

Medical Coverage Policy | Nusinersen for Spinal Muscular Atrophy



EFFECTIVE DATE: TBD
POLICY LAST UPDATED: TBD

OVERVIEW

Spinal muscular atrophy (SMA) is an inherited disorder caused by homozygous deletions or variants in the *SMN1* gene. As a consequence of absent or low levels of SMN1 protein, the motor neurons in spinal cord degenerate, resulting in atrophy of the voluntary muscles of the limbs and trunk. Nusinersen is a synthetic antisense oligonucleotide designed to bind to a specific sequence in exon 7 of the SMN2 transcript causing the inclusion of exon 7 in the SMN2 transcript, leading to production of full length functional SMN2 protein, which is very similar to SMN1.

MEDICAL CRITERIA

BlueCHiP for Medicare and Commercial

Nusinersen may be considered medically necessary for patients with infantile-onset or type I spinal muscular atrophy with a documented genetic diagnosis of spinal muscular atrophy.

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare and recommended for Commercial Products

POLICY STATEMENT

Nusinersen may be considered **medically necessary** for patients with infantile-onset or type I spinal muscular atrophy with a documented genetic diagnosis of spinal muscular atrophy.

Note: The recommended dosage is 12 mg (5 mL) administered intrathecally. Treatment is initiated with 4 loading doses; the first 3 loading doses should be administered at 14-day intervals while the fourth loading dose is administered 30 days after the third loading dose. Subsequent maintenance doses should be administered once every 4 months thereafter.

Nusinersen is considered not medically necessary for patients with type 0, II, III, and IV spinal muscular atrophy as the evidence is insufficient to determine the effects of the technology on health outcomes.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessary services.

BACKGROUND

Spinal Muscular Atrophy

Spinal muscular atrophy (SMA) is a rare autosomal recessive genetic disorder caused by homozygous deletions or variants in the *SMN1* gene in chromosome 5. This gene is responsible for producing the “survival of motor neuron” protein (SMN1). As a consequence of absent or low levels of SMN1, the motoneurons in the spinal cord degenerate, resulting in atrophy of the voluntary muscles of the limbs and trunk. During early development, these muscles are necessary for crawling, walking, sitting up, and head control. The more severe types of SMA can also affect muscles involved in feeding, swallowing, and breathing. The exact role of the SMN protein in motoneurons has not been completely elucidated and levels of the SMN protein required for optimal functioning are unknown. *SMN2* is a nearly identical modifying gene capable of producing nearly identical compensatory SMN2 protein. However, 70% to 90% of the transcripts produced from the *SMN2* gene produce a truncated protein that is defective and unstable due to lack of exon 7. Further, humans exhibit variability (range, 0-6) in the number of copies of the *SMN2* gene and

copy number is inversely proportional to severity of disease. These factors in tandem lead to wide variability in disease severity.

SMA is classified into 4 main categories (with additional subcategories) based on the age at the onset of symptoms. Generally, early onset of disease directly correlates to severity of symptom and rate of disease progression. There is no exact marker to classify these categories, and they are not well-distinguished by ICD-10-CM code.

- Type 0: The most severe form of SMA, symptoms can often be seen in the later stages of pregnancy. Fetal movements are less than expected and, after birth, the infant will have little ability to move and may not be able to breathe and swallow independently. Death occurs before the age of 6 months.
- Type I (also called infantile SMA or Werdnig-Hoffman disease and subcategorized as IA, IB and IC): Onset within for 6 months of birth and symptoms progress rapidly, and most infants die before 1 year of age from respiratory failure. About 60% of patients with SMA constitute of this phenotype.
- Type II (also called intermediate SMA or Dubowitz disease): Onset within 6 to 18 months with a less severe progression. Typically, a child can sit independently if positioned, but is unable to walk. More than 70% of patients live beyond 25 years of age with adequate supportive care.
- Type III (also called Kugelberg-Welander disease and subcategorized as IIIA and IIIB): Onset after 18 months of age. Lifespan is not affected, with wide-ranging reduction in muscle strength with a chronic course. The outcome depends primarily on the severity of muscle weakness at presentation rather than age of onset, but earlier onset tends to correlate with greater weakness.
- Type IV (also called adult-onset SMA): Usually presents in the third decade of life and is otherwise similar to SMA type III.

Infantile-Onset or Type I SMA

For individuals who have type I (infantile-onset) SMA (symptomatic or presymptomatic) who receive nusinersen, the evidence includes 2 randomized, double-blind, controlled trial (results not yet reported for one) and 1 single-arm open-label study. Relevant outcomes are overall survival, change in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related mortality and morbidity. Trial results in symptomatic patients has shown clinically meaningful improvement in motor milestones as well as event-free survival, which exceeded those seen in the control group, with an acceptable safety profile. The proportion of patients, who met the primary end point responder definition of achieving motor milestones, was 40% in the nusinersen arm compared to 0 in the sham-controlled arm. Further, the hazard ratio for event-free survival was 0.53 in favor of nusinersen versus sham controlled. It is notable, however, that most nusinersen-treated subjects did not achieve the primary end point motor milestone response. Given the limited data on durability of response, long-term safety, and lack of efficacy in substantial number of patients, continued risk-benefit assessment of long-term treatment with nusinersen is necessary. The open-label uncontrolled trial in presymptomatic infantile-onset SMA patients found a benefit of early treatment with nusinersen. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Type II and III SMA

For individuals who have type I or II SMA who receive nusinersen, the evidence includes 4 single-arm studies and 1 double-blind, randomized controlled trial. Relevant outcomes are overall survival, change in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related mortality and morbidity. Efficacy findings from single-arm studies of type II and III SMA are difficult to interpret because these trials used a wide range of nusinersen doses and lacked control arms. Results of the confirmatory phase 3 CHERISH trial are not yet available. The evidence is insufficient to determine the effects of the technology on health outcomes.

Type 0 or IV SMA

For individuals who have type 0 SMA or type IV SMA who receive nusinersen, no studies were identified. Relevant outcomes are change in disease status, morbid events, functional outcomes, health status measures,

quality of life, and treatment-related mortality and morbidity. The evidence is insufficient to determine the effects of technology on health outcomes

Regulatory Status

In December 23, 2016, Spinraza™ (nusinersen; Biogen) was approved by the U.S. Food and Drug Administration (FDA) for treatment of pediatric and adult patients with spinal muscular atrophy.

CODING

There is no specific HCPCS code at this time, claims must be filed with an unlisted code such as J3490 and the NDC number

RELATED POLICIES

None

PUBLISHED

Provider Update XXXX 2017

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