Mass General Brigham
Health Plan

Medical Necessity Guidelines
Skysona (elivaldogene autotemcel)

Policy Number: 065

Contents

Overview

Skysona is an autologous hematopoietic stem cell (HSC)-based gene therapy indicated for the treatment of patients with confirmed early, active cerebral adrenoleukodystrophy (CALD).

Medicare Advantage

Prior Authorization Required	Yes ☒ No ☐

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, Medicare 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 Initial Approval

   Authorization of a single treatment may be granted to members 4 to 17 years of age for treatment of early, active cerebral adrenoleukodystrophy (CALD) when **ALL** of the following criteria are met:

   A. Documentation of adrenoleukodystrophy as established by meeting BOTH of the following:

i. Elevated plasma very long chain fatty acid levels according to the standard reference values of the performing laboratory.

ii. The presence of a variant in the ABCD1 gene as detected by genetic testing.

B. Documentation of early, active CALD as defined by meeting ALL of the following:
   i. A Loes score between 0.5 and 9 (inclusive) on the 34-point scale.

   ii. A Neurologic Function Score (NFS) less than or equal to 1.

   iii. Gadolinium enhancement on MRI of demyelinating lesions.

C. The member is eligible for a hematopoietic stem cell transplant (HSCT) but an HLA-matched family donor is not available. HLA matching with family members should be explored to optimally inform transplant planning.

D. The member has not taken anti-retroviral medication(s) for at least one month prior to mobilization, OR the expected duration for elimination of the anti-retroviral medication(s) and until all cycles of apheresis are completed.

E. The member has not received a vaccination during the 6 weeks preceding the start of myeloablative conditioning, and until hematological recovery following treatment with Skysona.

F. The member does not test positive for HIV-1 and HIV-2, hepatitis B virus (HBV), or hepatitis C (HCV). and Human T-lymphotropic virus 1 & 2 (HTLV-1/HTLV-2) in accordance with clinical guidelines before collection of cells for manufacturing. Documentation of planned testing is required.

G. The member has been evaluated for hepatic function to ensure HSC transplantation is appropriate as defined by one of the following:
   i. Alanine transaminase (ALT) value less than 2.5x the upper limit of normal (ULN), or

   ii. Aspartate transaminase (AST) value less than 2.5x ULN, or

   iii. Total bilirubin value less than 3.0 milligram per deciliter (mg/dL), except if there is a diagnosis of Gilbert's Syndrome, and the member is otherwise stable.

H. The member does not have any current malignancies.

I. The member has not received Skysona or any other gene therapy.

2. Dosing and Administration
   - The recommended dose is a single dose, given intravenously, containing a minimum of 5.0 x 10^6 CD34+ cells/kg of body weight in which body weight is based on individual's weight prior to first apheresis.

   - Full myeloablative and lymphodepleting conditioning must be administered before infusion of Skysona.

3. Duration of Therapy
   - Single treatment course

   - The member should receive seizure, hepatic veno-occlusive disease, anti-fungal, and antibiotic prophylaxis as needed.

   - Additional courses of therapy are considered experimental/investigational.

4. Facility Criteria
    - The medication is prescribed by a hematologist, a neurologist, and/or a stem cell transplant specialist
    - The treatment will be administered at a Skysona Qualified Treatment Center.

Mass General Brigham ACO

Prior Authorization Required	Yes ☒ No ☐

Prior authorization requests for Skysona for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Skysona are found in Table 72: Agents not Otherwise Classified.

One Care and Senior Care Options (SCO)

Prior Authorization Required	Yes ☒ No ☐

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 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 ☐

Prior authorization for Skysona for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See the Prime Therapeutics policy for Skysona for more information.

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
J3387	Injection, elivaldogene autotemcel, per treatment

Summary of Evidence

Elivaldogene autotemcel (Skysona, eli-cel), a lentiviral gene therapy developed by Bluebird Bio, received FDA accelerated approval in September 2022 for the treatment of early, active cerebral adrenoleukodystrophy (CALD), a rare and fatal neurodegenerative disease. The pivotal STARBEAM (ALD-102) study evaluated eli-cel in a Phase 2/3 single-arm, open-label trial of boys aged ≤17 years with early-stage CALD. In this study, eli-cel was administered following conditioning with busulfan-cyclophosphamide. The initial report, by Eichler et al. (2017), reported on the first 17 patients, aged 4-13 (median 6). The study achieved its primary endpoint of major functional disability (MFD)-free survival, with a median follow-up of 29.4 months showing sustained disease stabilization in 94% of evaluable participants. A subsequent report of the same study, by Eichler et al. (2024), included 32 patients. Of those, 91% survived 24 months with no major functional disabilities, and at the most recent follow-up (median 60.2 months) 81% survived with no major functional disabilities. A second phase 2-3 study of the same agent, ALD-104, is in process and has not yet reported efficacy outcomes. The treatment protocol in ALD-104 differed from that of ALD-102 in that 104 used busulfan-fludarabine as the conditioning

regimen, used plerixafor mobilization consistently, and used a fixed dose of transducing viral particles relative to host cells (Duncan et al. 2024).

Despite the promising early efficacy data, recent reports of hematologic malignancy caused by insertional oncogenesis have raised major safety concerns. As reported by Duncan et al. (2024), 6 cases of myelodysplastic syndrome and 1 case of acute myeloid leukemia developed between 14-92 months post-treatment among 67 patients enrolled in the ALD-102 and ALD-104 studies, including 1/32 in ALD-102 and 6/35 in ALD-104. The malignant cells showed evidence of clonal vector insertion within oncogenes and clonal evolution with acquisition of somatic genetic defects. It has been hypothesized that the oncogenesis is related to the strong viral MND promoter used in eli-cel, and perhaps also to the profound immune suppression caused by fludarabine (Dunbar 2024). Other adverse events have included myelosuppression, infections, and immune-related complications; a REMS and black-box warning are in effect.

Based on these safety concerns, and the fact that long-term safety beyond 5 years remain unknown, consensus guidelines recommend allogeneic stem cell transplantation, rather than lentiviral gene therapy for most patients with early-stage CALD (Engelen M, et al. 2022). Eli-cel may still have a role, particularly for patients for whom no appropriate HLA-matched donor can be identified. MGB Health Plan considers eli-cel medically necessary for members without an appropriate donor and who otherwise meet inclusion criteria consistent with those in the pivotal trial reported by Eichler (2017).

Effective Dates

April 2026: Ad hoc update. Reformatted policy. Clarified Medicare Advantage section and hierarchy of criteria in One Care and SCO section. Added Prime Therapeutics information to Commercial and Qualified Health Plans section. Updated code list.
January 2026: Ad hoc update. Updated prior authorization table and added variation for One Care and SCO members.
October 2025: Annual update. Fixed code disclaimer.
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. Codes updated. Code disclaimer added.
September 2024: Ad hoc update. Added MassHealth variation. Fixed Medicare variation language. References updated.
May 2023: Effective Date.

References

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