

## PHARMACY / MEDICAL POLICY – 5.01.574

# Pharmacotherapy of Spinal Muscular Atrophy (SMA)

Effective Date: Jan. 1, 2024  
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Replaces: N/A

RELATED MEDICAL POLICIES:  
None

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## Introduction

Spinal muscular atrophy (SMA) is a rare disease that leads to muscle weakness and atrophy. SMA affects the muscles of the limbs and trunk. SMA is caused by changes to the survival motor neuron 1 gene (SMN1). This gene creates a protein called the survival motor neuron (SMN) protein. Too little of the SMN protein leads to muscle weakness that gets worse over time and muscles that waste away (atrophy). There are different types of SMA. Type 1 SMA, also known as Werdnig-Hoffman disease or infantile SMA, is the most severe form. Symptoms usually start before 6 months of age. The chance of survival to one year of age is 50 percent. Less severe forms are Type 2, also known as Dubowitz disease, and Type 3, or Kugelberg-Welander disease. Evrysdi (risdiplam), Spinraza (nusinersen), and Zolgensma (onasemnogene abeparvovec-xioi) are three treatments the Food and Drug Administration has approved for SMA. This policy discusses when the use of Evrysdi, Spinraza, and Zolgensma may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

Drug	Medical Necessity
<p><b>Evrysdi (risdiplam)</b></p> <p><b>Managed under Pharmacy benefit</b></p>	<p><b>Evrysdi (risdiplam) may be considered medically necessary for the treatment of spinal muscular atrophy (SMA) when:</b></p> <ul style="list-style-type: none"> <li>• Patient has a diagnosis of SMA Type 1, 2 or 3 attributed to the bi-allelic mutations of survival motor neuron 1 (SMN1) gene documented by genetic testing</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Prescribed by a neurologist with expertise treating SMA</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• The dose is limited to the following: <ul style="list-style-type: none"> <li>○ 0.15 mg/kg per day; less than 2 months of age</li> <li>○ 0.2 mg/kg per day; 2 months to less than 2 years of age</li> <li>○ 0.25 mg/kg per day; 2 years of age and older weighing less than 20 kg</li> <li>○ 5 mg per day; 2 years of age and older weighing 20 kg or more</li> </ul> </li> </ul> <p><b>Note:</b> Although Types 2 and 3 manifest in childhood, treatment may be continued throughout the patient's lifetime.</p>
<p><b>Spinraza (nusinersen)</b></p> <p><b>Managed under Medical benefit</b></p>	<p><b>Spinraza (nusinersen) may be considered medically necessary for the treatment of spinal muscular atrophy (SMA) when:</b></p> <ul style="list-style-type: none"> <li>• Patient has a diagnosis of SMA Type 1, 2 or 3 attributed to the bi-allelic mutations of survival motor neuron 1 (SMN1) gene documented by genetic testing</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Prescribed by a neurologist with expertise treating SMA</li> </ul> <p><b>Note:</b> Although Types 2 and 3 manifest in childhood, treatment may be continued throughout the patient's lifetime.</p> <p><b>Note:</b> The recommended dosage is 12 mg (5mL) per administration. Treatment with Spinraza should be initiated with 4 loading doses. The first 3 loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose. The maintenance dose for Spinraza is administered once every 4 months thereafter.</p>
<p><b>Zolgensma (onasemnogene abeparvovec-xioi)</b></p>	<p><b>Zolgensma (onasemnogene abeparvovec-xioi) may be considered medically necessary for the treatment of spinal muscular atrophy (SMA) when:</b></p>



Drug	Medical Necessity
Managed under Medical benefit	<ul style="list-style-type: none"> <li>• Patient is less than 2 years of age at the time of infusion</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Has a diagnosis of SMA attributed to the bi-allelic mutations of survival motor neuron 1 (SMN1) gene documented by genetic testing</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Documented genetic test confirms 4 or fewer copies of the SMN2 gene</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Patient does not have advanced SMA</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Baseline anti-adenovirus serotype 9 (AAV9) antibody levels are <math>\leq 1:50</math></li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Prescribed by a neurologist with expertise treating SMA</li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>• Zolgensma is administered as a one-time infusion</li> </ul> <p><b>Note:</b> The recommended dosage is <math>1.1 \times 10^{14}</math> vector genomes per kg of body weight administered as an intravenous infusion over 60 minutes</p>

Drug	Investigational
Evrysdi (risdiplam), Spinraza (nusinersen)	<p><b>All other uses of Evrysdi (risdiplam) and Spinraza (nusinersen) for conditions not outlined in this policy are considered investigational, including but not limited to:</b></p> <ul style="list-style-type: none"> <li>• SMA that is not attributed to the bi-allelic mutations of SMN1 gene</li> <li>• SMA type 4 (adult onset)</li> <li>• Evrysdi or Spinraza use after Zolgensma infusion</li> <li>• Evrysdi and Spinraza used in combination with each other</li> </ul>
Zolgensma (onasemnogene abeparvovec-xioi)	<p><b>All other uses of Zolgensma (onasemnogene abeparvovec-xioi) for conditions not outlined in this policy are considered investigational, including but not limited to:</b></p> <ul style="list-style-type: none"> <li>• SMA that is not attributed to the bi-allelic mutations of SMN1 gene</li> <li>• Patient's with 5 or more copies of the SMN2 gene</li> </ul>

Length of Approval	
Approval	Criteria
Initial authorization	<p><b>Evrysdi (risdiplam) and Spinraza (nusinersen) may be approved up to 1 year.</b></p> <p><b>Zolgensma (onasemnogene abeparvovec-xioi) may be approved as a one-time infusion.</b></p>
Re-authorization criteria	<p><b>Future re-authorization of Evrysdi (risdiplam) and Spinraza (nusinersen) may be approved up to 12 months in duration when clinical benefit/response at the time of re-authorization based on evidence show continued benefit.</b></p> <p><b>Future re-authorization of Zolgensma (onasemnogene abeparvovec-xioi) beyond a one-time infusion is considered investigational.</b></p>

Documentation Requirements
<ul style="list-style-type: none"> <li>Initial approval requires chart notes documenting the diagnosis and genetic testing documenting bi-allelic mutations of SMN1 gene and the copies of SMN2 gene</li> <li>Evrysdi (risdiplam) and Spinraza reauthorization requires chart notes documenting progress, including functional measures appropriate to the patient's current abilities such as ambulation, arm strength or pulmonary function.</li> </ul>

## Coding

Code	Description
HCPCS	
J2326	Injection, nusinersen (Spinraza), 0.1 mg
J3399	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10 <sup>15</sup> vector genomes (Zolgensma)

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).



## Related Information

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### Benefit Application

Evrysdi (risdiplam) is managed through the pharmacy benefit. Spinraza (nusinersen) and Zolgensma (onasemnogene abeparvovec-xioi) are managed through the medical benefit.

### Consideration of Age

Age limits specified in this policy for Zolgensma are determined according to the FDA-approved indication. The use of Evrysdi and Spinraza for SMA type 1, 2, and 3 is based on the clinical trial experience as described in the full prescribing information of the FDA label. The patients in these studies had or were likely to develop type 1, 2, or 3 SMA.

### Availability

Zolgensma is only available at certified treatment centers. Information on certified treatment centers is available by emailing [treatments@curesma.org](mailto:treatments@curesma.org).

## Evidence Review

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### Disease Background

Spinal muscular atrophy (SMA) is a rare recessive neurodegenerative disease that leads to muscle weakness and atrophy of the voluntary muscles of the limbs and trunk, due to the progressive loss of anterior horn cells of the spinal cord and brainstem nuclei.<sup>2</sup> SMA has an incidence of about 1:10,000 live births and is the leading genetic cause of infant death. It has a carrier frequency estimated to be between 1:40 to 1:60

SMA is caused by the homozygous deletion of the survival motor neuron 1 gene (SMN1), which encode stable survival motor neuron (SMN) protein. The absence of enough SMN leads to



increasing motor neuron dysfunction and progressive muscle weakness and atrophy. Cases are classified based on their severity and maximal achieved motor abilities, inversely correlating with the age of onset as well as the number of survival motor neuron 2 gene (SMN2) copies present. SMN2 encodes for SMN proteins that are less stable than those produced by SMN1 and do not have as lasting an impact on motor neuron function. SMN1 and SMN2 are nearly identical and encode the same protein. The critical sequence difference between the two genes is a single nucleotide in exon 7, which is thought to be an exon splice enhancer.

Type 1 SMA, also known as Werdnig-Hoffman disease or infantile SMA, is the most severe with symptomatic onset usually before 6 months and the probability of survival at 1 year is 50%.<sup>2,7</sup> Type 2 SMA is also called intermediate SMA or Dubowitz disease while type 3 SMA is also called juvenile SMA or Kugelberg-Welander disease, and both have slightly older age of onsets and more varied disease progression. Type 4 SMA is an adult onset form of SMA that is usually not symptomatic until later in life and rarely affects life expectancy.

**Table 1. Clinical Classification of SMA**

<b>SMA Type</b>	<b>Age of Onset</b>	<b>Highest Achieved Motor Function</b>	<b>Natural Age of Death</b>	<b>Typical Number of SMN2 Copies</b>
<b>0</b>	Prenatal/fetal	None	< 6 months	1
<b>I</b>	< 6 months	Sit with support only	< 2 years	2
<b>II</b>	6 – 18 months	Sit independently	> 2 years	3 or 4
<b>III</b>	> 18 months	Walk independently	Adulthood	3 or 4
<b>IV</b>	Adult (20s-30s)	Walk through adulthood	Adult	4 to 8

## Evrysdi (risdiplam)

Risdiplam is an orally administered/available, centrally and peripherally distributed, pyridazine derived, small molecule designed to modify the splicing of the survival motor neuron (SMN2) pre-mRNA and thus increase levels of functional SMN protein. The importance of adequate SMN protein levels which, are found to be depressed in SMA patients, is in the maintenance of motor neurons which control muscle movement. This increase in functional SMN protein allows SMA patients to achieve motor milestones and improve their functional abilities.



## Evidence of Efficacy

In the SUNFISH phase II/III two-part, randomized, placebo-controlled trial of SMA Types 2/3, being the only placebo-controlled trial in progress to date, initial results showed an average increase from baseline after 12 months of treatment in MFM-32 score (an assessment of motor function) of 2.66 ( $\pm 3.70$ ) and a  $\geq 3$ -point change (95% CI) for 58% (42–73%) for all patients with available data in part one of the study (N=43). The second part of the trial saw statistically significant improvements at 12 months of treatment in MFM-32 and Revised Upper Limb Module scores with risdiplam in comparison with placebo of 1.55 ( $p=0.0156$ ; N=170) and 1.59 ( $p=0.028$ ; N=186), respectively. Caregiver reported SMA Independence Scale changes showed statistically significant improvement at 12 months compared to placebo. However, the patient reported improvement was not statistically significant. Minimal important difference (MID) information is unavailable for the previously mentioned outcome measures. However, an MID of 3 points is proposed for MFM-32 although the research supporting this is not yet available. At 12 months the difference from placebo for Hammersmith Functional Motor Score – Expanded was not statistically significant at 0.58 ( $p=0.3015$ ) and failed to meet the MID of 3 points.

In the FIREFISH phase II/III two-part, open-label trial of SMA Type 1, initial results of part one (N=21) showed a median increase of 16 points in all patients as well as a  $\geq 4$ -point increase in 93% of patients in their CHOP-INTEND score at 245 days of treatment. Clinical and statistical significance of these results are uncertain due to lack of placebo control as well as lack of MID for this outcome measure. At 245 days of treatment, a  $\geq 40$ -point total score was achieved in 57% of patients which is rare and considered clinically meaningful in comparison with known natural history data.

In the JEWELFISH phase II open-label trial of SMA patients previously treated with other agents targeting SMN2 splicing, initial results for 4 patients (12 months of treatment; Study enrollment N=174) shows a  $>2$ -fold increase in median SMN protein levels in the blood compared to baseline. Clinical significance of this change is uncertain at this point.

The RAINBOWFISH study is an open-label, single-arm, multicenter clinical study designed to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of risdiplam 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 an 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 risdiplam for at least 12 months: four patients had 2 copies of the SMN2 gene, 2 patients had 3 copies, and 1 patient had 4 or more copies. Of



these 7 patients, the median age at first dose was 35 days (range: 16 to 40 days), 71% were female, 100% were Caucasian.

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 (5 patients could pivot/rotate and 1 patient achieved stable sit); 4 (67%) patients could stand (3 patients could stand unaided and 1 patient could stand with support), and 3 (50%) patients could walk independently. All 6 patients were alive at 12 months without permanent ventilation.

## Evidence of Safety

In the natural course of SMA common areas of complications include pulmonary issues, gastrointestinal/ digestive issues, and musculoskeletal issues among others. It is important to consider these issues in the natural course of SMA as well as the poor prognosis for SMA, especially in the case of earlier onset, in the evaluation of adverse events experienced during treatment and risk/benefit analysis.

In the SUNFISH phase II/III two-part, randomized, placebo-controlled trial of SMA Types 2/3, being the only placebo-controlled trial in progress to date, initial results showed no significant difference in serious adverse events (SAE) occurrence between the risdiplam and placebo groups at 20% (24/120) and 18.3% (11/60), respectively. The most common SAEs for patients taking risdiplam were pneumonia (n=9), gastroenteritis (n=2), bacteremia (n=2), influenza (n=2), and pyrexia (n=2). This study did note a trend towards more grade 3-4 AEs in the risdiplam group compared to placebo was seen at 17.5% (21/120) and 13.3% (8/60), respectively.

In the FIREFISH phase II/III two-part, open-label trial of SMA Type 1, initial results of part one showed at least one SAE in 47.6% (10/21; most commonly pneumonia) and at least one grade 3-5 AE in 38.1% (8/21). In part one of this study 3 deaths have occurred due to respiratory complications which were considered unrelated to risdiplam use.

In the JEWELFISH phase II open-label trial of SMA patients previously treated with other agents targeting SMN2 splicing, there have been no SAEs reported in 12 patients (57-512 days of drug exposure; Study enrollment N=174)) with available data.

In the RAINBOWFISH study at the time of interim analysis, the study had enrolled 18 patients with pre-symptomatic SMA between 16 and 40 days of age at the time of the first dose (weight range 3.1 to 5.7 kg). The median exposure duration was 8.7 months (range: 0.5 to 22.8 months). The safety profile of risdiplam in pre-symptomatic patients in Study 3 is consistent with the safety profile for symptomatic SMA patients treated with Evrysdi in clinical trials.





## Spinraza (nusinersen)

Spinraza is a SMN2 directed antisense oligonucleotide that increases the production of complete SMN protein by increasing exon 7 inclusion into SMN2 mRNA transcripts (alternative splicing). The resulting protein resembles those produced by SMN1 and is more stable than regular SMN protein produced by SMN2. SMN protein is involved in the maintenance of motor neurons which control muscle movement. This allows SMA patients to achieve motor milestones and improve their functional abilities.

In one clinical study, Spinraza resulted in platelet levels below the lower limit of normal in 6 of the 56 patients who had normal baseline levels; however none of these patients developed a sustained low platelet count. In two different studies, 17 out of 51 patients and 36 out of 52 patients on Spinraza had elevated urine protein. Common adverse reactions recorded in infantile SMA patients included lower respiratory infection (43%), upper respiratory infection (39%), and constipation (30%), while common adverse reactions recorded in later onset patients include headache (50%), back pain (41%), and post-lumbar puncture syndrome (41%) and were associated with the intrathecal administration.

## Evidence of Efficacy

Currently, there are ten clinical trials that evaluate the use of Spinraza for SMA treatment, with efficacy endpoints focused on survival, growth parameters, electro-physiology, and motor function. The ENDEAR study, which provided much of the efficacy evidence, was a phase 3 sham procedure controlled study which depicted a 29% reduction in risk of death or permanent ventilation in the nusinersen group compared to the sham procedure controlled group. Mean improvements in motor milestones for the nusinersen group was observable starting at 2 months post treatment initiation with an increased difference from the sham control patients as the study went on.

In another study, the interim analysis of 13 pre-symptomatic patients SMA patients demonstrated that patients treated with nusinersen exceeded expected outcomes with improvements in various motor functions and motor milestone measures. Compared to the Pediatric Neuromuscular Clinical Research natural-history studies of SMA patients that received standard of care, patients with type 1 SMA treated with nusinersen had a significant differentiation in age at death or permanent ventilation as well as increased motor function and nerve response. The CS2 and CS12 studies showed additional milestone attainment and



maintenance in type 2 and 3 SMA patients who received nusinersen compared to the decline in milestone maintenance commonly seen in SMA patients, with independent walking achieved in three patients and increased mean ambulation. Nusinersen has not been studied in type 4 patients.

## Evidence of Safety

In the limited studies available, Spinraza has been shown to be generally safe, with most adverse events associated with the route of administration or the natural progression of SMA. Elevated urine protein and low platelet levels have been observed in a few studies with nusinersen; however, the coagulation abnormalities, thrombocytopenia, and renal toxicity associated with antisense oligonucleotides has not been observed with nusinersen though they are still listed as precautions. The majority of adverse events associated with nusinersen were mild to moderate in severity and mirrored events seen in the controlled historical groups, including respiratory distress, respiratory failure, pneumonia, acute respiratory failure, atelectasis, pneumonia aspiration, rhinovirus infection, and cardiorespiratory arrest.

## Zolgensma (onasemnogene abeparvovec-xioi)

Zolgensma is a gene therapy that uses the adeno-associated virus serotype 9 vector (AAV9) to deliver a copy of the SMN gene to the nucleus of the patient's cells to replace the defective SMN1 gene without modifying the existing DNA of the patient.

## Evidence of Efficacy

A Phase I, single-arm, open-label trial evaluated Zolgensma for the treatment of 15 patients with genetically confirmed diagnosis of SMA1, homozygous SMN1 exon 7 deletions, and two copies of SMN2. Subjects were excluded if they had anti-AAV9 antibody titers > 1:50. Of the 15 study patients, the three patients in cohort 1 received a low dose of adeno-associated virus serotype 9 carrying SMN ( $6.7 \times 10^{13}$  vg per kg of body weight) and the 12 patients in cohort 2 received a high dose ( $2.0 \times 10^{14}$  vg per kg of body weight). The mean age of patients at the time of treatment was 6.3 months (range 5.9 to 7.2) in cohort 1 and 3.4 months (range 0.9 to 7.9) in cohort 2. As a result of serum aminotransferase elevations in Patient 1 in cohort 1, which led to a protocol amendment, Patients 2 to 15 received oral prednisolone at a dose of 1 mg per kg per day for approximately 30 days, starting 24 hours before the administration of gene therapy. The



gene vector was delivered in normal saline that was infused IV during a period of approximately 60 minutes.

The primary outcome was the determination of safety on the basis of any treatment-related adverse events (AEs) of grade 3 or higher. The secondary outcome was the time until death or the need for permanent ventilatory assistance. Permanent ventilatory assistance was defined as at least 16 hours of respiratory assistance per day continuously for at least 14 days in the absence of an acute, reversible illness or a perioperative state. As of August 7, 2017, all the patients had reached an age of at least 20 months and did not require permanent mechanical ventilation; the median age at their last pulmonary assessment was 30.8 months in cohort 1 and 25.7 months in cohort 2. At 29 months of age, one patient in cohort 1 required permanent ventilation because of hypersalivation. After salivary gland ligation, the requirement for the use of noninvasive ventilation was reduced by 25% to 15 hours per day.

Exploratory outcomes included motor-milestone achievements (particularly, sitting unassisted) and The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) scores. All the patients in cohorts 1 and 2 had increased scores from baseline on the CHOP INTEND scale and maintained these changes during the study. Patients in cohort 2 had mean increases of 9.8 points at 1 month and 15.4 points at 3 months ( $P < 0.001$  for both comparisons); 11 patients attained and sustained scores of more than 40 points. No patients in cohort 1 attained any motor milestones. A total of 11 of 12 patients in cohort 2 were able to sit unassisted for at least 5 seconds, 10 for at least 10 seconds, and 9 for at least 30 seconds. A total of 11 achieved head control, 9 could roll over, and 2 were able to crawl, pull to stand, stand independently, and walk independently. Eleven patients attained the ability to speak.

## Evidence of Safety

As of August 7, 2017, a total of 56 serious adverse events were observed in 13 patients in the two cohorts. Of these, 2 events were treatment-related grade 4 based on laboratory values. Patient 1 in cohort 1 had elevations in serum aminotransferase levels (31 times the ULN for ALT and 14 times the ULN for AST) without other liver-function abnormalities and without clinical manifestations. These elevations were attenuated by prednisolone treatment, which was subsequently administered to the remaining patients. One patient in cohort 2 required additional prednisolone to attenuate elevated serum ALT and AST levels. Of the 241 non-serious adverse events, 3 were deemed to be treatment-related and consisted of asymptomatic elevations in serum aminotransferase levels in 2 patients. The most common adverse events were upper respiratory tract infection (73%), vomiting (53%), constipation (53%), pyrexia (47%), nasal congestion (40%), and gastroesophageal reflux (40%).



In October 2021 Zolgensma received a black box warning noting that acute serious liver injury, acute liver failure, and elevated aminotransferases can occur and that patients with preexisting liver impairment may be at higher risk. Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing (eg, hepatic aminotransferases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], total bilirubin, and prothrombin time). Corticosteroids are to be administered to all patients before and after Zolgensma infusion and patients are to have liver function monitored for at least 3 months after infusion.

## **2018 Update**

A literature search from 1/1/17 to 3/30/18 did not reveal new clinical data requiring change to the above criteria. Added reauthorization period and criteria.

## **2019 Update**

Added criteria for Zolgensma (onasemnogene abeparvovec-xioi) which was approved by the FDA in May 2019. Reviewed prescribing information for Spinraza (nusinersen) and no new information was identified that would change coverage criteria.

## **2020 Update**

Reviewed prescribing information for Zolgensma (onasemnogene abeparvovec-xioi) and Spinraza (nusinersen) and no new information was identified that would change coverage criteria. Added criteria for Evrysdi (risdiplam) which is an oral medication that was approved by the FDA in August 2020 for the treatment of SMA in patients 2 months of age and older.

## **2021 Update**

Reviewed prescribing information for Evrysdi (risdiplam), Spinraza (nusinersen), and Zolgensma (onasemnogene abeparvovec-xioi). No new information was identified that would result in changes to policy statements. Added safety information to Zolgensma regarding a black box warning regarding acute serious liver injury and acute liver failure.



## 2021 Update

Reviewed prescribing information for Evrysdi (risdiplam), Spinraza (nusinersen), and Zolgensma (onasemnogene abeparvovec-xioi). Updated Evrysdi coverage criteria as the FDA approval for Evrysdi was expanded to include babies under 2 months of age with SMA based on interim efficacy and safety data from the RAINBOWFISH study. Updated Spinraza (nusinersen) criteria to include that Spinraza is prescribed by a neurologist with expertise treating SMA. All three drugs, Evrysdi, Spinraza, and Zolgensma now include identical language that the product is prescribed by a neurologist with expertise treating SMA.

## 2023 Update

Reviewed prescribing information of all drugs in this policy. Updated Zolgensma (onasemnogene abeparvovec-xioi) criteria to include coverage of individuals with 4 copies of the SMN2 gene.

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## History

Date	Comments
04/01/17	New policy, approved March 14, 2017. Add to Prescription Drug section. Nusinersen (Spinraza®) may be considered medically necessary to treat SMA when criteria are met; all other uses are considered investigational.
07/01/17	Coding update; added HCPCS code C9489 (new code effective 7/1/17).
11/01/17	Interim Review, approved October 10, 2017. Clarified Spinraza® (nusinersen) criteria to include Type 1, 2, and 3 information.
01/01/18	Coding update; added HCPCS code J2326 (new code effective 1/1/18).
05/01/18	Annual Review, approved April 3, 2018. Added reauthorization criteria and duration. Removed HCPCS C9489 (it was terminated 1/1/18) and J3490 from policy.
09/21/18	Minor update. Added Consideration of Age statement.
07/01/19	Annual Review, approved June 11, 2019. Added criteria for Zolgensma (onasemnogene abeparvovec-xioi). Added HCPCS code J3590.
11/01/20	Annual Review, approved October 13, 2020. Added criteria for Evrysdi (risdiplam) for the treatment of SMA Type 1, 2 or 3.
02/01/21	Coding update, Added HCPCS code J3399 and removed HCPCS code J3590.
01/01/22	Annual Review, approved December 2, 2021. No changes to policy statements.
08/01/22	Annual Review, approved July 25, 2022. Updated Evrysdi (risdiplam) criteria removing requirement patient is 2 months of age or older as Evrysdi is FDA approved in patients less than 2 months of age. Updated Spinraza (nusinersen) criteria to include that Spinraza is prescribed by a neurologist with expertise treating SMA.
10/01/23	Annual Review, approved September 11, 2023. No changes to the policy statements.
01/01/24	Interim Review, approved December 12, 2023. Updated Zolgensma (onasemnogene abeparvovec-xioi) criteria to include coverage of individuals with 4 copies of the SMN2 gene.



**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2024 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.





## Discrimination is Against the Law

Premera Blue Cross HMO (Premera HMO) complies with applicable Federal and Washington state civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, sex, gender identity, or sexual orientation. Premera HMO does not exclude people or treat them differently because of race, color, national origin, age, disability, sex, gender identity, or sexual orientation. Premera HMO provides free aids and services to people with disabilities to communicate effectively with us, such as qualified sign language interpreters and written information in other formats (large print, audio, accessible electronic formats, other formats). Premera HMO provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, contact the Civil Rights Coordinator. If you believe that Premera HMO has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, sex, gender identity, or sexual orientation, you can file a grievance with: Civil Rights Coordinator — Complaints and Appeals, PO Box 91102, Seattle, WA 98111, Toll free: 855-332-4535, Fax: 425-918-5592, TTY: 711, Email [AppealsDepartmentInquiries@Premera.com](mailto:AppealsDepartmentInquiries@Premera.com). You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Ave SW, Room 509F, HHH Building, Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>. You can also file a civil rights complaint with the Washington State Office of the Insurance Commissioner, electronically through the Office of the Insurance Commissioner Complaint Portal available at <https://www.insurance.wa.gov/file-complaint-or-check-your-complaint-status>, or by phone at 800-562-6900, 360-586-0241 (TDD). Complaint forms are available at <https://fortress.wa.gov/oic/online-services/cc/pub/complaintinformation.aspx>.

## Language Assistance

**ATENCIÓN:** si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 844-722-4661 (TTY: 711).

**注意:** 如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 844-722-4661 (TTY: 711)。

**CHÚ Ý:** Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 844-722-4661 (TTY: 711).

**주의:** 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 844-722-4661 (TTY: 711) 번으로 전화해 주십시오.

**ВНИМАНИЕ:** Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 844-722-4661 (телетайп: 711).

**PAUNAWA:** Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 844-722-4661 (TTY: 711).

**УВАГА!** Якщо ви розмовляєте українською мовою, ви можете звернутися до безкоштовної служби мовної підтримки.

Телефонуйте за номером 844-722-4661 (телетайп: 711).

**ប្រយ័ត្ន:** បើសិនជាអ្នកនិយាយ ភាសាខ្មែរ, សេវាជំនួយផ្នែកភាសា ដោយមិនគិតថ្លៃ គឺអាចមានសំរាប់អ្នក។ ចូរ ទូរស័ព្ទ 844-722-4661 (TTY: 711)។

**注意事項:** 日本語を話される場合、無料の言語支援をご利用いただけます。844-722-4661 (TTY: 711) まで、お電話にてご連絡ください。

**ማስታወሻ:** የሚናገሩት ቋንቋ ኣማርኛ ከሆነ የትርጉም ኣርዳታ ድርጅቶች፣ በኣኦ.ሊ.የግዝዎት ተዘጋጅተዋል። ወደ ሚከተለው ቁጥር ይደውሉ 844-722-4661 (መስማት ለተሳናቸው: 711)።

**XIYYEEFFANNAA:** Afaan dubbattu Oroomiffa, tajaajila gargaarsa afaanii, kanfaltiidhaan ala, ni argama. Bilbilaa 844-722-4661 (TTY: 711).

**ملحوظة:** إذا كنت تتحدث اذكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم 844-722-4661 (رقم هاتف الصم والبكم: 711).

**ਧਿਆਨ ਦਿਓ:** ਜੇ ਤੁਸੀਂ ਪੰਜਾਬੀ ਬੋਲਦੇ ਹੋ, ਤਾਂ ਭਾਸ਼ਾ ਵਿੱਚ ਸਹਾਇਤਾ ਸੇਵਾ ਤੁਹਾਡੇ ਲਈ ਮੁਫਤ ਉਪਲਬਧ ਹੈ। 844-722-4661 (TTY: 711) 'ਤੇ ਕਾਲ ਕਰੋ।

**ACHTUNG:** Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 844-722-4661 (TTY: 711).

**ໂປດຊາບ:** ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັຍຄ່າ, ຄວນມີພ້ອມໃຫ້ທ່ານ. ໂທ 844-722-4661 (TTY: 711).

**ATANSYON:** Si w pale Kreyòl Ayisyen, gen sèvis èd pou lang ki disponib gratis pou ou. Rele 844-722-4661 (TTY: 711).

**ATTENTION:** Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 844-722-4661 (ATS: 711).

**UWAGA:** Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 844-722-4661 (TTY: 711).

**ATENÇÃO:** Se fala português, encontram-se disponíveis serviços linguísticos, grátis. Ligue para 844-722-4661 (TTY: 711).

**ATTENZIONE:** In caso la lingua parlata sia l'italiano, sono disponibili servizi di assistenza linguistica gratuiti. Chiamare il numero 844-722-4661 (TTY: 711).

**توجہ:** اگر بہ زبان فارسی گفتگو می کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می باشد. با 844-722-4661 (TTY: 711) تماس بگیرید.