BlueCross BlueShield Federal Employee Program

TEGSEDI (inotersen)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Tegsedi (inotersen) 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 (1).

Regulatory Status

FDA-approved indication: Tegsedi is a transthyretin-directed antisense oligonucleotide indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR) in adults (1).

Tegsedi has a boxed warning for thrombocytopenia. Tegsedi can cause reductions in platelet count that may result in sudden and unpredictable thrombocytopenia that can be life-threatening. Tegsedi should not be initiated in patients with a platelet count below 100 x 10^9/L. Patients who are not able to adhere to the recommended laboratory monitoring or to the related treatment recommendations should not receive Tegsedi (1).

Tegsedi also has a boxed warning for glomerulonephritis. Tegsedi can cause glomerulonephritis that may require immunosuppressive treatment and may result in dialysis-dependent renal failure. Tegsedi-treated patients who develop glomerulonephritis will require monitoring and treatment for nephrotic syndrome and its manifestations. Tegsedi should generally not be initiated in patients with a urine protein to creatinine ratio (UPCR) of 1000 mg/g or greater, or eGFR below 45 mL/minute/1.73 m^2. If acute glomerulonephritis is confirmed, Tegsedi should be permanently discontinued. Serum creatinine, estimated glomerular filtration rate (eGFR), urinalysis, and UPCR should be monitored every 2 weeks during treatment with Tegsedi (1).

Tegsedi is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Tegsedi REMS Program, because of risks of serious bleeding caused by severe thrombocytopenia and because of glomerulonephritis (1).

Other warnings for Tegsedi include stroke and cervicocephalic arterial dissection; inflammatory and immune effects; liver effects; hypersensitivity reactions/antibody formation; uninterpretable platelet counts; and reduced serum vitamin A levels.

Various scales are used to capture the disease burden and progression of polyneuropathy in hATTR amyloidosis. The extent of disability is typically captured by the Familial Amyloidotic Polyneuropathy (FAP) staging system and/or the polyneuropathy disability (PND) scoring system. Neuropathy Impairment Score (NIS) can be used to quantify impairment and progression of neuromuscular conditions at time of diagnosis and during treatment (2). Tegsedi clinical trials included only Stage 1 and 2 FAP patients with a NIS score ≥ 10 and ≤130 (3).

The safety and effectiveness of Tegsedi in pediatric patients have not been established (1).

Summary

Tegsedi (inotersen) is an antisense oligonucleotide used to treat polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR). Tegsedi contains boxed warnings for thrombocytopenia and glomerulonephritis. Tegsedi is available only through the Tegsedi REMS program. The safety and effectiveness of Tegsedi in pediatric patients have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Tegsedi while maintaining optimal therapeutic outcomes.

References

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