

Zolgensma® (onasemnogene abeparvovec-xioi)

When requesting Zolgensma® (onasemnogene abeparvovec-xioi), the individual requiring treatment must be diagnosed with an FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Indication

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.

Coverage Guidelines

Treatment of spinal muscular atrophy (SMA)

An individual must meet **all** of the following criteria for approval:

- Has had a genetic test confirming the diagnosis of SMA with bi-allelic pathogenic variants in the *survival motor neuron 1 (SMN1)* gene (e.g., homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations) [documentation required];
- Is less than 2 years of age;
- If the individual is a premature neonate, full term gestational age of 39 weeks and 0 days has been met;
 - Note: Full-term gestational age can be defined as the postmenstrual age (gestational age plus chronological age) being ≥ 39 weeks and 0 days.
- Meets one of the following:
 - Has three or less *survival motor neuron 2 (SMN2)* gene copies [documentation required]; OR
 - Has four *survival motor neuron 2 (SMN2)* gene copies determined by a quantitative assay capable of distinguishing between four *SMN2* gene copies and five or greater *SMN2* gene copies [documentation required];
- Has baseline anti-AAV9 antibody titers of $\leq 1:50$ [documentation required];
- Has not received Zolgensma in the past;
- For a patient currently receiving or who has received prior treatment with Spinraza (nusinersen injection for intrathecal use), further therapy with Spinraza will be discontinued;
- For a patient currently receiving or who has received prior treatment with Evrysdi (risdiplam oral solution), further therapy with Evrysdi will be discontinued;
- Will be receiving systemic corticosteroids equivalent to oral prednisolone at a dose of 1 mg/kg per day starting 1 day prior to Zolgensma infusion and for a total of 30 days;
- Has undergone a renal function assessment within the last 30 days and has a creatinine level less than 1.0 mg/dL [documentation required];

- Has undergone a liver function assessment within the last 30 days and meets ALL of the following conditions [documentation required]:
 - o Alanine aminotransferase levels are $\leq 2x$ the upper limit of normal (ULN);
 - o Aspartate aminotransferase levels are $\leq 2x$ the ULN;
 - o Total bilirubin levels are $\leq 2x$ the ULN;
 - o Prothrombin time results are $\leq 2x$ the ULN
- Has obtained a complete blood count within the last 30 days and meets BOTH of the following conditions [documentation required]:
 - o White blood cell count is $\leq 20,000$ cells/mm³;
 - o Hemoglobin levels are between 8 g/dL and 18 g/dL;
- Zolgensma is prescribed by or in consultation with a physician who specializes in the management of spinal muscular atrophy and/or neuromuscular disorders.

Approval duration: One dose (lifetime)

Dosing Recommendation

Zolgensma is for single-dose intravenous infusion only.

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

References

1. Zolgensma® intravenous infusion [prescribing information]. Bannockburn, IL: Novartis; October 2023.
2. ACOG Committee Opinion No 579: Definition of term pregnancy. *Obstet Gynecol.* 2013;122(5):1139-1140.
3. Arnold ES, Fischbeck KH. Spinal muscular atrophy. *Handb Clin Neurol.* 2018;148:591-601.
4. Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. 2000 Feb 24 [Updated 2020 December 3]. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1352/>. Accessed on March 23, 2023.
5. Nicolau S, Waldrop MA, Connolly AM, Mendell JR. Spinal muscular atrophy. *Semin Pediatr Neurol.* 2021;37:100878.
6. Yeo CJJ, Darras BT. Overturning the paradigm of spinal muscular atrophy as just a motor neuron disease. *Pediatr Neurol.* 2020;109:12-19.
7. Spinraza® intrathecal injection [prescribing information]. Cambridge, MA: Biogen; February 2023.
8. Evrysdi® oral solution [prescribing information]. South San Francisco, CA: Genentech/Roche; February 2024.
9. Mendell JR, Al-Zaidy S, Shell R, et al. Single-dose gene replacement therapy for spinal muscular atrophy. *N Engl J Med.* 2017;377(18):1713-1722.
10. Mendell JR, Al-Zaidy SA, Lehman KJ, et al. Five-year extension results of the Phase I START trial of onasemnogene abeparvovec in spinal muscular atrophy. *JAMA Neurol.* 2021;78(7):834-841.
11. Day JW, Finkel RS, Chiriboga CA, et al. Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset muscular atrophy in patients with two copies of SMN2 (STR1VE): an open-label, single-arm, multicenter, phase 3 trial. *Lancet Neurol.* 2021;20:284-293.
12. Strauss KA, Farrar MS, 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. *Nat Med.* 2022;28:1390-1397.
13. Strauss KA, Farrar MS, 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. *Nat Med.* 2022;28:1381-1389.
14. Mercuri E, Muntoni F, Baranello G, et al. Onasemnogene abeparvovec gene therapy for symptomatic infantile-onset spinal muscular atrophy type 2 (STR1VE-EU): an open-label, single-arm, multicenter, phase 3 trial. *Lancet Neurol.* 2021;20:832-841.
15. Blair HA. Onasemnogene abeparvovec: a review of spinal muscular atrophy. *CNS Drugs.* 2022;36:995-1005.

16. 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;5:145-158.
17. Glascock J, Sampson J, Connolly AM, et al. Revised recommendations for the treatment of infants diagnosed with spinal muscular atrophy via newborn screening who have 4 copies of SMN2. *J Neuromuscul Dis.* 2020;7(2):97-100.