Sample Letter of Medical Necessity

The letter of medical necessity should be prepared by your office and submitted to insurers as part of the prior authorization or predetermination process. If you would like more information on how to utilize this template letter, please call AKCEA® CONNECT toll-free at 1-866-252-3289, Monday through Friday, 8 AM to 8 PM (ET).

Please see Indication and boxed WARNING regarding the risk of Thrombocytopenia and Glomerulonephritis on pg 4, additional Important Safety Information on the accompanying folder, and full Prescribing Information for TEGSEDI located in pocket of accompanying folder.

[Practice Letterhead]

[Date]

[Name of Medical Director] [Title]
[Name of Insurer]
[Address of Insurer]
[City, State, ZIP Code]

Re: [Patient's Name]
[Patient ID Number]
[Diagnosis code(s) and description(s)]

I am writing to provide additional information regarding the medical necessity of treating one of your members, **[Patient Name]**, with TEGSEDI® (inotersen) injection for subcutaneous, self-administered use. TEGSEDI was approved by the FDA on October 5, 2018 for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTR) in adults.[1] This letter provides information about my patient's medical history, and my rationale for use of TEGSEDI.

Disease Overview

Hereditary ATTR amyloidosis is a rare, systemic, and life-threatening disease.[2,3] Hereditary ATTR amyloidosis impacts multiple organ systems resulting in a range of complications that impair quality of life.[4-6] Over 130 mutational variants of the *TTR* gene have been identified and are expressed in an autosomal dominant manner with variable penetrance.[7,8] Hereditary ATTR amyloidosis is associated with a point mutation in the *TTR* gene, and ATTR presents with substantial clinical heterogeneity. Nonspecific symptoms and manifestations overlap with other disorders which may result in delayed differential diagnosis.[9,10] In addition, given the array of symptoms, many patients see multiple physicians and specialists prior to hereditary ATTR amyloidosis confirmation through tissue biopsy analysis and/or genetic testing.[9,10]

Patient's Diagnosis and History

The history and course of the polyneuropathy of hereditary ATTR amyloidosis for **[Patient Name]** are as follows:

Diagnosis of hereditary ATTR amyloidosis with E85.1 (Neuropathic heredofamilial amyloidosis):
[Insert comment / information regarding the date and method of diagnosis:

- **MUST include comment on genetic confirmation of the mutation for hereditary ATTR amyloidosis**
- **MAY include evidence of amyloid by tissue biopsy, immunohistochemistry/mass spectrometry results, and/or scintigraph (technetium-99m stannous pyrophosphate [PYP] scanning)**
- **SHOULD include clinical manifestations (e.g., past/present working diagnosis prior to hereditary ATTR amyloidosis confirmation such as polyneuropathy, nephropathy, ocular manifestations, bilateral carpal tunnel syndrome (CTS), lumbar spinal canal stenosis, etc.)]**

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Signs, Symptoms, Scoring / Staging of Polyneuropathy:
[Clinical signs and symptoms of disease progression

- **MUST include baseline Polyneuropathy Disability (PND) score and/or Familial Amyloidosis Polyneuropathy (FAP) stage**
- **MUST include clinical evidence of peripheral and/or autonomic polyneuropathy (e.g. symmetrical length–dependent peripheral sensorimotor polyneuropathy, orthostatic hypotension, sexual dysfunction, uncontrolled diarrhea, alternating diarrhea/constipation, etc.)**
- **SHOULD include impact on quality of life, activities of daily living, and/or impact upon the caregiver**
- **SHOULD include comment on patient hospitalizations, and/or frequency of office visits]**

Previous treatments: **[Insert comment / information on current therapy and previous treatments identified to manage or slow the progression of the disease and resulting symptoms, including but not limited to those related to neuropathy, CTS, spinal canal stenosis, GI symptoms, ocular manifestations, and renal failure.]**

Despite the use of a variety of therapies to treat the symptoms of the polyneuropathy of hereditary ATTR amyloidosis described in this letter, my patient continues to decline in daily function and quality of life is significantly impacted by the polyneuropathy of hereditary ATTR amyloidosis. It is my opinion that TEGSEDI® (inotersen) injection is the appropriate therapeutic treatment for my patient. TEGSEDI prevents the synthesis of the TTR protein in the liver through degradation of the TTR mRNA.[1,11] In clinical trials, initiation of TEGSEDI therapy substantially reduced TTR protein levels and sustained reductions through 65 weeks.[1] TEGSEDI has an established safety profile.[1]

TEGSEDI is available in a single-dose, prefilled syringe with a safety spring (284 mg/1.5 mL solution, 27-gauge, 8-mm needle), providing patients with a once-weekly subcutaneous injection,[1,12] and is available only through a restricted distribution program under a REMS due to the risk of thrombocytopenia and glomerulonephritis.[1] Regular monitoring for patients is delivered as part of the TEGSEDI REMS program[1], and patients have the ability to self-administer at a time and place that works for them.[1]

Treatment Description and Rationale

TEGSEDI is a transthyretin-directed antisense oligonucleotide (ASO) indicated for treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.[1] In clinical trials, TEGSEDI delivered significant, sustained improvement or stabilization in measures of both neuropathy and quality of life.[1] The efficacy of TEGSEDI was demonstrated in a robust, randomized, double-blind, placebo-controlled, multicenter clinical trial in adults with polyneuropathy caused by hereditary ATTR amyloidosis.[1] Patients were randomized in a 2:1 ratio to receive either TEGSEDI (n=112) or placebo (n=60), respectively, as a subcutaneous injection administered once per week for 65 weeks.[1] The coprimary efficacy end points were the change from baseline to week 66 in the modified Neuropathy Impairment Score +7 (mNIS+7) and Norfolk Quality of Life–Diabetic Neuropathy (QoL-DN) scores.[1]

TEGSEDI significantly improved or stabilized measures of neuropathic progression vs placebo.[1] Patients treated with TEGSEDI achieved a 19.7-point benefit at 66 weeks vs patients receiving placebo (P<0.001).[1,11] More than one-third of patients treated with TEGSEDI saw improvement or stabilization in neuropathy at 66 weeks (36% vs 19.2% on placebo, P=0.033).[13]

TEGSEDI significantly improved or stabilized quality of life vs placebo.[1] Patients treated with TEGSEDI achieved a clinically meaningful 11.7-point benefit on Norfolk QoL-DN at 66 weeks vs patients receiving placebo (P<0.001).[1,14,15] Half of patients treated with TEGSEDI saw improvement or stabilization or stabilization in quality of life at 66 weeks (50% vs 26.9% on placebo, P=0.08).[13] Patients treated with TEGSEDI experienced similar improvement or stabilization regardless of age, sex, race, region, Neuropathy Impairment Score, Val30Met mutation status, and disease stage.[1]

Given the seriousness of my patient's condition, and the sustained improvement or stabilization in measures of both neuropathy and quality of life[1,11] as described by the TEGSEDI clinical trials, it is my professional medical opinion that **[Patient Name]** should receive treatment with TEGSEDI.

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I certify that both the patient and the healthcare provider understand the requirements of, and are in compliance with, the parameters of the TEGSEDI REMS program.

Print Name: _____ Signature: _____ Date: _____

I trust that this information is helpful to you in understanding why I have prescribed treatment with TEGSEDI. If you require any additional information, please do not hesitate to contact me at **[(XXX) XXX-XXXX]**.

Sincerely,

[Physician's name], MD
Title
Address
City, State, ZIP
Phone
Email

Enclosures: **[Clinic notes, Prescribing Information, FDA approval letter, other supportive medical literature]**

Please see Indication and boxed WARNING regarding the risk of Thrombocytopenia and Glomerulonephritis on back, and full Prescribing Information for TEGSEDI located in pocket of accompanying folder.

References

1. TEGSEDI [package insert]. Boston, MA: Akcea Therapeutics, Inc; 2020.
2. Adams D, Amitay O, Coelho T. *Orphanet J Rare Dis.* 2015;10(suppl 1):58.
3. Conceição I, González-Duarte A, Obici L, et al. *J Peripher Nerv Syst.* 2016;21(1):5-9.
4. Coelho T, Maurer MS, Suhr OB. *Curr Med Res Opin.* 2013;29(1):63-76.
5. Suhr O, Danielsson A, Holmgren G, Steen L. *J Int Med.* 1994;235(5):479-85.
6. Hawkins PN, Ando Y, Dispenzeri A, Gonzalez-Duarte A, Adams D, Suhr OB. *Ann Med.* 2015;47(8):625-38.
7. Rowczenio DM, Noor I, Gillmore JD, et al. *Hum Mutat.* 2014;35(9):E2403-12.
8. Hou X, Aguilar MI, Small DH. *FEBS J.* 2007;274(7):1637-50.
9. Lousada I, Maurer M, Warner M, Guthrie S, Hsu K, Grogan M. *Orphanet J Rare Dis.* 2017;12(suppl 1):165.
10. Lousada I, et al. Presented at: the First European Congress on Hereditary ATTR Amyloidosis. November 2015; Paris, France.
11. Benson MD, Waddington-Cruz M, Berk JL, et al. *N Engl J Med.* 2018;379(1):22-31.
12. TEGSEDI [instructions for use]. Boston, MA: Akcea Therapeutics, Inc; 2018.
13. Benson MD, Waddington-Cruz M, Berk JL, et al. *N Engl J Med.* 2018;379(1):1-36 [supplemental appendix].
14. DOF/TEGSEDI Brand Blueprint append.
15. DOF/TEGSEDI Clinical Profile p28.

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INDICATION

TEGSEDI is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOCYTOPENIA AND GLOMERULONEPHRITIS

Thrombocytopenia

- **TEGSEDI causes reductions in platelet count that may result in sudden and unpredictable thrombocytopenia, which can be life-threatening. One clinical trial patient died from intracranial hemorrhage**
- **TEGSEDI is contraindicated in patients with a platelet count below 100 x 10^9/L**
- **Prior to starting TEGSEDI, obtain a platelet count. During treatment, monitor platelet counts weekly if values are 75 x 10^9/L or greater, and more frequently if values are less than 75 x 10^9/L**
- **If a patient develops signs or symptoms of thrombocytopenia, obtain a platelet count as soon as possible. The patient should not receive additional TEGSEDI unless a platelet count is determined to be interpretable and acceptable by a medical professional**
- **Following discontinuation of treatment for any reason, continue to monitor platelet count for 8 weeks, or longer if platelet counts are less than normal, to verify that platelet counts remain above 75 x 10^9/L**

Glomerulonephritis

- **TEGSEDI can cause glomerulonephritis that may require immunosuppressive treatment and may result in dialysis-dependent renal failure. One clinical trial patient who developed glomerulonephritis and did not receive immunosuppressive treatment remained dialysis-dependent. In clinical trials, cases of glomerulonephritis were accompanied by nephrotic syndrome, which can have manifestations of edema, hypercoagulability with venous or arterial thrombosis, and increased susceptibility to infection**
- **TEGSEDI should generally not be initiated in patients with urinary protein to creatinine ratio (UPCR) of 1000 mg/g or higher**
- **Prior to starting TEGSEDI, measure the serum creatinine, estimated glomerular filtration rate (eGFR), urine protein to creatinine ratio (UPCR), and perform a urinalysis. During treatment, monitor serum creatinine, eGFR urinalysis, and UPCR every 2 weeks. TEGSEDI should not be given to patients who develop a UPCR of 1000 mg/g or higher or eGFR below 45 mL/minute/1.73 m^2, pending further evaluation of the cause**
- **If a dose is held, once eGFR increases to ≥45 mL/minute/1.73 m^2, UPCR decreases to below 1000 mg/g, or the underlying cause of the decline in renal function is corrected, weekly dosing may be reinitiated. In patients with UPCR of 2000 mg/g or higher, perform further evaluation for acute glomerulonephritis, as clinically indicated. If acute glomerulonephritis is confirmed, TEGSEDI should be permanently discontinued**

TEGSEDI REMS Program

- **Because of the risks of serious bleeding caused by severe thrombocytopenia and because of glomerulonephritis, both of which require frequent monitoring, TEGSEDI is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called the TEGSEDI REMS Program**

sobi rare strength

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