ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Waskyra 2-10 × 10^6 cells/mL dispersion for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 General description

Waskyra (etuvetidigene autotemcel) is a genetically modified autologous CD34+ cell enriched population that contains haematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector encoding the human Wiskott-Aldrich Syndrome (WAS) gene.

2.2 Qualitative and quantitative composition

Each patient-specific infusion bag of Waskyra contains etuvetidigene autotemcel at a batch-dependent concentration of genetically modified autologous CD34+ cell enriched population.

The medicinal product is packaged in one or more infusion bags overall containing a dispersion for infusion of 2–10 × 10^6 cells/mL of viable $CD34^+$ enriched cell population suspended in a cryopreservative solution.

Each patient-specific infusion bag contains 10 to 20 mL of dispersion for infusion.

The quantitative information of medicinal product, including the batch dependent concentration and the number of infusion bags to be administered, is presented in the Lot information sheet (LIS) accompanying the medicinal product for treatment.

Excipients with known effect

This medicinal product contains 3.5 mg sodium per mL and 55 mg dimethylsulfoxide (DMSO) per mL (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersion for infusion.

A clear to slightly cloudy, colourless to yellow or pink dispersion.

4. CLINICAL PARTICULARS

4.1 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 no suitable human leukocyte antigen (HLA)-matched related haematopoietic stem cell donor is available.

4.2 Posology and method of administration

Waskyra must be administered in a qualified treatment centre by a physician with experience in haematopoietic stem cell transplantation (HSCT) and trained for administration and management of patients treated with the medicinal product.

Before mobilisation, apheresis and reduced intensity conditioning are initiated, it must be confirmed that haematopoietic stem cell (HSC) transplantation is appropriate for the patient.

Physicians should refer to the SmPCs of medicinal products used for pre-treatment, peripheral blood mobilisation and conditioning to ensure appropriate guidance to the patient.

Posology

Waskyra is intended for autologous use only and should be administered once (see section 4.4).

Treatment consists of a single dose for infusion containing a dispersion of viable $CD34^+$ cells in one or more infusion bags.

The dose of Waskyra to be administered is defined based on the patient's body weight at the time of infusion.

The minimum recommended dose is 7×10^6 $CD34^+$ cells/kg of body weight.

The maximum volume of Waskyra to be administered should remain < 20% of the patient's estimated plasma volume (see section 4.4 and section 6.6).

See the accompanying Lot Information Sheet (LIS) for additional information pertaining to dose.

Pre-treatment and conditioning

The treating physician should confirm that autologous HSPC gene therapy administration is clinically appropriate for the patient before rituximab and conditioning is initiated (see section 4.4).

Conditioning should not begin until the complete set of infusion bag(s) constituting the dose of Waskyra has been received and stored at the administration site, and the availability of the back-up collection is confirmed.

Peripheral blood mobilisation and apheresis

The autologous CD34+ cells are isolated from mobilised peripheral blood. This is achieved by apheresis procedure(s) following peripheral blood mobilisation.

To obtain CD34+ cells for medicinal product manufacturing and for autologous back up, patients are required to undergo haematopoietic stem and progenitor cell (HSPC) mobilisation with granulocyte-colony stimulation factor (G-CSF) and plerixafor followed by leukapheresis.

A total HSPC collection target of 40×10^6 CD34+ cells/kg is recommended for medicinal product manufacture. In addition to this, at least 3×10^6 CD34+ cells/kg should be collected as autologous back-up The back-up cells may be harvested either through mobilised peripheral blood apheresis or bone marrow harvest.

Pre-treatment with Rituximab and reduced intensity conditioning regimen

Busulfan and fludarabine are the recommended conditioning medicinal products.

	Days before the treatment infusion	**Dosing regimen**	**Dose**
Rituximab	Day-22 (+/- 1 day)	The infusion of a single dose of IV Rituximab, a monoclonal antibody anti-CD20, is recommended at Day –22 (+/- 1 day) before the infusion of Waskyra, with the aim to deplete B cells pre-treatment. Infusion rate is in accordance with the summary of product characteristics (SmPC) To reduce the occurrence of potential adverse reactions, Rituximab infusion should be preceded by appropriate premedication with IV antihistaminic medicinal product, paracetamol, and steroids, following standard procedures. These should be repeated after 6 hours.	375 mg/m^2
Busulfan	Day-4 to Day-2	Patients will receive body weight-based doses of IV busulfan. Patients are scheduled to receive a total of 8 doses, given every 6 hours from Day -4 to Day -2. If the target AUC of 48 000 ng/mL*h (± 10%) is not achieved with 8 doses, additional doses may be administered. Dosing will be stopped if the target AUC was reached prior to the eighth dose. Dose adjustment will be performed according to busulfan PK levels to achieve the target cumulative AUC of 48 000 ng/mL*h (± 10%). The Waskyra cell infusion will be scheduled to allow a washout time of at least 24 hours from the last dose of busulfan.	The starting dose of busulfan is based on patient's weight according to the following scheme: • 1 mg/kg/dose (< 9 kg); • 1.2 mg/kg/dose (9 - 16 kg); • 1.1 mg/kg/dose (> 16 - 23 kg); • 0.95 mg/kg/dose (> 23 - 34 kg); • 0.8 mg/kg/dose (> 34 kg). The subsequent doses of busulfan should be estimated from pharmacokinetics (PK) sampling and adjusted accordingly. The busulfan PK analysis should be performed by serial blood sampling before and after the infusion of at least two separate doses usually the first and fifth dose. Special attention should be kept on the busulfan dosing in order to achieve the target cumulative

			AUC of 48 000 ng/ml*h (± 10%). A dose adjustment should be performed if the total predicted AUC shows more than 10% deviation from the target (total predicted AUC is < 43 200 ng/mL*h or > 52 800 ng/mL*h). The number of doses of Busulfan may be decreased if the cumulative predicted AUC is too high.
Fludarabine	Day -4 and Day -3	Fludarabine is administered IV once daily in Day-4 and Day-3. The infusion rate should be in accordance with the fludarabine Summary of Product Characteristics (SmPC).	30 mg/m^2/day

C=area under the curve; IV=intravenous; PK=pharmacokinetic; m^2=square meter

Prevention and management of infections during pre-treatment

Prophylactic and empiric use of anti-infectives (bacterial, fungal, viral) should be considered for the prevention and management of infections especially during the neutropenic period following conditioning (see section 4.4). Infection control measures and isolation procedures should be employed during the hospitalisation according to local standards.

Premedication

Antiallergic medicinal products, such as intravenous chlorpheniramine, are recommended be administered 15-30 minutes before the infusion of Waskyra to reduce the possibility of an allergic reaction to the infusion.

Special populations

Elderly
Waskyra has not been studied in patients > 65 years of age.

Patients seropositive for human immunodeficiency virus (HIV), hepatitis B virus (HBV) or hepatitis C virus (HCV)
Waskyra has not been studied in patients with HIV-1, HIV-2, active HBV, or active HCV. Patients should be screened for HIV-1, HIV-2, HBV, and HCV and any other infectious agents in accordance with local guidelines before collection of cells for manufacturing.

Patients with serious haematological disorders
Waskyra has not been studied in patients with evidence of myelodysplasia, cytogenetic alterations characteristic of myelodysplastic syndrome and acute myeloid leukemia, or other serious hematological disorders. Treatment with Waskyra is not recommended in these patients.

Paediatric population

The safety and efficacy of Waskyra in patients < 6 months of age have not yet been established. No data are available.

Method of administration

Waskyra is for intravenous infusion only.

Prior to Waskyra infusion, it must be confirmed that the patient's identity matches the essential unique patient information on the Waskyra infusion bag(s) labels and accompanying documentation. When more than one bag of Waskyra is needed, only one bag of medicinal product should be infused at a time. The total number of infusion bags to be administered must also be confirmed with the patient specific information on the Lot Information Sheet (LIS) (see section 4.4).

Waskyra infusion will be scheduled to allow a washout time of at least 24 hours from the last dose of busulfan.

The timing of thaw and infusion of Waskyra should be coordinated. The infusion start time should be confirmed in advance and adjusted for thaw so that Waskyra is available for infusion when the patient is ready. To maintain product viability, as soon as thawing is complete, it is recommended that Waskyra is administered immediately. Administration must be completed within 2 hours from the time of thawing.

Administration
Administer the product as an intravenous infusion via a central venous catheter. When more than one bag of Waskyra is provided, one bag of medicinal product should be thawed at a time.
Each bag should be infused at an infusion rate which does not exceed 5 mL/kg/h, within approximately 30 minutes. The recommended administration set consists of a blood transfusion set equipped with a 200 μm filter.

Patients should be monitored closely prior to, during, and after infusion. Vital signs (blood pressure, heart rate, and oxygen saturation) and the occurrence of any symptom should be checked every ten minutes during the infusion and every hour, for 3 hours, after the infusion (see section 4.4).

Patients should be monitored frequently by complete blood count for at least 6 weeks after infusion or until recovery of haematopoiesis and infections managed according to standard guidelines and medical judgement (see section 4.4).

For detailed instructions on preparation, administration, measures to take in case of accidental exposure and disposal of Waskyra, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Previous treatment with haematopoietic stem cell gene therapy or with allogeneic HSC transplant with evidence of residual cells of donor origin.

4.4 Special warnings and precautions for use

Traceability

The traceability requirements of cell-based advanced therapy medicinal products must apply. To ensure traceability, the name of the product, the batch number and the name of the treated patient should be kept for a period of 30 years after expiry date of the product.

Autologous use

Waskyra is intended solely for autologous use and must not, under any circumstances, be administered to other patients. Waskyra must not be administered if the information on the product labels and Lot Information Sheet (LIS) do not match the patient's identity.

Age related adverse reactions

It is advisable to administer gene therapy at younger age. The risk of autoimmunity pre-GT, as well as the risk of incomplete reversal of clinical autoimmunity after gene therapy appeared higher in the age group > 5 years. Also, older patients may need to be carefully screened for conditions which may imply a higher risk for adverse reactions to conditioning.

Mobilisation, rituximab and conditioning medicinal products

Warnings and precautions of the mobilisation, rituximab and conditioning medicinal products must be considered before planning cell collection for manufacturing.

Central venous catheter (CVC) complications

Infections and bleeding related to the use of CVCs have been reported in clinical trials (see section 4.8). Patients should be closely monitored for potential infections and catheter-related complications.

Hypersensitivity and infusion-related reactions

Dimethylsulfoxide (DMSO), one of the excipients of Waskyra, is known to possibly cause serious hypersensitivity reactions, including anaphylaxis. Patients should be observed closely during and after infusion. Vital signs (blood pressure, heart rate, and oxygen saturation) and the occurrence of any symptom should be monitored prior to the start of the infusion, approximately every ten minutes during the infusion and every hour, for 3 hours, after the infusion.

It should be ensured prior to infusion that the total volume of DMSO administered should remain < 1% of the patient's estimated plasma volume. The maximum volume of Waskyra to be administered should therefore remain < 20% of the patient's estimated plasma volume (see section 6.6).

Prolonged cytopenia and engraftment failure

Patients may exhibit severe cytopenias, including severe neutropenia, defined as Absolute Neutrophil Count (ANC) < 500 /µL, for several weeks following reduced intensity conditioning and Waskyra infusion. Patients should be monitored frequently by complete blood count for at least 6 weeks after infusion or until recovery of hematopoiesis and infections managed according to standard guidelines and medical judgement. Supportive transfusion of irradiated packed red blood cells and platelets should be given according to medical judgement and institutional practice.

Failure of engraftment is a potentially important risk defined as not achieving an absolute neutrophil count (ANC) > 500 cells/µL, associated with no evidence of bone marrow recovery (i.e., hypocellular marrow), by day 60 after Waskyra infusion. In case of persisting neutropenia, G-CSF should be started to stimulate bone marrow recovery or earlier based on medical judgement. If failure of engraftment and neutropenia persist despite the use of granulocyte colony – stimulating factor, administration of the non-transduced back up autologous stem cells is recommended.

Transmission of an infectious agent

Although Waskyra is tested for sterility and mycoplasma, a risk of transmission of infectious agents exists. Healthcare professionals administering Waskyra must, therefore, monitor patients for signs and symptoms of infections after treatment and treat appropriately, if needed.

Serological testing

All patients should be tested for HIV-1/2, HTLV-1/2, HBV, HCV and mycoplasma prior to mobilisation to ensure acceptance of the cellular source material for Waskyra manufacturing.

Interference with HIV testing

Due to limited and short spans of identical genetic information between the lentiviral vector used to created Waskyra and HIV, some HIV nucleic acid tests (NAT) may give a false positive result.

Patients who have received Waskyra are therefore likely to test positive by polymerase chain reaction (PCR) assays for HIV due to lentiviral vector provirus insertion, resulting in a false positive test for HIV. Therefore, patients who have received Waskyra should not be screened for HIV infection using a PCR-based assay.

Anti-retroviral use

Patients should not take anti-retroviral medicinal products from at least one month prior to mobilisation until at least 7 days after Waskyra infusion (see section 4.5). If a patient requires anti-retroviral treatment following exposure to HIV/HTLV, initiation of Waskyra treatment should be delayed until an HIV/HTLV western blot and viral load assay have been performed at 6 months post-exposure.

Risk of insertional oncogenesis

There is a theoretical risk of leukaemia or lymphoma after treatment with Waskyra. In the event a malignancy is suspected or confirmed, the marketing authorisation holder must be contacted for detailed instructions on sample collection for vector integration-site analysis (ISA) and clonal proliferation testing (see the malignancy work up checklist and the contact details of the marketing authorisation holder in the Educational/safety advice tools).

Blood, organ, tissue and cell donation

Patients treated with Waskyra should not donate plasma, blood, organs, tissues and cells for transplantation at any time in the future. This information is provided in the Patient Card which should be given to the patient after treatment.

After Waskyra administration

After the infusion, standard procedures for patient management after HSPC transplantation should be followed.

The viral load for cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus-6 (HSV6) and adenovirus will be determined weekly by polymerase chain reaction (PCR) on peripheral blood until Day +90. If repeatedly negative, the testing interval could be prolonged after Day +90. If the subject is positive for CMV, preemptive therapy with ganciclovir, valganciclovir or foscarnet will be administered, according to local standards.

Pre-emptive therapy with rituximab will be administered if the subject is EBV- positive before or after gene therapy in case of repeated increase of EBV viral load, according to local standards.

Immunoglobulin G serum level should be maintained above 5 g/L to prevent potential infections associated with severe hypogammaglobinaemia, resulting from disease – related immune deficiency, rituximab administration and conditioning.

Any blood products required after Waskyra infusion should be irradiated.

Long-term follow-up

Patients who receive Waskyra are expected to be enrolled in a post-authorisation study and should be actively followed for up to 15 years after infusion. Treating physicians should schedule yearly clinical assessments (including haematology, biochemistry, and malignancy surveillance) in accordance with the agreed post-authorisation safety study.

Educational/safety advice tools

Educational/safety advice tools will be provided to healthcare professionals involved in Waskyra treatment of a patient with WAS, to the patients and/or their parents/carers with the aim to facilitate informed decision-making by healthcare professionals and patients, parents/carers based on the known benefits and risks of Waskyra and to minimise the risks to the patients.

Sodium content

This medicinal product contains 3.5 mg sodium per ml .

In adults this may range between 35–560 mg sodium per dose, depending on the volume of the medicinal product. This is equivalent to 2 to 28% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

The theoretical content of sodium in the medicinal product in a pediatric population may vary between 2.3 to 56% of the WHO recommended maximum daily intake for children, however this percentage may vary depending on their weight, age and medicinal product volume.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

The drug-drug interaction of mobilisation and myeloablative conditioning medicinal products must be considered

Patients should not take anti-retroviral medicinal products from at least one month prior to mobilisation until at least 7 days after Waskyra infusion (see section 4.4).

Live vaccines

The safety of immunisation with live viral vaccines during or following Waskyra treatment has not been studied. Vaccination is not recommended with live virus vaccines for 6 weeks before being given the conditioning medicine to prepare for Waskyra treatment, nor after treatment until immune reconstitution is completed following treatment with Waskyra.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no clinical data from the use of Waskyra in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with etuvetidigene autotemcel.

A negative serum pregnancy test must be confirmed prior to the start of each mobilisation cycle and re-confirmed prior to myeloablative conditioning.

Women of childbearing potential and men capable of fathering a child must use effective method of contraception from start of mobilisation through at least 6 months after administration of myeloablative conditioning. Please also refer to the Summary of Product Characteristics for the mobilization, pre-treatment, and myeloablative conditioning medicinal products.

Breast-feeding

It is unknown whether Waskyra is excreted in human milk or transferred to the breast-feeding child. There are no data available.

Breast-feeding should be discontinued during conditioning and Waskyra administration because of the potential risks associated with conditioning.

The decision to breast-feed after Waskyra treatment should be discussed with the treating physician, taking into account the benefit of breast-feeding for the child versus any potential adverse events from Waskyra or from the underlying condition.

Fertility

There are no data on the effects of Waskyra on human fertility. Effects on male and female fertility have not been evaluated in animal studies. Data are available on the risk of infertility with myeloablative conditioning. It is therefore advised to consider fertility preservation options such as cryopreservation of semen or ova before treatment if possible

4.7 Effects on ability to drive and use machines

Waskyra has no influence on the ability to drive and use machines. The effect of the mobilisation agents and the conditioning agents on the ability to drive or use machines must be considered.

4.8 Undesirable effects

Summary of the safety profile

Treatment with Waskyra is preceded by medical interventions, namely haematopoietic stem cell collection through peripheral blood mobilisation with G-CSF with plerixafor followed by apheresis, pre-treatment with rituximab (anti-CD20 monoclonal antibody) and reduced intensity conditioning, which carry their own risks. When assessing the safety of a treatment with Waskyra, the safety profile and product information of the medicinal products used for peripheral blood mobilisation, pre-treatment and reduced intensity conditioning should be considered, in addition to the risks linked to the gene therapy

Adverse reactions were attributed to pre-treatment (including mobilisation/leukapheresis) conditioning regimen and administration site conditions (device related infection, catheter site haemorrhage very commonly reported).

Tabulated list of adverse reactions

The safety of Waskyra was evaluated in 28 patients with WAS. The median duration of the follow up was 5.67 years (range: 0.37–13.26 years).

Given the small patient population, adverse reactions in the table below do not provide a complete perspective on the nature and frequency of these events.

Adverse reactions are listed by MedDRA body system organ class and by frequency. Frequencies are defined as: very common (≥1/10), and common (≥1/100 and <1/10).

Table 1 Adverse reactions attributed to mobilisation/apheresis and pre-treatment (G-CSF ± plerixafor, rituximab)

System organ class	Very common	Common
Infections and infestations		Aspergillus infection Influenza Urinary tract infections Pseudomonal sepsis Pneumonia aspiration
Blood and lymphatic system disorders		Anaemia
Immune system disorders		Drug hypersensitivity
Gastrointestinal disorders	Stomatitis	Abdominal pain Diarrhoea haemorrhagic Upper gastrointestinal bleeding Lip swelling
Skin and subcutaneous tissue disorders		Erythema
General disorders and administration site conditions		Pyrexia

Table 2 Adverse reactions attributed to reduced intensity conditioning regimen (busulfan and fludarabine)

System organ class	Very common	Common
Blood and lymphatic system disorders		Neutropenia Thrombotic microangiopathy
Vascular disorders		Shock
Gastrointestinal disorders	Stomatitis	Vomiting Aphthous ulcer
Hepatobiliary disorders		Veno occlusive liver disease
Skin and subcutaneous tissue disorders		Urticaria
General disorders and administration site conditions		Mucosal inflammation
Investigations		Hepatic enzyme increased
Injury, poisoning and procedural complications		Transfusional reaction

Administration site conditions very commonly reported were: device related infections and catheter site haemorrhage.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No data from clinical trials are available regarding overdose of Waskyra.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: not yet assigned, ATC code: not yet assigned

Mechanism of action

Etuvetidigene autotemcel is an *ex vivo* genetically modified autologous $CD34^+$ haematopoietic stem and progenitor cell gene therapy. Autologous $CD34^+$ haematopoietic stem and progenitor cells (HSPCs) are enriched from patient mobilised peripheral blood and transduced with a lentiviral vector (LVV), which inserts one or more copies of the human Wiskott-Aldrich Syndrome (WAS) complementary deoxyribonucleic acid (cDNA) into the cell's genome making the genetically modified cells capable of expressing the functional WAS protein. Following administration, the genetically modified cells engraft and repopulate the haematopoietic compartment. These genetically modified cells containing the corrected WAS protein (WASP) differentiate and produce biologically active lymphoid and myeloid progenitors whose progeny express WAS protein.

Clinical efficacy

The efficacy of Waskyra has been assessed in a clinical development program that includes data from a total of 27 subjects treated in a clinical trial with a fresh formulation (n=8), a clinical trial with a cryopreserved formulation (n=10) and patients treated with the fresh formulation under a compassionate use program (CUP) and Hospital Exemptions (HE), collectively referred as Expanded Access Program (EAP) (HE, n=3; and CUP, n=6).

Study OTL-103-4

The main evidence of efficacy comes from this clinical trial, in which 10 patients were treated with etuvetidigene autotemcel. All the 10 participants completed at least 2 years of follow-up, with eight participants completing 3 years of follow-up. Six participants had completed the 5-year follow-up visit.

Patients were eligible if they had a diagnosis of WAS defined by genetic mutation and at least one of the following criteria: a) Severe WAS mutation, b) Absent Wiskott-Aldrich syndrome protein (WASP) expression, c) Severe clinical score (Zhu clinical score ≥3) and no human leukocyte antigen-identical related donor available for hematopoietic stem cell transplantation (HSCT).

The WAS gene mutation was classified as severe in all but one participant, for whom severity of the mutation was not known. All participants had a history of bleeding events, recurrent infection, and skin disorders.

Patients who had end-organ dysfunction, severe active infection not responsive to treatment or other severe disease or clinical condition, malignant neoplasia (except local skin cancer) or a documented history of hereditary cancer syndrome; myelodysplasia, cytogenetic alterations characteristic of myelodysplastic syndrome and acute myeloid leukemia, or other serious hematological disorders were excluded from the studies.

Patients who had prior allogeneic HSCT, with evidence of residual cells of donor origin or previous GT, as well as patients with documented human immunodeficiency virus (HIV) infection (positive HIV RNA and/or anti-p24 antibodies) were excluded from the studies.

Results
Primary endpoint
The primary endpoints were annualized rate of severe infections from 6 to 18 months after GT compared with 1 year prior to GT and annualized rate of moderate and severe bleeding episodes up to 1 year after GT compared with 1 year prior to GT. Rate of events was estimated as number of events over person-years of observation.

Severe infections: The annualized rate of severe infections decreased from 2.40 per person-year of observation (PYO) in the 12 months before Waskyra infusion to 0.20 per PYO in the 6–18 months post-Waskyra. All severe infections were Grade 3 according to the Common Terminology Criteria for Adverse Events (CTCAE).

Moderate and severe bleeding episodes: The combined annualized rate of moderate and severe bleeding events decreased from 0.90 events per PYO in the 12 months before Waskyra infusion to 0.30 events per PYO in the first 12 months following Waskyra. One severe bleeding event (diarrhea hemorrhagic) was reported in the > 3-year period in one patient.

Main Secondary efficacy endpoints:
Overall survival: All 10 participants were alive with a median follow up duration of 5.02 years (range 2.32-5.43 years).

Annualized rate of severe infections and moderate and severe bleeding episodes at 2 and 3 years post treatment
The annualized rate of severe infections decreased from 2.40 per person-year of observation (PYO) in the 12 months before infusion to 0.10 per PYO in the 1-2 years post-infusion and to 0 in the 2-3 years post Waskyra.
The combined annualized rate of moderate and severe bleeding events decreased from 0.90 events per PYO in the 12 months before infusion to 0.20 events per PYO in the 1-2 years following Waskyra and 0 events per PYO in the 2-3 years post-Waskyra.

Integrated analysis of all treated patients

An integrated analysis of data from the two clinical trials (TIGET-WAS and OTL-103-4) and patients treated in the EAP has been performed in order to assess the overall clinical efficacy of Waskyra. The population for this analysis includes all the 27 participants who were enrolled and treated with Waskyra.

Patient characteristics
In the total population for the integrated analysis, the subjects' age at the time of GT ranged from 1.0 year to 35.1 years. Eighteen participants were aged < 5 years and nine were ≥ 5 years, of which two adults, both enrolled in the EAP. By study, the age range was 1.1 – 12.4 years in study Tiget-WAS, 1- 9 years in OTL-103-4, and 1.4 – 35.1 years in the EAP.

The WAS gene mutation was classified as severe in 22 participants and of unknown severity in the other five participants. Twenty-six participants had severe clinical features of WAS with a Zhu score ≥ 3.0 at baseline and one participant with milder clinical features (Zhu score of 2.0) was identified as having a severe *WAS* mutation.

Waskyra administration
The doses administered ranged between 7.0 and 31.0 CD34+ cells 10^6/kg. The median dose in the trial TIGET-WAS was lower than in the OTL-103-4 trial and EAP. In 5 participants of TIGET-WAS the cellular source for the GT drug product was obtained from bone marrow harvest. Mobilized peripheral blood, yielding a larger number of cells, was the CD34+ cell source in the remaining patients in TIGET-WAS and in the OTL-103-4 trial and EAP.

Results
Primary endpoints
The primary endpoints for the integrated analysis were overall survival and rate of severe infections and rate of moderate and severe bleeding events.

Overall survival: Overall, the follow-up duration in all 26 surviving participants ranges from 2.31 to 13.26 years. An overall 96% survival rate (95% CI: 82-99%) was observed following treatment

with Waskyra. One adult participant treated in the EAP died as a result of a fatal SAE unrelated to Waskyra.

Severe infections: The annualized rate of severe infections decreased from 2.00 events per person-year of observation (PYO) in the 12 months before Waskyra infusion to 0.12 in the 2-3 years post Waskyra.

Moderate and severe bleeding events: The combined annualized rate of moderate and severe bleeding events decreased from 2.00 events per Person-year(s) of observation (PYO) in the 12 months before GT to 0.16 events per PYO in the 2-3 years post-Waskyra

Table 3: Integrated analysis: Annualized rate of severe infections and rate of moderate / severe bleeding events

Severe infections	**Pre-treatment (N=27)**	**6–18 Months (N=26)**	**1–2 Years (N=26)**	**2-3 Years (N=26)**
Person-years of observation	26.99	26.08	25.98	24.97
Number (%) of participants with severe infection	19 (70.4)	4 (15.4)	4 (15.4)	3 (11.5)
Number of severe infections (rate)	54 (2.001)	4 (0.154)	4 (0.154)	3 (0.120)
95% confidence interval of the rate	1.5033 -2.6110	0.0418–0.3931	0.0419–0.3942	0.0248–0.3511

Moderate + Severe bleeding events	**Pre-treatment (N=27)**	**0-12 Months (N=27)**	**1-2 Years (N=26)**	**2-3 Years (N=26)**
Person-years of observation	26.99	26.35	25.98	24.97
Number (%) of participants with bleeding event	19 (70.4)	10 (37.0)	3 (11.5)	2 (7.7)
Number of bleeding events (Rate)	54 (2.001)	21 (0.797)	4 (0.154)	4 (0.160)
95% confidence interval of the rate	1.5033–2.6110	0.4933–1.2182	0.0419–0.3942	0.0436, 0.4102

Secondary endpoints
Durable and stable engraftment of gene corrected cells was observed from 1 month after the single administration of Waskyra and throughout post-treatment follow-up, in all evaluated participants (n=26) with a follow-up period ranging between 2 and 9 years after gene therapy (GT). All participants showed a marked increase in WASP expression in platelets and lymphocytes, and an increase in platelet count and improved T-cell functionality.

5.2 Pharmacokinetic properties

Waskyra is a gene therapy medicinal product consisting of autologous cells that have been genetically modified *ex vivo*. The nature of Waskyra is such that conventional studies on pharmacokinetics, absorption, distribution, metabolism, and elimination are not applicable.

5.3 Preclinical safety data

Due to the nature of Waskyra, a standard toxicological assessment was not applicable and conventional mutagenicity, carcinogenicity and reproductive and developmental toxicity studies have not been conducted.

The pharmacology, toxicology and genotoxicity of Waskyra were evaluated *in vitro* and *in vivo*. Due to the design of the WAS lentiviral vector (LVV) and reliance on co-expression of other interacting proteins, the WAS protein is not overexpressed, even at high vector copy numbers (VCNs). Therefore, no toxicity due protein overexpression has been seen.

Toxicity studies were performed *in vivo* in two different WAS knock-out mouse models transplanted with Lin- cells transduced with WAS LVV. These studies demonstrated normal engraftment, differentiation and seeding of lymphoid tissues with no adverse clinical signs, mortalities and no pathologic changes related to the integration of WAS LVV. No toxicities or increases in the tumourigenesis occurred in either model.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dimethyl sulfoxide
Sodium chloride
Human albumin solution

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

6 months.

Once thawed, maximum 2 hours at room temperature (20 °C - 25 °C). For products formulated at 2×10^6 cells/mL, the maximum time at room temperature should be 45 minutes.

6.4 Special precautions for storage

Waskyra infusion bags must be stored in the vapour phase of liquid nitrogen (< -130 °C) and must remain frozen until the patient is ready for treatment to ensure viable cells are administered to the patient.

Keep the infusion bag(s) in the metal cassette(s). Do not unseal the overwrap bag before thawing. Do not re-freeze after thawing.

For storage conditions after thawing of the medicinal product, see section 6.3.

6.5 Nature and contents of container

50 mL ethylene vinyl acetate (EVA) infusion bag(s) with two available spike ports, packed in an EVA overwrap bag placed inside a metal cassette.

Waskyra is shipped from the manufacturing facility to the treatment centre storage facility in a cryoshipper, which may contain multiple metal cassettes intended for a single patient.

Each metal cassette contains one infusion bag of Waskyra.

6.6 Special precautions for disposal and other handling

Precautions to be taken before handling or administering the medicinal product

Waskyra should be transported within the facility in closed, break-proof, leak-proof containers.

- This medicinal product contains genetically modified human blood cells. Healthcare professionals handling Waskyra should take appropriate precautions (wearing gloves, protective clothing and eye protection) to avoid potential transmission of infectious diseases.
- Waskyra must remain at < -130°C at all times, until the content of the bag is thawed for infusion.

Definition of the dose to be administered

- Careful consideration must be given to the volume of infusion in relation to age and weight of the patient. When the dose of Waskyra to be infused represents more than one bag, it should be ensured prior to infusion that the volume of medicinal product to be infused is compatible with the recommended limit of DMSO, i.e., the total volume of DMSO administered should remain < 1% of the patient's estimated plasma volume. Therefore, the maximum volume of Waskyra to be administered should remain < 20% of the patient's estimated plasma volume (see section 4.4).

Preparation for the infusion

- A patient may have multiple infusion bags. Each infusion bag is provided inside an overwrap bag, which is contained in a metal cassette.
- The overwrapped infusion bag(s) must be kept inside the metal cassette(s) in the vapour phase of liquid nitrogen at < -130 °C until ready to thaw and infuse.
- Account for all infusion bags and confirm each infusion bag is within the expiry date.

Checking prior to thawing

- Do not remove the metal cassette from cryogenic storage or thaw Waskyra until the patient is ready to be infused. The timing of thaw of the infusion bag(s) containing Waskyra and of the infusion should be coordinated. Confirm the infusion time in advance and adjust the start time for thaw so that the treatment is available for infusion when the patient is ready.
- Open the metal cassette and inspect the overwrap bag and infusion bag for any breaches of integrity before thawing. If an infusion bag is compromised, follow the local guidelines for handling of waste of human-derived material and contact Marketing Authorization Holder immediately.
- Prior to thawing Waskyra, it must be verified that the patient identity matches the unique patient information reported on the packaging labels and Lot Information Sheet (LIS). Waskyra is solely for autologous use. Do not thaw or infuse Waskyra if the information on the patient-specific label on the infusion bag does not match the intended patient. The total number of infusion bags to be administered must also be confirmed with the patient specific information on the Lot Information Sheet (LIS).

Thawing

- After careful removal from the metal cassette, thaw the infusion bag in its sealed overwrap bag at 37 °C in a controlled thawing device until there is no visible ice in the infusion bag.
- Once thawing is complete, the bag should be removed immediately from the thawing device. To maintain product viability, as soon as thawing is complete, it is recommended that Waskyra is administered immediately. Administration must be completed within 2 hours from the time of thawing.
- The overwrap bag should be carefully opened to remove the infusion bag which should be kept at room temperature (20 °C – 25 °C) until infusion. Gently massage the infusion bag to resuspend the cells. The content of the infusion bag should be inspected for any remaining visible cellular aggregates. Small clumps of cellular material should disperse with gentle manual mixing. Do not shake the bag.
- The infusion bag should not be washed, spun down, sampled and/or resuspended in new media prior to infusion.
- Waskyra should not be irradiated as irradiation could lead to inactivation of the product.

- If more than one infusion bag is provided for the patient treatment dose, the next bag should only be thawed after the content of the preceding bag has been fully infused.

Administration

- Waskyra should be administered as an intravenous infusion via a central venous catheter, per the administration site's standard procedures for cell therapy products.
- The recommended administration set consists of a blood transfusion set equipped with a 200 µm filter.
- Each bag should be infused by gravity within 2 hours of thaw, including any interruption during the infusion, to maintain maximum product viability.
- The maximum infusion rate is 5 mL/kg/h, and the content of each bag should be infused within approximately 30 minutes.
- When more than one bag of Waskyra is needed, one bag of medicinal product should be thawed at a time.
- Patients not previously exposed to DMSO should be observed closely. Vital signs (blood pressure, heart rate, and oxygen saturation) and the occurrence of any symptom should be monitored for up to 3 hours following the infusion.
- At the end of the infusion, flush all Waskyra remaining in the infusion bag and any associated tubing with sodium chloride 9 mg/mL (0.9%) solution for injection to ensure that as many cells as possible are infused into the patient. Careful consideration must be given to the volume of infusion in relation to the age and weight of the patient.

Precautions to be taken for the disposal of the medicinal product

- Unused medicinal products and all material that has been in contact with Waskyra (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling human-derived material.

Accidental exposure

- In case of accidental exposure, local guidelines on handling of human-derived material should be followed. Work surfaces and materials which have potentially been in contact with Waskyra must be decontaminated with appropriate disinfectant.

7. MARKETING AUTHORISATION HOLDER

Fondazione Telethon ETS
Via Varese 16/B
00185 Rome
Italy

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1996/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

AGC Biologics S.p.A.
Via Meucci 3
Openzone
20091 Bresso (MI)
Italy

Name and address of the manufacturer responsible for batch release

AGC Biologics S.p.A.
Via Meucci 3
Openzone
20091 Bresso (MI)
Italy

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to launch of Waskyra in each Member State, the Marketing Authorisation Holder (MAH) must agree about the content and format of the educational materials for parents/carers and health professionals, restricted prescription details and controlled access/product consent form, including communication media, distribution modalities, and any other aspects of the programme, with the National Competent Authority.

The educational/ safety advice tools for health professionals should highlight the important risks of Waskyra to healthcare professionals with guidance on how to minimise the risks, including the potential risk of leukaemia/lymphoma or solid organ malignancies and the need for monitoring treated patients for signs and symptoms of oncogenic transformation, leukaemia or lymphoma or solid organ malignancies and the potential risks of engraftment failure and make them aware of the importance of monitoring and long-term follow-up,

With regards to parents/carers the educational material indicates what actions to take and when and how to contact their specialist doctor in case of side effects, any symptoms or concerns and how to report adverse drug reactions and the importance of regular and long term monitoring.

The MAH shall ensure that, in each Member State where Waskyra is marketed, a system aimed to control its distribution beyond the level of control ensured by routine risk minimisation measures is implemented.

The following requirements need to be fulfilled before the product is prescribed, manufactured, dispensed and used:

- Waskyra will only be available through treatment centres qualified by the MAH to ensure traceability of the patient's cells and manufactured drug product between the treating hospital and manufacturing site.
- Waskyra will be administered at a specialist transplant centre, and by physicians with previous experience in the treatment and management of patients with Wiskott-Aldrich Syndrome and the use of autologous CD34+ ex vivo gene therapy products.
- A completed product consent form is required prior to initiating treatment.
- The selection of the treatment centres will be conducted in collaboration with national health authorities as appropriate.
- The healthcare professionals will receive training on the physician educational/ safety advice tools as part of the centre qualification process.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	**Due date**
Interventional post-authorisation safety study (PASS): In order to further characterise the long-term safety and efficacy of Waskyra in patients aged 6 months and older with Wiskott-Aldrich Syndrome (WAS) who have a mutation in the WAS gene for whom haematopoietic stem cell transplantation is appropriate and no suitable human leukocyte antigen-matched related haematopoietic stem cell donor is available, the MAH shall conduct and submit the results of an interventional post-authorisation study, according to an agreed protocol.	Final CSR: 31 December 2046

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

METAL CASSETTE

1. NAME OF THE MEDICINAL PRODUCT

Waskyra 2-10 × 10^6 cells/mL dispersion for infusion
etuvetidigene autotemcel ($CD34^+$ cells)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

This medicine contains human blood cells.

Each patient-specific infusion bag contains etuvetidigene autotemcel at a batch dependent concentration of an autologous $CD34^+$ cell enriched population that contains haematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector encoding the human Wiskott-Aldrich Syndrome (WAS) gene.

Each 10-20 mL infusion bag contains 2-10 × 10^6 cells/mL

3. LIST OF EXCIPIENTS

Also contains dimethyl sulfoxide, human albumin solution and sodium chloride. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for infusion

One infusion bag of 10-20 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

For autologous use only.

8. EXPIRY DATE

EXP

Shelf life after thawing: 2 hours at room temperature (20 °C-25 °C)

9. SPECIAL STORAGE CONDITIONS

Store and transport frozen (< -130 °C). Keep infusion bag in the metal cassette until ready for thaw and administration. Do not unseal the overwrap bag until after thaw. Once thawed do not re-freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Unused medicine or waste material must be disposed of in compliance with the local guidelines on handling of waste of human-derived material.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Fondazione Telethon ETS
Via Varese 16/B
00185 Rome
Italy

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1996/001

13. BATCH NUMBER, DONATION AND PRODUCT CODES

DIN:
COI ID:
SEC:
Lot:
Bag ID:

See Lot Information Sheet for number of infusion bags and $CD34^+$ cells per bag for this patient.

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OVERWRAPPING BAG

1. NAME OF THE MEDICINAL PRODUCT

Waskyra 2-10 × 10^6 cells/mL dispersion for infusion
etuvetidigene autotemcel ($CD34^+$ cells)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

This medicine contains human blood cells.

Each patient-specific infusion bag contains etuvetidigene autotemcel at a batch dependent concentration of an autologous $CD34^+$ cell enriched population that contains haematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector encoding the human Wiskott-Aldrich Syndrome (WAS) gene.

Each 10-20 mL infusion bag contains 2-10 × 10^6 cells/mL

3. LIST OF EXCIPIENTS

Also contains dimethyl sulfoxide, human albumin solution and sodium chloride.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for infusion

One infusion bag of 10-20 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

For autologous use only.

8. EXPIRY DATE

EXP:

Shelf life after thawing: 2 hours at room temperature (20 °C – 25 °C)

9. SPECIAL STORAGE CONDITIONS

Store and transport frozen (< -130 °C). Keep infusion bag in the metal cassette until ready for thaw and administration. Do not unseal the overwrap bag until after thaw. Once thawed do not re-freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

This medicine contains human blood cells. Unused medicine or waste material must be disposed of in compliance with the local guidelines on handling of waste of human-derived material.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Fondazione Telethon ETS
Via Varese 16/B
00185 Rome
Italy

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1996/001

13. BATCH NUMBER, DONATION AND PRODUCT CODES

DIN:
COI ID:
SEC:
Lot:
Bag ID:

See Lot Information Sheet for number of infusion bags and $CD34^+$ cells per bag for this patient.

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

INFUSION BAG

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Waskyra 2-10 × 10^6 cells/mL dispersion for infusion
etuvetidigene autotemcel ($CD34^+$ cells)
Intravenous use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP:

Shelf life after thawing: 2 hours at room temperature (20 °C – 25 °C)

4. BATCH NUMBER, DONATION AND PRODUCT CODES

Lot:
DIN:
SEC:
Bag ID:
COI ID:

See Lot Information Sheet for number of infusion bags and $CD34^+$ cells per bag for this patient.

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10-20 mL of cell dispersion per bag.

6. OTHER

For autologous use only.

PARTICULARS TO APPEAR ON THE LOT INFORMATION SHEET INCLUDED WITH EACH SHIPMENT FOR ONE PATIENT

1. NAME OF THE MEDICINAL PRODUCT

Waskyra 2-10 × 10^6 cells/mL dispersion for infusion
etuvetidigene autotemcel ($CD34^+$ cells)

2. STATEMENT OF ACTIVE SUBSTANCE

An autologous $CD34^+$ cell enriched population that contains haematopoietic stem and progenitor cells (HSPC) transduced *ex vivo* using a lentiviral vector encoding the human Wiskott-Aldrich Syndrome (WAS) gene.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT, AND DOSE OF THE MEDICINAL PRODUCT

INFORMATION ON SUPPLIED LOT(S)

The following lot(s) is (are) included in the shipment:

Lot number	**Bag ID**	**Volume of dispersion for infusion** (mL)	**Strength** ($x10^6$ cells/mL)	**Total $CD34^+$ cells** ($x10^6$)	**Expiry date** (DD-MMM-YYYY)

Total number of bags: _____
Total number of $CD34^+$ cells ($x10^6$): _____
The supplied dose (calculated based on patient's weight at time of cell harvest) is:
_____ × 10^6 $CD34^+$ cells/kg

The minimum recommended dose of Waskyra to be administered is 7 × 10^6 $CD34^+$ cells/kg. In clinical trials doses up to 31 × 10^6 $CD34^+$ cells/kg have been administered.

The ***dose to be infused*** should be defined by the treating physician based on the total number of $CD34^+$ cells supplied, the patient's weight at time of treatment, and the fact that any bag used should be administered in its entirety.

When more than one bag of Waskyra is needed, it should be ensured prior to infusion that the volume of medicinal product to be infused is compatible with the recommended ***limit of DMSO***, i.e., the total volume of DMSO administered should remain < 1% of the patient's estimated plasma volume.

The maximum volume of Waskyra to be administered should therefore remain < 20% of the patient's estimated plasma volume.

4. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

5. OTHER SPECIAL WARNINGS, IF NECESSARY

Save this document and have it available when preparing for administration of Waskyra

For autologous use only.

6. SPECIAL STORAGE CONDITIONS

INSTRUCTIONS FOR STORAGE AND USE

Store and transport frozen (< -130 °C). Keep infusion bag in the metal cassette until ready for thaw and administration. Do not unseal the overwrap bag until after thaw. Once thawed do not re-freeze.

Shelf life: 6 months at < -130 ºC. Shelf life after thawing: 2 hours at room temperature (20 ºC – 25 ºC)

7. EXPIRY DATE AND OTHER BATCH SPECIFIC INFORMATION

Information is presented in the table in section 3 above.

8. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

This medicine contains human blood cells. Unused medicine or waste material must be disposed of in compliance with the local guidelines on handling of waste of human-derived material.

9. BATCH NUMBER, DONATION AND PRODUCT CODES

COI ID:
Weight at First Collection (kg):
DIN:
SEC:

10. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Fondazione Telethon ETS
Via Varese 16/B
00185 Rome
Italy

11. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1996/001

B. PACKAGE LEAFLET

Package leaflet: Information for the patient or carer

Waskyra 2-10 × 10^6 cells/mL dispersion for infusion
etuvetidigene autotemcel

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you (or your child) are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- Your doctor or nurse will give you a Patient Card which contains important safety information about your treatment with Waskyra. Read it carefully and follow the instructions on it.
- Carry the Patient Card with you at all times and always show it to the doctor or nurse when you see them or if you go to the hospital.
- The information in this leaflet is for you or your child – but in the leaflet it will just say "you".

What is in this leaflet

1. What Waskyra is and what it is used for

Waskyra is a gene therapy product that contains the active substance etuvetidigene autotemcel. A gene therapy product works by delivering a gene into the body to correct a genetic defect. This medicine is made specially for you, from your own blood-forming cells.

Waskyra is used to treat a serious condition called Wiskott-Aldrich Syndrome (WAS) in people aged 6 months and older who have a mutation in the WAS gene for whom haematopoietic stem cell (HSC) transplantation is appropriate and there is no suitable match from a family member to donate haematopoietic stem cells for a transplant. Haematopoietic stem cells are immature cells that can develop into all types of blood cells, including white blood cells, red blood cells, and platelets (components that help the blood to clot).

People with WAS have a mutation (change) in the gene which provides instructions to make the WAS protein. The WAS protein helps white blood cells move and work properly to fight infections and helps platelets form correctly to stop bleeding. A mutation in the gene leads to a defective or missing WAS protein. This can lead to life-threatening complications such as bleeding episodes and infections.

Waskyra is prepared using your own haematopoietic stem cells which are modified in a laboratory using a virus. This virus has been modified so it cannot spread in the body but can deliver a correct copy of the WAS gene into the haematopoietic stem cells. The modified haematopoietic stem cells are given back to the patient via an infusion (drip) and can make blood cells that are able to produce the WAS protein, which is expected to improve the disease.

If you have any questions about how Waskyra works or why this medicine has been prescribed, ask your doctor.

2. What you need to know before you are given Waskyra

You must not be given Waskyra

- if you are allergic to any of the ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice

- if you have previously had gene therapy made from blood stem cells, or an allogeneic HSC transplant with evidence of residual cells of donor origin.

Warnings and precautions

Before you are given Waskyra
The doctor will:
- Check your lungs, heart, kidney, liver, brain, skin, thyroid, as well as vital parameters such as blood pressure. A general medical assessment is necessary before treatment.

- Look for signs of infection. Any infection should be treated before Waskyra is given to you.

- Check for hepatitis B, hepatitis C, human T-cell lymphotropic virus (HTLV), HIV or mycoplasma infection. If you have an active infection from one of these agents, your treatment with Waskyra may be postponed or withheld.

- Check your bone marrow to make sure you do not have signs of leukaemia or myelodysplasia (a condition where your bone marrow does not make enough healthy blood cells or platelets). If you have signs of these conditions, they may prevent you from undergoing Waskyra treatment.

Before the treatment with Waskyra
- Before it is given to you, Waskyra is tested to make sure there are no infectious microbes, since a theoretical risk of infection exists. The doctors and nurses will monitor for signs of infection throughout the infusion, like fever, chills, sweats, fatigue, sore throat etc. and provide treatment if needed. Consult your doctor if you experience the signs and symptoms,

When Waskyra is given to you
- Information about cell-based medicines like Waskyra must be kept for 30 years at the hospital. The information kept will be your name and the batch number of Waskyra you received.

After the treatment with Waskyra
- After receiving Waskyra, you will be monitored with regular blood tests. This will include measurement of antibodies, known as *immunoglobulins*, in the blood. If the immunoglobulin level is low, you may need immunoglobulin replacement therapy. Your doctor will discuss this with you if needed.

- You may be given anti-infectives (bacterial, fungal, viral) for the prevention and management of infections especially during the neutropenic period following conditioning. Infection control measures and isolation procedures should be employed during the hospitalisation according to local standards.

- The viral load for cytomegalovirus, Epstein-Barr virus, herpes simplex virus, and adenovirus will be determined weekly on peripheral blood until Day +90. If repeatedly negative, the testing interval could be prolonged after Day +90. If you are positive for cytomegalovirus, preemptive

therapy with ganciclovir, valganciclovir or foscarnet will be administered, according to local standards.

- You may exhibit severe decrease of the number of cells in the blood, including severe decrease in the number neutrophils for several weeks following conditioning and Waskyra infusion. You should, therefore, be monitored frequently by complete blood count for at least 6 weeks after infusion or until recovery of hematopoiesis and infections managed according to standard guidelines and medical judgement. You should consult your doctor if you experience fatigue and weakness, infections and easy bruising and bleeding. Supportive transfusion of irradiated packed red blood cells and platelets should be given according to medical judgement and institutional practice.

- Failure of engraftment is a potentially important risk after Waskyra infusion. In case of persisting decrease in the number neutrophils, a growing factor (Granulocytes –Colony Stimulating Fcator) should be started to stimulate bone marrow recovery or earlier based on medical judgement. If failure of engraftment and a low number of neutrophils persist despite the use of granulocyte colony – stimulating factor, administration of the non-transduced back up autologous stem cells is recommended.

- After the treatment, you may be asked to be followed for up to 15 years to better understand the long-term effects of Waskyra.

- If you require a blood transfusion before and after receiving Waskyra, blood products given to you should be irradiated. This means the white blood cells, called lymphocytes, have been reduced to minimise the risk of a reaction to the transfusion. Your doctor will monitor you for any blood transfusion reaction.

- Inserting a new gene into the stem cells could contribute to a risk of blood cancers such as leukaemia (cancer of the white blood cells) and lymphoma (cancer of lymphocytes, white blood cells involved in the body's defences). Although there is no evidence of this in the clinical trials so far, this remains possible because of the nature of the medicine. After the treatment, your doctor will monitor you for any signs of leukaemia or lymphoma or solid organ malignancies.

- Waskyra is prepared using parts of a virus, which have been altered so that they cannot cause infection. This may cause a false positive HIV test result. More specific tests can be used to exclude HIV infection in case of need.

- The active substance in Waskyra may temporarily be excreted through your blood, semen, breast milk or bodily waste, a process called shedding. After treatment with Waskyra, you will therefore not be able to donate blood, blood components (plasma), organs, tissues or cells.

When Waskyra treatment cannot be completed

Manufacturing of Waskyra may not be successful if the amount of stem cells collected from your blood is not enough or if there are difficulties in the preparation of the medicine after stem cells have been collected. In this case you may be asked to repeat the stem cell collection, if feasible, or offered another treatment.

Before receiving Waskyra, a conditioning medicine will be given to remove cells from the bone marrow providing space for the gene modified stem cells in Waskyra to take hold (*engraft)* in the bone marrow.

If Waskyra cannot be given after you have had the conditioning medicine, or if the modified stem cells do not take hold in your body, the doctor may give you an infusion of rescue cells from the previously collected backup sample (see also section 3, *"How Waskyra is given"*). The rescue cells do not have

the working *WAS* gene added to them and will not produce the WAS protein. For more details, please contact your doctor.

The safety and efficacy of Waskyra in patients younger than 6 months of age have not been established. No data are available and Waskyra cannot be given to patients under 6 months of age.

Other medicines and Waskyra

Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

- You should not take any medicines for HIV infection from at least one month before you are given the mobilisation medicines or have blood samples taken, until at least 7 days after Waskyra infusion since these medicines could impact on the production and early functioning of Waskyra.

- You must not be given vaccines called **live vaccines** for 6 weeks before being given the conditioning medicine to prepare for Waskyra treatment, nor after treatment while your immune system (the body's defence system) is recovering.

Driving and using machines

Waskyra has no influence on the ability to drive or use machines.

Pregnancy and lactation

This treatment must not be given during pregnancy because of the possible effects of the conditioning medicine. The effects of Waskyra in pregnant women are not known. Talk to your doctor about pregnancy after receiving Waskyra.

If you are pregnant or think you may be pregnant after treatment with Waskyra, talk to your doctor immediately.

If you are a woman who can get pregnant, you will be given a pregnancy test before starting mobilisation and conditioning medicines to make sure you are not pregnant.

Contraception in men and women

If you are a woman who can get pregnant, or a man capable of fathering a child, you must use an effective method of contraception (birth control) from the start of mobilisation treatment and for at least 6 months after receiving Waskyra. Talk to your doctor about which methods of contraception are appropriate.

Breast-feeding

Breast-feeding should be stopped during conditioning because of the possible effects of the conditioning medicine. It is not known whether the ingredients of Waskyra can pass into breast milk.

Your doctor will discuss with you the benefit of breast-feeding for your baby versus the potential risks of treatment.

Fertility in men and women

It may not be possible for you to become pregnant or father a child after you have had the conditioning medicine. You should discuss your options with your doctor before treatment. These may include storing reproductive material (for instance, eggs, sperm) to use at a later time.

Waskyra contains sodium and dimethylsulfoxide (DMSO)

This medicine contains 35-560 mg sodium (main component of cooking/table salt) in each dose. This is equivalent to 2% to 28% of the recommended maximum daily dietary intake of sodium for an adult. The recommended maximum level of intake of 2 g/day sodium in adults should be adjusted downward based on the energy requirements of children relative to those of adults.

This medicine contains 55 mg/mL DMSO (a substance used to preserve frozen cells) which can cause sudden, severe allergic reactions. The doctor or nurse should watch you closely for any reactions during the infusion and every hour, for 3 hours, after the infusion.

3. How Waskyra is made and given

Since Waskyra is made from your own haematopoietic stem cells, your blood will be collected to prepare the medicine about 2 to 3 months before treatment. The stem cells can be collected from your blood which is drawn from a vein. For more details, please ask your doctor.

When stem cells are collected from the blood:

- You will be given two types of medicines before you are given Waskyra:
    - **mobilisation medicine,** to move the blood stem cells from the bone marrow into the blood stream
    - **conditioning medicines,** to make space in the bone marrow for the new stem cells you will be given

Refer to the package leaflets of these medicines for more information.

(See section 3 *"How Waskyra was made and given"* and section 4 *"Possible Side Effects"* for more information on these medicines, including possible side effects).

- Collection of the blood stem cells will occur from a temporarily placed central venous catheter. A central venous catheter is a thin, flexible tube that is inserted by a doctor into a large vein to access your bloodstream. Another catheter will be placed before you start conditioning treatment to allow infusion of Waskyra and other medicines and blood collection for testing. There may be side effects, like infections and bleeding, when a catheter is inserted, although not everybody gets them. The doctor and nurses will monitor for any complications.

- You will first be given a so-called 'mobilisation' medicine to move the blood stem cells from the bone marrow into the blood stream (see section 2 *"Warnings and precautions"*).

- The blood stem cells can then be collected by a machine that separates blood components *(apheresis machine)*. It may take more than 1 day to collect enough blood stem cells to make Waskyra.

The collected stem cells from the blood will be divided into:

- The **backup sample**, which will be frozen and stored, to be given as rescue stem cells if Waskyra cannot be given or does not work (see *"When Waskyra treatment cannot be completed"* in section 2).

- The **treatment sample**, which will be provided to the manufacturer to make Waskyra by inserting a working copy of the WAS gene into the stem cells in the sample.

How you are given Waskyra

- Waskyra will be given in a qualified treatment centre and by doctors trained in using this type of medicine.

- Waskyra is given by a drip (infusion) into a vein (intravenously) through a central venous catheter. It is possible that more than one bag of medicine will be administered.

- The doctors will check that the Waskyra infusion bags are all identified as being made from your own sample.

- Waskyra is a one-time treatment. It will not be given to you again.

When	What happens	Why
About 2 months before Waskyra infusion	Mobilisation medicines are given by subcutaneous injection for 4 to 6 days	To move the blood stem cells from the bone marrow into the blood stream
About 2 months before Waskyra infusion	Mobilized blood is collected in 2 to 3 days	To obtain blood stem cells to make Waskyra. Part of the stem cells collected will be kept separately, to serve as rescue cells if needed
About 3 weeks before Waskyra infusion	A medicine called rituximab is given a single time into a vein through the catheter	To reduce the number of any white blood cells producing antibodies targeted towards your body, and help gene-corrected cells to establish after infusion of Waskyra
5 days before Waskyra infusion	Two conditioning medicines (busulfan and fludarabine) are given for 2–3 days in a hospital, into a vein through the catheter	To prepare the bone marrow for treatment. These medicines destroy cells in the bone marrow, so they can be replaced with the gene-corrected cells in Waskyra
15 to 30 minutes before Waskyra infusion	A medicine called an antihistamine may be given	To help prevent an allergic reaction to the infusion
Start of Waskyra infusion	Waskyra is given by a drip (infusion) into a vein. This will be done in a hospital and will take about 30 minutes for each infusion bag. The number of bags will vary by patient.	To inject stem cells containing the correct WAS gene into the blood stream which will deliver them to your bone marrow,
After Waskyra infusion	You will remain in the hospital for about 4–8 weeks	To recover. You will be monitored to check if the treatment is working and any side effects can be treated until the doctor is satisfied that it is safe for you to leave the hospital

4. Possible side effects

During the clinicals trials conducted with Waskyra no side effects have been assigned to the drug product itself. However, the procedures and medicines required to receive the medicine, in combination with your disease status, can cause side effects, although not everybody gets them.

Serious side effects — get medical help immediately

Seek urgent medical advice straight away if you notice any of the following (they can be serious):

A combination of several of the following symptoms: fever (≥38 °C), chills, cough, shortness of breath, fast heartbeat, confusion, feeling very unwell. This may point at serious infections (including Aspergillus infection), sepsis (including Pseudomonas sepsis) or aspiration pneumonia — seek medical help immediately.

Unusual bruising or bleeding, pale skin, extreme tiredness, confusion, reduced urination or swelling of legs/ankles can be indicative of blood clots in small blood vessels, so-called 'Thrombotic microangiopathy' — seek urgent medical help.

A combination of stomach/abdominal pain, swelling, sudden weight gain, yellowing of the skin or eyes (jaundice), and dark urine is suggestive of a severe liver disease (veno-occlusive liver disease) which can occur after receiving conditioning medicines — contact a doctor straight away.

Upper gastrointestinal bleeding: vomiting blood or material that looks like coffee grounds; black, tarry stools; feeling faint or dizzy — seek medical help immediately.

Severe hypersensitivity (allergic) reactions, which may include shock: rash or hives, itching, flushing, swelling of the lips, face, tongue or throat, wheezing or difficulty breathing, dizziness or fainting — seek urgent medical help immediately.

Transfusion reaction (during or after a transfusion): fever or chills, shortness of breath, chest/back pain, dark urine — seek medical help immediately.

Other side effects (listed by frequency, starting with the most frequent)

Very common (may affect more than 1 in 10 people)
Stomatitis (soreness or ulcers in the mouth)

Common (may affect up to 1 in 10 people)
Influenza (flu)
Urinary tract infections
Neutropenia (low white blood cells)
Anaemia (low red blood cells)
Abdominal pain
Diarrhoea, haemorrhagic (bloody diarrhoea)
Vomiting
Urticaria
Shock
Lip swelling
Aphthous ulcer (mouth ulcers)
Erythema (skin redness)
Pyrexia (fever)
Mucosal inflammation (inflammation of the lining of the mouth, nose/throat or gut)
Hepatic enzyme increased (increased liver enzymes seen in blood tests)

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Waskyra

This information is intended for doctors only.

As this medicine will be given in a hospital, the hospital is responsible for the correct storage of the medicine before and during its use, as well as for its correct disposal.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer container and infusion bag labels.

Do not use this medicine if the infusion bag is damaged or leaking.

Store at < -130 °C. Do not thaw the product until it is ready to be used. Once thawed, keep at room temperature (20 °C – 25 °C) and use within 2 hours. For products formulated at 2×10^6 cells/mL, the maximum time at room temperature should be 45 minutes. Do not refreeze.

Keep the infusion bag(s) in the metal cassette(s) until thawing.

Do not unseal the overwrap bag before thawing.

Unused medicine or waste material must be disposed of in compliance with the local guidelines on handling human-derived material.

6. Contents of the pack and other information

What Waskyra contains

The active substance is etuvetidigene autotemcel and consists of your own stem cells that contain working copies of the WAS gene.

Each patient-specific infusion bag of Waskyra contains 2-10 × 10^6 cells/mL of viable CD34+ enriched cell population at a batch-dependent concentration.

The other ingredients are dimethyl sulfoxide (DMSO), sodium chloride and human albumin solution (see section 2, *"Waskyra contains sodium and DMSO"*).

This medicine contains genetically-modified human blood cells.

What Waskyra looks like and contents of the pack

Waskyra dispersion for infusion is a clear to slightly cloudy, colourless to yellow or pink dispersion of cells.

Waskyra is supplied in 50 mL ethylene vinyl acetate (EVA) infusion bag(s) containing 10-20 mL of dispersion for infusion. Every infusion bag with two available spike ports is packed in an EVA overwrap bag placed inside a metal cassette.

Waskyra is shipped from the manufacturing facility to the treatment centre storage facility in a cryoshipper, which may contain multiple metal cassettes intended for a single patient. Each metal cassette contains one infusion bag of Waskyra.

Marketing Authorisation Holder
Fondazione Telethon ETS

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AGC Biologics S.p.A.
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This leaflet was last revised in .

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

The following information is intended for healthcare professionals only:

It is important that you read the entire content of this procedure prior to administering Waskyra.

Precautions to be taken before handling or administering the medicinal product

Waskyra should be transported within the facility in closed, break-proof, leak-proof containers.

- This medicine contains genetically modified human blood cells. Healthcare professionals handling Waskyra should take appropriate precautions (wearing gloves, protective clothing and eye protection) to avoid potential transmission of infectious diseases.

- Waskyra must remain at < -130 °C at all times, until the content of the bag is thawed for infusion.

- The total number of infusion bags to be administered must also be confirmed with the patient specific information on the Lot Information Sheet (LIS)

Defining the dose to be administered

- Careful consideration must be given to the volume of infusion in relation to the age and weight of the patient. When the dose of Waskyra to be infused represents more than one bag, it should be ensured prior to infusion that the volume of medicine to be infused is compatible with the recommended limit of DMSO, i.e., the total volume of DMSO administered should remain < 1% of the patient's estimated plasma volume. Therefore, the maximum volume of Waskyra to be administered should remain < 20% of the patient's estimated plasma volume.

Preparation for the infusion

- A patient may have multiple infusion bags. Each infusion bag is provided inside an overwrap bag, which is contained in a metal cassette.

- The overwrapped infusion bag(s) must be kept inside the metal cassette(s) in the vapour phase of liquid nitrogen at < -130 °C until ready to thaw and infuse.

- Account for all infusion bags and confirm each infusion bag is within the expiry date using the accompanying Lot Information Sheet.

Checking prior to thawing

- Do not remove the metal cassette from cryogenic storage and thaw Waskyra until the patient is ready to be infused. The timing of thaw of the infusion bag(s) containing Waskyra and of the infusion should be coordinated. Confirm the infusion time in advance and adjust the start time for thaw so that Waskyra is available for infusion when the recipient is ready.

- Open the metal cassette and inspect the overwrap bag and infusion bag for any breaches of integrity before thawing. If an infusion bag is compromised, follow the local guidelines on handling of waste of human-derived material and contact the Marketing Authorization Holder immediately.

- Prior to thawing Waskyra, it must be verified that the patient identity matches the unique patient information reported on the packaging labels. Waskyra is intended solely for autologous use. Do not thaw or infuse Waskyra if the information on the patient-specific label on the infusion bag does not match the intended patient.

Thawing

After careful removal from the metal cassette, thaw the infusion bag in its sealed overwrap bag at 37°C in a controlled thawing device until there is no visible ice in the infusion bag.

- Once thawing is complete, the bag should be removed immediately from the thawing device. To maintain product viability, as soon as thawing is complete, it is recommended that Waskyra is administered immediately.

- The overwrap bag should be carefully opened to remove the infusion bag which should be kept at room temperature (20 °C – 25 °C) until infusion.

- Gently massage the infusion bag to resuspend the cells. The content of the infusion bag should be inspected for any remaining visible cellular aggregates. Small clumps of cellular material should disperse with gentle manual mixing. Do not shake the bag.

- The infusion bag should not be washed, spun down, sampled and/or resuspended in new media prior to infusion.

- Waskyra should not be irradiated as irradiation could lead to inactivation of the product.

- If more than one infusion bag is provided for the patient treatment dose, the next bag should only be thawed after the content of the preceding bag has been fully infused.

Administration

- Waskyra should be administered as an intravenous infusion via a central venous catheter, per the qualified treatment centre’s standard procedures for cell therapy products.

- The recommended administration set consists of a blood transfusion set equipped with a 200 µm filter.

- Each bag should be infused by gravity within 2 hours of thaw, including any interruption during the infusion, to maintain maximum product viability.

- The maximum infusion rate is 5 mL/kg/h, and the content of each bag should be infused within approximately 30 minutes.

- When more than one bag of Waskyra is needed, only one bag of medicinal product should be thawed at a time.

- Patients not previously exposed to DMSO should be observed closely. Vital signs (blood pressure, heart rate, and oxygen saturation) and the occurrence of any symptom should be monitored for up to 3 hours following the infusion.

- At the end of the infusion, flush all Waskyra remaining in the infusion bag and any associated tubing with sodium chloride 9 mg/mL (0.9%) solution for injection to ensure that as many cells as possible are infused into the patient. Careful consideration must be given to the volume of infusion in relation to the age and weight of the patient.

Precautions to be taken for the disposal of the medicinal product

Unused medicinal products and all material that has been in contact with Waskyra (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling human-derived material.

Accidental exposure

- In case of accidental exposure, local guidelines on handling of human derived materials should be followed. Work surfaces and materials which have potentially been in contact with Waskyra must be decontaminated with appropriate disinfectant.