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 are 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) and the Hammersmith Functional Motor Scale (HFMS) (1-2).

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

**Related policies**
Emflaza, Exondys 51, 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) 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 showing 5q SMA of **ONE** of the following:
      i. Homozygous gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13)
      ii. Compound heterozygous mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2])
   b. Type I, II, or III SMA
c. Prescriber agrees to do a platelet count and coagulation test before each dose
d. Patient must have a platelet count of ≥ 50,000 cells per microliter
e. Prescriber agrees to do quantitative spot urine testing before each dose
f. Obtain a baseline motor milestone score from ONE the following assessments:
   i. HINE
   ii. CHOP-INTEND
   iii. Upper Limb Module (ULM)
   iv. Hammersmith Functional Motor Scale (HFMS)
g. Patient has not previously received gene therapy for SMA (see Appendix 1)

Prior – Approval Renewal Requirements

Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA) with ONE of the following:
   a. Type I SMA
      i. Improvement in motor milestone score from baseline
   b. Type II or III SMA
      ii. Improvement in motor milestone score of 2 points from baseline

AND ALL of the following:
   a. Prescriber agrees to do a platelet count and coagulation test before each dose
   b. Patient must have a platelet count of ≥ 50,000 cells per microliter
   c. Prescriber agrees to do quantitative spot urine testing before each dose
   d. 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 are 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
<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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<tbody>
<tr>
<td>February 2017</td>
<td>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.</td>
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<tr>
<td>April 2017</td>
<td>Addition of patient must have a platelet count of $\geq 50,000$ cells per microliter</td>
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<tr>
<td>June 2017</td>
<td>Annual review</td>
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<td>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])</td>
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<tr>
<td>September 2017</td>
<td>Annual review</td>
</tr>
<tr>
<td>September 2018</td>
<td>Annual review and reference update</td>
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<tr>
<td>June 2019</td>
<td>Addition of requirement that patient has not received gene therapy for SMA</td>
</tr>
<tr>
<td>September 2019</td>
<td>Annual review and reference update</td>
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**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.
Appendix 1 - List of Gene Therapies for SMA

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>Onasemnogene abeparvovec-xioi</td>
<td>Zolgensma</td>
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