics; October 2018.
3. Tegsedi (inotersen). IPD analytics. October 2018.
4. Adams D, Suhr OB, Hund E, et al. First European consensus for diagnosis, management, and treatment of transthyretin familial amyloid polyneuropathy. *Curr Opin Neurol*. 2016;29 Suppl 1:S14-26.
5. Gertz MA, Benson MD, Dyck PJ, et al. Diagnosis, prognosis, and therapy of transthyretin amyloidosis. J *Am Coll Cardiol*. 2015;66(21):2451-2466.
6. Benson MD, Waddington-Cruz M, Berk JL, Polydefkis M, Dyck PJ, Wang AK, et al. Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. New England Journal of Medicine. 2018May;379(1):22–31.
7. Inotersen and Patisiran for Hereditary Transthyretin Amyloidosis: Effectiveness and Value. Institute for Clinical and Economic Review. August 29, 2018

Prior approval is required for HCPCS Codes C9399, J3490

†When *unclassified drugs* (C9399, J3490) is determined to be Tegsedi

Edits and Denials:

Prior approval: Prior approval is required for Tegsedi **(HCPCS Codes C9399, J3490)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Codes C9399, J3490** will pend with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs