Jefferson Health Plans

DR.005.D ZOLGENSMA® (onasemnogene abeparvovec-xioi)

Original Implementation Date : 3/1/2020
Version [D] Date : 4/17/2024
Last Reviewed Date: April 2024

PRODUCT VARIATIONS

This policy applies to Jefferson Health Plans Medicaid, CHIP and Medicare product lines.

Gene therapy is a benefit exclusion for **Individual and Family (ACA) product lines** and therefore, non-covered.

POLICY STATEMENT

Jefferson Health Plans considers ZOLGENSMA® medically necessary when the prior authorization criteria listed in the policy are met.

OFF-LABEL USE

Authorization for off-labeled use of medication will be evaluated on an individual basis. Review of an off-labeled request by the Medical Staff will be predicated on the appropriateness of treatment and full consideration of medical necessity. For off label use Medical Directors will review scientific literature and local practice patterns.

FDA APPROVED INDICATIONS

ZOLGENSMA® is an adeno-associated virus vector-based gene therapy indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the *survival motor neuron 1 (SMN1)* gene.

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

1) Medication is prescribed by or in consultation with a physician who specializes in the treatment of spinal muscular atrophy (SMA); and

2) Member has a documented diagnosis of SMA with the following: genetically confirmed bi-allelic *SMN1* gene deletions or variants; and

3) Member does not have a diagnosis of advanced SMA disease (complete limb paralysis, invasive ventilation support, etc.)? *If NO, go to 4. If YES, refer to Medical Director.*

4) If born premature, the member will not be given their ZOLGENSMA® infusion until the corresponding full-time gestational age is reached.

5) The member is less than 2 years of age.

6) The member has a baseline anti-adeno-associated virus serotype 9 (AAV9) antibody titer ≤1:50 measured by enzyme-linked immunosorbent assay (ELISA.

7) The member will be given systemic corticosteroids, administered beginning one day prior to infusion for a total of 30 days.

8) The member has documentation for baseline liver function tests (AST, ALT, total bilirubin, and prothrombin time) and will they continue to be monitored for at least 3 months after the infusion or until results are unremarkable.

9) The member has documentation for baseline platelet count and troponin-I levels and will they continue to be monitored.

10) The member does not have signs and symptoms of infection.

11) The member's dose is prescribed within the FDA labeled dose of 1.1×10^{14} vector genomes per kilograms (vg/kg) of body weight.

RENEWAL CRITERIA

ZOLGENSMA® is meant for a one-time-only dose. The safety and effectiveness of repeat administration of ZOLGENSMA® has not been evaluated.

DOSAGE AND ADMINISTRATION

ZOLGENSMA® is for single-dose intravenous infusion only:

- Recommended dosage: ZOLGENSMA® 1.1×10^{14} vector genomes (vg) per kg of body weight.
- Administer ZOLGENSMA® as an intravenous infusion over 60 minutes through a venous catheter.
- Provided in a kit containing 2 to 9 vials, as a combination of 2 vial fill volumes (either 5.5 mL or 8.3 mL). All vials have a nominal concentration of 2.0×10^{13} vector genomes (vg) per mL.

- Requires premedication with systemic corticosteroids.
- Equivalent to oral prednisolone at 1 mg/kg per day beginning 1 day prior to infusion for a total of 30 days.
- ZOLGENSMA® is shipped frozen at ≤ -60 °C. Thaw prior to infusion. Store refrigerated. Must use within 14 days of receipt.
- Postpone ZOLGENSMA in patients with infections until the infection has resolved and the patient is clinically stable. Clinical signs or symptoms of infection should not be evident at the time of ZOLGENSMA infusions.
- At the end of the 30-day period of systemic corticosteroid treatment, check liver function by clinical examination and by laboratory testing. For patients with unremarkable findings, taper the corticosteroid dose gradually over the next 28 days. If liver function abnormalities persist, continue systemic corticosteroids (1 mg/kg/day) until findings become unremarkable, and then taper the corticosteroid dose gradually over the next 28 days or longer if needed.
- If liver function abnormalities continue to persist ≥ 2 × ULN after the 30-day period of systemic corticosteroids, promptly consult a pediatric gastroenterologist or hepatologist.

RISK FACTORS/SIDE EFFECTS

Most common adverse reactions (incidence ≥5%) noted in trials were elevated liver enzymes and vomiting.

Hepatic effects: acute serious liver injury and elevated aminotransferases were observed in clinical trials; assess liver function by clinical examination and laboratory testing. Administer systemic corticosteroids before and after ZOLGENSMA® infusion.

Thrombocytopenia: transient decreases in platelet count were observed at different time points through the trial after ZOLGENSMA® infusion. Monitor platelet counts before and periodically after ZOLGENSMA® infusion until return to baseline.

Thrombotic Microangiopathy (TMA): If clinical signs, symptoms and/or laboratory findings occur, consult a pediatric hematologist and/or pediatric nephrologist immediately to manage as clinically indicated.

Cardiac effects: transient increases in cardiac troponin-I level were observed after ZOLGENSMA® infusion; clinical importance is unknown. However, cardiac toxicity was observed in animal studies. Monitor troponin-I before and periodically after ZOLGENSMA® infusion until return to baseline.

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MONITORING

Efficacy:

Physical findings:

- Achievement of developmental milestones (e.g., kicking, head control, rolling, sitting, crawling, standing, walking) may indicate efficacy.

Toxicity:

- Laboratory parameters: obtain at baseline and then as directed below.
  - **Liver function:** (clinical exam, AST, ALT, total bilirubin, prothrombin time): weekly for the first month; then every other week for months 2 and 3, until results are unremarkable (normal clinical exam, total bilirubin, and prothrombin results, and ALT and AST levels below 2 × ULN).
  - **Platelet count**: weekly for the first month and then every other week for months 2 and 3 until platelet count returns to baseline.
  - **Troponin-I**: weekly for the first month and then monthly for months 2 and 3 until troponin-I level returns to baseline.

BLACK BOX WARNING

Acute serious liver injury and elevated aminotransferases can occur with ZOLGENSMA®.

- Cases of acute 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.
- An assessment of liver function of all patients by examination and laboratory parameters must be performed prior to infusion.
- Liver enzymes (AST, ALT), total bilirubin and prothrombin time.
- Liver function must be monitored for at least 3 months after administration.
- 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.

CLINICAL EVIDENCE

N/A

BACKGROUND

Spinal muscular atrophy (SMA) is a group of rare hereditary diseases caused by a genetic mutation in the *survival motor neuron 1 (SMN1)* gene. Typically, the *SMN1* gene encodes most of the survival motor neuron (SMN) protein within the body, whereas a smaller percentage of functional SMN protein is encoded by *the survival motor neuron 2 (SMN2)* gene. SMN protein is largely responsible for the health and normal function of specialized nerve cells called motor neurons. Motor neurons located on the brain and spinal cord control voluntary muscle movement; an insufficient amount of functional SMN protein leads to motor neuron death, muscle weakness, hypotonia and atrophy.

The SMA classification is determined based on a patient's age at disease onset, as well as by functional ability.

SMA Type	Age of Onset	Highest Functional Ability	Typical number of copies of *SMN2* gene present in majority of patients
Type I: Werdnig Hoffman	0-6 months	Never sits or rolls over	1-2 copies
Type II: intermediate	7-18 months	Sits, may stand, never walks	3 copies
Type III: mild, Kugelberg-Welander disease	≥ 18 months	Walks	3-4 copies
Type IV: adult	2nd or 3rd decade	Walks during adult years	4-6 copies

The diagnosis of SMA is based on molecular genetic testing of *SMN1/SMN2*; genetically confirmed bi-allelic deletions or variants of *SMN1* gene are diagnostic of SMA. The number of *SMN2* gene copies is not essential to diagnosis, but it will influence the severity of SMA.

218th European Neuromuscular Center (ENMC) International Workshop summarizes survival data from SMA Type 1 studies, concluding that the number of copies of *SMN2* gene is a strong predictive biomarker when looking at the rapidly declining survival curve for patient with 2 copies compared to those that have 3 copies of the *SMN2* gene.

Although current literature suggests there is a correlation between clinical phenotype/severity of disease and the number of copies of *SMN2* gene, the 2017 update for the consensus statement for standard of care in spinal muscular atrophy states that there are exceptions; in individual cases, the number of *SMN2* copies may not predict the severity of the phenotype.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT® is a registered trademark of the American Medical Association.

CPT Code	Description
N/A	

HCPCS Code	Description
J3399	Injection, onasemnogene abeparvovec-xioi, per treatment, up to 5x10

ICD-10 Codes	Description
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffman].
G12.1	Other inherited spinal muscular atrophy
G.12.9	Spinal muscular atrophy, unspecified

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making.

Policy Bulletins are developed by Jefferson Health Plans to assist in administering plan benefits and constitute neither offers of coverage nor medical advice.

This Policy Bulletin may be updated and therefore is subject to change.

For HealthChoices (Medicaid) and Children's Health Insurance Program (CHIP) products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
2024 Annual review. Statement added to Black Box Warning section.	D	4/17/2024
2023 Annual review. Revisions were made to the following sections of the policy: Prior Authorization Criteria, Dosage and Administration, Black Box Warning. References were updated according.	C	6/23/2023
2022 Annual review. Thrombotic Microangiopathy added to the "Risk Factor" section.	B	7/1/2022
2021 Annual review. J3399 was added to the coding table.	A	3/1/2020
2020 Annual review. No changes.	A	3/1/2020
New Policy.	A	3/1/2020

REFERENCES

1. Al-Zaidy S, et al. Health outcomes in spinal muscular atrophy type 1 following AVXS-101 gene replacement therapy. Pediatr Pulmonol. 2019 Feb; 54(2):179-185.

2. FDA approves innovative gene therapy to treat pediatric patients with spinal muscular atrophy, a rare disease and leading genetic cause of infant mortality [Internet]. U.S. Food and Drug Administration. FDA; [cited 2019 Sep 5]. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease.

3. Finkle RS, et al, European Neuromuscular Center (ENMC) SMA Workshop Study Group (2017). 218th ENMC International Workshop: Revisiting the consensus on standards of care in SMA Naarden, The Netherlands, 19-21 February 2016. Neuromuscular Disorders. 2017 Jun; 27(6):596-605.

4. Mercuri E, et al. Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscular Disorders. 2018 ;(28): 103–115.

5. National Institutes of Health Spinal Muscular Atrophy Fact Sheet. National Institute of Neurological Disorders and Stroke. May 2019. *NIH Publication No. 19-NS-5597.Available from:* https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Spinal-Muscular-Atrophy-Fact-Sheet.

6. ZOLGENSMA ® [prescribing information]. AveXis Inc., Bannockburn, IL. 2/2023. Last viewed 2/20/2024.