

## Treatment for Spinal Muscular Atrophy

**Policy # 00550**

Original Effective Date: 04/19/2017

Current Effective Date: 07/01/2025

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

### When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

### nusinersen (Spinraza<sup>TM</sup>)

Based on review of available data, the Company may consider nusinersen (Spinraza<sup>TM</sup>)<sup>†</sup> for the treatment of spinal muscular atrophy (SMA) to be **eligible for coverage**.\*\*

#### Patient Selection Criteria

Coverage eligibility for nusinersen (Spinraza) will be considered when the following criteria are met:

#### **Initial**

- Patient has a diagnosis of types I, II, or III spinal muscular atrophy (SMA) established by, or in consultation with a neuromuscular specialist or neurologist and confirmed by either:
  - SMA diagnostic test results confirming 0 copies of *SMN1*; OR
  - Bi-allelic mutations in the *SMN1* gene; AND

*(Note: The restriction to types I-III SMA is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Documentation of genetic testing confirming 2-4 copies of *SMN2*; AND
 

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Patient is not currently enrolled in a clinical trial for any experimental therapy for SMA; AND
 

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Patient has NOT received treatment with onasemnogene abeparvovec-xioi (Zolgensma<sup>TM</sup>)<sup>‡</sup>; AND
- Spinraza will not be used in combination with risdiplam (Evrysdi<sup>TM</sup>)<sup>‡</sup>; AND

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- Patient does NOT have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, or tracheostomy); AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- The medication will be administered by or under the direction of a healthcare professional experienced in performing lumbar punctures; AND
- The requested dose is consistent with the Food and Drug Administration (FDA)-approved dosing of 12 milligrams (mg) administered with 4 loading doses; the first 3 loading doses should be administered at 14 day intervals. The 4<sup>th</sup> loading dose should be administered 30 days after the 3<sup>rd</sup> dose. A maintenance dose should be administered once every 4 months thereafter.

### Continuation

- The “initial” criteria are met; AND
- There is documentation of clinically significant improvement in SMA-associated symptoms (for example, progression of motor function, stabilization of motor function, or decreased decline in motor function) compared to the predicted natural history trajectory of disease; AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Dosing will be in accordance with FDA-approved labeling: maximum dosing of 12 mg every 4 months starting 4 months after the last loading dose.

## When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of nusinersen (Spinraza) when the number of copies of *SMN2* criteria are not met, patient has advanced SMA, patient has types 0 or IV SMA, or when the patient is enrolled in a clinical trial to be **not medically necessary.\*\***

Based on review of available data, the Company considers the continued use of nusinersen (Spinraza) when there is NO documentation of clinically significant improvement in spinal muscular atrophy-associated symptoms (for example, progression of motor function, stabilization of motor function, or decreased decline in motor function) compared to the predicted natural history trajectory of disease to be **not medically necessary.\*\***

## When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of nusinersen (Spinraza) when the patient selection criteria are not met (except those denoted as **not medically necessary\*\***) to be **investigational.\***

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## When Services May Be Eligible for Coverage

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- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

### **onasemnogene abeparvovec-xioi (Zolgensma<sup>TM</sup>)**

Based on review of available data, the Company may consider onasemnogene abeparvovec-xioi (Zolgensma) for the treatment of spinal muscular atrophy (SMA) to be **eligible for coverage**.\*\*

#### Patient Selection Criteria

Coverage eligibility for onasemnogene abeparvovec-xioi (Zolgensma) will be considered when the following criteria are met:

- Patient has a diagnosis of spinal muscular atrophy established by, or in consultation with a neuromuscular specialist or neurologist and confirmed by either:
  - SMA diagnostic test results confirming 0 copies of the survival motor neuron (*SMN1*) gene; OR
  - Bi-allelic mutations in the *SMN1* gene; AND
- Patient is younger than 2 years of age (and will still be younger than 2 years of age at the time of infusion); AND
- Patient has less than or equal to 4 copies of *SMN2*; AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Patient does NOT have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, or tracheostomy); AND
- Patient has documentation of a test confirming anti-adenovirus serotype 9 antibody titer  $\leq 1:50$ ; AND
- Patient weight is less than or equal to 21 kg; AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Patient does not have a contraindication or intolerance to corticosteroids; AND
- Patient has not received prior treatment with Zolgensma or any other gene therapy for SMA and is not currently enrolled in a clinical trial for any experimental therapy for SMA; AND  
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- If the patient has previously received Spinraza or Evrysdi, it will be discontinued prior to administration of Zolgensma (NOTE: member's medical record will be reviewed and any current authorizations for Spinraza or Evrysdi will be terminated upon Zolgensma approval); AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*

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- The requested one-time dose is consistent with the Food and Drug Administration (FDA)-approved dosing of  $1.1 \times 10^{14}$  vector genomes per kg of body weight.

Note: Authorization will be for no longer than 12 weeks from approval, or until 2 years of age, whichever is first.

### When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of onasemnogene abeparvovec-xioi (Zolgensma) when the patient has more than 4 copies of the *SMN2* gene, weighs more than 21 kg, has received prior treatment with Zolgensma or any other gene therapy, is currently enrolled in a clinical trial for an experimental therapy for SMA, or will be continuing treatment with Spinraza or Evrysdi to be **not medically necessary**.\*\*

### When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of onasemnogene abeparvovec-xioi (Zolgensma) when the patient selection criteria are not met (except those denoted as **not medically necessary**\*\*) to be **investigational**.\*

### When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

### risdiplam (Evrysdi™)

Based on review of available data, the Company may consider risdiplam (Evrysdi) for the treatment of spinal muscular atrophy (SMA) to be **eligible for coverage**.\*\*

#### Patient Selection Criteria

Coverage eligibility for risdiplam (Evrysdi) will be considered when the following criteria are met:

#### **Initial**

- Patient has a diagnosis of types I, II, or III spinal muscular atrophy confirmed by either:
  - SMA diagnostic test results confirming 0 copies of *SMN1*; OR
  - Bi-allelic mutations in the survival motor neuron 1 (*SMN1*) gene; AND*(Note: The restriction to types I-III SMA is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*

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- Documentation of genetic testing confirming 2-4 copies of *SMN2*; AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Patient is not currently enrolled in a clinical trial for any experimental therapy for SMA; AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Patient has NOT received treatment with onasemnogene abeparvovec-xioi (Zolgensma); AND
- If the patient is a female of childbearing potential, patient is NOT currently pregnant and is willing to utilize effective contraception; AND
- Patient does NOT have evidence of hepatic impairment; AND
- Patient does NOT have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, or tracheostomy); AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Evrysdi will not be used concomitantly with nusinersen (Spinraza); AND
- Dosing of Evrysdi meets **ONE** of the following based on current patient weight and age:
  - If the patient is < 2 months of age: 0.15 mg/kg once daily; OR
  - If the patient is 2 months to < 2 years of age: 0.2 mg/kg once daily; OR
  - If the patient is  $\geq$  2 years of age and weighs < 20 kg: 0.25 mg/kg once daily; OR
  - If the patient is  $\geq$  2 years of age and weighs  $\geq$  20 kg: 5 mg once daily.

### Continuation

- The “initial” criteria are met; AND
- There is documentation of clinically significant improvement in SMA-associated symptoms (for example, progression of motor function, stabilization of motor function, or decreased decline in motor function) compared to the predicted natural history trajectory of disease; AND  
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*
- Dosing of Evrysdi meets **ONE** of the following based on current patient weight and age:
  - If the patient is 2 months to < 2 years of age: 0.2 mg/kg once daily; OR
  - If the patient is  $\geq$  2 years of age and weighs < 20 kg: 0.25 mg/kg once daily; OR
  - If the patient is  $\geq$  2 years of age and weighs  $\geq$  20 kg: 5 mg once daily.

## When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of risdiplam (Evrysdi) for the treatment of types 0 or IV SMA, for patients without the specified number of copies of *SMN2*, for patients currently enrolled in a clinical trial for an experimental therapy for SMA, or for patients with advanced SMA to be **not medically necessary.\*\***

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Based on review of available data, the Company considers the continued use of risdiplam (Evrysdi) when there is NO documentation of clinically significant improvement in SMA-associated symptoms (for example, progression, stabilization, or decreased decline in motor function) compared to the predicted natural history trajectory of disease to be **not medically necessary.\*\***

## When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of risdiplam (Evrysdi) when the patient selection criteria are not met (except those denoted as **not medically necessary\*\***) to be **investigational.\***

## Background/Overview

Spinraza is an SMN2-directed antisense oligonucleotide indicated for the treatment of SMA in pediatric and adult patients. Spinraza is administered intrathecally at 12 mg per administration. Spinraza is initiated with four loading doses. The first three loading doses should be administered at 14 day intervals. The fourth loading dose should be administered 30 days after the 3<sup>rd</sup> dose; a maintenance dose should be given once every 4 months thereafter.

Zolgensma is a one-time gene replacement therapy currently available as an intravenous infusion for patients younger than 2 years of age with SMA. It is composed of an adeno-associated viral vector containing a transgene encoding the human survival motor neuron (SMN) protein. The transgene does not integrate into the host cell DNA and is equipped with a promoter that allows it to continuously express the SMN1 protein. Because motor neurons are nondividing cells, it has been suggested that once the *SMN* gene is incorporated in the cells, it would be retained over time and allow for long-term, sustained SMN protein expression with a one-time dose and provide a durable therapeutic effect.

Evrysdi is an *SMN2* splicing modifier indicated for the treatment of SMA in pediatric and adult patients. It is the first oral treatment for this disease and should be dosed daily based on the patient's age and weight. For patients less than 2 months of age, the dose is 0.15 mg/kg/day. For patients 2 months to < 2 years of age, the dose is 0.2 mg/kg/day. For patients  $\geq$  2 years of age and < 20 kg, the dose is 0.25 mg/kg/day. For patients  $\geq$  2 years of age and  $\geq$  20 kg, the dose is 5 mg daily. It is available in a liquid formulation for doses less than or equal to 5 mg per day and a 5 mg tablet for patients receiving the 5 mg per day dose.

## **Spinal Muscular Atrophy (SMA)**

SMA is an inherited disorder (autosomal recessive) that occurs due to homozygous deletions or variants in the *SMN1* gene. As a consequence of absent or low levels of the SMN protein, the motor neurons in the spinal cord degenerate resulting in atrophy of the voluntary muscles of the limbs and trunk. *SMN2* is a nearly identical modifying gene capable of producing nearly identical

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compensatory SMN protein. However, 70% to 90% of the transcripts produced from the *SMN2* gene produce a truncated protein that is defective and unstable due to lack of exon 7. Further, humans exhibit variability (range, 0-6) in the number of copies of the *SMN2* gene, and copy number is inversely proportional to severity of disease. Spinraza is a synthetic genetic material that is designed to bind to a specific sequence in exon 7 of the *SMN2* transcript causing the inclusion of exon 7 in the *SMN2* transcript leading to production of full length functional SMN protein. Similarly, Evrysdi is an *SMN2* splicing modifier that increases exon 7 inclusion in *SMN2* messenger RNA to increase the production of full-length SMN protein. In contrast, Zolgensma contains a transgene that encodes for the SMN protein, allowing neurons to continuously produce the protein.

Despite being a rare disease, SMA is the most common genetic cause of death in infants. The incidence of spinal muscular atrophy is estimated to be 1 per 6,000 to 10,000 live births and is estimated to impact as many as 10,000 to 25,000 children and adults in the United States. The carrier frequency is 1 in 40 to 1 in 60, equating to approximately 6,000,000 carriers in the United States. SMA is classified into 5 main categories (Types 0-IV) based on the age at onset of symptoms. Generally, early onset of disease directly correlates to severity of symptoms and rate of disease progression. There is no exact marker to classify these categories, and they are not well-distinguished by ICD-10-CM code. Type I SMA is the most common form of SMA and is categorized by SMA symptom onset at or before 6 months of age.

- Type 0: The most severe form of SMA, symptoms can often be seen in the later stages of pregnancy. Fetal movements are less than expected and, after birth, the infant will have little ability to move and may not be able to breathe and swallow independently. Death occurs before the age of 6 months.
- Type I: Onset within 6 months after birth and symptoms progress rapidly, with most infants dying before 1 year of age from respiratory failure. About 60% of patients with SMA constitute this phenotype.
- Type II: Onset is within 6 to 18 months with less severe progression. Typically, a child can sit independently if positioned, but is unable to walk. More than 70% of patients live beyond 25 years of age with adequate supportive care.
- Type III: Onset is after 18 months of age. Lifespan is not affected, with wide-ranging reductions in muscle strength with a chronic course. The outcome depends primarily on the severity of muscle weakness at presentation rather than age of onset, but earlier onset tends to correlate with greater weakness.
- Type IV: Onset usually presents in the third decade of life and is otherwise similar to type III SMA.

## **FDA or Other Governmental Regulatory Approval**

### **U.S. Food and Drug Administration (FDA)**

Spinraza is FDA approved for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

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Zolgensma is FDA approved for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1 (SMN1)* gene.

Evrysdi is FDA approved for the treatment of spinal muscular atrophy in pediatric and adult patients.

### **Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

#### **Spinraza**

Spinraza was studied in a multicenter, randomized, double-blind, sham-procedure controlled study in 121 symptomatic infants (symptom onset before 6 months of age). Patients had 2 copies of *SMN2*. Patients were randomized to either receive Spinraza or a sham injection. The primary endpoint assessed at the time of the interim analysis was the proportion of responders: patients with an improvement in motor milestones according to section 2 of the Hammersmith Infant Neurologic Exam (HINE). A greater percentage of patients who received Spinraza achieved a motor milestone response versus those that received the sham procedure control (40% vs. 0%,  $p < 0.0001$ ).

Currently, the evidence for use of Spinraza in Type II or III SMA consists of 4 single-arm studies and 1 double-blind randomized controlled trial. The single-arm studies included small numbers of patients and used multiple doses of Spinraza, but the results of those trials did not stratify by dose or type of SMA. The randomized, controlled trial evaluated 126 non-ambulatory patients with genetic documentation 5q SMA with the onset of signs and symptoms at more than 6 months and between ages 2 and 12 years at screening as well as the presence of the following features at screening: the ability to sit independently, no history of the ability to walk independently, and a Hammersmith Functional Motor Scale—Expanded (HFMSE) score between 10 and 54. Children were excluded if they had a severe contracture, evidence of severe scoliosis on radiography, respiratory insufficiency, or a gastric tube placed to provide adequate nutrition. Participants were randomized 2:1 to receive either Spinraza or a sham injection. The primary end point was change in HFMSE score compared with baseline. HFMSE scores range from 0 to 66, with higher scores indicating better motor function. A higher percentage of children in the nusinersen group (57%) than in the control group (26%;  $p < 0.001$ ) had an increase from baseline to month 15 in the HFMSE score of at least 3 points, which was considered meaningful.

The results of the sham-controlled trial in infantile-onset and later-onset SMA patients were supported by an open-label uncontrolled trial conducted in presymptomatic SMA patients ( $n = 25$ ), who ranged in age from 3 days to 42 days at the time of first dose and had a minimum of 2 but less than 4 copies of *SMN2*. Patients received 12 mg Spinraza as a series of loading doses administered intrathecally followed by maintenance doses administered every 4 months. Interim results from this



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study demonstrated that 100% of patients were alive, 100% achieved sitting without support, 88% achieved walking with assistance, and 68% achieved walking alone after 27 months of median follow-up. Early treatment resulted in the achievement of motor milestones among patients who were not likely to attain them without treatment.

There are currently no studies assessing the safety and efficacy of Spinraza in patients with Type 0 or IV SMA. Therefore, the criteria for coverage presented in this medical policy represent coverage for types I, II, and III SMA only. More information is needed to assess the safety and clinical utility of Spinraza in broader patient populations of SMA.

### **Zolgensma**

Zolgensma was approved based on a phase 1 study as well as preliminary data from the ongoing STRIVE-US phase 3 study. In the phase 1 study, 12 of 15 infants with 2 copies of the *SMN2* gene received the proposed dose while 3 received a minimally effective dose. At the end of the 2-year follow-up, all 15 infants survived and none of the 12 patients who received the proposed therapeutic dose required permanent ventilation. All 12 patients also achieved at least 1 motor milestone, with 92% of those achieving CHOP INTEND scores greater than 40. The observed treatment effect on survival, event-free survival, and achievement of motor functions is beyond what is typical based on the known natural history of patients with SMA type 1 with two copies of *SMN2*. The available published data support a durable treatment effect through 2 years.

For individuals who are presymptomatic with a genetic diagnosis of SMA and less than 3 copies of *SMN2* who receive Zolgensma, the evidence includes a prospective cohort with a planned enrollment of 44 patients and a planned follow-up of 18-24 months. This single prospective cohort study (SPRINT) is currently ongoing. At the March 2019 update, 18 patients had been treated with a median follow up of 2.9 months. All 18 children were alive and “event free.” Among 8 patients with 2 copies of *SMN2*, all reportedly achieved age-appropriate motor milestones including 4 who could sit without support and 1 who could stand with assistance. Data was much more limited for patients with 3 copies of *SMN2*. However, early increases in mean Bayley-III Gross Motor score were observed.

### **Evrysdi**

Evrysdi was approved based on two pivotal trials in infants with Type 1 SMA (FIREFISH) and patients  $\geq 2$  years to  $\leq 25$  years of age with Type 2 or 3 SMA (SUNFISH). Two non-pivotal trials are also ongoing in assessing Evrysdi in patients up to 60 years of age (JEWELFISH) and infants up to 6 weeks of age with pre-symptomatic SMA (RAINBOWFISH).

FIREFISH is an ongoing open-label Phase II/III pivotal study evaluating Evrysdi in infants with Type 1 SMA (symptom onset between 28 days and 3 months of age) with two *SMN2* gene copies. It is a two part study with 17/21 patients in part 1 and all 41 patients in part 2 receiving the FDA-approved dose. In part 1, the median treatment duration for patients receiving the FDA-approved dose was 14.8 months. After 12 months of treatment, 41% of these patients were able to sit

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independently for at least 5 seconds. After a minimum of 23 months of treatment, 81% of patients were alive without permanent ventilation. In part 2, at 12 months of Evrysdi therapy, 29% of infants were able to sit without support for at least 5 seconds.

SUNFISH is an ongoing Phase II/III, two-part, randomized, double-blind, placebo-controlled, multicenter, pivotal trial assessing Evrysdi in patients (2 to 25 years of age) with Type 2 or Type 3 SMA. Most patients had 3 *SMN2* gene copies (88%). Part 1 was dose-finding and exploratory (n = 51). Part 2 (n = 180) involved non-ambulatory patients who were randomized 2:1 to Evrysdi or placebo for 12 months, after which all patients received Evrysdi for an additional 12 months. In part 2 (mean age of 9 years at the start of treatment), the treatment difference vs placebo in the baseline Motor Function Measure-32 Items (MFM-32) score at Month 12 was 1.55 points (p=0.0156). The difference vs placebo in the Revised Upper Limb Module (RULM) score from baseline was 1.59 points (p = 0.0028).

RAINBOWFISH is an ongoing open-label, single-arm, multicenter study to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of Evrysdi in infants up to 6 weeks of age (at first dose) who have been genetically diagnosed with SMA but do not yet present with symptoms. At the time of interim analysis, a total of 18 patients with pre-symptomatic SMA were enrolled in Study 3. The efficacy in pre-symptomatic SMA patients was evaluated in 7 patients who had been treated with Evrysdi for at least 12 months: 4 patients had 2 copies of the *SMN2* gene, 2 patients had 3 copies, and 1 patient had 4 or more copies. The 6 patients with 2 or 3 copies of *SMN2* achieved the following motor milestones as measured by the HINE-2 at Month 12: 6 (100%) patients achieved sitting, 4 (67%) patients could stand, and 3 (50%) patients could walk independently. All 6 patients were alive at 12 months without permanent ventilation.

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## **Policy History**

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04/06/2017	Medical Policy Committee review
04/19/2017	Medical Policy Implementation Committee approval. New policy.
05/03/2018	Medical Policy Committee review
05/16/2018	Medical Policy Implementation Committee approval. Updated policy to include patients with later-onset SMA due to results of the CHERISH trial.
08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. Added new drug, Zolgensma, to policy with relevant background and criteria. Updated Spinraza criteria to improve consistency in diagnostic criteria and add criterion noting that use of Spinraza after Zolgensma is considered investigational.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. Added new drug, Evrysdi, to policy with relevant background and criteria. Updated Spinraza criteria to clarify that coverage is for SMA types I-III, removed criterion requiring onset of symptoms prior to 20 months of age, and improve consistency among criteria for all drugs.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. No change to coverage.
06/02/2022	Medical Policy Committee review
06/08/2022	Medical Policy Implementation Committee approval. Updated Evrysdi criteria and background information to reflect FDA approval in adult patients. Updated Zolgensma criteria to include coverage of patients with 4 copies of the <i>SMN2</i> gene.
06/01/2023	Medical Policy Committee review
06/14/2023	Medical Policy Implementation Committee approval. Updated weight limit in Zolgensma criteria to reflect label change including higher doses/weights.
06/06/2024	Medical Policy Committee review
06/12/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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06/05/2025 Medical Policy Committee review

06/11/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Updated background information to include new Evrysdi tablet dosage form.

Next Scheduled Review Date: 06/2026

### **Coding**

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2326, J3399 Delete codes effective 07/01/2025: C9399, J3490, J3590
ICD-10 Diagnosis	All Related Diagnoses

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

## Treatment for Spinal Muscular Atrophy

Policy # 00550

Original Effective Date: 04/19/2017

Current Effective Date: 07/01/2025

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with technology evaluation center(s);
  2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  3. Reference to federal regulations.

**\*\*Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

**NOTICE:** Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.