Medical Policy

BlueCross BlueShield Kansas
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Blue Cross Blue Shield Association

Title: Zolgensma Medical Drug Criteria

Professional / Institutional
Original Effective Date: August 25, 2022
Latest Review Date: April 8, 2025
Current Effective Date: September 21, 2023

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

CLINICAL RATIONALE

Spinal Muscular Atrophy	Spinal muscular atrophy (SMA) is the second most common autosomal recessive neurodegenerative disorder, caused by deletion or loss of function mutation of the survival motor neuron 1 (SMN1) gene.(2,11) SMA is characterized by dysfunction and then loss of the alpha motor neurons in the spinal cord that causes progressive muscle atrophy and weakness.(10) There are two forms of survival motor neuron (SMN), SMN1 and SMN2, which are located on chromosome 5q13.2.(5) SMN1 is the primary gene responsible for functional production of SMN protein.(3) SMN1 can be absent because of deletion or SMN1-to-SMN2 conversion.(5) SMN2 preferentially excludes exon 7 during splicing and, as a result, produces only a small fraction of functional SMN protein as compared with SMN1. Because SMN2 produces a reduced number of SMN proteins, it can only partially compensate for the loss of SMN1 gene. SMA has an incidence of approximately 1 in 10,000 live births and a carrier frequency

	of approximately 1 in 54. It is one of the leading causes of infant mortality.(3) Molecular genetic testing of SMN1/SMN2 is highly reliable and is the standard tool for the diagnosis of SMA.(2,4,10) Genetic testing for homozygous deletion will confirm the disease in 95% of patients. Essentially all other patients with SMN-related SMA will be compound heterozygotes with a single SMN1 deletion and a mutation in the other SMN1 copy.(4) With newborn screening (NBS) becoming more widespread, infants can be diagnosed and receive early disease-modifying treatment, even before they become symptomatic. SMA newborns identified by NBS and before treatment initiation should be characterized by SMN2 copy number (probable Type), current motor function, age at symptom onset, and severity of symptoms. Early diagnosis and treatment will give infants with SMA the best outcomes and a healthier life.(10,12) SMA was historically classified into Types 0-4 based on age of onset of symptoms and motor milestone achievement. Applied retroactively, it was most applicable to older children and adults.(2,9) Type 0 is very rare with symptoms beginning prior to birth and survival being only a few months. Type 1 is the most common and severe form and usually diagnosed during the first six months of life. Type 2 is usually diagnosed after six months of age but before 2 years of age. Type 3, known as juvenile SMA, is typically diagnosed after 18 months of age and before 3 years of age. However, some SMA Type 3 patients can be diagnosed as late as the teenage years. Type 4 is very rare, less than 1% of cases, and usually symptoms appear as early as 18 years of age but most commonly after 35 years of age.(9) SMN2 copy number is predictive of phenotype severity. The more copies of SMN2, the milder phenotypic presentation.(10) For example, in a large German study, 80% of SMN Type 1 patients had two or less copies of SMN2, 82% with SMN Type 2 patients had three copies, and 96% of SMN Type 3 patients had 3 or 4 copies. The most severe is Type 0 with a single copy of SMN2. Infants with two or three SMN2 copies are likely to develop SMA Type 1 or 2. Type 4 usually has 4 or more SMN2 copies.(4,10) Therefore, determination of SMN2 copy number is a powerful predictor of disease and appropriate treatments.(10) With the approval of SMN-enhancing treatments and the addition of NBS, a dramatic changed in the natural history of SMA across all ages and has led to a shift in disease management.(9) According to the updated treatment algorithm from the SMA NBS Multidisciplinary Working Group, infants diagnosed through NBS with up to four SMN2 gene copies require immediate treatment. Patients with five (or more) SMN2 gene copies should be observed and screened for symptoms.(7,9,10) Guidelines recommend the use of age-appropriate function assessments to advise initiation and follow-up of drug therapy in SMA patients. They acknowledge that the tests vary in availability, physician expertise and preference, and the patient's ability, based on age, to participate. The function assessments that were considered for use in SMA patients were CHOP-INTEND, Hammersmith Infant Neurological Examination (HINE-2), Hammersmith Functional Motor Scale-Expanded (HFMSE), six-minute walk test (6MWT), Revised Upper Limb Module (RULM) test, and Bayley Scales of Infant and Toddler Development (BSID). Risdiplam efficacy trials utilized Bayley Scales of Infant and Toddler development, Third Edition (BSID-III), and Motor Function Measurement score (MFM32).(10)

Efficacy	Zolgensma is a gene therapy that is given as a one-time IV administration that delivers a copy of SMN in a self-complementary adeno-associated viral serotype 9 (scAAV9). This has induced SMN expression in motor neurons and peripheral tissues.(3) The efficacy of Zolgensma in pediatric patients less than 2 years of age with SMA with bi-allelic mutations in the SMN1 gene were evaluated in three clinical trials; Study 1 (STR1VE NCT03306277), Study 2 (START NCT02122952), and Study 3 (SPR1NT NCT03505099). Patients experienced onset of clinical symptoms consistent with SMA before 6 months of age. All patients had genetically confirmed bi-allelic SMN1 gene deletions, 2 copies of the SMN2 gene, and absence of the c.859G>C modification in exon 7 of SMN2 gene. All patients had a baseline anti-AAV9 antibody titers of less than or equal to 1:50, measured by ELISA. In Zolgensma clinical trials, patients were required to have baseline anti-AAV9 antibody titers of less than or equal to 1:50, measured using an enzyme-linked immunosorbent assay (ELISA). The safety and efficacy of Zolgensma in patients with anti-AAV9 antibody titers above 1:50 have not been evaluated. Starting one day prior to Zolgensma infusion, patients should receive systemic corticosteroids equivalent to oral prednisolone at 1 mg/kg of body weight per day for a total of 30 days. At the end of systemic corticosteroid treatment, check liver function be clinical examination and by laboratory testing.(1) **STR1VE** This was a Phase 3 open label, single-arm clinical trial that enrolled 21 symptomatic patients with SMA Type 1 and less than 6 months of age at the time of infusion, none of which required non-invasive ventilator support, and all could exclusively feed orally. During the study, one patient died from respiratory failure deemed unrelated to treatment and another patient withdrew before the 18-month end-of-study-visit. Primary endpoints were event-free survival and functional, independent sitting for at least 30 seconds at the 18-month-of-age visit. At the 14-month-of-age study visit (primary endpoint, 20/22 (91%) of patients were alive and free of permanent ventilation and results were maintained through 18 months of age. At the 18-month-of-age study visit (primary endpoint), 13/22 (59%) of patients achieved sitting without support for at least 30 seconds. Secondary endpoints met included 41% of patients meeting all 3 criteria for ability to thrive (composite endpoint, maintains weight at greater than or equal to 3rd percentile [does not receive nutrition through mechanical support, and has ability to tolerate thin liquids as demonstrated through a formal swallowing test]) at 18 months of age, 4/22 patients required ventilatory support at 18 months of age (vs most patients with SMA Type 1 in natural history of disease, requiring respiratory support by 12 months of age), and 95% of patients achieved or maintained a CHOP-INTEND score of at least 40 (vs historical controls not typically achieving and maintaining a score greater than or equal to 40).(1) **START** This was a Phase 1, open-label, single-arm, ascending-dose clinical trial to support the efficacy of Zolgensma that enrolled 15 patients with SMA Type 1, symptomatic, and less than 6 months of age at time of infusion. Of the 16 patients screened, one was excluded because of persistently elevated anti-AAV9 titers greater than 1:50. Three patients were assigned to the low-dose (6.7x10^13 vg/kg) cohort, the remaining 12 received high dose (2.0x10^14 vg/kg). The average age for cohort 1 at time of treatment was 6.3 months, while average age in cohort 2 was 3.4

	months. Patient 1 in cohort 1 resulted with serum aminotransferase elevations, which led to a protocol amendment. Patients 2 through 15 received oral prednisolone 1mg/kg daily for 30 days, starting 24 hours before the administration of Zolgensma. The primary outcome was the determination of safety based on any treatment-related adverse events of grade 3 or higher. The secondary outcome was the time until death or the need for permanent ventilatory assistance. Exploratory outcomes included motor-milestone achievements and CHOP-INTEND scores. At the end of the study, all patients had reached an age of at least 20 months and did not require permanent mechanical ventilation. At 29 months of age, one patient required permanent ventilation because of hypersalivation. All patients had increased scores from baseline on the CHOP-INTEND scale and maintained these changes during the study. Eleven of twelve patients in cohort 2 were able to sit unassisted for at least 5 seconds, ten for at least 10 seconds, and 9 for at least 30 seconds. Other motor milestones were also positive, and eleven of twelve attained the ability to speak. No patients in historical cohorts had achieved any of these motor milestones and rarely achieved the ability to speak.(3) **SPR1NT** This was a Phase 3, open-label, single-arm study, that evaluated safety and efficacy in pre-symptomatic SMA patients with 2 copies (cohort 1) or 3 copies (cohort 2) of SMN2 treated at less than or equal to 6 weeks of life. In cohort 1, all 14 children with two copies of *SMN2*, expected to develop SMA Type 1, achieved the primary endpoint of sitting without support for greater than or equal to 30 seconds up to the 18 month-of-age-visit (Bayley-III item #26; $P < 0.001$; 11 within the normal developmental window). All survived without permanent ventilation at 14 months as per protocol; 13 maintained body weight (greater than or equal to 3rd WHO percentile) through 18 months. No child used nutritional or respiratory support. In cohort 2, all 15 children with three SMN2 copies, expected to develop SMA Type 2, stood independently before 24 months ($P < 0.0001$; 14 within normal developmental window), and 14 walked independently ($P < 0.0001$; 11 within normal developmental window). All survived without permanent ventilation at 14 months; ten (67%) maintained body weight (greater than or equal to 3rd WHO percentile) without feeding support through 24 months; and none required nutritional or respiratory support. Zolgensma was effective and well-tolerated for children expected to develop SMA Type 1 and Type 2, highlighting the urgency for universal newborn screening.(6,8)
Safety	Zolgensma has no FDA labeled contraindications for use.(1) Zolgensma has the following boxed warnings:(1) • Cases of acute serious liver failure with fatal outcomes have been reported. Acute serious liver injury and elevated aminotransferases can also occur with Zolgensma. • Patients with pre-existing liver impairment may be at higher risk. • Prior to infusion, assess liver function of all patients by clinical examination and laboratory testing. Administer systemic corticosteroid to all patients before and after Zolgensma infusion. Continue to monitor liver function for at least 3 months after infusion, and at other times as clinically indicated.

See package insert for FDA preshttps://dailymed.nlm.nih.gov/dailymed/index.cfm

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Number	Reference
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3	Mendell JR, Al-Zaidy S, Shell R, et al. Single-Dose Gene Replacement Therapy for Spinal Muscular Atrophy. *N Engl J Med* 2017;377:1713-22
4	Arnold WA, Kassar D, Kissel JT. Spinal Muscular Atrophy: Diagnosis and Management in a New Therapeutic Era. *Muscle Nerve* 2015 Feb;51(2):157-167. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4293319/.
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6	Strauss KA, Farrar MA, Muntoni F, et al. Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial. *Nature Medicine*. 2022;28(7):1381-1389. doi:10.1038/s41591-022-01866-4
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8	Strauss KA, Farrar MA, Muntoni F, et al. Onasemnogene abeparvovec for presymptomatic infants with three copies of SMN2 at risk for spinal muscular atrophy: the Phase III SPR1NT trial. *Nature Medicine*. 2022;28(7):1390-1397. doi:10.1038/s41591-022-01867-3
9	Spinal Muscular Atrophy - Symptoms, Causes, Treatment. National Organization for Rare Disorders. Updated April 2024. https://rarediseases.org/rare-diseases/spinal-muscular-atrophy/.
10	Glascock J, Sampson J, Haidet-Phillips A, et al. Treatment Algorithm for Infants Diagnosed with Spinal Muscular Atrophy through Newborn Screening. *J Neuromuscul Dis*. 2018;5(2):145-158.
11	Keinath MC, Prior DE, Prior TW. (2021). Spinal Muscular Atrophy: Mutations, Testing, and Clinical Relevance. *The application of clinical genetics*, *14*, 11-25. https://doi.org/10.2147/TACG.S239603
12	Schroth M, Deans J, Arya K, et al. *Spinal Muscular Atrophy Update in Best Practices Recommendations for Diagnosis Considerations*.; 2024. doi:10.1212/CPJ.00200310

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPCS Codes	Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J3399	Zolgensma 10.1-10.5 kg ; Zolgensma 10.6-11.0 kg ; Zolgensma 11.1-11.5 kg ; Zolgensma 11.6-12.0 kg ; Zolgensma 12.1-12.5 kg ; Zolgensma 12.6-13.0 kg ; Zolgensma 13.1-13.5 kg ; Zolgensma 13.6-14.0 kg ; Zolgensma 14.1-14.5 kg ; Zolgensma 14.6-15.0 kg ; Zolgensma 15.1-15.5 kg ; Zolgensma 15.6-16.0 kg ; Zolgensma 16.1-16.5 kg ; Zolgensma 16.6-17.0 kg ; Zolgensma 17.1-17.5 kg ; Zolgensma 17.6-18.0 kg ; Zolgensma 18.1-18.5 kg ; Zolgensma 18.6-19.0 kg ; Zolgensma 19.1-19.5 kg ; Zolgensma 19.6-20.0 kg ; Zolgensma 2.6-3.0 kg ; Zolgensma 20.1-20.5 kg ; Zolgensma 20.6-21.0 kg ; Zolgensma 3.1-3.5 kg ; Zolgensma 3.6-4.0 kg ; Zolgensma 4.1-4.5 kg ; Zolgensma 4.6-5.0 kg ; Zolgensma 5.1-5.5 kg ; Zolgensma 5.6-6.0 kg ; Zolgensma 6.1-6.5 kg ; Zolgensma 6.6-7.0 kg ; Zolgensma 7.1-7.5 kg ; Zolgensma 7.6-8.0 kg ; Zolgensma 8.1-8.5 kg ; Zolgensma 8.6-9.0 kg ; Zolgensma 9.1-9.5 kg ; Zolgensma 9.6-10.0 kg	onasemnogene abeparvovec-xioi	10x8.3 ML ; 11x8.3 ML ; 12x8.3 ML ; 13x8.3 ML ; 14x8.3 ML ; 1x5.5ML & 10x8.3ML ; 1x5.5ML & 11x8.3ML ; 1x5.5ML & 12x8.3ML ; 1x5.5ML & 13x8.3ML ; 1x5.5ML & 2x8.3ML ; 1x5.5ML & 3x8.3ML ; 1x5.5ML & 4x8.3ML ; 1x5.5ML & 5x8.3ML ; 1x5.5ML & 6x8.3ML ; 1x5.5ML & 7x8.3ML ; 1x5.5ML & 8x8.3ML ; 1x5.5ML & 9x8.3ML ; 2x5.5ML & 10x8.3ML ; 2x5.5ML & 11x8.3ML ; 2x5.5ML & 12x8.3ML ; 2x5.5ML & 1x8.3ML ; 2x5.5ML & 2x8.3ML ; 2x5.5ML & 3x8.3ML ;	M ; N ; O ; Y	N		

HCPCS Codes	Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
			2x5.5ML & 4x8.3ML ; 2x5.5ML & 5x8.3ML ; 2x5.5ML & 6x8.3ML ; 2x5.5ML & 7x8.3ML ; 2x5.5ML & 8x8.3ML ; 2x5.5ML & 9x8.3ML ; 2x8.3 ML ; 3x8.3 ML ; 4x8.3 ML ; 5x8.3 ML ; 6x8.3 ML ; 7x8.3 ML ; 8x8.3 ML ; 9x8.3 ML				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Zolgensma 10.1-10.5 kg ; Zolgensma 10.6-11.0 kg ; Zolgensma 11.1-11.5 kg ; Zolgensma 11.6-12.0 kg ; Zolgensma 12.1-12.5 kg ; Zolgensma 12.6-13.0 kg ; Zolgensma 13.1-13.5 kg ; Zolgensma 13.6-14.0 kg ; Zolgensma 14.1-14.5 kg ; Zolgensma 14.6-15.0 kg ; Zolgensma 15.1-15.5 kg ; Zolgensma 15.6-16.0 kg ; Zolgensma 16.1-16.5 kg ; Zolgensma 16.6-17.0 kg ; Zolgensma 17.1-17.5 kg ; Zolgensma 17.6-18.0 kg ; Zolgensma 18.1-18.5 kg ; Zolgensma 18.6-19.0 kg ; Zolgensma 19.1-19.5 kg ; Zolgensma 19.6-20.0 kg ; Zolgensma 2.6-3.0 kg ; Zolgensma 20.1-20.5 kg ; Zolgensma 20.6-21.0 kg ; Zolgensma 3.1-3.5 kg ; Zolgensma 3.6-4.0 kg ; Zolgensma 4.1-4.5 kg ; Zolgensma 4.6-5.0 kg ; Zolgensma 5.1-5.5 kg ; Zolgensma 5.6-6.0 kg ; Zolgensma 6.1-6.5 kg ; Zolgensma 6.6-7.0 kg ; Zolgensma 7.1-7.5 kg ; Zolgensma 7.6-8.0 kg ; Zolgensma 8.1-8.5 kg ; Zolgensma 8.6-9.0 kg ; Zolgensma 9.1-9.5 kg ; Zolgensma 9.6-10.0 kg	onasemnogene abeparvovec-xioi	10x8.3 ML ; 11x8.3 ML ; 12x8.3 ML ; 13x8.3 ML ; 14x8.3 ML ; 1x5.5ML & 10x8.3ML ; 1x5.5ML & 11x8.3ML ; 1x5.5ML & 12x8.3ML ; 1x5.5ML & 13x8.3ML ; 1x5.5ML & 2x8.3ML ; 1x5.5ML & 3x8.3ML ; 1x5.5ML & 4x8.3ML ; 1x5.5ML & 5x8.3ML ; 1x5.5ML & 6x8.3ML ; 1x5.5ML & 7x8.3ML ; 1x5.5ML & 8x8.3ML ; 1x5.5ML & 9x8.3ML ; 2x5.5ML & 10x8.3ML ; 2x5.5ML & 11x8.3ML ; 2x5.5ML & 12x8.3ML ; 2x5.5ML & 1x8.3ML ; 2x5.5ML & 2x8.3ML ; 2x5.5ML & 3x8.3ML ; 2x5.5ML & 4x8.3ML ; 2x5.5ML & 5x8.3ML ; 2x5.5ML & 6x8.3ML ; 2x5.5ML & 7x8.3ML ; 2x5.5ML & 8x8.3ML ; 2x5.5ML & 9x8.3ML ; 2x8.3 ML ; 3x8.3 ML ; 4x8.3 ML ; 5x8.3 ML ; 6x8.3 ML ; 7x8.3 ML ; 8x8.3 ML ; 9x8.3 ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. The patient has a diagnosis of spinal muscular atrophy (SMA) **AND** 2. The patient has bi-allelic mutations in the survival motor neuron 1 (SMN1) gene as confirmed by genetic testing (medical records required) **AND** 3. The patient has 4 or fewer copies of the SMN2 gene **AND** 4. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 5. The patient has baseline anti-AAV9 antibody titers of less than or equal to 1:50 **AND** 6. The patient's pre-treatment liver function has been assessed by clinical examination and laboratory testing (e.g., hepatic aminotransferases [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)], total bilirubin, and prothrombin time) **AND** 7. The patient will have their liver function monitored for at least 3 months after infusion **AND** 8. The patient has been assessed for concurrent infections and no clinical signs or symptoms of infection are evident **AND** 9. Pre-infusion blood work, including creatinine, complete blood count (including hemoglobin and platelet count) and troponin-I, has been completed **AND** 10. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist, geneticist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 11. The patient will receive systemic corticosteroids before and after Zolgensma (onasemnogene abeparvovec-xioi) infusion **AND** 12. The patient has NOT previously been administered Zolgensma (onasemnogene abeparvovec-xioi) **AND** 13. The patient does NOT have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence [defined as invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in absence of an acute reversible illness, excluding perioperative ventilation]) **AND** 14. The patient will NOT receive the requested agent in combination with SPINRAZA (nusinersen) or Evrysdi (risdiplam) for the requested indication **AND** 15. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 16. The requested dose is within FDA labeled dosing for the requested indication **Length of Approval:** Once per lifetime

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

REVISIONS	
08-25-2022	Policy added to the bcbsks.com web site.
10-13-2022	Updated Policy Section ▪ Added to Section A and A1 Onasemnogene Abeparvovec-Xioi: "(High-Control)" ▪ Added Section Ae: "Documentation of baseline laboratory assessments such as AST, ALT, total bilirubin, and prothrombin time." ▪ Added Section B: "Onasemnogene Abeparvovec-Xioi (Low-Control)" 1. Onasemnogene abeparvovec-xioi (Low-Control) may be considered medically necessary if ALL of the following conditions are met: a. Diagnosis of spinal muscular atrophy confirmed by genetic testing demonstrating bi-allelic mutations in the survival motor neuron 1 (SMN1) gene as stated below I. deletion of both copies of the SMN1 gene OR II. compound heterozygous mutations of the SMN1 gene (defined below): i. pathogenic variant(s) in both copies of the SMN1 gene ii. pathogenic variant in 1 copy and deletion of the second copy of the SMN1 gene. AND b. Documentation of signs and symptoms consistent with a clinical diagnosis of spinal muscular atrophy. AND c. Documentation of a genetic test confirms no more than 3 copies of the SMN2 gene. AND d. The patient is less than 2 years of age at the time of infusion of onasemnogene abeparvovec-xioi. AND e. Documentation of baseline laboratory assessments such as AST, ALT, total bilirubin, and prothrombin time. AND f. The patient does not have advanced spinal muscular atrophy (e.g., complete paralysis of limbs, permanent ventilator dependence). AND g. Baseline anti-adeno-associated virus serotype 9 (AAV9) antibody titers < 1:50. AND h. Prescribed by a neurologist with expertise in treating spinal muscular atrophy. 2. Repeat treatment or ante-partum use of onasemnogene abeparvovec-xioi is considered experimental / investigational. 3. Onasemnogene abeparvovec-xioi is considered experimental /investigational for all other indications. 4. Concurrent use of onasemnogene abeparvovec-xioi with nusinersen and/or risdiplam is considered experimental / investigational. 5. Use of nusinersen and/or risdiplam after administration of onasemnogene abeparvovec-xioi is considered experimental / investigational.
	Updated Policy Guideline Section ▪ Added: Dosing Limits A. 1 injection per lifetime
02-09-2023	Updated Policy Section ▪ Removed Section A Onasemnogene Abeparvovec-Xioi (High-Control) A. Onasemnogene Abeparvovec-Xioi (High-Control) 1. Onasemnogene abeparvovec-xioi (High-Control) may be considered medically necessary if ALL of the following conditions are met: a. Diagnosis of spinal muscular atrophy confirmed by genetic testing demonstrating bi-allelic mutations in the survival motor neuron 1 (*SMN1*) gene as stated below I. deletion of both copies of the *SMN1* gene OR II. compound heterozygous mutations of the *SMN1* gene (defined below): i. pathogenic variant(s) in both copies of the *SMN1* gene ii. pathogenic variant in 1 copy and deletion of the second copy of the *SMN1* gene. AND b. Documentation of onset of symptoms consistent with a clinical diagnosis of type I spinal muscular atrophy less than 6 months of age.

REVISIONS	
	AND c. Documentation of a genetic test confirms no more than 2 copies of the SMN2 gene. AND d. The individual is less than 6 months of age at the time of infusion of onasemnogene abeparvovec-xioi. AND e. Documentation of baseline laboratory assessments such as AST, ALT, total bilirubin, and prothrombin time. AND f. The individual does not have advanced spinal muscular atrophy (e.g., complete paralysis of limbs, permanent ventilator dependence). AND g. Baseline anti-adeno-associated virus serotype 9 (AAV9) antibody titers < 1:50. AND h. Prescribed by a neurologist with expertise in treating spinal muscular atrophy. 2. Repeat treatment or ante-partum use of onasemnogene abeparvovec-xioi is considered experimental/investigational. 3. Onasemnogene abeparvovec-xioi is considered experimental/investigational for all other indications. 4. Concurrent use of onasemnogene abeparvovec-xioi with nusinersen and/or risdiplam is considered experimental/investigational. 5. Use of nusinersen and/or risdiplam after administration of onasemnogene abeparvovec-xioi is considered experimental / investigational. ▪ Section B (new A) Onasemnogene Abeparvovec-Xioi (Low-Control) • Added A1a "Diagnosis of spinal muscular atrophy based on the results of SMA newborn screening" • Removed A1c "Documentation of signs and symptoms consistent with a clinical diagnosis of spinal muscular atrophy."
09-21-2023	Adopted Prime Therapeutics Zolgensma policy. Policy now maintained by Prime Therapeutics LLC.
06-27-2024	Policy was reviewed by Prime Therapeutics LLC with no updates.
04-08-2025	Updated PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL Section: ▪ Standardization of criteria per template: 1) Update of "approved" to "labeled", 2) Removing "information has been provided" or "prescriber has provided information" to "there is support" ▪ Removed documentation requirement for SMN2 copy confirmation
	Policy maintained by Prime Therapeutics LLC.