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Pharmacy Clinical Policy Document: Spinal Muscular Atrophy (SMA) Medications Prior Authorization	**Replaces Effective Policy Dated:** 12/7/2022
Reference #: PC/S008	**Page:** 1 of 5

PURPOSE:
The intent of the Spinal Muscular Atrophy (SMA) Medications Pharmacy Clinical Policy is to ensure services are medically necessary.

Please refer to the member's benefit document for specific information. To the extent there is any inconsistency between this policy and the terms of the member's benefit plan or certificate of coverage, the terms of the member's benefit plan document will govern.

POLICY:
Benefits must be available for health care services. Health care services must be ordered by a provider. Health care services must be medically necessary, applicable conservative treatments must have been tried, and the most cost-effective alternative must be requested for coverage consideration.

Table 1: SMA targeted therapies

Drug	Generic/ Molecule Name	Generic/ Biosimilar available	Route of Administration	Recommended Age
Spinraza	nusinersen	N	intrathecal	pediatric and adult
Zolgensma	onasemnogene abeparvovec-xioi	N	intravenous	less than 2 years of age

GUIDELINES:
Medical Necessity Criteria - Must satisfy the following: I, and one of II - IV

I. Prescribed by or in consultation with a physician who specializes in the management of spinal muscular atrophy and/or neuromuscular disorders.

II. Request for Spinraza[4,5,6] – must satisfy any of the following: A or B

A. Initial request for treatment – must satisfy all of the following: 1 - 6
1. Genetic testing of SMN1 gene in chromosome 5q shows one of the following: a or b
a. Homozygous gene deletion or mutation, eg, deletion of exon 7 at locus 5q13; or
b. Compound heterozygous mutation, eg, deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2).

2. SMA phenotypes – must satisfy any of the following: a or b
a. SMA I as confirmed by either of the following: i or ii
i. 2 or less copies of SMN2 gene; or
ii. Must satisfy both of the following: 1) and 2)
1) 3 copies of the SMN2 gene; and
2) Absence of the c.859G>C single base substitution modification in exon 7

b. SMA II or SMA III with impaired motor function and/or delayed motor milestone.
3. Member is not *ventilator dependent.*

4. A pretreatment baseline examination has been performed using any of the following: a - d

a. Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)
b. Hammersmith Functional Motor Scale Expanded (HFMSE)
c. Upper Limb Module (ULM) Test (Non ambulatory)
d. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)

5. The member will not be receiving concurrent SMN modifying or gene therapy (eg, Evrysdi or Zolgensma).

6. Approve for 4 doses for 3 months (see Table 2).

Table 2: Spinraza Dosage and Administration

Recommended Dosage	Loading Dose	Maintenance Dose
12mg (5mL) per administration	Initiate treatment with 4 loading doses: the first three loading doses should be administered at 14-day intervals; the 4th loading dose should be administered 30 days after the 3rd dose	A maintenance dose should be administered once every 4 months thereafter

Day 0, 14, 28 ⟶ Day 58 ⟶ Day 180 ⟶ Day 300

B. Continuation request - must satisfy all of the following: 1 - 3
1. Documentation supports a positive clinical response from pretreatment baseline as demonstrated on the most recent (within the last 30 days) examination – must satisfy one of the following: a – f
   a. The member has patient experienced both of the following HINE milestones: i and ii
      i. Improvement or maintenance of a previous improvement of at least a 2 point (or maximal score) increase in ability to kick or improvement or maintenance of a previous improvement of at least a 1 point increase in any other HINE milestone (eg, head control, rolling, sitting, crawling, etc.), excluding voluntary grasp; and
      ii. Improvement or maintenance of a previous improvement in more HINE motor milestones than worsening from pretreatment baseline (net positive improvement) or member has achieved and maintained any new motor milestones from pretreatment baseline when they would otherwise be unexpected to do so (eg, sit unassisted, stand, walk.)
   b. The member has experienced one of the following HFMSA milestones: i or ii
      i. Improvement or maintenance of a previous improvement of at least a 3 point increase in score from pretreatment baseline; or
      ii. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so.
   c. The member has experienced one of the following ULM milestone: i or ii
      i. Improvement or maintenance of a previous improvement of at least a 2 point increase in score from pretreatment baseline; or
      ii. Member has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so.
   d. The member has experienced one of the following CHOP INTEND milestones: i or ii

i. Improvement or maintenance of a previous improvement of at least a 4 point increase in score from pretreatment baseline; or
ii. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so.

e. The member has experienced an improvement or maintenance from baseline or from previous assessment.
f. If *ventilator dependent*, there has been an improvement in respiratory function, as evidenced by less time on ventilatory support.

2. The member will not be receiving concurrent SMN modifying or gene therapy (eg, Evrysdi or Zolgensma).

3. Approve 3 doses over 12 months (see Table 2).

III. Request for Zolgensma[7,8,9] – must satisfy the following: A - H

A. Member is less than age 2.

B. Genetic testing of SMN1 gene in chromosome 5q shows one of the following: 1 or 2
1. Homozygous gene deletion or mutation, eg, deletion of exon 7 at locus 5q13; or

2. Compound heterozygous mutation, eg, deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2).

C. SMA I phenotype confirmed by either of the following: 1 or 2
1. 2 or less copies of SMN2 gene; or

2. Both of the following: a and b
a. 3 copies of the SMN2 gene; and
b. Absence of the c.859G>C single base substitution modification in exon 7.

D. Member is not *ventilator dependent.*

E. The member's anti-AAV9 antibodies are less than or equal to 1:50.

F. A pretreatment baseline examination has been performed – must have one of the following: 1 - 4
1. Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)
2. Hammersmith Functional Motor Scale Expanded (HFMSE)
3. Upper Limb Module (ULM) Test (Non ambulatory)
4. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)

G. Other SMN gene or modifying therapy – must satisfy both of the following: 1 and 2
1. The member has never received prior treatment with Zolgensma; and
2. The member will not be receiving concurrent SMN gene or modifying therapy (eg, Evrysdi or Spinraza).

H. Approve appropriate weight-based dose. (see Table 3)

Table 3: Zolgensma Dosage and Administration

Recommended Dosage	
1.1 $x10^{14}$ vector genomes per kg of body weight	Administer as an intravenous infusion over 60 minutes

DEFINITIONS:

Clinically significant:
A T-score > 59

Non-invasive ventilation:
Use of ventilatory support with a ventilator without using an invasive artificial airway (endotracheal tube or tracheostomy).

Ventilator dependent:
Ventilatory support with an invasive artificial airway (endotracheal tube or tracheostomy), or use of *non-invasive ventilation*, beyond use for naps and nighttime sleep, eg, more than 16 hours day continuously for 14 days or more in the absence of acute reversible illness, eg, pneumonia.

BACKGROUND:

This clinical policy is based on U.S. Food and Drug Administration (FDA) approved indications, expert consensus opinion and/or available reliable evidence.

Prior Authorization: Yes, per network provider agreement – initial authorize for up to 12 months. This is subject to the member's contract benefits.

CODING:

CPT/HCPCS
J2326 Injection, nusinersen, 0.1 mg
J3399 Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes

REFERENCES:

1. Medical Management Process Manual UR015 Use of Medical Policy and Criteria
2. Clinical Policy: MP/C009 Coverage Determination Guidelines
3. Pharmacy Clinical Policy: PP/T002 Therapeutic Equivalence
4. Spinraza [package insert]. Cambridge, MA: Biogen; 2/2023.
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6. Finkel RS, Mercuri E, Darras BT, Connolly AM, Kuntz NL, Kirschner J. Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy. *N Engl J Med*. 2017 Nov 2;377(18):1723-1732.
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9. Al-Saidy S, Pickard AS, Kotha K, Alfano LN, Lowes L, Paul G, et al. Health outcomes in spinal muscular atrophy type 1 following AVXS-101 gene replacement therapy. *Pediatr Pulmonol* 2019 Feb;54(2):179-185.
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11. Lunn MR, Wang CH. Spinal muscular atrophy. *Lancet.* 2008; 371:2120-2133
12. Prior TW, Finanger E. Spinal Muscular Atrophy. Last Revision: 12/03/20. GeneReviews. - https://www.ncbi.nlm.nih.gov/books/NBK1352/. Accessed 9/14/2023.

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Attachment A

Classification of Disease Subtypes in Spinal Muscular Atrophy

Type	Frequency	SMN 2 copies	Age Onset	Max motor	Survival	Comorbidities
0	<1%	1	Prenatal	Never sit	< 6 months	Respiratory failure Dysphagia Contractures Decreased fetal movement
I	50-60%	2,3	0-6 months	Never sit	< 2 years	Respiratory failure Dysphagia Weak cough Paradoxical breathing Contractures Severe weakness
II	30%	2,3,4	<18 months	Sit	>2 years/adult	Respiratory insufficiency Weak cough Tremor Scoliosis Contractures Weakness
III	10%	3-4	18 months-21 years	Walk	Adult	Variable weakness Joint contractures Scoliosis
IV	1%	4+	Late childhood-adult	Walk	Adult	Mild weakness

Retrieved from: Bharucha-Goebel D, Kaufmann P. Treatment Advances in Spinal Muscular Atrophy. *Curr Neurol Neurosci Rep* (2017) 17:

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

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Room 509F, HHH Building
Washington, D.C. 20201
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