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| Department of Origin: Pharmacy | Effective Date: 12/06/2023 |
| Approved by: Pharmacy and Therapeutics Quality Management Subcommittee | Date approved: 12/06/2023 |
| 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

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- 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

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- 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)

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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 5x10¹⁵ vector genomes

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DOCUMENT HISTORY:

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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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PO Box 1062
Minneapolis, MN 55440
Phone: 1.866.631.5404 (TTY: 711)
Fax: 763.847.4010
Email: customerservice@aspirushealthplan.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Nondiscrimination Grievance 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 Avenue, 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>.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë. Telefononi në 1.866.631.5404 (TTY: 711).

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Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.866.631.5404 (TTY: 711).

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Lao: ໄປດຊາຍ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັຽຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທ 1.866.631.5404 (TTY: 711).