# Medical Policy

**Healthcare Services Department**

| Policy Name | Policy Number | Scope |
|---|---|---|
| Spinraza (nusinersen) | MP-RX-FP-84-23 | ☒ MMM MA ☒ MMM Multihealth |

## Service Category

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

## Service Description

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).

**Background Information**

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).

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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 |

**Approved Indications**

A. Treatment of childrens and adults spinal muscular atrophy (SMA)

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## Applicable Codes

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.

| HCPCS | Description |
|---|---|
| J2326 | Injection, nusinersen, 0.1 mg [SPINRAZA] |

| ICD-10 | Description |
|---|---|
| G12.0<br>G12.1 | Infantile spinal muscular atrophy, type I (Werdnig-Hoffman)<br>Other inherited spinal muscular atrophy [includes types II, III (Kugelberg-Welander) and IV] |

## 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.

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

Spinraza (nusinersen)

**A. Criteria For Initial Approval**

i. 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:
1. homozygous gene deletion; or
2. homozygous conversion mutation; or
3. compound heterozygote;
AND
II. Documentation is provided that individual has either:
A. Genetic testing confirming no more than 2 copies of SMN2 (Finkel 2017); OR
B. Onset of SMA-associated signs and symptoms before 21 months of age (Mercuri 2018).
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.

ii. 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 (for example, loss of motor milestone) since receipt of gene therapy.

**B. Criteria For Continuation of Therapy**

i. I. When initial therapy was determined to meet the above criteria;
AND
II. 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;
AND
III. Documentation is provided that individual has clinically significant improvement in spinal muscular atrophy-associated signs and symptoms (i.e., progression, stabilization, or

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decreased decline in motor function) compared to the predicted natural history trajectory of disease.

**C. Authorization Duration**

i. Approval Duration:

a. Initial Approval Duration: 6 months

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| Policy Name | Policy Number | Scope |
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## Limits or Restrictions

A. Therapeutic Alternatives

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 | Limit |
|---|---|
| Spinraza (nusinersen) 12 mg/5 mL vial* | 1 vial (12 mg) per 4 months |
| **Exceptions** | |
| *For initiation of therapy, may approve 4 loading doses of 12 mg (1 vial) each in the first 4 months of therapy | |

## Reference Information


1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. Finkel RS, Mercuri E, Darras BT, et al. Nusinersen versus Sham Control in Infant-Onset Spinal Muscular Atrophy. N Engl J Med 2017;377:1723-1732.
3. 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.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
6. 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.
7. Mercuri E, Darras BT, Chiriboga CA, et al. Nusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy. N Engl J Med 2018;378:625-635.

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## Policy History

| Revision Type | Summary of Changes | P&T Approval Date | MPCC Approval Date |
|---|---|---|---|
| Policy Inception | Elevance Health's Medical Policy adoption. | N/A | 11/30/2023 |

Revised: 11/18/22