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# 5.75.15

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| <b>Section:</b>    | Prescription Drugs   | <b>Effective Date:</b>       | July 1, 2022     |
| <b>Subsection:</b> | Neuromuscular Agents | <b>Original Policy Date:</b> | January 13, 2017 |
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**Last Review Date:** June 16, 2022

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## Spinraza

### Description

#### Spinraza (nusinersen)

#### Background

Spinraza is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. It contains nusinersen, which is a modified antisense oligonucleotide designed to treat SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Nusinersen binds to a specific sequence in the intron downstream of exon 7 of the SMN2 transcript. Using in vitro assays and studies in transgenic animal models of SMA, Spinraza was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein (1).

#### Regulatory Status

FDA-approved indication: Spinraza is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients (1).

Physicians should obtain a platelet count and appropriate coagulation laboratory testing at baseline and before each dose. No patient had a platelet count less than 50,000 cells per microliter in these studies. Additionally, due to the risk of renal toxicity, quantitative spot urine testing is required at baseline and before each dose (1).

In the clinical studies done for Spinraza the patients in these studies had or were likely to develop Type I, II, or III SMA. The clinical studies did not include Type 0 and IV (1).

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Multiple tools have been developed in order to determine a baseline motor milestone score for patients with SMA. These assessments can also be utilized to measure improvement and include: Hammersmith Infant Neurologic Exam (HINE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), Upper Limb Module (ULM), Hammersmith Functional Motor Scale (HFMS) / Hammersmith Functional Motor Scale - Expanded (HFMS-E), Motor Function Measure 32 (MFM32), and the Revised Upper Limb Module (RULM) (1-3).

The safety and effectiveness of Spinraza in pediatric patients from newborn to 17 years have been established (1).

## Related policies

Evrysdi, Zolgensma

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Spinraza may be considered **medically necessary** in patients with spinal muscular atrophy (SMA) and if the conditions indicated below are met.

Spinraza may be considered **investigational** for all other indications.

## Prior-Approval Requirements

### Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA)

**AND ALL** of the following:

- a. Diagnosis confirmed by genetic testing demonstrating bi-allelic mutations in the survival motor neuron 1 (SMN1) gene with **ONE** of the following:
  - i. Deletion of both copies of the SMN1 gene **OR**
  - ii. Compound heterozygous mutation of the SMN1 gene (defined below)

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- a) Pathogenic variant(s) in both copies of the SMN1 gene
- b) Pathogenic variant in 1 copy and deletion of the second copy of the SMN1 gene
- b. Patient has **ONE** of the following:
  - i. Patient is symptomatic with documentation of a genetic test confirming 2 to 4 copies of the SMN2 gene
  - ii. Patient is asymptomatic with documentation of a genetic test confirming 2 to 3 copies of the SMN2 gene
- c. The patient is not on permanent ventilator dependence
- d. Obtain a baseline motor milestone score from **ONE** the following assessments:
  - i. Hammersmith Infant Neurologic Exam (HINE)
  - ii. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
  - iii. Upper Limb Module (ULM)
  - iv. Hammersmith Functional Motor Scale (HFMS) / Hammersmith Functional Motor Scale - Expanded (HFMSSE)
  - v. Motor Function Measure 32 (MFM32)
  - vi. Revised Upper Limb Module (RULM)
- e. Prescriber will not exceed the FDA labeled dose of 12 mg (5 mL) per administration
- f. Prescribed by a neurologist, neuromuscular specialist, or pediatrician with expertise in treating SMA
- g. **NOT** used in combination with risdiplam
- h. Patient has not previously received gene therapy for SMA (see Appendix 1)
- i. Patient is not concurrently enrolled in a clinical trial for an experimental therapy for SMA

## Prior – Approval *Renewal* Requirements

### Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA)

**AND ALL** of the following:

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- a. Clinically meaningful improvement or stabilization in motor milestones from baseline
- b. **NOT** used in combination with risdiplam
- c. Patient has not previously received gene therapy for SMA (see Appendix 1)

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 4 doses (20mL)  
**Duration** 3 months

### Prior – Approval *Renewal* Limits

**Quantity** 4 doses (20mL)  
**Duration** 12 months

## Rationale

### Summary

Spinraza is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. It contains nusinersen, which is a modified antisense oligonucleotide designed to treat SMA caused by mutations in chromosome 5q that lead to SMN protein deficiency. Due to the risk of thrombocytopenia and coagulation abnormalities, it is required to obtain a platelet count and appropriate coagulation laboratory testing at baseline and before each dose. Additionally, due to the risk of renal toxicity, quantitative spot urine testing is required at baseline and before each dose (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Spinraza while maintaining optimal therapeutic outcomes.

### References

1. Spinraza [package insert]. Cambridge, MA: Biogen Inc.; June 2020.

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2. Mazzone E, Bianco F, et al. Assessing upper limb function in nonambulant SMA patients: Development of a new module. *Neuromuscular Disorders* 21 (2011) pg:406–412.
3. Finkel RS, Chiriboga CA, et al. Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study. *Lancet*. 2016 Dec 17; 388(10063): 3017-3026.

## Policy History

| Date           | Action   |
|----------------|--|
| January 2017   | Addition to PA   |
| February 2017  | Addition of the following requirements: diagnosis was confirmed by genetic testing, Type I, II, or III SMA, addition of new assessments that can be used and the improvement in motor milestone score of 2 points for Type II or III in the renewal section.                                   |
| April 2017     | Addition of patient must have a platelet count of $\geq 50,000$ cells per microliter   |
| June 2017      | Annual review<br>Addition of the genetic testing showing 5q SMA of ONE of the following: homozygous gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13) or compound heterozygous mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2]) |
| September 2017 | Annual review  |
| September 2018 | Annual review and reference update   |
| June 2019      | Addition of requirement that patient has not received gene therapy for SMA   |
| September 2019 | Annual review and reference update   |
| September 2020 | Annual editorial review and reference update. Added the options of HFMSE, MFM32, or RULM scores per FEP. Added no dual therapy with risdiplam  |
| December 2020  | Annual review  |
| September 2021 | Annual review  |

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| April 2022 | Per FEP: Updated genetic testing requirement. Added requirements for: exclusion of patients on permanent ventilator dependence and patients enrolled in clinical trials for SMA. Added requirement for prescriber agreement to FDA dosing and prescriber needing to have expertise in treating SMA. Removed requirements for: platelet and coagulation testing, platelet count $\geq 50,000$ and spot urine testing. Removed continuation requirement for 2 point decrease in motor milestone score for type II and type III SMA. Added less specific continuation requirement for improvement and stabilization in motor milestones from baseline. |
| June 2022  | Annual review   |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.**

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## Appendix 1 - List of Gene Therapies for SMA

| Generic Name                     | Brand Name |
|----------------------------------|------------|
| Onasemnogene<br>abeparvovec-xioi | Zolgensma  |