

Medical Necessity Guidelines Zolgensma (onasemnogene abeparvovec)

Policy Number: 060

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Overview

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.

Medicare Advantage

Prior Authorization Required	Yes ☒ No ☐
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Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, CMS had:**

- [Medicare Benefit Policy Manual Chapter 15: Covered Medical and Other Health Services](#)

When CMS documentation references FDA labeling, Mass General Brigham Health Plan develops coverage criteria to clarify medical necessity of the requested services. Mass General Brigham Health Plan coverage criteria align with FDA labeling without contradicting existing determinations and enhance the clarity of medical necessity requirements, documentation requirements, and clinical indications.

Criteria

1. Criteria for Approval (The member must meet **all** of the following requirements):
 - a. The member has confirmed and symptomatic genetic diagnosis documented by biallelic mutations in the SMN1 gene AND four or fewer copies of SMN2 gene; and

- b. The member has an anti-adenoviral vector, serotype 9 (AAV9) antibody titer less than or equal to 1:50; and
 - c. The member is less than 2 years of age; and
 - d. The member has not previously received Zolgensma; and
 - e. The member does not have concomitant illness such as severe kidney or liver disease, active viral infection, or symptomatic cardiomyopathy; and
 - f. If the member is receiving treatment with nusinersen, risdiplam, or other SMN modifying therapies, that treatment will be discontinued.
2. Dosing and Administration
- a. The member will receive a single-dose Zolgensma intravenous infusion in accordance with the FDA approved labeling; 1.1×10^{14} vector genomes (vg) per kilogram of body weight.

Exclusions

- 1. The member has advanced SMA as evidenced by, but not limited to, complete paralysis of limbs, invasive ventilatory support (tracheostomy), or use of non-invasive respiratory support for more than 16 hours per day; or
- 2. The member has previously been treated with Zolgensma or another gene therapy for SMA; or
- 3. The member is receiving treatment with another SMN modifying therapy that would not be discontinued upon approval for Zolgensma; or
- 4. The member is a neonate who has not reached 40 weeks postconceptual age; or
- 5. The member has contraindications to systemic corticosteroids.

Mass General Brigham ACO

Prior Authorization Required	Yes ☒ No ☐
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Prior authorization requests for Zolgensma for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Zolgensma are found in [Table 76: Neuromuscular Agents – Duchenne Muscular Dystrophy and Spinal Muscular Atrophy](#).

One Care and Senior Care Options (SCO)

Prior Authorization Required	Yes ☐ No ☐
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Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, or the member does not meet all of the medical necessity criteria for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. **See Medicare Advantage criteria and exclusions above. If Medicare Advantage criteria are not met, then MassHealth criteria are applied.**

Commercial and Qualified Health Plans

Prior Authorization Required	Yes ☒ No ☐
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Prior authorization for Zolgensma for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See the [Prime Therapeutics policy for Zolgensma](#) for more information.

Related Policies

- [Medical Necessity Guidelines Itvisma](#)

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Authorized Code	Code Description
J3399	Injection, Onasemnogene abeparvovec-xioi, per treatment, up to 5×10^{15} vector genomes

Summary of Evidence

The therapeutic potential of onasemnogene abeparvovec in treating spinal muscular atrophy (SMA) has been extensively evaluated in clinical trials, with outcomes highlighting efficacy and safety across different patient populations and stages of disease progression. Mendell et al. (2017) conducted a phase 1 trial to assess its impact in symptomatic infants with SMA Type 1. Patients in the low-dose and therapeutic-dose cohorts, with mean ages at treatment of 6.3 months and 3.4 months respectively, demonstrated remarkable improvements in motor function. By 20 months, none required permanent mechanical ventilation, with cohort 1 reaching a median age of 30.8 months and cohort 2 reaching 25.7 months at their last pulmonary assessments. Motor function improvements were quantified using CHOP INTEND scores, which increased by an average of 7.7 points in cohort 1 and 24.6 points in cohort 2. Notably, nearly all patients in cohort 2 achieved critical motor milestones, including independent sitting and walking. Adverse events were limited to transient elevated aminotransferase levels, successfully managed with prednisolone. Following median 5.2 years of follow-up, among patients in the therapeutic-dose cohort, no patient required initiation of permanent ventilation, all motor milestones attained in the initial START study were attained, and 2/10 attained the ability to stand with assistance (Mendell et al. 2021).

Building on these findings, the STRIVE-US trial (Day et al., 2021), a single-arm phase 3 study, evaluated the effect of onasemnogene abeparvovec on symptomatic or presymptomatic infants <6 months with SMA1. Patients who had tracheostomy, who required ventilatory support >6h/day, who had baseline hypoxia, or who had evidence of aspiration were excluded. The trial reported a mean dosing age of 3.7 months and demonstrated statistically significant improvements compared to historical controls. At 14 months, 91% of patients survived without permanent ventilation, and 82% remained ventilation-free at 18 months. A key co-primary endpoint, independent sitting, was achieved by 59% of patients at a median age of 12.6 months, an outcome previously unattainable for untreated SMA Type 1 patients. CHOP INTEND motor function assessments showed sustained improvement, with 95% of participants scoring 40 points or higher. These results emphasized both the early and long-term benefits of treatment, particularly in achieving developmental milestones and reducing reliance on ventilatory support.

The STRIVE-EU trial (Mercuri et al., 2021) had a similar design to that of the STRIVE-US trial but had somewhat more permissive inclusion criteria (permitting those who required up to 12 hours per day of ventilatory support). Mean dosing age was 4.1 months, and outcomes were similar to those in STRIVE-US, with 44% achieving functional independent sitting for at least 10s by the 18-month visit and 97% surviving to 14 months free of ventilatory support.

The single-arm phase 3 SPRINT trial (Strauss et al., 2022) shifted focus to presymptomatic infants, further underscoring the importance of early intervention. Fifteen infants with three SMN2 copies were treated within six weeks of birth. All patients survived without permanent ventilation at 14 months, and 14 achieved



independent walking before 24 months. Moreover, 67% maintained body weight above the 3rd WHO percentile without feeding support, and none required nutritional or respiratory assistance. No treatment-related serious adverse events were reported, bolstering the safety profile of early administration. Per Glascock et al. (2020), Cure SMA convened a working group which revised earlier decisions and recommended that infants diagnosed with SMA who have four copies of SMN2 receive immediate treatment.

Despite these promising outcomes, safety remains a significant consideration. Chand et al. (2021) and Friesen et al. (2021) documented hepatotoxicity as a prominent adverse event, with up to 90% of patients experiencing elevated transaminase levels. While most cases resolved by the observation period's end, the prevalence (76.7%) of baseline elevations in presymptomatic patients highlights the need for careful monitoring. Mitigation strategies include prophylactic corticosteroid use, routine hepatology evaluations, and avoidance of hepatotoxic medications. Saffari et al. (2019) also identified immune-mediated complications linked to the adeno-associated virus vector, reinforcing the importance of corticosteroid prophylaxis.

Real-world data from Waldrop et al. (2020), Goedecker et al. (2024), and Weiß et al. (2024) validate the efficacy and safety of onasemnogene abeparvovec in clinical settings, supporting its role as a transformative therapy for SMA and highlighting an inverse correlation between outcomes and age at treatment. Based on evidence from the STRIVE trials, the SPRINT trial, and subsequent studies and recommendations, Mass General Brigham Health Plan considers onasemnogene to be medically necessary for individuals with non-advanced SMA who meet inclusion criteria based on those trials.

Effective Dates

December 1, 2026: Annual review. Reformatted policy. Added link to Itvisma medical necessity guidelines. Expanded exclusions based on FDA label. References updated.

January 2026: Ad hoc review. Updated prior authorization table and added variation for One Care and SCO members.

December 2025: Annual review. Fixed code disclaimer. Criteria updated to include children with up to 4 copies of SMN2 and to note that children receiving any treatment for SMA need to discontinue therapy to receive onasemnogene abeparvovec. Summary of evidence and references updated.

April 2025: Ad hoc review. MassHealth variation updated to include new prior authorization process.

March 2025: Ad hoc review. Summary of evidence added. References updated.

October 2024: Annual review. Clarified Medicare variation language.

September 2024: Ad hoc review. MassHealth variation added.

October 2023: Annual review. Medicare Advantage added to table.

October 2022: Annual review. References updated.

October 2021: Annual review. References updated.

October 2020: Annual review. References updated.

July 2020: Ad hoc review. Added code.

April 1, 2020: Ad hoc review. Updated table and added Criteria section to reflect MassHealth coverage.

December 2019: Effective date.

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