Medical Policy:

Zolgensma® (onasemnogene abeparvovec-xioi) injection

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.194	January 2, 2025	

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. **Spinal Muscular Atrophy – Treatment**. Approve if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, L, M, and N):

A. Patient is less than 2 years of age; **AND**

B. If the patient is a premature neonate, full-term gestational age of 39 weeks and 0 days has been met; **AND**

Note: Full-term gestational age can be defined as the postmenstrual age (gestational age plus chronological age) being equal to ≥ 39 weeks and 0 days.

C. Patient has not received Zolgensma in the past [verification in claims history required]; **AND**

Note: If no claim for Zolgensma is present (or if claims is not available), the prescribing physician confirms that the patient has not previously received Zolgensma.

D. 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 [documentation required]; **AND**

Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.

E. Patient meets ONE of the following (i or ii):

i. Patient has three or fewer survival motor neuron 2 (SMN2) gene copies [documentation required]; **OR**

ii. Patient meets BOTH of the following (a and b):

a. Patient has four SMN2 gene copies [documentation required]; **AND**

b. The number of SMN2 gene copies has been determined by a quantitative assay capable of distinguishing between four SMN2 gene copies and five or greater SMN2 gene copies; **AND**

F. According to the prescribing physician, patient has started or will receive systemic corticosteroids equivalent to oral prednisolone at a dose of 1 mg/kg per day commencing 1 day prior to Zolgensma infusion for a total of 30 days; **AND**

G. Baseline anti-AAV9 antibody titers are ≤ 1:50 [documentation required]; **AND**

H. Patient has undergone liver function testing within the past 30 days and meets ALL of the following (i, ii, iii, and iv):

i. Alanine aminotransferase levels are ≤ 2 times the upper limit of normal [documentation required]; **AND**

ii. Aspartate aminotransferase levels are ≤ 2 times the upper limit of normal [documentation required]; **AND**

iii. Total bilirubin levels are ≤ 2 times the upper limit of normal [documentation required]; **AND**

Note: Patient with elevated bilirubin levels due to neonatal jaundice are acceptable.

iv. Prothrombin time results are ≤ 2 times the upper limit of normal [documentation required]; **AND**

I. Patient has undergone a renal function assessment within the past 30 days and has a creatinine level < 1.0 mg/dL [documentation required]; **AND**

J. A complete blood count has been obtained within the past 30 days and the patient meets BOTH of the following (i and ii):

i. White blood cell count is ≤ 20,000 cells per mm3[documentation required]; **AND**

ii. Hemoglobin levels are between 8 g/dL and 18 g/dL [documentation required]; **AND**

K. For a patient currently receiving or who has received prior treatment with Spinraza (nusinersen intrathecal injection), the prescribing physician confirms that further therapy with Spinraza will be discontinued; **AND**

L. For a patient currently receiving or who has received prior treatment with Evrysdi (risdiplam oral solution), the prescribing physician confirms that further therapy with Evrysdi will be discontinued; **AND**

M. Medication is prescribed by a physician who has consulted with or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; **AND**

N. Current patient body weight has been obtained within the past 14 days [documentation required]

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	1/2/2025	Annual Review: Changed order and wording of the criteria. Reworded: "Patient has four SMN2 gene copies [documentation required]; **AND** The number of SMN2 gene copies has been determined by a quantitative assay capable of distinguishing between four SMN2 gene copies and five or greater SMN2 gene copies; **AND** According to the prescribing physician, patient has started or will receive systemic corticosteroids equivalent to oral prednisolone at a dose of 1 mg/kg per day commencing 1 day prior to Zolgensma infusion for a total of 30 days; **AND"** Added: "Total bilirubin levels are ≤ 2 times the upper limit of normal [documentation required]; **AND** Prothrombin time results are ≤ 2 times the upper limit of normal [documentation required]; **AND** White blood cell count is ≤ 20,000 cells per mm3[documentation required]; **AND** Hemoglobin levels are between 8 g/dL and 18 g/dL [documentation required]; **AND** For a patient currently receiving or who has received prior treatment with Evrysdi (risdiplam oral solution), the prescribing physician confirms that further therapy with Evrysdi will be discontinued; **AND** Current patient body weight has been obtained within the past 14 days"
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: <u>Length of Authorization:</u> 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." <u>Initial Criteria:</u> 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.