BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.75.015

Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Neuromuscular Agents	**Original Policy Date:**	January 13, 2017
Subject:	Spinraza	**Page:**	1 of 7

Last Review Date: September 6, 2024

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).

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 (HFMSE), 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** 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)
        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 (HFMSE)
    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:
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.; April 2024.
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 ≥ 50,000 cells per microliter
June 2017	Annual review 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
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 ≥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
September 2023	Annual review and reference update. Changed policy number to 5.75.015
December 2023	Annual review
September 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.

Appendix 1 - List of Gene Therapies for SMA

Generic Name	Brand Name
Onasemnogene abeparvovec-xioi	Zolgensma