DRUG DETERMINATION POLICY

Title: DDP-40 Zolgensma Gene Therapy

Effective Date: 03/17/2020

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Zolgensma is an adeno-associated virus gene specialty therapy indicated for a very specific diagnosis and is associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnosis and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

A. Zolgensma (onasennogene beparvovec).

   1. Age:

      a. Six months to less than two years.

      b. Prematurity: full-term gestational age reached before use.

   2. Prescriber: neurologist.

   3. Diagnosis and severity.

      a. Spinal muscular atrophy (SMA) diagnosis (must meet all below):

         i. Symptomatic disease that is diagnosed by a neurologist with expertise in SMA.

         ii. Diagnosis of likely Type I or II SMA based on SMA newborn screening.

iii. Medical records documenting that the patient has three or less copies of the SMA2 gene.

b. Genetic testing (must meet one below):

i. Homozygous gene deletion of genes or mutation of SMN1 gene (e.g., deletion of SMN1 exon 7 at locus 5q13); or

ii. Compound heterozygous mutation of SMN1 gene (e.g., deletion of SMB1 exon7 [allele 1] and mutation of SMN1 [allele 2]).

c. Severity (must meet both below):

i. Severity score: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disease (CHOP INTEND) score of at least 40 indicating disease severity is not advanced stage. http://columbiasma.org/docs/cme-2010/CHOP%20INTEND%20for%20SMA%20Type%20I%20-%20Score%20Sheet.pdf.

ii. Degree of ventilation assistance: use of non-invasive ventilation only during naps and nighttime sleep.

4. Other therapies: Spinraza (nusinersen) (must meet both below):

a. Received before six months of age or within six months of diagnosis of late onset SMA.

b. Positive clinical response or no evidence of clinical decline while on Spinraza.

5. Dosage regimen (must meet all below):

a. 1.1 x 10 4 vector genomes (vg) per Kg of body weight (limit of one kit of Zolgensma).

b. Weight not above 13.5 Kg.

c. Receive prophylactic prednisolone (or glucocorticoid equivalent) prior to and following receipt of Zolgensma as indicated by the package insert.

6. Approval.

a. Initial: one month.

b. Re-approval: limited to one injection per lifetime.

7. Exclusions.

a. Treatment of pre-symptomatic patients diagnosed by newborn screening who are unlikely to develop Type I or II SMA.

b. Late-onset SMA more than two years old.

c. SMA without chromosome 5q deletions.

d. Anti-AAV9 antibody titer at or above 1:50 before administration.

e. Combination of SMA with concomitant SMN modifying therapy (e.g., Spinraza).

4.0 Coding:

AFFECTED CODES				
Code	**Brand Name**	**Generic Name**	**Billing Units (1U)**	**Prior Approval**
NA	Zolgensma	Onasemnogene abreparvovec-XIOI	NA	Y
MEDICAL DIAGNOSIS CODES				
G12.0	Infantile spinal muscular atrophy Type 1			N
G12.1	Other inherited spinal muscular atrophy			N
G12.9	Spinal muscular atrophy, unspecified			N

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Zolgensma, accessed October 2019.
2. Single-dose gene-replacement therapy for spinal muscular atrophy. N Engl J med. 2017;377:1713-22.
3. Treatment algorithm for infants diagnosed with spinal muscular atrophy through newborn screening. Journal of Neuromuscular Disease. 2018;5(2):145-58.

6.0 Appendices:

Appendix I - Monitoring and patient safety

Drug	Adverse Reactions	Monitoring & Contraindications	REMS
Zolgensma Onasemnogene abreparvovec-XIOI	• Hepatic: increased liver function tests LFT) (27%) • Immunologic: antibody development (100%)	• Labs: anti-AAV9 antibody testing (pre); LFT/platelets/ Troponin-I (pre, weekly x 1 month, biweekly x 2 months, then until normal	• None needed

7.0 Revision History:

Original Effective Date: 03/17/2020

Next Review Date: 03/17/2021

Revision Date	Reason for Revision