Prior Authorization Review Panel

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CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review. Policies submitted without this form will not be considered for review.

<table>
<thead>
<tr>
<th>Plan: PA Health &amp; Wellness</th>
<th>Submission Date: 02/01/2020</th>
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<tbody>
<tr>
<td>Policy Number: PA.CP.PHAR.421</td>
<td>Effective Date: 01/15/2020</td>
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<tr>
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<td>Revision Date: 01/15/2020</td>
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<tr>
<td>Policy Name: Onasemnogene Abeparvovec (Zolgensma)</td>
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Type of Submission – **Check all that apply:**

- ✓ New Policy
- □ Revised Policy*
- □ Annual Review - No Revisions
- □ Statewide PDL - Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any changes or clarifying information for the policy below:

New Policy Created

<table>
<thead>
<tr>
<th>Name of Authorized Individual (Please type or print):</th>
<th>Signature of Authorized Individual:</th>
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<tbody>
<tr>
<td>Francis G. Grillo, MD</td>
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</tbody>
</table>
Clinical Policy: Onasemnogene Abeparvovec (Zolgensma)
Reference Number: PA.CP.PHAR.421
Effective Date: 01/15/2020
Last Review Date: 01/15/2020

Description
Onasemnogene abeparvovec (Zolgensma®) is an adeno-associated virus (AAV) vector-based gene therapy.

FDA Approved Indication(s)
Zolgensma is indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in survival motor neuron 1 (SMN1) gene.

Limitation(s) 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Zolgensma is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Spinal Muscular Atrophy (must meet all):
      1. Diagnosis of SMA;
      2. Genetic testing confirms the presence of one of the following (a, b, or c):
         a. Homozygous deletions of SMN1 gene (e.g., absence of the SMN1 gene);
         b. Homozygous mutation in the SMN1 gene (e.g., biallelic mutations of exon 7);
         c. Compound heterozygous mutation in the SMN1 gene (e.g., deletion of SMN1 exon 7 (allele 1) and mutation of SMN1 (allele 2));
      3. Prescribed by or in consultation with a neurologist;
      4. Age < 2 years;
      5. Documentation of one of the following baseline scores (see Appendix D) (a or b):
         a. Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorder (CHOP-INTEND) score;
         b. Hammersmith Infant Neurological Examination (HINE) Section 2 motor milestone score;
      6. Documentation of both of the following (a and b):
         a. Baseline laboratory tests demonstrating Anti-AAV9 antibody titers ≤ 1:50 as determined by ELISA binding immunoassay;
         b. Baseline liver function test, platelet counts, and troponin-I;
7. Member does not have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence, tracheostomy);
8. Member has not been previously treated with Zolgensma;
9. Zolgensma is not prescribed concurrently with Spinraza®;
10. If the member is currently on Spinraza, provider submits attestation of intention to discontinue Spinraza prior to treatment with Zolgensma;
11. Total dose does not exceed $1.1 \times 10^{14}$ vector genomes (vg) per kilogram (kg).

Approval duration: 4 weeks (one time infusion per lifetime)

B. Other diagnoses/indications
   1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy
   A. Spinal Muscular Atrophy
      1. Re-authorization is not permitted.
      Approval duration: Not applicable

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;
   B. Advanced SMA.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   
   ELISA: enzyme-linked immunosorbent assay  
   FDA: Food and Drug Administration  
   SMA: spinal muscular atrophy  
   SMN: survival motor neuron

   Appendix B: Therapeutic Alternatives
   Not applicable

   Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s): none reported
   • Boxed warning(s): acute serious liver injury and elevated aminotransferases

   Appendix D: General Information
   • SMA is an autosomal recessive genetic disorder. It is caused by mutations in the SMN1 (survival motor neuron) gene that is found on chromosome 5 (hence the name 5q-SMA). To develop SMA, an individual must inherit two faulty (deletion or mutation) SMN1 genes, one from each parent.
• There are other types of SMA that are not related to chromosome 5 or SMN. Safety and efficacy of Zolgensma in non-SMN-related SMA have not been established.
• SMN-related SMA is classified as type 1 through 4 depending on time of onset. The age of disease onset of symptoms correlates with disease severity: the earlier the age of onset, the greater the impact on motor function. Children who display symptoms at birth or in infancy typically have the lowest level of functioning (type 1). SMA onset in children (types 2 and 3), teens or adults (type 4) generally correlates with increasingly higher levels of motor function.
• SMN2 gene copy and SMA types
  o SMN2 gene copy numbers are variable in individuals with spinal muscular atrophy. Higher numbers typically correlate with less severe disease.
  o More than 95% of individuals with spinal muscular atrophy retain at least 1 copy of the SMN2 gene
  o About 80% of individuals with Type I spinal muscular atrophy have 1 or 2 copies of the SMN2 gene
  o About 82% of individuals with Type II spinal muscular atrophy have 3 copies of the SMN2 gene
  o About 96% of individuals with Type III spinal muscular atrophy have 3 or 4 copies of the SMN2 gene
• SMA Type I: onset of symptoms (e.g., hypotonia, muscle weakness, weak cry, lack of reflexes, difficulty swallowing, poor head control, round shoulder posture, inability to sit without support, tongue fasciculations, pooling secretions, poor suck and swallow reflexes, increased risk of aspiration, and failure to thrive) prior to the age of 6 months.
• Advanced SMA: complete paralysis of limbs, permanent ventilator dependence
• Permanent Ventilation: 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.
• Active infections include HIV, HBC, HCV, Zika, upper or lower respiratory tract infection, non-respiratory tract infection within 2 weeks of administration.
• The CHOP-INTEND score is a validated 16-item, 64-point scale shown to be reliable and sensitive to change over time for SMA Type 1. In a prospective cohort study of SMA type I patients (n = 34), the mean rate of decline in the CHOP-INTEND score was 1.27 points/year (95% CI 0.21-2.33, p = 0.02). A CHOP-INTEND score greater than 40 is considered a clinically meaningful change.
• The HINE Section 2 motor milestone exam is an easily performed and relatively brief standardized clinical neurological examination that is optimal for infants aged between 2 and 24 months with good inter-observer reliability. This endpoint evaluates seven different areas of motor milestone development, with a maximum score between 2-4 points for each, depending on the milestone, and a total maximum score of 26 points.

V. Dosage and Administration

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<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tr>
<td>SMA</td>
<td>Administer Zolgensma as a single-dose IV infusion over 60 minutes at the dose of $1.1 \times 10^{14}$ vg/kg.</td>
<td>Once</td>
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</table>
### Indication | Dosing Regimen | Maximum Dose
--- | --- | ---
None | One day prior to Zolgensma infusion, begin administration of systemic corticosteroids equivalent to oral prednisolone at 1mg/kg/day for a total of 30 days. Afterwards, evaluate liver function. No liver abnormalities, taper corticosteroids over the next 28 days. If liver abnormalities persist, continue systemic corticosteroids until resolution then taper over the next 28 days. |  

### VI. Product Availability
Zolgensma is shipped frozen in 10 mL vials with either 5.5 mL or 8.3 mL fill volumes. Each vial has a nominal concentration is 2.0 x 1013 vg/mL.

The customized kits come in differing vial quantities based on the patient’s weight in kilograms as reflected within the package insert.

### VII. References

**Coding Implications**
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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**Reviews, Revisions, and Approvals**

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<thead>
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<th>Date</th>
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