Mass General Brigham
Health Plan

Medical Policy
Zolgensma (Onasemnogene Abeparvovec)

Policy Number: 060

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization required	X	X	X
Authorization not required			

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.

Criteria (Commercial)

1. Criteria for Approval (The member must meet **all** of the following requirements):
    - Member has confirmed and symptomatic genetic diagnosis documented by bi-allelic mutations in the SMN1 gene AND three or less copies of SMN2 gene
    - Member has an anti-adeno-associated viral vector, serotype 9 (AAV9) antibody titer less than or equal to 1:50
    - Member is less than 2 years of age
    - Member has not previously received Zolgensma
    - Member does not have concomitant illness such as severe kidney or liver disease, active viral infection, or symptomatic cardiomyopathy
    - If the member is receiving treatment with Spinraza, that treatment will be discontinued
2. Dosing and Administration
    - Member will receive a single-dose Zolgensma intravenously infusion within accordance of the FDA approved labeling; 1.1×10^{14} vector genomes (vg) per kilogram of body weight.
3. Duration of Therapy
    - Single-dose one-time intravenous infusion per lifetime
4. Exclusions
    - The member has advanced SMA as evidenced 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.

MassHealth Variation
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.

Medicare Variation
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage 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 coverage determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for coverage determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, CMS had no NCD or LCD for onasemnogene abeparvovec.**

Codes

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

This list of codes applies to commercial and MassHealth plans only.

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 STR1VE-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 STR1VE-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 STR1VE-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 SPR1NT 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.

Despite these promising outcomes, safety remains a significant consideration. Chand et al. (2021) and Friese 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 Weiβ 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 STR1VE trials, the SPR1NT trial, and subsequent studies, MGB Health Plan considers onasmnogene to be medically necessary for individuals with non-advanced SMA who meet inclusion criteria based on those trials.

Effective
April 2025: Ad hoc update. MassHealth variation updated to include new prior authorization process.
March 2025: Ad hoc update. Summary of evidence added. References updated.
October 2024: Annual update. Clarified Medicare variation language.
September 2024: Ad hoc update. MassHealth variation added.
October 2023: Annual update. Medicare Advantage added to table.
October 2022: Annual update. References updated.
October 2021: Annual update. References updated.
October 2020: Annual update. References updated.
July 2020: Ad hoc update. Added code.
April 1, 2020: Ad hoc update. Updated table and added Criteria section to reflect MassHealth coverage.
December 2019: Effective date.

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