Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Onasemnogene abeparvovec-xioi (Zolgensma®)	**MP-RX-FP-186-26**	☒ **MMM MA** ☒ **MMM MultiHealth**	**5/6/2026**	**5/6/2026**
			Last Review Date: **5/6/2026**	**Frequently Revision:** **Annual**

Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: Part B Drugs

Service Description:

This document addresses the use of Onasemnogene abeparvovec-xioi (Zolgensma®), a gene replacement therapy approved by the U.S. Food and Drug Administration (FDA) for the treatment of pediatric patients less than two years of age with spinal muscular atrophy (SMA). Zolgensma is an adeno-associated virus vector-based therapy designed to deliver a functional copy of the survival motor neuron (SMN) gene to motor neuron cells, thereby addressing the underlying genetic cause of SMA through a one-time intravenous infusion.

Background Information:

Spinal muscular atrophy (SMA) is a rare inherited neuromuscular disorder caused by mutations in the SMN1 gene, which is responsible for producing survival motor neuron (SMN) protein. This protein is essential for the health and function of motor neurons in the spinal cord and brainstem. When adequate SMN protein is not produced, motor neurons progressively degenerate, leading to muscle weakness, loss of motor function, respiratory complications, and, in severe cases, early death.

SMA presents along a spectrum of severity, typically categorized by age of onset and clinical progression. The infantile-onset form is the most severe and most frequently diagnosed subtype. Affected infants may exhibit symptoms within the first few months of life, including poor muscle tone, limited head control, feeding difficulties, and impaired breathing. Without treatment, this form of SMA is associated with significant morbidity and reduced survival.

Zolgensma (onasemnogene abeparvovec-xioi) is a gene replacement therapy indicated for pediatric patients less than two years of age with SMA. It utilizes an adeno-associated viral vector to deliver a functional copy of the SMN gene to motor neurons through a one-time intravenous infusion. By enabling production of the missing SMN protein, the therapy addresses the underlying genetic cause of the disease rather than only managing symptoms. The dose is determined based on patient weight at the time of administration.

The efficacy of Zolgensma was evaluated in two open-label, single-arm clinical trials: START (NCT02122952) and STR1VE-US (NCT03306277), conducted in pediatric patients less than two years of age with infantile-onset spinal muscular atrophy (SMA), confirmed biallelic mutations in the *SMN1* gene, two copies of the *SMN2* gene, and baseline anti-AAV9 antibody titers ≤1:50. In both studies, Zolgensma was administered as a single intravenous infusion. Efficacy was primarily assessed based on event-free survival (defined as survival without permanent ventilation) and the attainment of developmental motor milestones, such as independent sitting. In the pivotal study, most treated patients remained alive without permanent ventilation beyond 14 months

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of age, and a meaningful proportion achieved independent sitting—outcomes that exceed those expected based on the natural history of untreated infantile-onset SMA. Results across studies were consistent and demonstrated a dose-response relationship, supporting the clinical effectiveness of the therapy.

The most commonly observed adverse effects include transient elevations in liver enzymes and gastrointestinal symptoms such as vomiting. The therapy carries a boxed warning for the risk of acute serious liver injury. Liver function testing is required prior to treatment and should continue for at least three months following infusion. Because corticosteroids are administered in conjunction with therapy, vaccination schedules may require temporary adjustment, particularly for live vaccines.

Approved Indications

A. For the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1* (*SMN1)* gene.
B. Limitations of use:
    a. The safety and efficacy of administering more than one dose of Zolgensma have not been studied, and repeat treatment has not been established. In addition, clinical data are lacking in individuals with advanced-stage spinal muscular atrophy, such as those with complete limb paralysis or those who require permanent ventilatory support; therefore, outcomes in this population are unknown.

Other Uses

A. None

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Zolgensma® (onasemnogene abeparvovec-xioi)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Treatment with Zolgensma (onasemnogene abeparvovec-xioi) may be considered medically necessary when all of the following criteria are met:

i. Zolgensma has been prescribed by or in consultation with a neurologist who specializes in spinal muscular atrophy; **AND**
ii. The individual has a confirmed diagnosis of spinal muscular atrophy (SMA) supported by genetic testing demonstrating biallelic pathogenic mutations (e.g., deletion or loss-of-function mutation) in the *SMN1* gene (genetic confirmatory laboratory testing results must be submitted); **AND**
iii. The individual is less than two (2) years of age at the time of infusion; **AND**
iv. The individual does not have advanced disease defined as:
   A. Permanent ventilator dependence (≥16 hours per day of respiratory support for ≥14 consecutive days in the absence of an acute reversible illness); **OR**
   B. Invasive ventilatory support (tracheostomy); **OR**
   C. Complete and irreversible paralysis of all limbs;

AND

v. The prescribing provider attests that:
   A. Baseline liver function testing (e.g., AST, ALT, total bilirubin) has been completed prior to administration; **AND**
   B. Individual does not have an active infection; **AND**
   C. Systemic corticosteroids will be administered per FDA labeling to reduce the risk of hepatotoxicity; **AND**
   D. Liver function will be monitored for at least three (3) months following infusion;

AND

vi. Individual has an anti-adeno-associated virus 9 (AAV9) antibody titer less than or equal to 1:50 as determined by Enzyme- linked Immunosorbent Assay (ELISA) binding immunoassay; **AND**
vii. The individual has not received Zolgensma before; **AND**
viii. Zolgensma will be administered as a one-time intravenous infusion in an appropriate healthcare setting capable of monitoring and managing potential adverse events.

B. Criteria For Continuation of Therapy

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i. Zolgensma is administered as a single, one-time intravenous infusion. Repeat dosing is not supported by current evidence and is not recommended; therefore, continuation or reauthorization criteria do not apply.

C. Authorization Duration

i. Authorization will be provided for one (1) single intravenous infusion. Reauthorization is not applicable, as Zolgensma is administered as a one-time treatment.

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Repeat administration (more than one lifetime dose); **OR**

ii. Individuals with advanced spinal muscular atrophy characterized by permanent ventilator dependence or complete irreversible limb paralysis; **OR**

iii. When the above criteria in Section A: Criteria for Initial Approval are not met, and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Approved Indication	Recommended Dosing/Limits
Spinal Muscular Atrophy	1.1×10^{14} vector genomes (vg) per kg of body weight as a one-time intravenous infusion
Exceptions	
None	

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
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

HCPCS Codes:

Codes	Description
J3399	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10

CPT Codes:

Codes	Description
96365 - 96368	Intravenous infusion administration

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Reference Information:

1. Bodamer O. *Spinal muscular atrophy.* In: Nordli DR Jr, Firth HV, Martin RJ, eds. UpToDate. Waltham, MA: UpToDate, Inc. Available at: https://www.uptodate.com . Accessed February 23, 2026.
2. Day JW, Finkel RS, Chiriboga CA, et al. Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicentre, phase 3 trial. *Lancet Neurol.* 2021;20(4):284–293.
3. Mendell JR, Al-Zaidy S, Shell R, et al. Single-dose gene-replacement therapy for spinal muscular atrophy. *N Engl J Med.*2017;377(18):1713–1722.
4. Novartis Gene Therapies, Inc. *Zolgensma® (onasemnogene abeparvovec-xioi) injection, for intravenous use.* Prescribing Information. Bannockburn, IL: Novartis Gene Therapies, Inc.; February 2025.
5. U.S. Food and Drug Administration (FDA). *FDA approves innovative gene therapy to treat pediatric patients with spinal muscular atrophy, a rare disease and leading genetic cause of infant mortality.* FDA News Release. May 24, 2019. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease. Accessed February 23, 2026.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	New Policy Creation	3/9/2026	5/6/2026