Medical Drug Clinical Criteria

Subject:	Spinraza (nusinersen)		
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Overview

This document addresses the use of Spinraza (nusinersen), a drug approved by the Food and Drug Administration (FDA) for the treatment of children and adults with spinal muscular atrophy (SMA). SMA is a rare and often fatal autosomal recessive genetic disease affecting muscle strength and movement. SMA is caused by a deficiency in SMN (survival motor neuron) 1-related proteins resulting from either deletion of both SMN1 genes, or mutations within the SMN1 gene. This deficiency results in degeneration of motor neurons causing muscle atrophy, particularly in the limbs and the muscles that control the mouth, throat, and respiration. SMA is most often diagnosed by an SMN1 gene deletion test using PCR but can also be detected by genetic testing of the SMN1 gene itself. SMA is one of the leading genetic causes of death in infants but can affect individuals at any stage of life. The five main types of SMA are defined based on the severity of muscle weakness and the age of symptom onset.

Spinal Muscular Atrophy Classification

SMA Type	Predicted SMN2 Copy Number	Age of Onset	Life Expectancy	Highest motor function
0	0-1	Prenatal	<6 months	None; require respiratory support
I	1-3	0-6 months	<2 years	Never sit
II	2-4	<18 months	10-40 years	Sit alone
III	2-4	>18 months	Adult	Stand alone; walk assisted
IV	>4	>5 years to adult	Adult	Stand alone; walk unassisted

SMA type and severity of disease can correlate with the number of copies of the SMN2 gene. SMN2 is a closely related gene to SMN1; thus, this increased production can compensate for the genetic SMN1 deficiency and modify the SMA phenotype to be potentially less severe. While the number of copies of SMN2 can correlate and predict disease severity and type, the relationship is not exact, and exceptions can occur. Importantly, patients are confirmed as belonging to an SMA type retrospectively, based on the motor milestones they achieve. Treatment decisions must be made early in the disease, when only genetic information, and possibly initial clinical characteristics, are known. Current treatment for SMA may include supportive care, Spinraza (nusinersen), Zolgensma (onasemnogene abeparvovec-xioi), or Evrysdi (risdiplam). Evrysdi (risdiplam) in an mRNA splicing modifier administered orally daily while Zolgensma is a one-time gene therapy treatment. All three drug treatments were studied in separate but overlapping populations. The optimal treatment for eligible patients is unknown. The efficacy, safety, and clinical utility of concomitant treatment with Spinraza, Evrysdi, and/or Zolgensma is also unknown.

Spinraza (nusinersen) is an antisense oligonucleotide drug administered by intrathecal injection that modifies splicing of the SMN2 gene to increase production of normal, full-length survival motor neuron (SMN) proteins. To date, benefits of Spinraza have been demonstrated in two major phase-3 studies: Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy (ENDEAR trial) and Nusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy (CHERISH trial). Relevant inclusion criteria are shown in the table below.

Trial	Diagnosis	Number of SMN2 copies	Symptom Onset	Age
ENDEAR	Homozygous deletion or mutation in the *SMN1* gene	2 copies	<6 months of age	<7 months
CHERISH	Homozygous deletion, mutation, or compound heterozygote in *SMN1* gene	Not specified; Results showed 88% had 3 copies	>6 months of age; Results showed 100% of participants had symptom onset before 21 months of age	2-12 years

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Spinraza (nusinersen)

Initial requests for Spinraza (nusinersen) may be approved if the following criteria are met:

I. Documentation is provided that individual has a diagnosis by *either*:
   A. Spinal Muscular Atrophy (SMA) diagnostic test results verifying 0 copies of SMN1; **OR**
   B. Molecular genetic testing of 5q SMA for any of the following:
      1. homozygous gene deletion; or
      2. homozygous conversion mutation; or
      3. compound heterozygote;

AND

II. Documentation is provided that individual has SMA-associated signs and symptoms;

AND

III. Documentation is provided that individual has baseline motor ability assessments that support diagnosis based on age and motor ability (baseline motor ability assessments include but are not limited to the following: Hammersmith Infant Neurological Examination, The Children's Hospital of Philadelphia Infant Test of Neurological Disorders (CHOP INTEND), Hammersmith Function Motor Scale – Expanded (HFMSE), 6-Minute Walk Test (6MWT), Revised Upper Limb Module (RULM);

AND

IV. Requested medication has been prescribed by or in consultation with a neurologist who specializes in spinal muscular atrophy;

AND

V. Individual does not require use of invasive ventilatory support (tracheotomy with positive pressure) or use of non-invasive ventilator support (BiPAP) for more than 16 hours per day as a result of advanced SMA disease.

Initial requests for Spinraza following treatment with Zolgensma (onasemnogene abeparvovec-xioi) may be approved if the following criteria are met:

I. When Spinraza therapy is determined to meet the above criteria; **AND**
II. Documentation is provided that individual has experienced a decline in clinical status (including but not limited to loss of motor milestone) since receipt of gene therapy.

Continuation requests for Spinraza (nusinersen) may be approved if the following criteria are met:

I. When initial therapy was determined to meet the above criteria; **AND**
II. Documentation is provided that individual has motor ability assessments that support improvement or stabilization compared baseline motor ability assessments (baseline motor ability assessments include but are not limited to the following: Hammersmith Infant Neurological Examination, The Children's Hospital of Philadelphia Infant Test of Neurological Disorders (CHOP INTEND), Hammersmith Function Motor Scale – Expanded (HFMSE), 6-Minute Walk Test (6MWT), Revised Upper Limb Module (RULM); **AND**
III. Individual does not require use of invasive ventilatory support (tracheotomy with positive pressure) or use of non-invasive ventilator support (BiPAP) for more than 16 hours per day as a result of advanced SMA disease.

Requests for Spinraza (nusinersen) may not be approved for the following:

I. When the above criteria are not met and for all other indications; **OR**
II. When used in combination therapy with Evrysdi (risdiplam).

Approval Duration:
Initial and continuation requests: 6 months

Quantity Limits

Spinraza (nusinersen) Quantity Limits

Drug	Limit
Spinraza (nusinersen) 12 mg/5 mL vial*	1 vial (12 mg) per 4 months

Override Criteria
*For initiation of therapy, may approve 4 loading doses of 12 mg (1 vial) each in the first 4 months of therapy

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

96450	Chemotherapy administration, into CNS (eg, intrathecal), requiring and including spinal puncture [when associated with administration of nusinersen (SPINRAZA)]

HCPCS

J2326	Injection, nusinersen, 0.1 mg [SPINRAZA]

ICD-10 Diagnosis

G12.0	Infantile spinal muscular atrophy, type I (Werdnig-Hoffman)
G12.1	Other inherited spinal muscular atrophy
G12.20	Motor neuron disease, unspecified
G12.21	Amyotrophic lateral sclerosis
G12.22	Progressive bulbar palsy
G12.23	Primary lateral sclerosis
G12.24	Familial motor neuron disease
G12.25	Progressive spinal muscle atrophy
G12.29	Other motor neuron disease
G12.8	Other spinal muscular atrophies and related syndromes
G12.9	Spinal muscular atrophy, unspecified

Document History

Revised: 08/16/2024
Document History:

- 08/16/2024 – Annual review: Removing requirement of genetic testing verifying no more than 2 copies of SMN2; removing requirement of onset of SMA signs and symptoms before 21 months of age. Add individual has SMA-associated signs and symptoms for clarity. Add requirement of baseline motor ability assessments. Added requirement for requested medication to be prescribed by or in consultation with neurologist who specializes in SMA. Clarified continuation requirements defining improvement based on motor ability assessments compared to baseline. Wording and formatting changes. Coding Reviewed: Expanded ICD-10-CM from G12.0, G12.1 to include all codes under the parent code G12.0-G12.9.
- 11/17/2023 – Annual review: Wording and formatting changes. Coding Reviewed: No changes.
- 11/18/2022 – Annual review: No changes. Coding Reviewed: No changes.
- 11/19/2021 – Annual review: Wording and formatting changes. Coding reviewed: No changes.
- 11/20/2020 – Annual review: Add ventilation independence as initial criterion for approval; wording and formatting changes for clarity. Coding Reviewed: No changes.
- 08/12/2020 – Select review: Add may not be approved section.
- 11/15/2019 – Annual review: Add quantity limit based on FDA label. Coding reviewed: No changes.
- 08/16/2019 – Select review. Update criteria for use of Spinraza after gene therapy to require a decline in clinical status. Coding Review: Delete ICD-10 code Z13.79.
- 06/10/2019 – Select review. Minor wording change/ administrative update.
- 05/17/2019 – Select review. Add criteria for use of Spinraza after gene therapy for SMA. Coding Reviewed: No changes.
- 11/16/2018 – Annual review. Initial P&T review of Spinraza (nusinersen). No changes to criteria, add references.

References

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