



5.75.027

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Subsection:	Neuromuscular Agents	Original Policy Date:	June 14, 2019
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Last Review Date: December 13, 2024

Zolgensma

Description

Zolgensma (onasemnogene abeparvovec-xioi)

Background

Zolgensma is a recombinant AAV9-based gene therapy designed to deliver a copy of the gene encoding the human SMN protein. Spinal muscular atrophy (SMA) is caused by a bi-allelic mutation in the *SMN1* gene, which results in insufficient SMN protein expression. Intravenous administration of Zolgensma that results in cell transduction and expression of the SMN protein has been observed in two human case studies (1).

Regulatory Status

FDA approved indication: Zolgensma is an adeno-associated virus vector-based gene therapy indicated 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 (1).

Limitations of Use: (1)

- The safety and effectiveness of repeat administration of Zolgensma have not been evaluated.
- The use of Zolgensma in patients with advanced SMA (e.g., complete paralysis of limbs, permanent ventilator-dependence) has not been evaluated.

Zolgensma has a boxed warning regarding acute serious liver injury and acute liver failure. Patients with pre-existing liver impairment may be at higher risk. Prior to infusion, liver function of all patients should be assessed by clinical examination and laboratory testing [e.g., hepatic aminotransferases (AST and ALT), total bilirubin, and prothrombin time]. Systemic

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corticosteroids should be administered to all patients before and after Zolgensma infusion. Liver function should be monitored for at least 3 months after infusion (1).

The recommended dose of Zolgensma is 1.1×10^{14} vector genomes per kilogram (vg/kg) of body weight (1).

Prior to Zolgensma infusion: patients should be assessed for liver function; platelet counts and troponin-I should be measured; baseline testing for the presence of anti-AAV9 antibodies should be performed; one day prior to Zolgensma infusion, administration of systemic corticosteroids equivalent to oral prednisolone at 1 mg per kg of body weight for a total of 30 days should be started; Zolgensma is administered as a single-dose intravenous infusion through a venous catheter (1).

Administration of Zolgensma to premature neonates before reaching full-term gestational age is not recommended, because concomitant treatment with corticosteroids may adversely affect neurological development. Delay Zolgensma infusion until the corresponding full-term gestational age is reached (1).

The safety of Zolgensma was studied in pediatric patients who received Zolgensma infusion at age 0.3 to 7.9 months (weight range 3.0 kg to 8.4 kg). The efficacy of Zolgensma was studied in pediatric patients who received Zolgensma infusion at age 0.5 to 7.9 months (weight range 3.6 kg to 8.4 kg) (1).

Related policies

Evrysdi, Spinraza

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zolgensma may be considered **medically necessary** if the conditions indicated below are met.

Zolgensma may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age Less than 24 months of age at the time of infusion

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Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA)

AND ALL of the following:

- a. Diagnosis of SMA based on the results of SMA newborn screening
- b. Diagnosis confirmed by genetic testing demonstrating bi-allelic mutations in the survival motor neuron 1 (SMN1) gene with **ONE** of the following:
 - i. Deletion of both copies of the SMN1 gene **OR**
 - ii. Compound heterozygous mutations of the SMN1 gene (defined below):
 - a) Pathogenic variant(s) in both copies of the SMN1 gene
 - b) Pathogenic variant in 1 copy and deletion of the second copy of the SMN1 gene
- c. Baseline anti-adenovirus serotype 9 (AAV9) antibody titers \leq 1:50
- d. Documentation of a genetic test confirming no more than 3 copies of the SMN2 gene
- e. Documentation of baseline laboratory assessments for AST, ALT, total bilirubin, and prothrombin time
- f. Patient does not have advanced spinal muscular atrophy (e.g., complete paralysis of limbs, permanent ventilator dependence)
- g. Prescribed by a neurologist, neuromuscular specialist, or pediatrician with expertise in treating SMA
- h. Patient has not previously received gene therapy for SMA (see Appendix 1)
- i. **NO** concurrent use with nusinersen or risdiplam

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

None

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Prior - Approval Limits

Quantity 1 injection per lifetime

Duration 1 month

Prior – Approval *Renewal* Limits

None

Rationale

Summary

Zolgensma is a recombinant AAV9-based gene therapy designed to deliver a copy of the gene encoding the human SMN protein. Spinal muscular atrophy (SMA) is caused by a bi-allelic mutation in the *SMN1* gene, which results in insufficient SMN protein expression. Intravenous administration of Zolgensma that results in cell transduction and expression of the SMN protein has been observed in two human case studies. The safety of Zolgensma was studied in pediatric patients who received Zolgensma infusion at age 0.3 to 7.9 months (weight range 3.0 kg to 8.4 kg). The efficacy of Zolgensma was studied in pediatric patients who received Zolgensma infusion at age 0.5 to 7.9 months (weight range 3.6 kg to 8.4 kg) (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Zolgensma while maintaining optimal therapeutic outcomes.

References

1. Zolgensma [package insert]. Bannockburn, IL: Novartis Gene Therapies, Inc.; July 2024.

Policy History

Date	Action
June 2019	Addition to PA. Changed requirement to 2 or fewer copies of the SMN2 gene per FEP
September 2019	Annual review
September 2020	Annual editorial review. Addition of no dual therapy with risdiplam
December 2020	Annual review
December 2021	Annual review and reference update

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April 2022	Per FEP: Added that patient must be less than 24 months of age at time of infusion. Updated genetic testing requirement and added requirement for genetic testing confirming no more than 3 copies of the SMN2 gene. Added requirement for documentation of SMA signs/symptoms and baseline laboratory testing. Added exclusion of advanced SMA. Removed requirements for: infusion delay for neonates, lab monitoring, systemic corticosteroid administration and agreement to FDA dosing.
June 2022	Annual editorial review and reference update
September 2022	Annual review. Per FEP, removed requirement “documentation of onset of SMA-associated signs and symptoms consistent with a clinical diagnosis of SMA” and added requirement “diagnosis of SMA based on the results of SMA newborn screening”
December 2023	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.

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Appendix 1 - List of Gene Therapies for SMA

Generic Name	Brand Name
Onasemnogene abeparvovec-xioi	Zolgensma