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
- 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 elevated aminotransferases. 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 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 $1.1 \times 10^{14}$ 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
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 in patients with spinal muscular atrophy (SMA) 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

Diagnosis

Patient must have the following:

1. Spinal Muscular Atrophy (SMA)

AND ALL of the following:

a. Diagnosis confirmed by genetic testing showing ALL of the following:
   i. Bi-allelic SMN1 5q gene variants or deletions
   ii. Two or fewer copies of the SMN2 gene
b. Onset of SMA-associated signs and symptoms before 6 months of age
c. Baseline anti-adeno-associated virus serotype 9 (AAV9) antibody titers ≤ 1:50
d. **Premature neonates only**: Zolgensma infusion will be delayed until the corresponding full-time gestational age is reached
e. Prescriber agrees to monitor AST, ALT, total bilirubin, and prothrombin time
f. Prescriber agrees to monitor platelet counts and troponin-I
g. Systemic corticosteroids will be administered beginning one day prior to infusion for a total of 30 days
h. Prescriber will not exceed the FDA labeled dose of 1.1 x 10^{14} vector genomes per kilogram (vg/kg) of body weight
i. Prescribed by a neurologist, neuromuscular specialist, or pediatrician with expertise in treating SMA
j. Patient has not previously received gene therapy for SMA (see Appendix 1) **AND** is not concurrently enrolled in a clinical trial for an experimental therapy for SMA
k. **NO** concurrent use with Spinraza (nusinersen)

Prior – Approval **Renewal Requirements**

None

**Policy Guidelines**

**Pre - PA Allowance**

None
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**


Policy History

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<tr>
<th>Date</th>
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<tbody>
<tr>
<td>June 2019</td>
<td>Addition to PA. Changed requirement to 2 or fewer copies of the SMN2 gene per FEP</td>
</tr>
<tr>
<td>September 2019</td>
<td>Annual review</td>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.
### Appendix 1 - List of Gene Therapies for SMA

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<tr>
<th>Generic Name</th>
<th>Brand Name</th>
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