14 November 2025
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

Waskyra (etuvetidigene autotemcel)
Treatment of Wiskott-Aldrich syndrome
EU/3/12/998

Sponsor: Fondazione Telethon Ets

Note

Assessment report as adopted by the COMP with all information of a commercially confidential nature deleted

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1. Product and administrative information

Product	
Designated active substance(s)	Autologous CD34+ cells transfected with lentiviral vector containing the Wiskott-Aldrich syndrome protein gene
Other name(s)	-
International Non-Proprietary Name	Etuvetidigene autotemcel
Tradename	Waskyra
Orphan condition	Treatment of Wiskott-Aldrich syndrome
Sponsor's details:	Fondazione Telethon Ets Via Varese 16 B 00185 Rome RM Italy
Orphan medicinal product designation procedural history	
Sponsor/applicant	Fondazione Telethon
COMP opinion	12 April 2012
EC decision	6 June 2012
EC registration number	EU/3/12/998
Post-designation procedural history	
Transfer of sponsorship	Transfer from Fondazione Telethon to GlaxoSmithKline Trading Services Limited – EC decision of 5 December 2014. 2nd transfer from GlaxoSmithKline Trading Services Limited to Orchard Therapeutics Ltd – EC decision of 25 July 2018. 3rd transfer from Orchard Therapeutics Ltd to Orchard Therapeutics (Netherlands) B.V. – EC decision of 17 April 2019. 4th transfer from Orchard Therapeutics (Netherlands) B.V. to Fondazione Telethon Ets – EC decision of 24 March 2023.
Marketing authorisation procedural history	
Rapporteur / Co-rapporteur	Violaine Closson Carella / Joseph DeCourcey
Applicant	Fondazione Telethon Ets
Application submission	24 November 2024
Procedure start	24 December 2024
Procedure number	EMA/H/C/006525
Invented name	Waskyra

Proposed therapeutic indication	Waskyra is indicated for the treatment of patients aged 6 months and older with Wiskott-Aldrich Syndrome (WAS) who have a mutation in the WAS gene for whom haematopoietic stem cell (HSC) transplantation is appropriate and for whom no suitable human leukocyte antigen (HLA)-matched related haematopoietic stem cell donor is available. Further information can be found in the European public assessment report (EPAR) on the Agency's website https://www.ema.europa.eu/en/medicines/human/EPAR/Waskyra.
CHMP opinion	13 November 2025
COMP review of orphan medicinal product designation procedural history	
COMP rapporteur(s)	Gloria Maria Palomo Carrasco / Julian Isla
Sponsor's report submission	5 September 2025
COMP discussion	4-6 November 2025
COMP opinion (adoption via written procedure)	14 November 2025

2. Grounds for the COMP opinion

Orphan medicinal product designation

The COMP opinion that was the basis for the initial orphan medicinal product designation in 2012 was based on the following grounds:

Whereas, the Committee for Orphan Medicinal Products (COMP), having examined the application, concluded:

- Wiskott-Aldrich syndrome (hereinafter referred to as "the condition") was estimated to be affecting approximately 0.01 in 10,000 persons in the European Union, at the time the application was made based on literature and databases;
- the condition is life-threatening and chronically debilitating due to thrombocytopenia leading to prolonged bleeding episodes, immunodeficiency leading to recurrent infections that may result in sepsis, autoimmunity resulting in cytopenias, as well as due to the development of haemopoietic malignancies;
- there is, at present, no satisfactory treatment that has been authorised in the European Union for patients affected by the condition.

The COMP recommends the designation of this medicinal product, containing Autologous CD34+ cells transfected with lentiviral vector containing the Wiskott-Aldrich syndrome protein gene, as an orphan medicinal product for the orphan indication: treatment of Wiskott-Aldrich syndrome.

Article 3(1)(a) of Regulation (EC) No 141/2000

Intention to diagnose, prevent or treat a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand people in the Community when the application is made

Condition

Wiskott-Aldrich syndrome (WAS) is an X-linked primary immune deficiency and platelet disorder, characterised by thrombocytopenia and associated bleeding, eczema, recurrent infections, with increased susceptibility to autoimmunity, and lymphoreticular malignancies (lymphoma, leukaemia, and myelodysplasia). WAS is caused by mutations in the WAS gene. These pathogenic mutations lead to defects in the Wiskott-Aldrich Syndrome protein (WASP), which disrupt immune cell function and platelet formation.

Wiskott-Aldrich Syndrome is a life-threatening illness associated with a severely reduced life expectancy and median survival of 14.5 years without definitive intervention; the majority of patients fail to reach adulthood.

The approved therapeutic indication "Waskyra is indicated for the treatment of patients aged 6 months and older with Wiskott-Aldrich Syndrome (WAS) who have a mutation in the WAS gene for whom haematopoietic stem cell (HSC) transplantation is appropriate and for whom no suitable human leukocyte antigen (HLA)-matched related haematopoietic stem cell donor is available" falls within the scope of the designated orphan condition "treatment of Wiskott-Aldrich syndrome".

Intention to diagnose, prevent or treat

The medical plausibility has been confirmed by the positive benefit/risk assessment of the CHMP, see EPAR.

Chronically debilitating and/or life-threatening nature

The most common abnormality in WAS is thrombocytopenia (usually platelet count <70 000/mm3 in the absence of splenectomy) with small platelet volume (mean platelet volume usually <5fl) and is present from birth. As a consequence, the majority of patients present with related complications, which vary from minor purpura to life-threatening gastrointestinal or intracranial haemorrhage. In

general, a platelet count <10 000/mm3 is predictive of severe bleeding complications, although higher counts are not necessarily protective. Progressive decrease in T cell number (in peripheral blood and lymphoid tissue) and function during childhood is associated with restricted defects in proliferative responses of WAS T cells (particularly CD3-mediated proliferation, but also depressed responses to mitogens), deficient antibody responses to polysaccharide (PS) and protein antigens, and low or absent levels of isohaemagglutinins. Quantitative abnormalities of immunoglobulin levels evolve in many patients, manifesting typically as low levels of IgM and increased levels of IgA, IgD, and IgE. Immune dysregulation may also manifest as food allergy, or as autoimmune disease, including haemolytic anaemia, vasculitis, inflammatory polyarthritis, and inflammatory bowel disease (IBD). The median survival for WAS patients is now around 15 years, and the usual causes of death (unrelated to transplantation procedures) are infection (44%), bleeding (23%), and malignancy (26%). Older patients and those patients with autoimmune disease are at particular risk for the development of malignancy. The reasons for this association are unclear but may relate in part to the use of immunosuppressive therapy.

In conclusion the condition is chronically debilitating and life threatening due to thrombocytopenia leading to prolonged bleeding episodes, immunodeficiency leading to recurrent infections that may result in sepsis, autoimmunity resulting in cytopenias, as well as due to the development of haemopoietic malignancies.

Number of people affected or at risk

The sponsor proposes that the prevalence of WAS is 0.01 in 10,000 persons and has not changed since the orphan designation agreement in 2012.

The sponsor describes the prevalence calculation as presented at time of orphan designation and complements it with a gap analysis from 2012 up until 2025.

Original assessment of the prevalence of WAS in the EU (2012):

In a global study of primary immunodeficiency diseases from the Jeffrey Modell Foundation (Modell et al, 2011), the updated total number of identified WAS patients in the world (up to 2011) is 1000 (181 from USA, 819 from other countries). In the European database of ESID (www.esid.org), 14506 PID patients have been reported as of February 2011. Among those, 384 WAS patients have been identified since 1993, but the prevalence of the disease has not been determined. Surveys of single country registries confirm that WAS is a rare condition. The estimated prevalence in the population in these surveys ranges from 0.002 to 0.018 in 10,000 (Hayakawa et al, 1981; Stray-Pedersen et al, 2000; Fasth et al, 1982; Ryser et al, 1988; Baumgart et al, 1997). Thus, using a total patient population estimate of 384, it was estimated that Wiskott-Aldrich Syndrome affects approximately 0.008 in 10,000 people in the European Union (EU), using the current total population estimate for the European Union (EU27) of 502,519,978 (Eurostat 2011).

Gap analysis assessment of prevalence of WAS in the EU for the years 2012 to 2025:

The gap analysis examined all relevant peer reviewed journals from 1 January 2012 to 29 September 2025. The most direct assessment of prevalence of WAS in the EU came from data from a Spanish hospital registry, which concluded that the mean annual incidence of WAS in Spain was 1.1 per 10,000,000 inhabitants and that there was 1 case of WAS per 100,000 births (Espego, et al 2023). This was based on a population based retrospective study of all WAS patients that attended any Spanish hospital from 1997 to 2017. The European Society for Immunodeficiencies patient registry (ESID-R) summarised patient datasets from 33 mainly European countries from 30,628 patients with inborn errors of immunity (IEI), within this registry 543 patients with WAS were identified over the 30-year (1994-2025) lifespan of the registry (Kindle, et al 2025). A direct assessment of prevalence of WAS was not provided in this analysis, but the overall prevalence of patients with IEI, based on the 30,628 patient data sets, across the 33 country registries ranged from 14.32 / 100,000 inhabitants (Slovakia) to 0.02 / 100,000 inhabitants (Sweden).

Data from The French National Reference Center for Primary Immune Deficiencies (CEREDIH) identified 189 patients with WAS across the France between 1987 and 2017 (Cheminant, et al, 2019). No direct assessment of prevalence of WAS was provided.

Data from other regions confirms that WAS is a very rare condition. Data from a hospital in patient data base in US identified 383 WAS patients between 2006 and 2012 across 47 US states. No direct prevalence of WAS was provided (Agarwal, et al 2021). Data from the national registry of IEI in Algeria, identified 887 IEI patients between 1985 and 2021, with a prevalence of 1.97/100,000. Of these 887 IEI patients, 40 cases of WAS were identified (Yagoubi, et al, 2022). The South Korean national medical registry identified 152 PID patients between 2001 and 2005, the period prevalence of

PID in Korea in 2005 was calculated to be 11.25 per million children. Of these 152 PID patients, 6 WAS patients were identified (Woo Rhim, et al, 2012). One final paper assessed the effectiveness of newborn screening across Zhejiang province in China. This testing identified 1 WAS mutation in 103,240 births (Chen, et al 2024). Data from Spain and China agree that that approximately 1 in 100,000 children are born with WAS.

In conclusion, the COMP agreed that the data from the initial application from 2012 and the additional supportive gap analysis of data from 2012-2025, indicates that the prevalence of Wiskott-Aldrich Syndrome affects approximately 0.01 in 10,000 people in the European Union (EU).

Article 3(1)(b) of Regulation (EC) No 141/2000

Existence of no satisfactory methods of diagnosis prevention or treatment of the condition in question, or, if such methods exist, the medicinal product will be of significant benefit to those affected by the condition.

Existing methods

There are no authorised medicinal products available in the EU for the treatment of WAS.

Current treatment approaches include allogeneic haematopoietic stem cell transplantation (HSCT), in which stem cells are obtained from a donor. When successful, HSCT leads to an increase in overall survival with improvement in platelet count and immune function and to the resolution of eczema. However, matched related HSCT donors (MRDs) are only available to about 30% of patients [Besse et al, 2016; Tiercy et al, 2016]. Consequently, allogeneic HSCT is not considered a satisfactory method for the entirety of the target patient population.

Conventional supportive treatments, which only manage the clinical manifestations of the disease, include platelet transfusions, anti-fibrinolytic agents or off-label TPO receptor agonists, antimicrobials, IgRT, and immunosuppressive drugs, corticosteroids, and anti-CD20 monoclonal antibody rituximab for the management of autoimmune diseases.

Splenectomy can be an effective treatment for thrombocytopenia, but it does not correct the underlying defect in platelets and carries a significant long-term risk of bacterial sepsis and may not be effective in the setting of autoimmune thrombocytopenia.

In conclusion, currently available treatment approaches are not considered to be satisfactory methods, for the purpose of this procedure.

Significant benefit

Not applicable.

3. COMP position adopted on 14 November 2025

The COMP concluded that:

- the proposed therapeutic indication falls entirely within the scope of the orphan condition of the designated Orphan Medicinal Product;
- the condition is life-threatening and chronically debilitating due to thrombocytopenia leading to prolonged bleeding episodes, immunodeficiency leading to recurrent infections that may result in sepsis, autoimmunity resulting in cytopenia, as well as due to the development of haematological malignancies;
- the condition was estimated to be affecting approximately 0.01 in 10,000 persons in the European Union, at the time the application was made;
- at present, no satisfactory method for the treatment of the condition has been authorised in the European Union for patients affected by the condition.

The COMP, having considered the information submitted by the sponsor and on the basis of Article 5(12)(b) of Regulation (EC) No 141/2000, is of the opinion that:

- the criteria for designation as set out in the first paragraph of Article 3(1)(a) are satisfied;
- the criteria for designation as set out in Article 3(1)(b) are satisfied.

The Committee for Orphan Medicinal Products has recommended that Waskyra, Autologous CD34+ cells transfected with lentiviral vector containing the Wiskott-Aldrich syndrome protein gene, etuvetidigene autotemcel for treatment of Wiskott-Aldrich syndrome (EU/3/12/998) is not removed from the Community Register of Orphan Medicinal Products.