Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Zolgensma Medical Drug Criteria

Professional / Institutional
Original Effective Date: August 25, 2022
Latest Review Date: June 27, 2024
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 bi-allelic loss or dysfunction of the survival motor neuron 1 (SMN1) gene.(2,6) SMA is characterized by dysfunction and then loss of the alpha motor neurons in the spinal cord that causes progressive muscle atrophy and weakness.(5) The SMN1 and SMN2 genes are all located on chromosome 5q13.2, an unstable chromosomal region that is prone to deletion, duplication, and gene conversion. There are two forms of survival motor neuron (SMN), SMN1 and SMN2, that differ by only five nucleotides.(9) SMN1 is the primary gene responsible for functional production of SMN protein. SMN1 produces a full-length transcript that encodes functional SMN protein.(3) SMN1 can be absent because of deletion or SMN1-to-SMN2 conversion.(9) The most common mutation causing SMA is a homozygous deletion of the SMN1 exon 7.(6) SMN2 preferentially excludes exon 7 during splicing and, as a result, produces only a small fraction of functional SMN protein as compared with SMN1.(3) Because SMN2 produces a reduced number of full-length transcripts, the number of SMN2 copies can modify the clinical phenotype and is an essential predictive factor.(3,6) About 94% of SMA patients have a

homozygous deletion of SMN1 exon 7. SMA has an incidence of approximately 1 in 10,000 live births and a carrier frequency of approximately 1 in 54.(3)

SMA is classified into four subtypes (1-4) based on age of onset of symptoms and motor milestone achievement. This variability in the clinical phenotype is largely a result of the number of copies of the survival motor neuron 2 (SMN2) gene. The SMA type 1 (SMA1) phenotype is the most severe.(2) The presence of two copies of SMN2 is associated with SMA1. Infants with SMN1 bi-allelic deletions and two copies of SMN2 have a 97% risk of SMA1.(3)

Clinical Classification of SMA(6)

SMA Type	Number of SMN2 Copies	Percent of Cases	Age of Onset	Highest Achieved Motor Function	Natural Age of Death Prior to Disease Modifying Therapy
0	1	Rare, less than 1%	Prenatal, at birth	Non-sitter, no head control	Death within weeks of birth
1	1-2	45%	0-6 months	Non-sitter	Death by age 2
2	3	20%	6-18 month	Sit independently, never stands or ambulates	Most alive at 25 years
3	3-4	30%	3a: 18 months-3 years 3b: 3-30 years	Ambulates independently	Normal lifespan
4	Greater than or equal to 4	Less than 5%	Greater than 30 years	Ambulates independently	Normal lifespan

The onset of symptoms for SMA1 occurs shortly after birth and prior to six months of age with a clinical hallmark of the inability to achieve independent sitting.(2) A historical cohort showed that the median age at symptom onset among infants with the disease was 1.2 months (range, 0 to 4 months).(3) Infants with SMA1 rapidly lose motor function and ultimately succumb to respiratory complications often within the first year of life. Studies of SMA1 infants with two SMN2 copies offered standard of care showed a median age of death or permanent ventilation (greater than or equal to 16h/day for at least 14 consecutive days) that ranged from 8 to 10.5 months.(2) Patients with SMA1 do not achieve major milestones in function and have a decline in function, as measured on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) scale, which ranges from 0 to 64, with higher scores indicating better motor function. In a historical analysis of 34 patients with SMA1, all but one of the patients did not reach a score of at least 40 after 6 months of age. In another cohort, CHOP-

	INTEND scores decreased by a mean of 10.7 points from 6 months to 12 months of age.(3) Molecular genetic testing is the standard tool for diagnosis of SMA. 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) Guidelines recommend use of age-appropriate testing 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), Hammersmith Functional Motor Scale-Expanded (HFMSE), six-minute walk test (6MWT), 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).(5) In addition to Zolgensma, there are two additional FDA-approved therapies for SMA, Evrysdi and Spinraza. Evrysdi, modifies pre-mRNA splicing of SMN2, increasing the production of SMN2. Evrysdi is administered as an oral solution dosed once daily.(6,8) Spinraza, a modified antisense oligonucleotide the binds SMN2 mRNA to modify splicing, causing an increase in SMN protein production. Spinraza is administered as an intrathecal injection dosed every four months after completing a loading dose series.(6,7)
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 an open label, single-arm clinical trial (ongoing) and an open-label, single-arm, ascending-dose clinical trial (completed). 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.(1) Efficacy was established based on survival and achievement of developmental motor milestones. Survival was defined as time from birth to either death or permanent ventilation. Efficacy was also supported by assessments of ventilator use, nutritional support, and scores on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND).(1) The ongoing trial enrolled 21 patients were enrolled, none of which required non-invasive ventilator support, and all could exclusively feed orally. At the time of cutoff, 19 patients were alive without permanent ventilation (i.e., event-free survival) and continuing in the trial. One patient died at age 7.8 months due to disease progression, and one patient withdrew at age 11.9 months. Thirteen of nineteen patients reached 14 months of age without permanent ventilation. In addition, 47.6% of patients achieved the ability to sit without support for greater than or equal to 30 seconds at the mean age of 12.1 months. Based on the natural history of the disease, patients who met the study entry criteria would not attain the ability to sit without support, and only approximately 25% of these patients would be expected to survive without permanent ventilation beyond 14 months of age.(1)

	The complete clinical trial enrolled 15 patients. 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) 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)
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

REFERENCES

Number	Reference
1	Zolgensma prescribing information. Novartis Gene Therapies, Inc. February 2023.
2	Al-Zaidy S, Pickard AS, Kotha K, et al. Health outcomes in spinal muscular atrophy type 1 following AVXS-101 gene replacement therapy. *Pediatr Pulmonol.* 2019;54(2):179-185.
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/
5	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.
6	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
7	Spinraza Prescribing Information. Biogen. February 2023.
8	Evrysdi prescribing information. Genentech, Inc. March 2023.
9	Fang P, Li L, Zeng J, et al. Molecular Characterization and Copy Number of SMN1, SMN2 and NAIP in Chinese Patients with Spinal Muscular Atrophy and Unrelated Healthy Controls. *BMC Musculoskelet Disord.* 2015;16(1):11.

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

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(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	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 &	M ; N ; O ; Y	N		

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
	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		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				

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 ;	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	Commercial ; HIM ; ResultsRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
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		; 5x8.3 ML ; 6x8.3 ML ; 7x8.3 ML ; 8x8.3 ML ; 9x8.3 ML	

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. Information has been provided that indicates 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 (medical records required) **AND** 4. If the patient has an FDA approved 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. The prescriber has provided information in support of 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) **AND** 15. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**

Module	Clinical Criteria for Approval
	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)

REVISIONS	
	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. 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.