

Zolgensma (onasemnogene abeparvovec-xioi)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Spinal Muscular Atrophy (SMA) is a rare, severe genetic disorder characterized by the loss of motor neurons in the spinal cord and brainstem, leading to progressive muscle weakness and atrophy. It is caused by mutations in the survival motor neuron 1 (SMN1) gene, resulting in insufficient production of the survival motor neuron (SMN) protein essential for motor neuron survival and function. The disease is classified into several types based on age of onset and severity, with Type 1 being the most severe and common infantile form.

Zolgensma (onasemnogene abeparvovec-xioi) is a gene replacement therapy designed to address the genetic root cause of SMA. It is delivered as a one-time, intravenous infusion and uses a modified, non-replicating adeno-associated virus (AAV9) vector to deliver a functional copy of the human SMN gene to motor neuron cells. This therapy aims to restore SMN protein production, potentially halting or reversing the progression of SMA.

- Zolgensma is indicated for the treatment of pediatric patients less than 2 years of age with SMA with bi-allelic mutations in the SMN1 gene. It is particularly effective when administered early,

ideally before the onset of symptoms, as it may prevent or significantly delay the loss of motor neurons and subsequent muscle degeneration.

- Other treatment options for SMA include nusinersen (Spinraza), an intrathecally administered antisense oligonucleotide, and risdiplam (Evrysdi), an orally administered small molecule SMN2 splicing modifier. However, Zolgensma is unique in its potential to provide a one-time treatment that addresses the genetic cause of the disease.

Definitions

“Gene therapy” is a technique that replaces a mutated gene with a healthy gene, inactivates a mutated gene, or introduces a new gene that helps fight against diseases and disorders.

“Permanent ventilation” is defined as requiring invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in the absence of an acute reversible illness, excluding perioperative ventilation.

“Spinal muscular atrophy (SMA)” is a genetic disease that affects the nervous systems and voluntary muscle movement. There is a loss of motor neurons in the spinal cord that cannot send signals for the muscles to move, resulting in weak and smaller muscles.

Medical Necessity Criteria for Authorization

The Plan considers **Zolgensma (onasemnogene abeparvovec-xioi)** medically necessary when **ALL** of the following criteria are met:

1. The prescriber is a neurologist or neuromuscular specialist with expertise in the diagnosis and management of spinal muscular atrophy (SMA); **AND**
2. The member is less than (<) 2 years of age at time of treatment; **AND**
3. The member is diagnosed with autosomal recessive 5q13-linked (genetically proven) Spinal Muscular Atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene; **AND**
4. The member has 1-3 copies of the SMN2 gene, confirmed by genetic testing (i.e., submission of medical records confirming the member has 3 copies or less of the SMN2 gene); **AND**
5. The member does not have advanced SMA (e.g. complete paralysis of limbs or permanent ventilator dependence); **AND**
6. The member has baseline anti-adenovirus 9 (anti-AAV9) antibody titer $\leq 1:50$ measured by ELISA (enzyme-linked immunosorbent assay); **AND**

7. The following baseline laboratory testing has been conducted:
 - a. liver function (clinical exam, AST, ALT, total bilirubin, prothrombin time); **and**
 - b. platelet counts; **and**
 - c. troponin-I; **AND**
8. The requested medication will not be used concurrently with other SMA therapies such as Spinraza (nusinersen) or Evrysdi (risdiplam); **AND**
9. The member does not have a history of prior treatment with Zolgensma (onasemnogene abeparvovec-xioi) or any other gene transfer therapy for SMA; **AND**
10. Zolgensma (onasemnogene abeparvovec-xioi) is dosed at 1.1×10^{14} vector genomes per kilogram (vg/kg) of body weight administered as a one-time intravenous infusion.

If the above criteria are met, Zolgensma (onasemnogene abeparvovec-xioi) will be approved for one-time administration at the recommended dosing.

Please note:

1. *Approval is provided for one-time single IV infusion only, in alignment with FDA-approved labeling.*
2. *Retreatment with Zolgensma (onasemnogene abeparvovec-xioi) is considered investigational, as safety and efficacy of repeat administrations have not been clinically established.*

Experimental or Investigational / Not Medically Necessary

Zolgensma (onasemnogene abeparvovec-xioi) for any other indication is considered experimental or investigational. Non-covered indications include, but are not limited to, the following:

- Advanced SMA, including but not limited to:
 - Complete paralysis of limbs.
 - Permanent ventilator dependence (defined as ≥ 16 hours of respiratory assistance per day continuously for >14 days in the absence of an acute reversible illness or perioperative state).
- Treatment in premature infants before reaching full-term gestational age.
 - Rationale: Concomitant use of corticosteroids may adversely affect neurological development.
- Treatment in members with 4 or more copies of the SMN2 gene.
 - Rationale: These patients are more likely to develop milder forms of SMA and the risk-benefit profile of treatment is less clear.
- Treatment in members with anti-AAV9 antibody titers $>1:50$.

- Rationale: Higher antibody levels may affect treatment efficacy and safety.
- Repeat administration of Zolgensma.
 - Rationale: Safety and effectiveness of repeat administration have not been evaluated.

Applicable Billing Codes (HCPCS/CPT Codes)

CPT/HCPCS Codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
J3399	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10 ¹⁵ vector genomes
ICD-10 codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffman]
G12.1	Other inherited spinal muscular atrophy
G12.8	Other spinal muscular atrophies and related syndromes
G12.9	Spinal muscular atrophy, unspecified

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