Molina Clinical Policy
Waskyra (etuvetidigene autotemcel)
Policy No. 479

Last Approval: 06/10/2026
Next Review Due By: February 2027

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy covers the use of Waskyra (etuvetidigene autotemcel) for the treatment of Wiskott Aldrich Syndrome (WAS).

Wiskott–Aldrich Syndrome is a hematopoietic-specific actinopathy that manifests as a primary immunodeficiency. WAS is defined by a unique set of features including immunodeficiency, micro-thrombocytopenia, eczema, autoimmune disorders, and lymphoid malignancies (Ochs et al. 2009). WAS is caused by pathogenic variants in the WAS gene. The WAS gene codes for the WAS protein. The WAS protein (WASP) helps reorganize the actin cytoskeleton upon signaling allowing dynamic control of cell shape, cell movement and membrane functions. Errors in the WAS protein impair cytoskeletal changes important for cell migration, adhesion, cell division, and formation of immune-synapses necessary for communication through cell contact. WASP dysfunction impairs platelet formation, T-cell response to infections, B cell regulation, and i-NTK cells are less able to surveil for cancer and suppress autoimmunity.

The WAS gene is located on the X chromosome making WAS an X-linked disorder primarily affecting males. Severity varies from the mildest form (e.g., X- linked thrombocytopenia) to the more severe life-threatening form (e.g., classic WAS). Another phenotypic variation of WAS, called X-linked neutropenia (XLN), is exceedingly rare and due to gain of function mutations in the WAS gene. XLN has a more moderate course but still includes recurrent infections and a high risk of myelodysplasia. Although WAS is X linked, there is some early literature suggesting female carriers may have mild features of WAS (Chandrakasan et al. 2025). Onset of classic WAS begins at birth with petechiae, bruises, and bloody diarrhea. Typical survival in severe WAS is only 15 years with supportive treatment. Overall, the prognosis is poor without stem cell transplant.

It is important to note there is a phenocopy of WAS caused by mutations in a gene that works closely with WASP. That protein is called WISP (WAS Interacting Protein). It is important to confirm patients with a WAS phenotype have a pathogenic variant in the WAS gene before considering a gene therapy aimed at compensating only for mutations in the WAS gene.

Incidence of WAS is 1 in 4 million live male births (WAS Foundation 2025). There are approximately 500 individuals with classic WAS in the United States.

Treatment options focus on symptom management unless a stem cell transplant donor is available. The primary unmet need for treatment in WAS is in those without an available donor. Therefore, the FDA approved Waskyra in December 2025 after successfully meeting the standards for the FDA's accelerated approval pathway. Waskyra is an ex vivo gene therapy using a lentiviral system to introduce a functional WAS gene into patient cells. Manufacture and quality control of the genetically engineered autologous stem cells may take several weeks and myeloablative conditioning is required.

COVERAGE POLICY

All Gene Therapy requests require Molina Medical Director review.

Waskyra (Etuvetidigene autotemcel) for the treatment of Wiskott Aldrich Syndrome (WAS) may be **considered medically necessary** when ALL the following criteria are met:

1. Diagnosis of severe Wiskott Aldrich syndrome confirmed by genetic analysis and at least one of the following criteria:
    a. Severe WAS mutation ("nonsense mutations, deletions and insertions resulting in absent WAS protein [WASP] expression or truncated WASP.")
    b. Absence of Wiskott Aldrich syndrome protein expression (Absent defined as WASP expression < 5%)
    c. Severe clinical score (Zhu clinical score ≥ 3; See supplemental section below for scoring system)
2. Member is > 6 months of age
3. Member does not have an HLA-identical sibling donor, or suitable 10/10 matched unrelated donor, or suitable 6/6 unrelated cord blood donor
4. Member is negative for HIV-infection and Hepatitis C RNA testing
5. Member does not have neoplasia (apart from local skin cancer)
6. Member does not have cytogenetic alterations typical of myelodysplastic syndrome/acute myeloid leukemia
7. Member does not have end-organ dysfunction or any other severe disease which would make them intolerant to reduced intensity conditioning required for Waskyra therapy
8. Member has not undergone allogeneic hematopoietic stem cell transplantation in the previous 6 months
9. Member has not had allogeneic hematopoietic stem cell transplantation with evidence of residual cells of donor origin
10. Member has not had previous treatment with hematopoietic stem cell gene therapy

ADMINISTRATION SETTING: This gene therapy is ex-vivo. For ex-vivo route, *inpatient administration* is generally anticipated.

QUANTITY LIMITATIONS: **FDA approved dosing with one-time dose per lifetime.** Additional infusions of Waskyra will not be authorized.

CONTINUATION OF THERAPY: Waskyra is indicated as a one-time infusion only. Repeat treatment or re-administration of a dose is not supported by labeling or compendia and is not considered medically necessary.

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Waskyra completed the accelerated approval pathway and became FDA approved in December 2025 based on evidence from trial NCT01515462 (TIGET-WAS) and other interim data taken from both the expanded access program and the ongoing phase 3 trial (NCT03837483).

Interim data from the TIGET-WAS trial were published by Ferrua et al. (2019) after the first 8 patients completed ≥3 years of follow-up. The TIGET-WAS trial was a non-randomized, open-label, phase ½ study evaluating the safety and efficacy of a single infusion of etuvetidigene therapy (OTL-103) in pediatric patients with severe WAS. The average participant age was 2.2 years. Severity was defined by: WAS gene mutation, absent WAS protein (WASP) expression, or Zhu clinical score ≥3 (Zhu et al. 1995). Participants were excluded if they had an HLA-identical sibling donor available. Children less than 5 years were allowed if they did not have a suitable 10/10 matched unrelated donor or 6/6 cord blood donor.

Primary safety endpoints were safety of the conditioning regimen and safety of lentiviral gene transfer into hematopoietic stem/progenitor cells (HSPCs). At more than 3 years follow-up there have been no abnormal clonal proliferation reported. Post gene therapy infections occurred and were attributed to conditioning. Recorded infections resolved 6 months after gene therapy. Per published records no adverse events have been attributed to Waskyra.

Efficacy endpoints were overall survival, sustained engraftment, expression of corrected WAS protein, improved T-cell function, platelet count and platelet volume as well as antigen specific vaccine responses. Overall survival was 100%. All had favorable outcomes with respect to infections and bleeding events. All patients successfully engrafted the engineered Waskyra cells & protein expression was observed in vivo. Baseline expression of WASP as measured from lymphocyte fractions was 3.9 percent, which rose to 66.7% 12 months after treatment. Measures of WASP expression in platelets also increased from 19.1% to 76.6%. Clinically, patients had fewer severe infections, from an average of 2.38 per year before treatment to 0.17 per year by the third year post-treatment. Immunoglobulin supplementation was stopped in 7 out 8 patients at the time of data cutoff (2016). Markers of autoimmunity were lower, and eczema was less or resolved in 7 of 8 patients. Bleeding was also reduced and platelet counts were higher, rising from 20 $x10^9$ / liter to 50 $x10^9$ / liter. In two participants, platelets were greater than 100 $x10^9$ per liter allowing those individuals to stop platelet transfusions. Days in the hospital decreased substantially. Four patients were living in a protected environment prior to Waskyra and were able to enter the community (i.e., go to school etc.) after gene therapy. Five patients became eligible to start childhood vaccinations and responded to those vaccinations with antibody responses.

A phase 3 study (NCT03837483) is active but incomplete. This study is an open label single arm study to evaluate the safety and efficacy of Waskyra in those with WAS. Ten participants have been enrolled. Interim participant data was used from this trial to support the FDA approval process.

Additional data from the FDA label shows a total of 30 patients treated with Waskyra (several from the expanded access program). Participants showed a continuation of the positive outcomes. Data is not published in peer reviewed journal yet.

National and Specialty Organizations

Currently, there are no national guidelines addressing the use of Waskyra.

SUPPLEMENTAL INFORMATION

Wiskott Aldrich Scoring System Per Zhu et al. (1995)

The severity of WAS-associated symptoms was scored from 1 to 5, based on the following criteria.

- Score of 1: Patients with thrombocytopenia and small sized platelets without any other symptoms or clinical findings.
- Score of 2: Patients with platelet abnormalities and a history of mild, transient eczema, with or without minor infections.

- Score of 3: Patients with persistent but manageable eczema, with or without recurrent infections.
- Score of 4: Patients with persistent and difficult to control eczema, with frequent potentially life-threatening infections.
- Score of 5: Patients presenting with eczema and/or frequent infections who developed autoimmune disease.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

CPT	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System) Codes

HCPCS	Description
J3386	Injection, etuvetidigene autotemcel, per treatment [Effective 07/01/2026]
C9399	Unclassified drugs or biologicals [when specified as Waskyra (Etuvetidigene autotemcel)]
J3590	Unclassified biologics [when specified as Waskyra (Etuvetidigene autotemcel)]

CODING DISCLAIMER: Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

06/10/2026	Inpatient setting recommendation added to Administration section of coverage criteria.
02/11/2026	New policy. IRO Peer Review February 5, 2026, by a Board-certified physician in Pediatric Hematology/Oncology.

REFERENCES

1. Chandrakasan S, Westbrook A, Griffith LM, et al. Clinical spectrum of Wiskott-Aldrich syndrome carriers: Self-reported survey of 193 carriers. Clin Immunol. 2025 Dec 17;283:110658. doi: 10.1016/j.clim.2025.110658. Epub ahead of print. PMID: 41419161.
2. ClinicalTrials.gov. National Library of Medicine; NCT01515462. Gene Therapy for Wiskott-Aldrich Syndrome (TIGET-WAS). Accessed December 20, 2025. Updated April 4, 2025 https://clinicaltrials.gov/study/NCT01515462?term=NCT01515462&rank=1
3. ClinicalTrials.gov. National Library of Medicine; NCT03837483. A Clinical Study to Evaluate the Use of a Cryopreserved Formulation of OTL-103 in Subjects With Wiskott-Aldrich Syndrome. Accessed December 20, 2025. Updated September 29, 2025.
4. Ferrua F, Cicalese MP, Galimberti S, et al. Lentiviral haemopoietic stem/progenitor cell gene therapy for treatment of Wiskott-Aldrich syndrome: interim results of a non-randomised, open-label, phase 1/2 clinical study. Lancet Haematol. 2019 May;6(5):e239-e253. doi: 10.1016/S2352-3026(19)30021-3. Epub 2019 Apr 10. PMID: 30981783; PMCID: PMC6494976.
5. Hayes. Etuvetidigene Autotemcel (Waskyra; The San Raffaele Telethon Institute For Gene Therapy) for Wiskott-Aldrich Syndrome. Emerging technology report Published 12/18/2025. Accessed 12/20/25. https://evidence.hayesinc.com/.
6. Ochs HD, Filipovich AH, Veys P, et al. Wiskott-Aldrich syndrome: diagnosis, clinical and laboratory manifestations, and treatment. Biol Blood Marrow Transplant. 2009 Jan;15(1 Suppl):84-90. doi: 10.1016/j.bbmt.2008.10.007. PMID: 19147084.
7. Vallée TC, Glasmacher JS, Buchner H, et al. Wiskott-Aldrich syndrome: a study of 577 patients defines the genotype as a biomarker for disease severity and survival. Blood. 2024 Jun 13;143(24):2504-2516. doi: 10.1182/blood.2023021411. PMID: 38579284.
8. Wiskott Aldrich Foundation 2025. https://www.wiskott.org/About-WAS/understanding-was/-epidemiology-and-disease-mechanism
9. Zhu Q, Zhang M, Blaese RM, et al. The Wiskott-Aldrich syndrome and X-linked congenital thrombocytopenia are caused by mutations of the same gene. Blood. 1995 Nov 15;86(10):3797-804. PMID: 7579347.