EXPRESS SCRIPTS®

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Immune Disorders – Gene Therapy – Waskyra UM Medical Policy
- Waskyra® (etuvetidigene autotemcel intravenous infusion – Fondazione Telethon ETS)

REVIEW DATE: 04/29/2026

OVERVIEW

Waskyra, an autologous hematopoietic stem cell (HSC)-based gene therapy, is indicated for the treatment of **Wiskott-Aldrich Syndrome (WAS) in pediatric patients ≥ 6 months of age and adults** who have a **mutation in the *WAS* gene** and for whom a **hematopoietic stem cell transplantation (HSCT) is appropriate** and **no suitable human leukocyte antigen (HLA)-matched related stem cell donor is available**.[1]

Waskyra is prepared from the patient's own HSCs, which are obtained via mobilization/apheresis procedure(s).[1] The CD34+ cells collected from the patient are then transduced *ex vivo* with a replication-incompetent, self-inactivating lentiviral vector encoding for human *WAS* complementary deoxyribonucleic acid (cDNA). The modified cells are re-infused into patients after a conditioning regimen.

Waskyra is given one-time (per lifetime) as a single dose; the minimum recommended dose is 7 x 10^6 cluster of differentiation 34+ (CD34+) cells/kg of body weight.[1] Waskyra is given as an intravenous (IV) infusion. Each dose of Waskyra is provided in one to eight infusion bags; each bag contains 10 mL to 20 mL of Waskyra.

Disease Overview

WAS, a rare X-linked primary immunodeficiency, is characterized by microthrombocytopenia, recurrent infections, eczema, and an increased risk for autoimmunity and lymphoid malignant diseases.[2] The estimated incidence of WAS is 1 to 10 per million live male births; WAS occurs almost exclusively in males.

WAS results from changes in the *WAS* gene, which encodes the Wiskott-Aldrich Syndrome protein (WASP).[2] WASP is an intracellular key regulator and is crucial for normal cell function, particularly for cells of the immune system and platelets.[2,3] Clinical manifestations of WAS include bleeding, immunodeficiency, eczema, autoimmune manifestations, and malignancies.[2] Severity of immunodeficiency depends on the type of WAS variant and resulting protein expression. Patients with the most severe forms of disease have severely decreased or absent WASP and tend to have poor prognosis.[2,3] Patients with milder disease tend to have decreased WASP and generally have good prognosis and life expectancy is close to that of the normal population.

Clinical Efficacy

The clinical program for Waskyra included two clinical studies (Study 1 and Study 2) and an expanded access program.[1,4] Pooled data for all of the patients who have received Waskyra for the treatment of WAS (n = 27) are reported.

All of the enrolled patients had a diagnosis of WAS confirmed by genetic testing and at least one of the following: 1) severe clinical score (Zhu clinical score ≥ 3); 2) severe *WAS* variant; 3) absent WASP

expression.[1] The Zhu score is a five-point scale that assesses disease severity and considers factors such as thrombocytopenia, eczema, immunodeficiency, infections, autoimmunity, and malignancies.[4] Severe *WAS* variants generally include nonsense changes, deletions, and insertions that lead to either no (or absent) WASP expression or the production of a shortened WASP. Absent WASP expression was defined as < 5% of lymphocytes expressing WASP. In addition, patients could not have a suitable HLA-matched donor.[1,4] Key exclusion criteria were patients who had a prior allogeneic HSCT within the past 6 months or with evidence of residual cells of donor origin; patients who have had prior gene therapy; and patients with human immunodeficiency virus (HIV) infection and cytogenetic alterations.[1]

Patients received a single infusion of Waskyra at a dose of 7 to 31 x 10^6 CD34+ cells/kg (median dose, 16.90 x 10^6 CD34+ cells/kg).[1,4]

There were three primary efficacy endpoints for the integrated analysis: overall survival; the rate of severe infections (defined as Grade 3 or above) from 6 months to 18 months after treatment compared to the 12 months before treatment; and the rate of moderate and severe bleeding events in the first 12 months after treatment compared to the 12 months before treatment.[1,4] At the end of follow-up, overall survival was 96%. The median duration of patient follow-up in all surviving patients was 5.72 years.[4] The rate of severe infections was reduced from 2.0 infections per patient-year observation in the 12 months before Waskyra treatment to 0.2 infections per patient-year observation during the 6 to 18 months after Waskyra treatment.[1,4] The rate of moderate and severe bleeding events decreased from 2.0 events per patient-year observation in the 12 months before Waskyra administration to 0.8 events per patient-year observation in the 12 months following Waskyra treatment.

Treatment of WAS

There is presently no consensus regarding the management of patients with WAS.[2] Supportive care for patients with WAS includes broad-spectrum antibiotics, antivirals, and/or antifungals, platelet transfusions (to prevent bleeding), and topical corticosteroids (to treat eczema). Other therapies used to manage patients with WAS include IV immune globulin, eltrombopag, and immunosuppressives. Allogeneic HSCT is the only proven curative treatment.[2,3,6] Cells in the bone marrow (stem cells) are abnormal and need to be replaced with healthy donor stem cells. HSCT may not be an option for all patients due to a lack of a suitable donor.[6] Furthermore, HSCT is associated with risks such as graft-versus-host disease and side effects from the conditioning regimen.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Waskyra. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Waskyra as well as the specialized training required for administration of Waskyra, approval requires Waskyra to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one time (per lifetime) as a single dose. The approval duration is 1 year to allow for an adequate timeframe to prepare and administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. In the criteria for Waskyra, as appropriate, the symbol (†) is noted next to the specified gender. In this context, the specified gender is defined as follows: females/males are defined as individuals with the biological traits of a woman/man, regardless of the individual's gender identity or gender expression.

All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation. Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with EviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@EviCore.com prior to completing the review.

Documentation: Documentation is required for use of Waskyra as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Waskyra is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Wiskott-Aldrich Syndrome.** Approve a one time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, and L):
   - **A)** Patient is ≥ 6 months of age; AND
   - **B)** Patient has not received Waskyra in the past **[verification in claims history required]**; AND
     Note: If there is no claim for Waskyra (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Waskyra.
   - **C)** According to the prescribing physician, a hematopoietic stem cell transplantation is appropriate for the patient; AND
   - **D)** If the patient had a prior allogeneic hematopoietic stem cell transplantation (HSCT), patient meets BOTH of the following (i and ii):
     - **i.** The prior allogeneic HSCT was completed at least 6 months ago; AND
     - **ii.** Patient does not have evidence of residual cells of donor origin; AND
   - **E)** Patient meets ONE of the following (i or ii):
     - **i.** Patient does not have a Human Leukocyte Antigen (HLA)-matched donor; OR
     - **ii.** Patient has an HLA-matched donor, but the individual is not able or is not willing to donate; AND
   - **F)** Diagnosis of Wiskott-Aldrich Syndrome was confirmed by BOTH of the following (i and ii) **[documentation required]**:
     - **i.** Genetic variant in the Wiskott-Aldrich Syndrome gene; AND
     - **ii.** Patient meets ONE of the following (a, b, or c):
       - **a)** Severe clinical phenotype (Zhu clinical score ≥ 3); OR
       - **b)** Severe Wiskott-Aldrich Syndrome variant; OR
       - **c)** Absent Wiskott-Aldrich Syndrome protein (WASP) expression; AND
   - **G)** Patient does not have any of the following (i, ii, and iii):
     - **i.** Prior or current human immunodeficiency virus (HIV) infection; AND
     - **ii.** Prior or current neoplasia; AND
     - **iii.** Prior or current cytogenetic alterations typical of malignancies; AND
       Note: Examples of cytogenetic alterations include those typical of myelodysplastic syndrome or acute myeloid leukemia.
   - **H)** According to the prescribing physician, the patient meets ALL of the following (i, ii, and iii):

i. Patient will undergo mobilization, apheresis, and myeloablative conditioning; AND
ii. A granulocyte-colony stimulating factor product will be utilized for mobilization; AND
Note: Filgrastim products are examples of a granulocyte-colony stimulating factor therapy.
iii. Busulfan and fludarabine will be used for myeloablative conditioning; AND

I) According to the prescribing physician, a patient of reproductive potential meets ONE of the following (i or ii):
i. A female† of reproductive potential meets BOTH of the following (a and b):
a) A negative serum pregnancy test will be confirmed prior to the start of mobilization and re-confirmed prior to conditioning procedures and before administration of Waskyra; AND
b) Patient will use an effective method of contraception from the start of mobilization through at least 6 months after administration of Waskyra; OR
ii. A male† of reproductive potential will use an effective method of contraception from the start of mobilization through at least 6 months after administration of Waskyra; AND

J) The medication is prescribed by a hematologist or a stem cell transplant physician; AND
K) Current patient body weight has been obtained within 30 days **[documentation required]**; AND
L) If criteria A through K are met, approve one dose of Waskyra by intravenous infusion to provide a one-time (per lifetime) single dose, which contains a minimum of 7 x 10^6 CD34+ cells/kg of body weight **[verification required]**.
Note: A single dose of Waskyra consists of one to eight infusion bag(s).

† Refer to the Policy Statement.

Dosing. The recommended dose of Waskyra is a one time (per lifetime) single intravenous infusion of a minimum of 7 x 10^6 CD34+ cells per kg body weight.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Waskyra is not recommended in the following situations:

1. **Prior Receipt of Gene Therapy.** Patients who have had prior gene therapy were excluded from the Waskyra clinical studies. Waskyra has not been studied in a patient who has received prior gene therapy.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Waskyra® intravenous infusion [prescribing information]. Rome, Italy: Fondazione Telethon ETS; December 2025.
2. Malik MA, Masab M. Wiskott-Aldrich Syndrome. In: StatPearls (internet). Treasure Island (FL): StatPearls Publishing. Updated June 2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK539838/. Accessed on March 23, 2026.
3. Wiskott-Aldrich Foundation. Available at: https://www.wiskott.org/About-WAS/treatment-of-was. Accessed on March 23, 2026.
4. Waskyra – FDA summary basis for regulatory action. Available at: https://www.fda.gov/media/190281/download?attachment. Accessed on March 23, 2026.
5. 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-randomized, open-label, phase 1/2 clinical study. *Lancet Haematol*. 2019;6:e239-e253.
6. Alexander JL, Davila Saldana BJ, Brazauskas R, et al. Hematopoietic cell transplantation for Wiskott-Aldrich syndrome: A Primary Immune Deficiency Treatment Consortium (PIDTC) Report. *Blood Adv*. 2026;10:1783-1798.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	04/29/2026