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Etuvetidigene autotemcel

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

Etuvetidigene autotemcel (Waskyra™) **may be considered medically necessary** for individuals meeting **ALL** the following criteria:

- Individual has a diagnosis of Wiskott-Aldrich Syndrome (WAS) with a confirmed genetic mutation in the WAS gene with at least one of the following:
  - Severe clinical score (Zhu clinical score ≥ 3); or
  - Severe WAS mutation; or
  - Absent Wiskott-Aldrich Syndrome protein (WASP) expression; and
- Individual is ≥6 months of age; and

- Individual is an appropriate candidate for hematopoietic stem cell transplantation (HSCT) but lacks a suitable human leukocyte antigen (HLA)-matched related stem cell donor; and
- If prior allogenic HSCT has occurred, there is documentation that the individual has no residual cells of donor origin; and
- Dosing is limited to one treatment per lifetime.

Etuvetidigene autotemcel (Waskyra™) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration (FDA) approved indications, and when the above criteria are not met.

Policy Guidelines

The U.S. Food and Drug Administration (FDA) label for etuvetidigene autotemcel (Waskyra™) lists several warnings and precautions for use. The following may occur after treatment:

- Hypersensitivity and infusion-related reactions.
- Failure of stem cell engraftment.
- Cytopenias (including anemia, neutropenia and thrombocytopenia).
- Serious infections.
- Hepatic veno-occlusive disease.
- False positive human immunodeficiency virus (HIV) test results are possible when using polymerase chain reaction (PCR) assays for HIV testing. Alternative methods for HIV screening should be used.
- There is also a risk of developing cancers later in life after treatment.
- Because Waskyra is manufactured using human and bovine-related components, there is a risk of transmission of infectious diseases or agents.

The label also notes that individuals treated with Waskyra should not donate blood, organs, tissues or cells for transplantation at any time in the future.

Description

Wiskott-Aldrich Syndrome

Wiskott-Aldrich syndrome (WAS) is a rare X-linked disorder with a characteristic triad of immunodeficiency, thrombocytopenia, and eczema. (2) It occurs almost exclusively in boys with an incidence of 4 in 1 million live male births in the United States. There are approximately 500 WAS patients in the United States. The disease has a similar incidence in countries around the world. (3)

A defect of the WAS gene on the short arm of the X chromosome causes the disease. The WAS gene allows cells to produce Wiskott-Aldrich Syndrome protein (WASp) which expressed by non-erythroid hematopoietic cells. The WASp regulates and helps organize the scaffolding (cytoskeleton) of the cell which is made up of filaments of the protein actin. The actin cytoskeleton regulates many functions within the cell such as growth, cell movement and

signaling within the cell. Over 300 WAS gene mutations have been identified. The WAS gene mutation results in cells with either no WASp or a deficiency of WASp, which affects the ability of cells to function properly. In most cases, there is an association between the specific mutation and the physical manifestations of WAS. Different defects in the WAS gene lead to different disease traits, such as Classic WAS, X-linked thrombocytopenia (XLT), intermittent thrombocytopenia and X-linked neutropenia (XLN), all of which are classified together as WAS Related Disorders. (2, 3)

The Classic (severe) form of WAS presents in early childhood. Thrombocytopenia is present at birth and affected individuals may manifest symptoms such as prolonged bleeding from the umbilical stump or after circumcision. Bruising, gastrointestinal bleeding, bloody urine and intracranial bleeding my occur. Sufferers with a severe WAS phenotype may have recurrent infections in early infancy. However, in most patients with classic WAS, the frequency of infections increases with age. Extensive eczema is noted, often with superinfection. Enlargement of the lymph nodes, spleen and liver may occur. Patients with classic WAS tend to develop autoimmune complications and lymphoma or other malignancies, often leading to early death. (4)

Treatment

Conventional treatment and supportive care for Classic WAS may include steroids, prophylactic medications to prevent injection, and transfusions of blood products such as platelets. Intravenous immune globulin (IVIG) therapy is indicated for individuals with severe antibody deficiency. Immunosuppressive treatment may be required to treat autoimmune manifestations. Splenectomy may be considered in carefully selected individuals to reverse the thrombocytopenia and arrest the bleeding tendency by increasing the number of circulating platelets. (4)

Hematopoietic cell transplantation (HCT) was previously the only potentially curative treatment for Classic WAS. Excellent results have been reported for individuals with human leukocyte antigen (HLA)-matched family or unrelated donors or partially matched cord-blood donors, achieving 100 percent overall survival in a 2018 report of 34 transplanted patients with WAS. Gene therapy has also been investigated as an alternative and potentially curative therapy for those with WAS without a suitable donor for HCT. (4)

Etuvetidigene autotemcel (Waskyra^{TM}) is an autologous hematopoietic stem cell (HSC)-based gene therapy. (1) It is prepared from the patient's own HSCs, which are collected using apheresis procedure(s). The autologous cells are enriched for CD34+ cell and then transduced ex vivo with a replication incompetent self-inactivating (SIN) human immunodeficiency virus-1 (HIV1)-based lentiviral vector (LVV) that has been modified to carry the WAS gene sequence under the control of the human WAS promoter. The transduced CD34+ cells are washed, formulated into a suspension, and then cryopreserved.

Etuvetidigene autotemcel (Waskyra) is manufactured for each individual patient into infusion bags, which are cryopreserved before being thawed prior to administration. After infusion, the

genetically modified cells engraft in the bone marrow, repopulate the hematopoietic compartment, and restore functional WASp expression in affected cells. (1)

Regulatory Status
In December 2025, the U.S. Food and Drug Administration (FDA) approved Etuvetidigene autotemcel (Waskyra) for the treatment of pediatric patients aged 6 months and older and adults with WAS who have a mutation in the WAS gene for whom hematopoietic stem cell transplantation (HSCT) is appropriate and no suitable human leukocyte antigen (HLA)-matched related stem cell donor is available. It is administered as a single intravenous infusion.

The safety and effectiveness of Waskyra have not been established in pediatric patients younger than 6 months of age. (1)

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for etuvetidigene autotemcel (Waskyra™).

Etuvetidigene autotemcel (Waskyra) (1)
The efficacy of Waskyra was evaluated in two clinical studies, Study 1 (201228; NCT01515462) and Study 2 (OTL-103-4; NCT03837483) as well as in patients from an expanded access program (EAP). Study 1 was a prospective, open-label, single-arm, single-center study (n=8) that evaluated the safety and efficacy of Waskyra fresh formulation compared to 12-month pre-treatment outcomes. Study 2 is an ongoing, open-label, single-arm, multicenter study (n=10) evaluating the efficacy of Waskyra cryopreserved formulation compared to 12-month pre-treatment outcomes. The expanded access program included Hospital Exemption (HE) 205030 (n=3), and Compassionate Use Program (CUP) 206257 (n=6) which provided Waskyra treatment to patients with Wiskott-Aldrich syndrome (WAS).

The studies and the expanded access program enrolled patients who had a diagnosis of WAS confirmed by genetic mutation and at least one of the following criteria: 1) severe clinical score (Zhu clinical score ≥ 3), 2) severe WAS mutation, or 3) absent Wiskott-Aldrich syndrome protein (WASP) expression. All patients lacked a suitable human leukocyte antigen (HLA)-matched donor. Patients with prior allogeneic hematopoietic stem-cell transplantation (HSCT) within 6 months or evidence of residual cells of donor origin, prior gene therapy, human immunodeficiency virus (HIV) infection and cytogenetic alterations were excluded.

Patients underwent hematopoietic stem-cell (HSC) collection by bone marrow collection (n=5), from apheresis following the administration of HSC mobilizing agents (n=21), or from both sources (n=1). Prior to treatment, patients received rituximab and a conditioning regimen with busulfan, and fludarabine. Rituximab was administered as a single dose of 375 mg/m² on Day –22 (+/-1). Busulfan was given in eight doses every 6 hours from Days -4 to -2, with dosing adjusted based on pharmacokinetic monitoring to achieve a target cumulative area under the

curve (AUC) of 48,000±10% ng/mL per hour. Fludarabine was given at a total dose of 60 mg/m², split into two doses on Days -4 and -3. Patient then received a single infusion of Waskyra through a central venous access at a dose range of 7– 31×10^6/kg $CD34^+$ cells (median dose: 16.90×10^6/kg).

The demographic characteristics were as follows: median age was 2.6 years (range 1 to 35 years), all patients (100%) were male, 20 patients (74%) were White, 4 patients (15%) were Asian, 2 patients (7%) were African American, and 1 patient was American Indian or Alaska Native. Three patients (11%) were Hispanic or Latino. Twenty-six out of 27 patients were included in efficacy evaluation. One patient did not receive Waskyra treatment due to mobilization failure and was excluded from the analyses.

The major efficacy outcomes were the rate of severe infections during the 6-to-18-month period after Waskyra infusion compared with the 12-month pre-treatment period, and the rate of moderate or severe bleeding episodes during the 12-month period after Waskyra infusion compared with the 12-month pre-treatment period.

The rate of severe infections decreased from 2.0 (95% confidence interval [CI]: 1.50, 2.61) infections per patient year observation (PYO) in the 12 months pre-treatment period to 0.2 (95% CI: 0.04, 0.40) per PYO infections in 6-18 months post-gene therapy.

The rate of moderate and severe bleeding events decreased from 2.0 (95% CI: 1.50, 2.61) events per PYO in the 12 months pre-treatment to 0.8 (95% CI: 0.49, 1.22) events per PYO in the 12 months after Waskyra treatment.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J3386

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. Prescribing Label: Waskyra (etuvetidigene autotemcel) suspension, for intravenous use. December 2025. Available at <https://www.accessdata.fda.gov/scripts/cder/daf.index.cfm> (accessed April 10, 2026).

Other:

2. Malik MA, Masab M. Wiskott-Aldrich Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; (Updated June 26, 2023). Available at <https://www.ncbi.nlm.nih.gov> (accessed April 21, 2026).
3. Wiskott-Aldrich Foundation. Epidemiology and Disease Mechanism. n.d. Available at <https://www.wiskott.org> (accessed April 21, 2026).
4. Ochs, Hans D. Wiskott-Aldrich syndrome. In: UpToDate, Puck JM (Ed), UpToDate. Waltham, MA: UpToDate Inc. Available at <https://www.uptodate.com> (accessed April 21, 2026).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
07/01/2026	New medical document. Etuvetidigene autotemcel (Waskyra™) may be considered medically necessary for individuals meeting ALL the following criteria: Individual with a diagnosis of Wiskott-Aldrich Syndrome (WAS) with a confirmed genetic mutation in the WAS gene with at least one of the following: Severe clinical score (Zhu clinical score ≥ 3); or Severe WAS mutation; or Absent Wiskott-Aldrich Syndrome protein (WASP) expression; and Individual is ≥6 months of age; and Individual is an appropriate candidate for hematopoietic stem cell transplantation (HSCT) but lacks a suitable human leukocyte antigen (HLA)-matched related stem cell donor; and If prior allogenic HSCT has occurred, there is documentation that member has no residual cells of donor origin; and Dosing is limited to one treatment per lifetime. Etuvetidigene autotemcel (Waskyra™) is considered experimental, investigational and/or unproven for all other non-Food and Drug Administration (FDA) approved indications, and when the above criteria are not met.