Pharmacy Management Drug Policy

SUBJECT: Spinal Muscular Atrophy (SMA) - Spinraza (nusinersen) and Zolgensma (onasemnogene abeparovec-xioi)

POLICY NUMBER: Pharmacy-68
EFFECTIVE DATE: 03/02/2017
LAST REVIEW DATE: 09/27/2019

If the member’s subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Spinal Muscular Atrophy (SMA) is a rare genetic condition that causes increasing weakness in muscles. Patients have inadequate amounts of survival motor neuron protein 1 (SMN1). The disease can be classified into five types with infantile onset (Type 1) being the most common. Symptoms and rate of disease progression can vary based on the type of SMA. Approximately 450-500 infants are born with SMA in the US annually.

Spinraza (nusinersen) is indicated for the treatment of SMA in pediatric and adult patients. It’s mechanism of action involves an increase of full-length SMN protein by targeting the process through which it is produced by the SMN2 gene. It was the first drug approved to treat SMA.

Zolgensma (onasemnogene abeparovex-xioi) is an adenoassociated virus vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age of with SMA with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene.

POLICY:

SPINRAZA

Based upon our assessment and review of the peer-reviewed literature, Spinraza has been medically proven to be effective and therefore, medically appropriate for the following:

1. Must be prescribed by or in consultation with a provider who specializes in the treatment of Spinal Muscular Atrophy (SMA) and/or neuromuscular disorders AND
2. Must have a diagnosis of Type I, II, or III Spinal Muscular Atrophy
   a. Confirmed by targeted mutation analysis
      i. Homozygous deletions of SMN1 gene OR
      ii. Homozygous mutation in the SMN1 gene (e.g. biallelic mutations of exon 7) OR
      iii. Compound heterozygous mutation in the SMN1 gene (e.g. deletion of SMN1 exon 7 and mutation of SMN1) AND
3. Must have genetic testing confirming 1, 2, or 3 copies of the SMN2 gene AND
4. Progress notes containing results of at least one of the following baseline exams must be submitted to establish baseline motor ability:
   a. Hammersmith Infant Neurological Exam (HINE) OR
   b. Hammersmith Functional Motor Scale Expanded (HFMSE) OR
   c. Upper Limb Module (ULM) Test/Revised Upper Limb Module Test (RULM) OR
d. Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) AND

5. Dosing should not exceed 12mg (5mL) per dose. Initiated with 4 loading doses; the first 3 loading doses should be administered at 14-day intervals; the 4th loading dose administered 30 days after the 3rd dose. A maintenance dose is then administered once every 4 months thereafter AND

6. Spinraza will not be approved for use in patients that have previously been treated with Zolgensma AND

7. Initial approval will be for 6 months and continued approval will be at 12-month intervals for commercial, exchange, and Medicaid members. Subsequent approval will require documentation of positive response to therapy from pretreatment baseline status as evidenced by at least one of the following exams:
   a. HINE milestones:
      i. One of the following:
         1. Improvement or maintenance of previous improvement of at least 2 point (or maximal score) increase in ability to kick OR
         2. Improvement or maintenance of previous improvement of at least 1-point increase in any other HINE milestone (e.g, head control, rolling, sitting, crawling, etc)
   b. HFMSE:
      i. One of the following:
         1. Improvement or maintenance of previous improvement of at least a 3-point increase in score from pretreatment baseline OR
         2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
   c. ULM/RULM:
      i. One of the following:
         1. Improvement or maintenance of previous improvement of at least a 2-point increase in score from pretreatment baseline OR
         2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so
   d. CHOP-INTEND
      i. One of the following:
         1. Improvement or maintenance of previous improvement of at least a 4-point increase in score from pretreatment baseline
         2. Patient has achieved and maintained any new motor milestone from pretreatment baseline when they would otherwise be unexpected to do so.
ZOLGENSMA:

Based upon our assessment and review of the peer-reviewed literature, Zolgensma has been medically proven to be effective and therefore, medically appropriate for the following:

1. Must be prescribed by or in consultation with a provider who specializes in the treatment of Spinal Muscular Atrophy (SMA) and/or neuromuscular disorders AND
2. Must be less than 2 years of age at the time of treatment and weigh \( \leq 13.5 \) kg AND
3. Must have a diagnosis of Spinal Muscular Atrophy with bi-allelic mutations in the SMN1 gene
   a. Confirmed by targeted mutation analysis
      i. Homozygous deletions of SMN1 gene OR
      ii. Homozygous mutation in the SMN1 gene (e.g. biallelic mutations of exon 7) OR
      iii. Compound heterozygous mutation in the SMN1 gene (e.g. deletion of SMN1 exon 7 and mutation of SMN1) AND
4. Must have genetic testing confirming 1, 2, or 3 copies of the SMN2 gene AND
5. Must have baseline anti-AAV9 antibody titers of \( \leq 1:50 \) AND
6. Must not have received previous Zolgensma treatment AND
7. Patients with advanced SMA (i.e complete paralysis of limbs, permanent ventilator dependence) will be excluded from treatment due to lack of literature support
   a. Permanent ventilation defined as required invasive ventilation (tracheostomy) , or invasive/noninvasive respiratory assistance for \( \geq 16 \) hours daily for \( \geq 14 \) days in the absence of an acute reversible illness and excluding perioperative ventilation AND
8. Zolgensma will not be approved for use in combination with Spinraza AND
9. Dosage should not exceed \( 1.1 \times 10^{14} \) vector genomes (vg) per kg of body weight administered as an IV infusion over 60 minutes. Systemic corticosteroids (equivalent to oral prednisolone at 1mg/kg of body weight) must be administered starting one day prior to Zolgensma infusion and continuing for a total of 30 days

POLICY GUIDELINES:

1. Spinraza is administered intrathecally and Zolgensma is administered intravenously. Both products will be covered under the medical benefit.
2. Ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract. Codes may not be covered under all circumstances. Please read the policy and guidelines statements carefully. Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.
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HCPCS:
J2326 Spinraza

UPDATES:

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REFERENCES:
1. Biogen Inc. Spinraza Package Insert; December 2016
3. FDA Summary review for regulatory action: application number 209531Orig1s000. Available at: <https://www.accessdata.fda.gov/drugsatfda> Accessed 6 March 2017
5. AveXis, Inc. Zolgensma Package Insert; May 2019
8. AveXis, Inc. Zolgensma Package Insert; May 2019