Medical Policy:

ZOLGENSMA® (onasemnogene abeparvovec-xioi) injection

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.194	January 2, 2024	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

The medication listed in this policy is not covered by the pharmacy benefit. Zolgensma is covered by the medical benefit and must be obtained by Accredo, our preferred medical specialty provider.

Length of Authorization

Coverage will be provided for one dose, per lifetime and may not be renewed.

Dosing Limits [Medical Benefit]

Spinal muscular atrophy, Bi-allelic survival motor neuron 1 (SMN1) gene mutations

The recommended dose of Zolgensma is 1.1×10^{14} vector genomes per kilogram (vg/kg) of body weight

Premedication, initiate systemic corticosteroids equivalent to oral prednisolone 1 mg/kg/day 1 day prior to infusion and continue for a total of 30 days.

Guideline

I. INITIAL APPROVAL CRITERIA

1. **<u>Spinal Muscular Atrophy (SMA)</u>** Approve for one treatment per lifetime in patients who meet ALL of the following criteria (A-N):
   A. Submission of medical records (e.g., chart notes, laboratory values) confirming the following: Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene; **AND**
   Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.
   B. Diagnosis of SMA by a neurologist with expertise in the diagnosis of SMA; **AND**
   C. Submission of medical records (e.g., chart notes, laboratory values) confirming that patient has 4 copies or less of SMN2 gene; **AND**
   D. For use in a neonatal patient born prematurely, the full-term gestational age has been reached; **AND**
   E. Patient must not have advanced disease (i.e., Invasive ventilation or tracheostomy, complete limb paralysis); **AND**
   F. Zolgensma is prescribed by a neurologist with expertise in the treatment of SMA; **AND**
   G. Patient is not to receive routine concomitant SMN modifying therapy (e.g., Spinraza) (patient's medical record will be reviewed and any current authorizations for SMN modifying therapy will be terminated upon Zolgensma approval; patient access to subsequent SMN modifying therapy will be assessed according to respective coverage policy of concomitant agent); **AND**
   H. Physician attests that the patient will be assessed for the presence of anti-AAV9 antibodies and managed accordingly; **AND**
   I. Physician attests that the patient will not receive Zolgensma if the most recent pre-treatment anti-AAV9 antibody titer is above 1:50*; **AND**
   J. Patient will receive prophylactic prednisolone (or glucocorticoid equivalent) prior to and following receipt of Zolgensma within accordance of the United States Food and Drug Administration (FDA) approved Zolgensma labeling; **AND**
   K. Patient will receive Zolgensma intravenously within accordance of the FDA approved labeling, 1.1×10^{14} vector genomes (vg) per kg of body weight; **AND**
   L. Patient has never received Zolgensma treatment in their lifetime; **AND**
   M. The following laboratory tests will be evaluated prior to administration of Zolgensma:
      i. Liver function tests (normal clinical exam, total bilirubin, and prothrombin results, and ALT and AST levels below 2 × ULN) **AND**
      ii. Complete blood count, including platelet counts **AND**
      iii. Patient has undergone a renal function assessment within the last 30 days and has a creatinine level < 1.0 mg/dL **AND**
   N. Authorization will be for no longer than 14 days from approval or until 2 years of age, whichever is first.

II. RENEWAL CRITERIA

Safety and effectiveness of repeat administration of Zolgensma have not been evaluated.

Limitations/Exclusions

Zolgensma is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.
Other Exclusions:

1. Age older than 2 years of age.
2. Combination treatment of SMA with concomitant SMN modifying therapy (e.g. Spinraza) or past treatment with a SMN modifying therapy.
3. SMA without chromosome 5q mutations or deletions.
4. Safety and effectiveness of repeat administration of Zolgensma have not been evaluated
5. Patient has pre-existing hepatic insufficiency

Applicable Procedure Codes

Code	Description
J3399	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes (Zolgensma)

Applicable NDCs

Code	Description
71894-0120-xx	Zolgensma 2.6-3.0 kg Intravenous Kit (2x8.3 mL)
71894-0121-xx	Zolgensma 3.1-3.5 kg Intravenous Kit (2x5.5mL & 1x8.3mL)
71894-0122-xx	Zolgensma 3.6-4.0 kg Intravenous Kit (1x5.5mL & 2x8.3mL)
71894-0123-xx	Zolgensma 4.1-4.5 kg Intravenous Kit (3x8.3 mL)
71894-0124-xx	Zolgensma 4.6-5.0 kg Intravenous Kit (2x5.5mL & 2x8.3mL)
71894-0125-xx	Zolgensma 5.1-5.5 kg Intravenous Kit (1x5.5mL & 3x8.3mL)
71894-0126-xx	Zolgensma 5.6-6.0 kg Intravenous Kit (4x8.3 mL)
71894-0127-xx	Zolgensma 6.1-6.5 kg Intravenous Kit (2x5.5mL & 3x8.3mL)
71894-0128-xx	Zolgensma 6.6-7.0 kg Intravenous Kit (1x5.5mL & 4x8.3mL)
71894-0129-xx	Zolgensma 7.1-7.5 kg Intravenous Kit (5x8.3 mL)
71894-0130-xx	Zolgensma 7.6-8.0 kg Intravenous Kit (2x5.5mL & 4x8.3mL)
71894-0131-xx	Zolgensma 8.1-8.5 kg Intravenous Kit (1x5.5mL & 5x8.3mL)
71894-0132-xx	Zolgensma 8.6-9.0 kg Intravenous Kit (6x8.3 mL)
71894-0133-xx	Zolgensma 9.1-9.5 kg Intravenous Kit (2x5.5mL & 5x8.3mL)
71894-0134-xx	Zolgensma 9.6-10.0 kg Intravenous Kit (1x5.5mL & 6x8.3mL)
71894-0135-xx	Zolgensma 10.1-10.5 kg Intravenous Kit (7x8.3 mL)
71894-0136-xx	Zolgensma 10.6-11.0 kg Intravenous Kit (2x5.5mL & 6x8.3mL)
71894-0137-xx	Zolgensma 11.1-11.5 kg Intravenous Kit (1x5.5mL & 7x8.3mL)
71894-0138-xx	Zolgensma 11.6-12.0 kg Intravenous Kit (8x8.3 mL)
71894-0139-xx	Zolgensma 12.1-12.5 kg Intravenous Kit (2x5.5mL & 7x8.3mL)
71894-0140-xx	Zolgensma 12.6-13.0 kg Intravenous Kit (1x5.5mL & 8x8.3mL)
71894-0141-xx	Zolgensma 13.1-13.5 kg Intravenous Kit (9x8.3 mL)
71894-0142-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 10mL

71894-0143-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 10mL
71894-0144-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 10mL
71894-0145-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 11mL
71894-0146-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 11mL
71894-0147-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 11mL
71894-0148-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 12mL
71894-0149-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 12mL
71894-0150-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 12mL
71894-0151-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 13mL
71894-0152-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 13mL
71894-0153-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 13mL
71894-0154-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 14mL
71894-0155-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 14mL
71894-0156-xx	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes 14mL

ICD-10 Diagnoses

Code	Description
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffmann]

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/2/2024	**Annual Review:** Length of Authorization: Removed "Coverage will be provided: For no longer than 14 days from approval or until 2 years of age, whichever is first" Replaced with: "Coverage will be provided for one dose per lifetime and may not be renewed." Initial Criteria: Previously, a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic mutations in the survival motor neuron 1 gene reported as at least one of the following was required: homozygous deletion, homozygous mutation, or compound heterozygous mutation This was revised to state that a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 gene is required with a Note added stating that pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations. Removed: "Troponin-I levels; AND" Replaced with " Patient has undergone a renal function assessment within the last 30 days and has a creatinine level < 1.0 mg/dL AND" Removed ICD-10 G12.1 and G12.9 Added: NDC codes: 71894-0142-xx 71894-0143-xx 71894-0144-xx 71894-0145-xx 71894-0146-xx

		71894-0147-xx 71894-0148-xx 71894-0149-xx 71894-0150-xx 71894-0151-xx 71894-0152-xx 71894-0153-xx 71894-0154-xx 71894-0155-xx 71894-0156-xx
EmblemHealth & ConnectiCare	3/23/2023	**Annual Review:** No changes
EmblemHealth & ConnectiCare	06/28/2022	**Annual Revision**: Removal of the word "symptomatic" in Diagnosis of symptomatic SMA by a neurologist with expertise in the diagnosis of SMA Removal of "Diagnosis of likely Type I or II SMA based on the results of SMA newborn screening" Removal of " Patient is less than or equal to 6 months of age; and ▪ Patient does not have advanced SMA at baseline (e.g., complete paralysis of limbs); OR All of the following: ▪ Patient is greater than 6 months of age, but less than 2 years of age; and ▪ One of the following: • Both of the following: o Patient has previously received Spinraza (nusinersen) for the treatment of Type I, or likely Type I or II SMA before 6 months of age with positive clinical response; AND Submission of medical records (e.g., chart notes, laboratory values) confirming patient does not have advanced SMA as defined by the fact that the patient has not shown evidence of clinical decline while receiving Spinraza therapy; OR • Both of the following: Patient has previously received Spinraza (nusinersen) for the treatment of later-onset SMA before 2 years of age with positive clinical response; AND o Submission of medical records (e.g., chart notes, laboratory values) confirming patient does not have advanced SMA as defined by the fact that the patient has not shown evidence of clinical decline while receiving Spinraza therapy; OR • Patient has recently been diagnosed with symptomatic later-onset SMA within the previous 6 months" Removal of : "Submission of medical records (e.g., chart notes, laboratory values) confirming patient does not have advanced SMA as defined by the fact that patient's most recent CHOP INTEND score is greater than or equal to 40" Removal of : "Patient is less than or equal to 13.5 kg" Removal of: "Dose to be administered does not exceed one kit of Zolgensma" Removal of: "Physician attests that the patient, while under the care of the physician, will be assessed by one of the following exam scales during subsequent office visits for a period not to exceed 3 years*† o Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) scale during subsequent office visits while the patient is 2 to 3 years of age or younger*†; or o Hammersmith Functional Motor Scale Expanded (HFMSE) during subsequent office visits while the patient is 2 to 3 years of age or older; AND • Physician acknowledges that EmblemHealth and ConnectiCare may request documentation, not more frequently than biannually, of follow-up patient assessment(s) including, but not necessarily

		limited to, serial CHOP INTEND or HFMSE assessments while the patient is under the care of the physician*" Addition of: "The following laboratory tests will be evaluated prior to administration of Zolgensma: Liver function tests (normal clinical exam, total bilirubin, and prothrombin results, and ALT and AST levels below 2 × ULN), Complete blood count, including platelet counts, Troponin-I levels" Removal of: "Patient has previously received a gene therapy for SMA" from Exclusion Criteria Addition of: "Pre-existing hepatic insufficiency" to exclusion criteria Removal of: "Pre-symptomatic treatment for patients who are unlikely to develop Type 1 or Type 2 SMA" from exclusion criteria
EmblemHealth & ConnectiCare	06/11/2020	Added J-Code (J3399): Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10^15 vector genomes (Zolgensma). Effective Date: 07/01/2020

References

1. Product Information: ZOLGENSMA® intravenous suspension, onasemnogene abeparvovec-xioi intravenous suspension. AveXis Inc (per manufacturer), Bannockburn, IL, 2021.