Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Onasemnogene Abeparvovec-xioi (Zolgensma)

Reference Number: CP.PHAR.421
Effective Date: FDA Approval Date
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s) [Pending]

Zolgensma is indicated for the treatment of pediatric patients between 2 to 17 years of age with spinal muscular atrophy (SMA).

Limitation(s) of use: [XXX]

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.

All requests reviewed under this policy **require medical director review.**

It is the policy of health plans affiliated with Centene Corporation® that Zolgensma is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Spinal Muscular Atrophy (must meet all)**:**

1. Diagnosis of SMA confirmed by 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));
2. Genetic testing quantifying number of copies of SMN2 gene and one of the following (a or b):*
   a. One, two, or three copies of SMN2 gene;
   b. Four copies of SMN2 gene, determined by a quantitative assay that is able to distinguish between four SMN2 gene copies and five or more SMN2 gene copies;
3. Request is for intrathecal formulation;*
4. Prescribed by or in consultation with a neurologist;*
5. Age 2 years to < 18 years;*

6. Documentation that member is able to sit independently;
7. Documentation of one of the following baseline scores (a, b, c, d, or e; *see Appendix D*):*
   a. Hammersmith functional motor scale expanded (HFMSE) score;
   b. Revised Hammersmith Scale (RHS);
   c. Upper Limb Module (ULM);
   d. Revised Upper Limb Module (RULM);
   e. 6-Minute Walk Test (6MWT);
8. 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;
9. Member does not require tracheostomy, invasive, noninvasive ventilation for > 12 hours/day, or awake noninvasive ventilation for > 6 hours/day;*
10. Member has not been previously treated with Zolgensma;*
11. Zolgensma is not prescribed concurrently with Spinraza® or Evrysdi™;*
12. If the member is currently on Spinraza or Evrysdi, one of the following (a or b):*
    a. Spinraza or Evrysdi is being used as a bridge therapy to Zolgensma;
    b. Both of the following (i and ii):
       i. Provider must submit evidence of clinical deterioration (e.g., sustained decrease in HFMSE score over a period of 3 to 6 months) upon completion of all loading doses of Spinraza;
       ii. Documentation of provider attestation of clinical deterioration and Spinraza/Evrysdi discontinuation;
13. Member does not have an active viral infection (*see Appendix D*);*
14. Dose does not exceed 1.2 x 10^{14} vector genomes (vg).*

Approval duration: 4 weeks (one time intrathecal dose per lifetime)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Spinal Muscular Atrophy

1. Continued therapy will not be authorized as Zolgensma is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HFMSE: Hammersmith functional motor scale expanded
RHS: Revised Hammersmith scale
RULM: Revised upper limb module
SMA: spinal muscular atrophy
SMN: survival motor neuron
ULM: upper limb module
6MWT: 6-minute walk test

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

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.
- 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
  - SMN2 gene copy numbers are variable in individuals with spinal muscular atrophy. Higher numbers typically correlate with less severe disease.
  - More than 95% of individuals with spinal muscular atrophy retain at least 1 copy of the SMN2 gene
  - About 80% of individuals with Type I spinal muscular atrophy have 1 or 2 copies of the SMN2 gene
  - About 82% of individuals with Type II spinal muscular atrophy have 3 copies of the SMN2 gene
  - About 96% of individuals with Type III spinal muscular atrophy have 3 or 4 copies of the SMN2 gene
- Active infections include HIV, HBC, HCV, Zika, upper or lower respiratory tract infection, non-respiratory tract infection within 2 weeks of administration.
- The HFSME score combines the Hammersmith Functional Motor Scale with a 13-item expansion module for ability to distinguish motor skills among individuals who may be older or with SMA types II and III. Each item is graded from 0 to 3, with 0 signifying no response, with a total of 66 points. HFMSE has demonstrated reliability and validity in patients with SMA. An increase of greater than 2 points in total score is unlikely in untreated SMA.
- The RHS is an ordinal scale which consist of 33 items with grades of 0,1 and 2. For individuals who can achieve the task without any compensation it is given a score of 2. For those who only attempt the movement or finish it with some form of compensation is scored 1 and sore of 0 is given when patients are unable to perform any part of the item. The total maximum score is 69 points.
- The RULM is a set of 19 tasks that measure motor function in non-ambulatory SMA patients. Each task is assessed with a 3-point ordinal scale, with a total maximum score of 37 points. Meanwhile, the maximum score for ULM was 18.
- The 6MWT is a clinical outcome measure for ambulatory SMA that has been determined to be functionally meaningful and capable of capturing disease severity.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
SMA*	Administer Zolgensma as a single-dose intrathecal injection of 1.2 x 10^{14} vg*	1.2 x 10^{14} vg once*

VI. Product Availability [Pending]

Pending

VII. References

1. ClinicalTrials.gov. Efficacy and safety of intrathecal OAV101 (AVXS-101) in pediatric patients with type 2 spinal muscular atrophy (SMA) (STEER). Available at: https://clinicaltrials.gov/study/NCT05089656#participation-criteria. Accessed January 30, 2025.
2. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard of care in spinal muscular atrophy. *Journal of Child Neurology.* 2007; 22:1027-1049.
3. Maitre NL, Chorna O, Romeo DM, and Guzzetta A. Implementation of the Hammersmith infant neurological examination in a high-risk infant follow-up program. *Pediatric Neurology.* 2016; 65:31-38.
4. Dunaway Young S, Montes J, Kramer SS, et al. Six-minute walk test is reliable and valid in spinal muscular atrophy. *Muscle and Nerve.* 2016. 54: 836-842.
5. Ramsey D, Scoto M, Mayhew A, et al. Revised Hammersmith scale for spinal muscular atrophy: A SMA specific clinical outcome assessment tool. *PLoS ONE*. 2017; 12(2): e0172346. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0172346.
6. Mercuri E, Finkel RS, Muntoni F, et al. Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. *Neuromuscul Disord*. 2018;28(2):103-115.
7. Finkel RS, Mercuri E, Meyer OH, et al. Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements, and immunizations; other organ systems; and ethics. *Neuromuscul Disord*. 2018;28(3):197-207.
8. Schroth M, Deans J, Arya K, et al. Spinal muscular atrophy update in best practices: recommendations for diagnosis considerations. Neurol Clin Pract. 2024 Aug;14(4):e200310. doi: 10.1212/CPJ.0000000000200310.

Coding Implications [Pending]

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.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	03.11.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.