

DRUG DETERMINATION POLICY

Title: DDP-40 Spinal Muscular Atrophy Agents

Effective Date: December 14, 2022



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. Medications within this policy may/will be sent out for independent review and final approval by Health Plan Medical Director.

2.0 Background or Purpose:

Zolgensma and Evrysdi are agents used to treat spinal muscular atrophy and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the severity of disease and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

- I. Zolgensma intravenous (onasemnogene beparovvec-xioi IV) [must meet all listed below]:
 - A. Age [must meet both listed below]:
 1. Six months to less than two years.
 2. Prematurity: full-term gestational age reached before use.
 - B. Prescriber: neurologist.
 - C. Diagnosis and severity.
 1. Spinal muscular atrophy (SMA) diagnosis [must meet all listed below]:
 - a. Symptomatic disease that is diagnosed by a neurologist with expertise in SMA.
 - b. Diagnosis of likely Type I or II SMA based on SMA newborn screening.
 - c. Medical records documenting that the patient has three or less copies of the SMA2 gene.
 2. Genetic testing [must meet one listed below]:

- a. Homozygous gene deletion of genes or mutation of SMN1 gene (e.g., deletion of SMN1 exon 7 at locus 5q13); or
- b. Compound heterozygous mutation of SMN1 gene (e.g., deletion of SMB1 exon7 [allele 1] and mutation of SMN1 [allele 2]).

3. Severity [must meet all listed below]:

- a. 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%201%20-%20Score%20Sheet.pdf>.
- b. Degree of ventilation assistance: use of non-invasive ventilation only during naps and nighttime sleep.
- c. Degree of paralysis: does not have paralysis of all limbs.

D. Other therapies: none required.

E. Dosage regimen [must meet all listed below]:

- 1. 1.1×10^4 vector genomes (vg) per Kg of body weight (limit of one kit of Zolgensma).
- 2. Weight not above 13.5 Kg.
- 3. Receive prophylactic prednisolone (or glucocorticoid equivalent) prior to and following receipt of Zolgensma as indicated by the package insert.

F. Approval.

- 1. Initial: one month.
- 2. Re-approval: limited to one injection per lifetime.

II. Evrysdi (risdiplam) [must meet all listed below]:

A. Age: at or above two months to 25 years.

B. Prescriber: neurologist.

C. Diagnosis and severity.

1. Spinal muscular atrophy (SMA) diagnosis [must meet all listed below]:

- a. Symptomatic disease that is diagnosed by a neurologist with expertise in SMA.
- b. Diagnosis: Type I, II or III SMA .
- c. Medical records documenting that the patient has three or less copies of the SMA2 gene.

2. Genetic testing [must meet one listed below]:

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

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

3. Severity [must meet both listed below]:

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

b. Degree of paralysis: does not have complete paralysis of all limbs.

D. Other therapies: none required.

E. Dosage regimen: Evrysdi (risdiplam).

1. Two months to below two years: 0.2 mg per Kg once daily.

2. Above two years and weighs below 20 Kg: 0.25mg per Kg once daily.

3. Above two years and weighs above 20Kg: 5mg once daily.

F. Approval.

1. Initial: four months.

2. Re-approval:

a. Duration: six months.

b. Documentation of a positive response to therapy as demonstrated by clinical significant improvement or maintenance of function from pretreatment baseline status.

III. Exclusions [meets any listed below]:

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) or previous treatment with Spinraza with evidence of clinical decline while receiving it.

F. Prior use of gene replacement therapy for the treatment of SMA (e.g. Zolgensma – nasemnogene abeparvovee-xioi).

4.0 Coding:

AFFECTED CODES

Code	Brand Name	Generic Name	Billing Units (1U)	Prior Approval
NA	Zolgensma	Onasemnogene abrepavovec-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. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Zolgensma, Evrysdi accessed J October 2021.
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.
4. Cure SMA: Clinical Guidelines. <https://www.curesma.org/clinical-guidelines/> accessed October 2022.

6.0 Appendices:

See page 5.

7.0 Revision History:

Original Effective Date: 12/23/2022

Next Review Date: 12/7/2022

Revision Date	Reason for Revision
11/20	Annual review, no changes
1/21	Off cycle review, changed policy name to Spinal Muscular Atrophy Agents, added drug Evrysdi, clarified Spinraza exclusion
10/21	Annual review; replaced abbreviations
10/22	Annual review: added reference

Appendix I - Monitoring and Patient Safety

Drug	Adverse Reactions	Monitoring & Contraindications	REMS
Zolgensma Onasemnogene abeparvovecxiol	<ul style="list-style-type: none"> • Hepatic: increased liver function tests liver function tests) (27%) • Immunologic: antibody development (100%) 	<ul style="list-style-type: none"> • Labs: anti-AAV9 antibody testing (pre); liver function tests/platelets/ Troponin-I (pre, weekly x 1 month, biweekly x 2 months, then until normal 	<ul style="list-style-type: none"> • None needed
Evrysdi (risdiplam)	<ul style="list-style-type: none"> • Dermatologic: skin rash (17%); • Gastrointestinal: constipation (infants: ≥10%), diarrhea (17%), vomiting (infants: ≥10%) • Respiratory: pneumonia (infants: ≥10%), upper respiratory tract infection (infants: ≥10%) • Miscellaneous: fever (22%) 	<ul style="list-style-type: none"> • None listed in Lexi-comp 	<ul style="list-style-type: none"> • None needed