UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Spinal Muscular Atrophy – Spinraza Utilization Management Medical Policy
- Spinraza® (nusinersen intrathecal injection – Biogen)

REVIEW DATE: 07/22/2026

OVERVIEW

Spinraza, a survival motor neuron 2 (SMN2)-directed antisense oligonucleotide, is indicated for the treatment of spinal muscular atrophy in pediatric and adult patients.[1]

Disease Overview

Spinal muscular atrophy is a genetic, autosomal recessive, progressive, neuromuscular disorder caused by biallelic deletions or pathogenic variants in the survival motor neuron 1 (SMN1) gene which can be identified by genetic testing.[2-5] The subsequent reduced levels of survival motor neuron (SMN) protein impacts brainstem and spinal cord motor neurons. The estimated incidence in the US is one in 11,000.[3] The phenotypic expression of the disease is impacted by the SMN2 gene copy number.[3-5] Patients with a higher number of SMN2 gene copies often have less severe disease with milder progression. Table 1 describes disease types. Of note, various motor ability assessments and different functional motor scales are used in clinical practice to characterize impairment in patients with spinal muscular atrophy. When motor neuron function is lost, it cannot be regained, which greatly impacts patients who have experienced progression (e.g., patients with complete paralysis of limbs or permanent ventilator dependence). A different manner of patient categorization classifies the three most common types as "non-sitters", "sitters", and "walkers".

Table 1. Types of Spinal Muscular Atrophy.[4,5]

	Age at Onset	Features/Clinical Presentation/Motor Milestones*	Lifespan*	SMN2 Gene Copy Number
Type 0 (< 1% of patients)	Birth	Severe hypotonia and weakness with respiratory failure at birth. There is no achievement of motor milestones.	A few weeks to days (< 6 months)	1
Type 1 (50% of patients)	< 6 months	Poor muscle tone and lack of movement. Respiratory assistance may be needed. Patients are never able to sit without support.	< 2 years	1 to 2 for 80% of patients
Type 2 (30% of patients)	6 to 18 months	Patients are able to sit. However, patients are unable to walk or stand without assistance.	Close to normal	2 to 3 for over 90% of patients
Type 3 (10% to 20% of patients)	> 18 months	Walks independently but may lose this ability as the disease progresses. There is loss of motor skills.	Normal	3 to 5 for most patients
Type 4 (< 1% of patients)	> 18 years	Independent walking. Fatigue and proximal muscle weakness.	Normal	4 for 75% of patients; 5 or 6 for 25% of patients

* With supportive care only; SMN2 – Survival motor neuron 2.

Clinical Efficacy

Spinraza was investigated in a pivotal trial called ENDEAR, which was a Phase III, multicenter, multinational, randomized, double-blind, sham-procedure controlled study involving 121 symptomatic infants diagnosed with infantile-onset spinal muscular atrophy (Type 1).[1,6] Patients were randomized 2:1 to receive either Spinraza Low Dose Regimen (n = 80) or sham injection (n = 41).[1] Eligible patients were ≤ 7 months of age at the time of the first dose and diagnosed with spinal muscular atrophy with a symptom onset prior to 6 months of age. Baseline demographics were balanced between the Spinraza and control groups with the exception of age at first treatment (median age of 175 and 206 days, respectively).[1] At

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baseline, all infants were symptomatic, hypotonic and weak, which are features consistent with a phenotype that is most likely to be categorized as spinal muscular atrophy Type 1.[6] Patients had two SMN2 gene copies. The median time of treatment was 261 days (range 6 days to 442 days).[1] Those who received Spinraza compared with sham-control experienced improvement on achieving motor milestone responses. Outcomes assessing survival also revealed improvements for patients receiving Spinraza vs. sham control.

CHERISH was a multicenter, double-blind, sham-controlled, Phase III trial which involved children with symptomatic later-onset spinal muscular atrophy who were 2 to 12 years of age (n = 126) with likely Type 2 or 3 disease (symptom onset after 6 months of age).[1,7] Patients were randomized (2:1) to receive Spinraza Low Dose Regimen or sham injection. Three SMN2 gene copies were reported among 88% of patients; approximately 8% of patients had two SMN2 gene copies. The median age at screening was 4 years and 3 years in the Spinraza and sham procedure control groups, respectively.[1,7] Patients who received Spinraza experienced more improvement in motor milestones compared with sham control.

NURTURE was an open-label uncontrolled trial involving patients with presymptomatic spinal muscular atrophy who ranged in age from 3 days to 42 days at the time of the first dose (n = 25).[1,8] Patients were required to have two or three SMN2 gene copies.[8] Some patients who were given Spinraza Low Dose Regimen prior to the onset of symptoms related to spinal muscular atrophy survived without requiring permanent ventilation beyond what would be anticipated based on their SMN2 copy number. Also, some patients also met age-appropriate growth and development motor milestones (e.g., ability to sit unassisted, stand, or walk). Data are available from almost a median of 3-year follow-up.

The EMBRACE trial showed benefits of Spinraza in infants/children with infantile- or later-onset spinal muscular atrophy who were not eligible for the ENDEAR or CHERISH studies.[9] Data also support the efficacy of the Spinraza High-Dose Regimen.[1,12]

Dosing

Spinraza is given intrathecally by, or under the direction of, healthcare professionals experienced in performing lumbar punctures.[1] There are two dosing regimen options for Spinraza. The Low-Dose Regimen involves administration of a total of four loading doses as follows: one 12 mg dose once every 14 days for three doses, followed by a fourth 12 mg dose once every 30 days after the third dose. The maintenance dose of 12 mg should be given once every 4 months starting 4 months after the last loading dose. For the High-Dose Regimen, administer a total of two loading doses with one 50 mg dose followed by a second 50 mg dose 14 days later. The maintenance dose is administered as 28 mg once every 4 months starting 4 months after the last loading dose. For a patient transitioning from the Spinraza Low-Dose Regimen to the High-Dose Regimen, administer a single 50 mg bolus dose at least 4 months after the last 12 mg maintenance dose, followed by a 28 mg maintenance dose once every 4 months thereafter. There are additional recommendations in patients who have missed doses.

Guidelines

The Spinal Muscular Atrophy Newborn Screening Multidisciplinary Working Group is comprised of clinicians and geneticists with expertise in spinal muscular atrophy who developed a treatment algorithm in 2018 for infants who have positive results from a newborn screening test for spinal muscular atrophy.[10] Spinal muscular atrophy Types 1 and 2 comprise a large majority of cases and account for many patients who screen positively for spinal muscular atrophy with three or fewer SMN2 gene copies. Immediate treatment is recommended in patients with two or three SMN2 gene copies. Treatment recommendations for patients who screen positive for spinal muscular atrophy and have only one SMN2 gene copy is more complicated.[10] In 2020, the Working Group updated recommendations that infants diagnosed with spinal muscular atrophy via newborn screening with four SMN2 gene copies should receive immediate

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treatment.[11] Also, patients with five (or more) SMN2 gene copies should be observed and screened for symptoms.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Spinraza. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Due to the specialized skills required for evaluation and diagnosis of patients treated with Spinraza as well as the monitoring required for adverse events and long-term efficacy, approval requires Spinraza to be prescribed by a physician who has consulted with or who specializes in the condition. If claims history is available, verification is required in certain criteria as noted by **[verification in claims history required]**. All reviews will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

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1. **Spinal Muscular Atrophy – Treatment.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Baseline motor ability assessment that suggest spinal muscular atrophy (based on age, motor ability, and development) has been performed from ONE of the following exams (a, b, c, d, e, f, or g) **[documentation required]**:
       - **a)** Bayley Scales of Infant and Toddler Development; OR
       - **b)** Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR
       - **c)** Hammersmith Functional Motor Scale Expanded (HFMSE); OR
       - **d)** Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR
       - **e)** Motor Function Measure-32 Items (MFM-32); OR
       - **f)** Revised Upper Limb Module (RULM) test; OR
       - **g)** World Health Organization motor milestone scale; AND
     - **ii.** Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene **[documentation required]**; AND
       Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.
     - **iii.** Patient meets ONE of the following (a or b):

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a) Patient has two or three survival motor neuron 2 (SMN2) gene copies **[documentation required]**; OR

b) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has four survival motor neuron 2 (SMN2) gene copies **[documentation required]**; AND

(2) Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3 **[documentation required]**; AND

iv. Patient has not received Zolgensma (onasemnogene abeparvovec-xioi intravenous infusion) or Itvisma (onasemnogene abeparvovec-brve intrathecal injection) in the past **[verification in claims history required]**; AND

Note: If no claim for Zolgensma or Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Zolgensma or Itvisma.

v. Medication is prescribed by a physician who has consulted with or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; OR

B) Patient Currently Receiving Spinraza Therapy. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, and v):

i. Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene; AND

Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.

ii. Patient meets ONE of the following (a or b):

a) Patient has two or three survival motor neuron 2 (SMN2) gene copies; OR

b) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has four survival motor neuron 2 (SMN2) gene copies; AND

(2) Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3; AND

iii. Each Spinraza dose is to be administered once every 4 months as maintenance therapy; AND

iv. Medication is prescribed by a physician who has consulted with or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; AND

v. Patient must meet ONE of the following (a or b):

a) Patient must have had a positive clinical response (for example, improvement or stabilization) from pretreatment baseline status with Spinraza from ONE of the following [(1), (2), (3), (4), (5), (6), or (7)] **[documentation required]**:

(1) Bayley Scales of Infant and Toddler Development; OR

(2) Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR

(3) Hammersmith Functional Motor Scale Expanded (HFMSE); OR

(4) Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR

(5) Motor Function Measure-32 Items (MFM-32); OR

(6) Revised Upper Limb Module (RULM) test; OR

(7) World Health Organization motor milestone scale; OR

b) According to the prescribing physician, the patient has responded to Spinraza and continues to benefit from ongoing Spinraza therapy by the most recent physician monitoring/assessment tools **[documentation required]**.

Note: Examples include pulmonary function tests showing improvement, bulbar function test results suggest benefits, reduced need for respiratory support, decrease in the frequency of respiratory infections or complications, and/or prevention of permanent assisted ventilation.

Dosing. Approve the following dosing regimens (A, B, and/or C):

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A) Low-Dose Regimen: Approve if the patient meets ONE of the following (i, ii, and/or iii):
- **i.** Initially give 12 mg intrathecally as four loading doses of which the first three loading doses should be given at 14-day intervals and the fourth loading dose should be given 30 days after the third dose; AND/OR
- **ii.** The maintenance dose is 12 mg intrathecally once every 4 months and is started 4 months after the last loading dose; AND/OR
- **iii.** Missed maintenance doses must meet ONE of the following (a, b, c, and/or d):
  - **a)** Less than 8 months from the last dose: Approve one 12 mg intrathecal dose to be given as soon as possible, then administer the next maintenance dose on the originally scheduled date (as long as these two doses are administered at least 14 days apart); AND/OR
    Note: Thereafter, the regular maintenance dose schedule should be followed.
  - **b)** At least 8 months but less than 16 months from the last dose: Approve one 12 mg intrathecal dose to be given as soon as possible, followed by one additional dose 14 days later; AND/OR
    Note: Thereafter, the regular maintenance dose scheduled should be followed.
  - **c)** At least 16 months but less than 40 months from the last dose: Approve one 12 mg intrathecal maintenance dose to be given as soon as possible, followed by two additional doses that must be given 14 days apart; AND/OR
    Note: Thereafter, the regular maintenance dose schedule should be followed.
  - **d)** At least 40 months from the last dose: Dosing should be restarted as recommended in criteria Ai and Aii; OR

B) Transitioning from the Low-Dose Regimen to the High-Dose Regimen: Approve one 50 mg intrathecal dose given at least 4 months after the last 12 mg maintenance dose; OR
Note: Thereafter, the regular maintenance dose should be followed in criterion C.ii.

C) High-Dose Regimen: Approve if the patient meets ONE of the following (i, ii, and/or iii)
- **i.** The initial dose is 50 mg intrathecally followed by a second 50 mg dose 14 days later; AND/OR
- **ii.** The maintenance dose is 28 mg intrathecally once every 4 months and is started 4 months after the last loading dose; AND/OR
- **iii.** Missed maintenance doses must meet ONE of the following (a, b, and/or c):
  - **a)** Less than 8 months from the last dose: Approve one 28 mg dose to be given as soon as possible, then administer the next maintenance dose on the originally scheduled date (as long as these two doses are administered at least 14 days apart); AND/OR
    Note: Thereafter, the regular maintenance dose schedule should be followed.
  - **b)** At least 8 months but less than 40 months after the last dose: Approve one 50 mg loading dose to be given as soon as possible; AND/OR
    Note: Thereafter, the regular maintenance dose schedule should be followed.
  - **c)** At least 40 months from the last dose: Dosing should be restarted as recommended in criteria Ci and Cii.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Spinraza is not recommended in the following situations:

1. **Patient has Complete Paralysis of All Limbs.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Spinraza.

2. **Patient has Permanent Ventilator Dependence.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Spinraza.

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3. **Concurrent Use with Evrysdi (risdiplam oral solution and tablets).** Further study is needed to determine if use of Spinraza with Evrysdi is efficacious and safe.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Regarding Documentation, medical test results and prescription receipts were added as examples; the example provided of laboratory "tests" was changed to laboratory "results". In the Policy Statement, regarding verification of claims history, the phrase "if claims history is available" was added to account for situations in which claims history is not present. **Spinal Muscular Atrophy – Treatment:** In criteria that the patient has not received Zolgensma in the past (with verification in claims history required), the Note was revised to account for situations in which a claims history is not available.	10/02/2024
Early Annual Revision	Regarding documentation, the following exception was removed: "In subsequent coverage reviews for a patient who has previously met the documentation requirements and related criteria in the Spinal Muscular Atrophy – Spinraza Prior Authorization Policy through the Coverage Review Department, and who is requesting reauthorization, the criteria utilized do NOT require resubmission of documentation for reauthorization, except for the criterion requiring documentation of response or benefit to Spinraza therapy." In addition, the following changes were made: **Spinal Muscular Atrophy – Treatment:** For initial therapy and for a patient currently receiving Spinraza, the following requirement was removed: "A patient currently receiving or who has received prior treatment with Evrysdi, the prescribing physician confirms that further therapy with Evrysdi will be discontinued." For a patient currently receiving Spinraza, the documentation requirement was removed from the following criteria: 1) patient has a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 gene; 2) patient has two or three survival motor neuron 2 gene copies; 3) patient has four survival motor neuron 2 gene copies, and 4) patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3. For a patient currently receiving Spinraza, the requirement that the patient has not received Zolgensma in the past was removed; the related Note and that verification was required in claims history were also removed. **Conditions Not Recommended for Approval:** Concurrent use with Evrysdi was added.	07/30/2025
Selected Revision	**Spinal Muscular Atrophy – Treatment:** For initial therapy, Itvisma was added as a gene therapy that the patient should not have received in the past. The Note now includes that if no claim for Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Itvisma.	01/28/2026
Selected Revision	**Spinal Muscular Atrophy – Treatment:** For a patient currently receiving Spinraza therapy the duration was changed to 1 year; previously it was one dose (for a dose to be used once within the next 4 months as maintenance therapy). The requirement that 4 months has elapsed since the last dose was changed to each Spinraza dose is to be administered once every 4 months as maintenance therapy.	02/18/2026
Selected Revision	**Spinal Muscular Atrophy – Treatment:** Dosing was revised to divide dosing into three sections: 1) Low-Dose Regimen, 2) Transitioning from the Low-Dose Regimen to the High-Dose Regimen, and 3) High-Dose Regimen.	04/08/2026
Update	07/01/2026: No criteria changes. Updated the dosing section in the overview.	NA
Annual Revision	No criteria changes.	07/22/2026

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