Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Nusinersen (Spinraza®)	**MP-RX-FP-84-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	**11/30/2023** **Last Review Date:** **7/1/2026**	**7/1/2026** **Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses the use of nusinersen (Spinraza®) , a drug approved by the Food and Drug Administration (FDA) for the treatment of children and adults with spinal muscular atrophy (SMA).

Background Information:

This document addresses the use of Spinraza (nusinersen), a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide that targets the SMN2 gene to promote inclusion of exon 7 in its mRNA, leading to the production of full-length SMN protein. This protein is essential for motor neuron survival and function, addressing the root cause of 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) is 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.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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			Last Review Date: 7/1/2026	Frequently Revision: Annual

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. Spinraza is now FDA-approved with two recommended dosing regimen options: a low-dose regimen and a high-dose regimen, each consisting of loading doses followed by maintenance dosing. The high-dose regimen includes two 50 mg loading doses administered 14 days apart, followed by 28 mg once every 4 months. Backed by more than 10 years of clinical data supporting the Low Dose Regimen of Spinraza (12 mg), High Dose Spinraza was designed to deliver a higher concentration of drug through both the loading and maintenance dosing phases, to provide a new option in response to the ongoing needs of the community.

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). The efficacy of the high-dose regimen was demonstrated in Study 4, a double-blind, randomized, external-controlled trial in patients with symptomatic infantile-onset and later-onset SMA. The overall findings from these trials support the effectiveness of Spinraza administered with either the low-dose regimen or the high-dose regimen across a range of ages and disease severities in patients with SMA. 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

Approved Indications

A. Treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

Other Uses

A. None.

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Nusinersen (Spinraza®)	MP-RX-FP-84-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/1/2026
			Last Review Date: 7/1/2026	Frequently Revision: Annual

Medical Necessity Guidelines:

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.

Nusinersen (Spinraza®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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

i. Documentation is provided that individual has a confirmatory diagnosis by either:
   A. Spinal Muscular Atrophy (SMA) diagnostic test results confirming 0 copies of SMN1; **OR**
   B. Molecular genetic testing of 5q SMA for any of the following:
      a. homozygous gene deletion; **OR**
      b. homozygous conversion mutation; **OR**
      c. 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.
   a. 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:

Policy Name: Nusinersen (Spinraza®)	Policy Number: MP-RX-FP-84-23	Scope: ☒ MMM MA ☒ MMM MultiHealth	Origination Date: 11/30/2023	Effective Date: 7/1/2026
			Last Review Date: 7/1/2026	Frequently Revision: Annual

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.

Transition requests for Spinraza following the treatment from the Low Dose Regimen to the High Dose Regimen may be approved if the following criteria are met:

i. When initial therapy was determined to meet the above criteria; **AND**
ii. The treating physician is required to provide a detailed clinical justification, supported by objective evidence from recognized clinical literature or compendia, to substantiate the medical necessity of transitioning from a low-dose regimen to a high-dose regimen.

B. Criteria For Continuation of 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 baseline motor ability assessments that support improvement or stabilization compared to baseline motor ability assessments.
    a. 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.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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ii. When used in combination therapy with Evrysdi (risdiplam).

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

This medical policy may be subject to Step Therapy. Please refer to the document published on the MMM Website: https://www.mmm-pr.com/planes-medicos/formulario-medicamentos

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Dosing
Spinraza® (nusinersen) 12 mg/5 mL SDV 28 mg/5ml SDV 50 mg/5ml SDV	• *Low Dose Regimen*: o Loading Dose: 12 mg (120 HCPCS units) every 14 days for 3 doses, then a fourth 12 mg dose 30 days after the third dose. o Maintenance Dose: 12 mg 120 (HCPCS units) once every 4 months • *High Dose Regimen:* o Loading Dose: 50 mg (500 HCPCS units) followed by a second 50 mg dose 14 days later o Maintenance Dose: 28 mg (280 HCPCS units) once every 4 months starting 4 months after the last loading dose
	Exceptions
• For initiation of low-dose therapy, may approve 4 loading doses of 12 mg (120 HCPCS units; 1 vial) each in the first 4 months of therapy. • For initiation of high-dose therapy, may approve 2 loading doses of 50 mg (500 HCPCS units; 1 vial) administered 14 days apart. • If transitioning from the Low Dose Regimen to the High Dose Regimen, administer a single 50 mg (500 HCPCS units) dose at least 4 months (+/- 14 days) after the last 12 mg maintenance dose, followed by 28 mg (280 HCPCS units) once every 4 months thereafter. • Conduct the following laboratory tests at baseline and prior to each dose of Spinraza, and as clinically needed: o Platelet count o Prothrombin time and activated partial thromboplastin time\ o Quantitative spot urine protein testing	

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
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 spinal muscular atrophies and related syndromes
G12.8	Other spinal muscular atrophies and related syndromes
G12.9	Spinal muscular atrophy, unspecified

HCPCS Codes:

Codes	Description
J2326	Injection, nusinersen, 0.1 mg [SPINRAZA] (J2326 is billed per 0.1 mg. Therefore, 12 mg = 120 units, 28 mg = 280 units, and 50 mg = 500 units)

CPT Codes:

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

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Reference Information:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Biogen Inc. Spinraza (nusinersen) injection, for intrathecal use: Prescribing information. Revised March 2026. Accessed April 27, 2026.
4. Finkel, R. S., Crawford, T. O., Mercuri, E., et al. High-dose nusinersen for spinal muscular atrophy: A phase 3 randomized trial. *Nature Medicine, 32*, 1095–1104. 2026. https://doi.org/10.1038/s41591-025-04193-6
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
6. Finkel RS, Mercuri E, Darras BT, et al. Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy. N Engl J Med. 2017;377(18):1723-1732. doi:10.1056/NEJMoa1702752.
7. De Vivo DC, Bertini E, Swoboda KJ, et al, on behalf of NURTURE Study Group, Nusinersen initiated in infants during the presymptomatic stage of spinal muscular atrophy: Interim efficacy and safety results from the Phase 2 Nurture study, Neuromuscular Disorders. 2019; 29 (11):842-856.
8. Mendell JR, Al-Zaidy S, Shell R, et al. Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy. N Engl J Med. 2017 Nov 2;377(18):1713-1722. doi: 10.1056/NEJMoa1706198.
9. Mercuri E, Darras BT, Chiriboga CA, et al. Nusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy. N Engl J Med. 2018;378(7):625-635. doi:10.1056/NEJMoa1710504.
10. Acsadi G, Crawford TO, Müller-Felber W, et al. Safety and efficacy of nusinersen in spinal muscular atrophy: The EMBRACE study. Muscle Nerve. 2021;63(5):668-677. doi:10.1002/mus.27187.
11. Mercuri E, Finkel RS, Muntoni F, et al. Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscul Disord. 2018;28(2):103-115. doi:10.1016/j.nmd.2017.11.005.
12. Pierzchlewicz K, Kępa I, Podogrodzki J, Kotulska K. Spinal Muscular Atrophy: The Use of Functional Motor Scales in the Era of Disease-Modifying Treatment. Child Neurol Open. 2021;8:2329048X211008725. Published 2021 Apr 27. doi:10.1177/2329048X211008725.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Nusinersen (Spinraza®)	MP-RX-FP-84-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	7/1/2026
			Last Review Date: 7/1/2026	Frequently Revision: Annual

Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Updated the policy to incorporate the FDA-approved Spinraza high-dose regimen, including the new 28 mg and 50 mg vial strengths, high-dose loading and maintenance dosing, transition dosing from the low-dose to high-dose regimen, and corresponding HCPCS billing units. Added laboratory monitoring requirements consistent with prescribing information. Clarified dosing limits and exceptions for low-dose initiation, high-dose initiation, and transition dosing. Updates reference list. Administrative update to incorporate new policy template.	6/19/2026	7/1/2026
Annual Review	Minimal changes; Word Formatting. Coding reviewed: No changes.	8/25/2025	9/8/2025
Annual Review	Updated sections: Applicable Codes, Medical Necessity Guidelines (Initial and Continuation Criteria, Approval Duration, and Conditions not covered), and Reference Information. 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: Added CPT code 96450 and ICD-10 codes: G12.0, G12.9 to include all codes under the parent code G12.0.	3/14/2025	4/2/2025
Policy Inception	11/18/23: Elevance Health's Medical Policy adoption.	N/A	11/30/2023