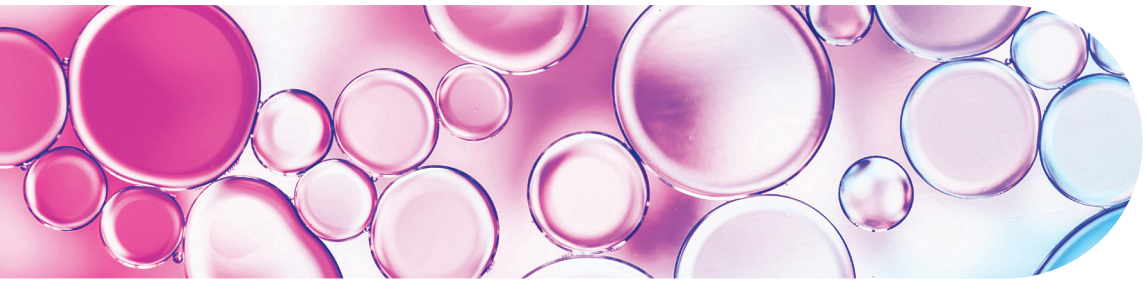
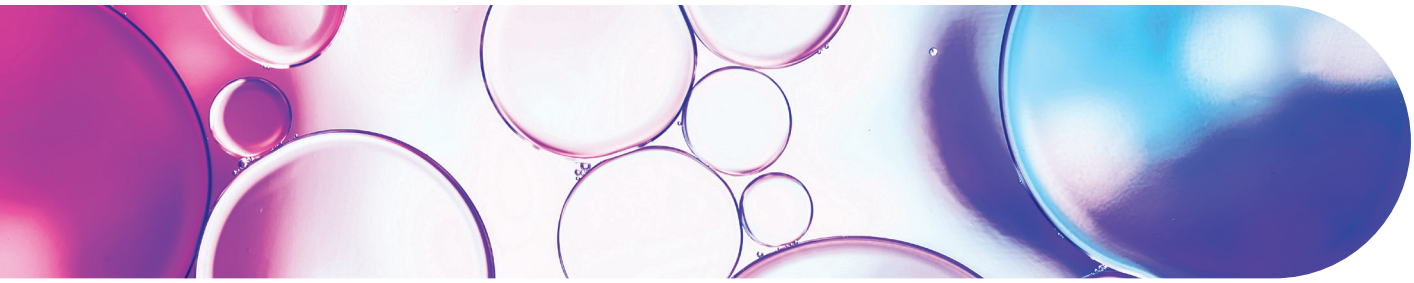
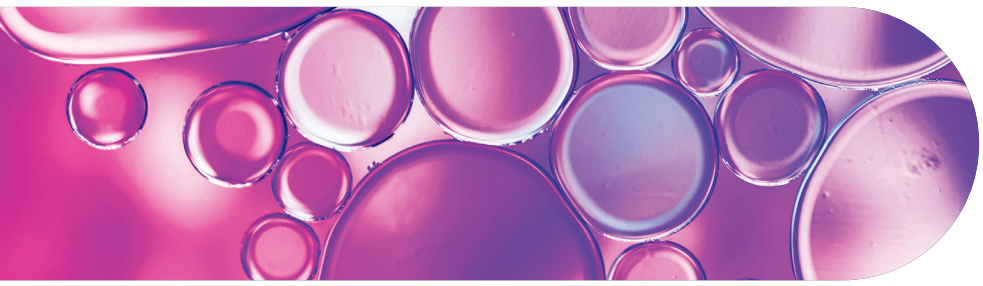
EBVALLO®▼
tabelecleucel

Preparation and Administration Guide





A preparation and administration guide to help you receive, store and administrate EBVALLO.



Pierre Fabre

▼ *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.*

EBVALLO® tabelecleucel

Preparation and Administration Guide

Glossary

- **ALT:** Alanine transaminase
- **APIN:** Atara Patient Identification number
- **AST:** Aspartate transaminase
- **CMV:** Cytomegalovirus
- **CR:** Complete response
- **EBV:** Epstein-Barr virus
- **EBV+ PTLD:** Epstein-Barr Virus Positive Post-Transplant Lymphoproliferative Disease
- **FDP:** Finished Drug Product
- **HLA:** Human Leukocyte Antigen
- **HCT:** Hematopoietic Stem Cell Transplant
- **IR:** Indeterminate response
- **LIS:** Lot Information Sheet
- **LN2:** liquid nitrogen
- **MFD:** Manufacturing Date
- **ORR:** Objective Response Rate
- **OS:** Overall Survival
- **PD:** Progressive disease
- **PR:** Partial response
- **PTLD:** Post-transplant Lymphoproliferative Disease
- **SD:** Stable disease
- **SOT:** Solid Organ Transplant

References

1. Dierickx D, et al. Post-Transplantation Lymphoproliferative Disorders in Adults. N Engl J Med. 2018;378:549–562. **2.** Nijland ML, et al. Epstein-Barr virus-positive posttransplant lymphoproliferative disease after solid organ transplantation: pathogenesis, clinical manifestations, diagnosis, and management. Transplant Direct. 2016;2(1):e48. **3.** Dharnidharka V., Thirumalai D., Jaeger U., et al. Clinical Outcomes of Solid Organ Transplant Patients with Epstein-Barr Virus-Driven (EBV +) Post-Transplant Lymphoproliferative Disorder (PTLD) Who Fail Rituximab Plus Chemotherapy: A Multinational, Retrospective Chart Review Study. Blood 2021 138 Supplement 1 (2528-). **4.** Sanz J., Storek J., Socié G., et al. Clinical Outcomes of Patients with Epstein-Barr Virus-Driven Post-Transplant Lymphoproliferative Disease Following Hematopoietic Stem Cell Transplantation Who Fail Rituximab: A Multinational, Retrospective Chart Review Study. Blood 2021 138 Supplement 1 (1454-). **5.** EBVALLO Summary of Product Characteristics. **6.** Mahadeo KM, et al. New and Updated Results from a Multicenter, Open-Label, Global Phase 3 Study of Tabelecleucel (Tab-cel) for Epstein-Barr Virus-Positive Post-Transplant Lymphoproliferative Disease (EBV+ PTLD) Following Allogeneic Hematopoietic Cell (HCT) or Solid Organ Transplant (SOT) after Failure of Rituximab or Rituximab and Chemotherapy (ALLELE). Blood 2022; 140 (Supplement 1): 10374–10376. doi: https://doi.org/10.1182/blood-2022-157766. **7.** EBVALLO EPAR.

SUMMARY

1. EBV+ PTLD OVERVIEW [1-4]

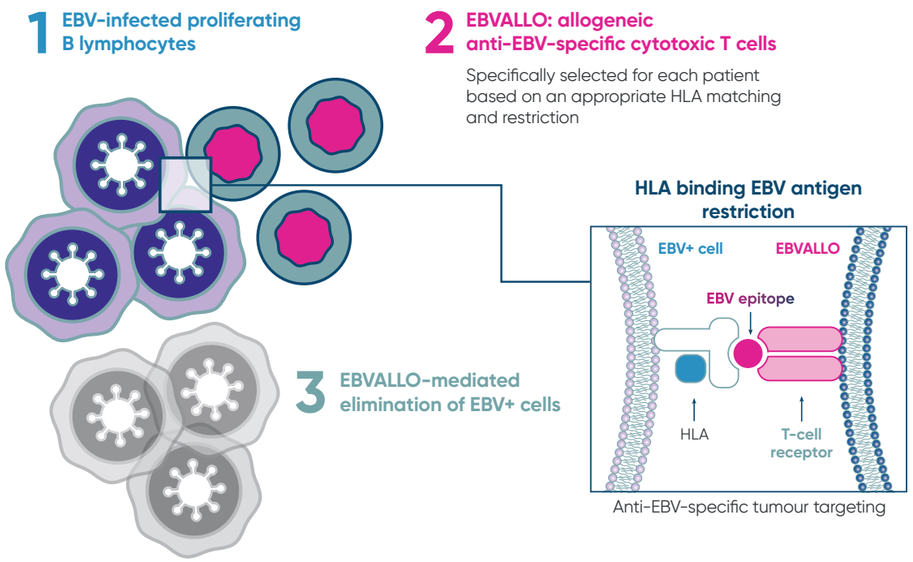
Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD) is a rare, acute and potentially life-threatening group of lymphoid disorders that arise after transplantation:[1-2]

- **EBV** infection primarily infects B-cells.
- **In immunocompetent host :**
  - T-cells kill infected B-cells during intermittent EBV lytic phases, keeping the infection under control.
  - At the same time, EBV DNA integrates in infected B-cells DNA, and establishes a latent infection that the immune system can usually control but cannot clear.
- **In immunosuppressed transplanted patients:**
  - Suppression of T-cell activity causes the EBV infection to remain undetected by the immune system.
  - EBV-infected B-cells may transform and rapidly proliferate causing PTLD.

The **poor patient prognosis** associated with EBV+ PTLD upon rituximab-based treatment failure calls for an urgent intervention. The median OS post rituximab +/- chemotherapy failure is **0.7 months** post HCT (hematopoietic cell transplantation) and **4.1 months** post SOT (solid organ transplantation).[3-4]

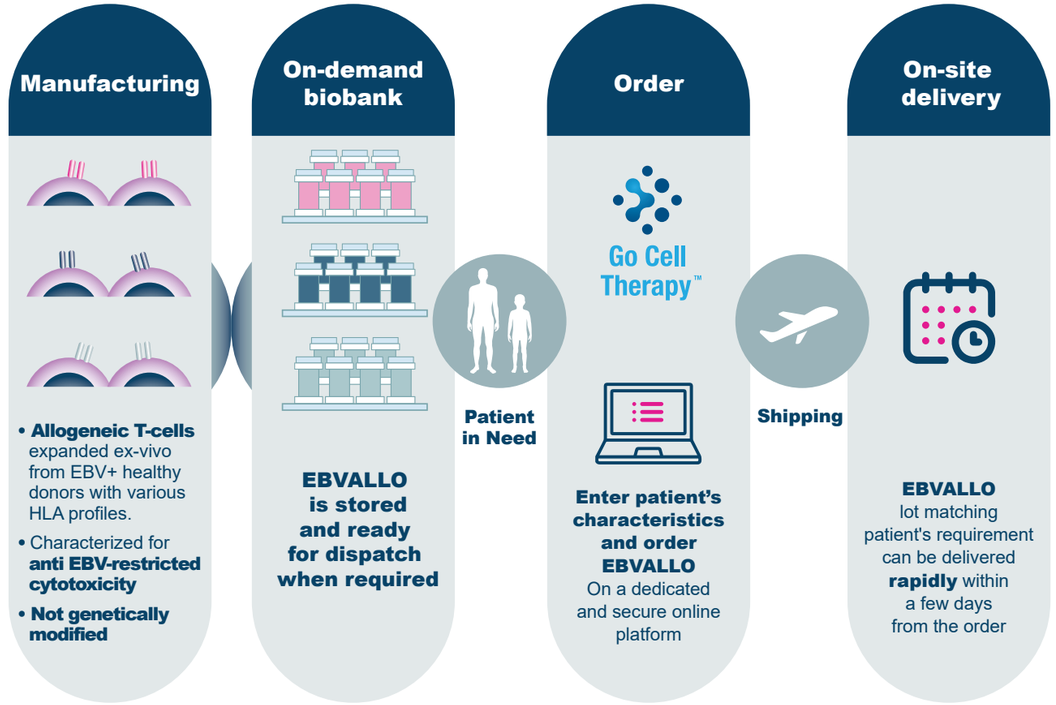
2. EBVALLO OVERVIEW

A • WHAT IS EBVALLO ? [5]



EBVALLO (tabelecleucel) is an allogeneic Epstein-Barr virus (EBV)-specific T-cell immunotherapy which targets and eliminates EBV-infected proliferating cells in a human leukocyte antigen (HLA)-restricted manner

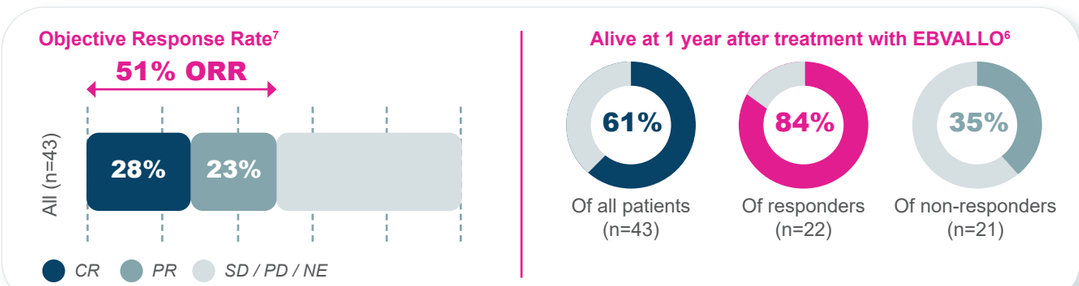
EBVALLO® tabelecleucel



B • INDICATION [5]

- EBVALLO is indicated as monotherapy for treatment of adult and paediatric patients 2 years of age and older with relapsed or refractory Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy.
- For solid organ transplant patients, prior therapy includes chemotherapy unless chemotherapy is inappropriate.

C • EFFICACY [6,7]

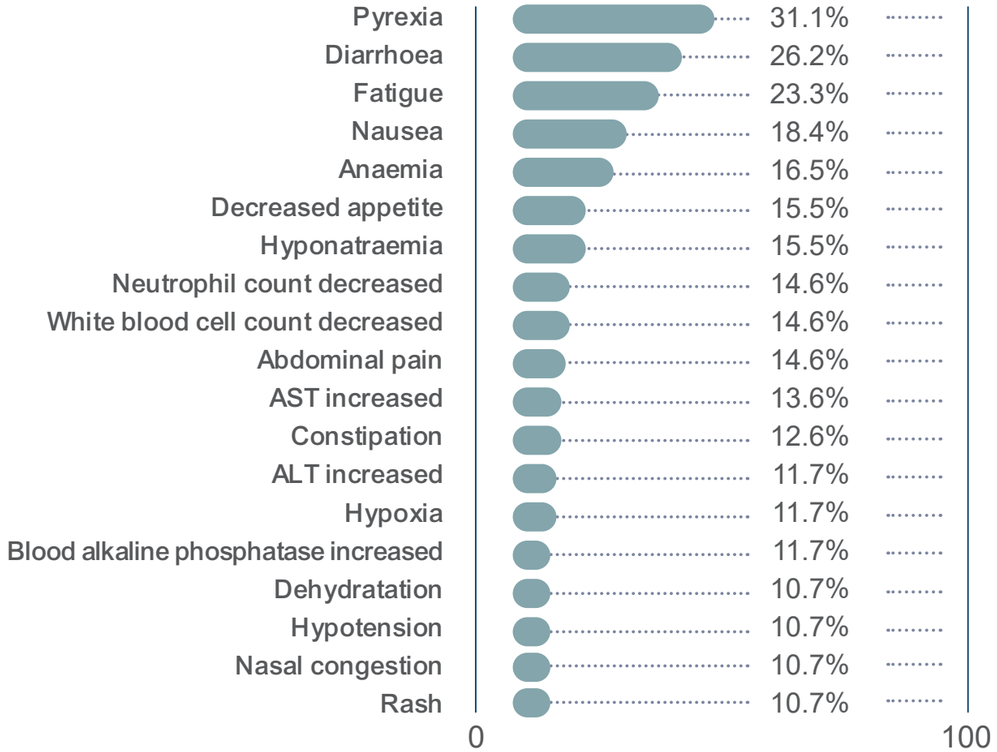


ORR: Objective Response Rate ; OS: Overall Survival ; CR: complete response ; PR: partial response ; SD: stable disease ; PD: progressive disease ; NE: includes not evaluable, missing, and indeterminate response.

D • SAFETY [5]

Frequencies of adverse reactions with EBVALLO were evaluated in 103 patients in PTLD development program:

Most common Adverse Reactions [5]



Most serious Adverse Reactions [5]

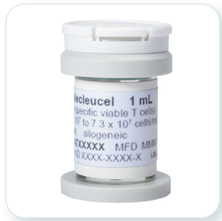
Adverse events	Nb of patients (%)	Grade	Outcome
Tumour flare reaction	1 (1%)	3	Recovered
Graft-versus-host disease	5 (4,9%)	2 grade 1 1 grade 2 1 grade 3 1 grade 4	No fatal events were reported. 4 patients recovered from GvHD.

3. EBVALLO ORDERING, DELIVERY & STORAGE

A • PRODUCT & PACKAGING DESCRIPTION [5]

- EBVALLO is a translucent, colourless to slightly yellow cell dispersion for injection.
- Each vial contains **1 mL** deliverable volume of EBVALLO at a concentration of 2.8×10^7 to 7.3×10^7 viable T-cells/mL dispersion for injection.
- Excipients : dimethyl sulfoxide DMSO (100mg/mL), human serum albumin, phosphate buffered saline.

EBVALLO vials are packaged in a carton containing between 1 and 6 vials, depending on the weight of the patient :



tabelecleucel 1 mL
(EBV-specific viable T cells)
2.8×10^7 to 7.3×10^7 cells/mL
IV use; allogeneic
Lot ATXXXXX MFD MMM YYYY
Donor ID XXXX-XXXX-X

Primary packaging* :

- Nominal cell concentration
- Lot number
- Manufacturing date
- Donor ID

** On some primary packagings, Atara Biotherapeutics may also be mentioned as manufacturer of the product.*

Secondary packaging :

- <u>For 1 injection:</u> 1 box of EBVALLO (dimensions 129 mm x 129 mm x 49 mm), containing up to 6 vials of product (depending on patient's weight)
- You will either receive product for 1 injection (1 box), or 1 cycle (3 injections ie 3 boxes), depending on your order

The Lot Information Sheet (LIS), placed on the cryoshipper, contains:

- <u>Patient information:</u> Pierre Fabre Patient Identification Number (PFPIN), Institution Patient Identification (to allow you to reconcile product with patient at your institution), patient weight.
- <u>Lot information:</u> lot number, donor ID, finished drug product (FDP) number, number of vials, actual concentration (viable T-cells/mL), expiry date, donor cytomegalovirus (CMV) status.
- <u>Lot HLA profile</u>

B • GO CELL THERAPY PLATFORM: ORDERING & MANAGEMENT

Go Cell Therapy™

Please scan the QR Code to access to the **Go Cell Therapy** platform.

www.go-cell-therapy.com is the ordering and management platform for EBVALLO.

PRESCRIPTION :

1. The physician completes patient's information and requests a lot of EBVALLO on Go Cell Therapy platform.
2. If a lot is available, the physician receives a lot proposal, and decides to confirm it or not.

ORDERING :

2. Once the lot is confirmed by the physician, the pharmacist has to order the lot on Go Cell Therapy platform.

SHIPMENT :

Pierre Fabre

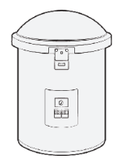
3. Once both confirmation from physician, and order from pharmacist, are available in Go Cell Therapy platform, Pierre Fabre will ship the EBVALLO lot.
4. Based on the exchanges at site activation, the hospital will receive either a full cycle (3 injections), or 1 injection at a time.
5. The pharmacist can follow the shipment and exchange with Pierre Fabre upon need directly on Go Cell Therapy platform.

For more information, please refer to the Go Cell Therapy platform user guide.

C • SHIPMENT

-150°

In a shipper charged with **liquid nitrogen** (LN2) at a temperature ≤ -150°C.



Shipper **sealed,** secured with a tamper evident tag, and shipped to the processing site by a **qualified carrier.**

Shipper equipped with a **monitoring device** that transmits real-time temperature, location and other data.

Go Cell Therapy™

You can access the **tracking link** in the Go Cell Therapy platform.

EBVALLO® tabelecleucel

D • RECEPTION

- Make sure the shipper is **sealed** with an intact tamper evident seal.
- Access the Connected Data Viewer and check the temperature records to ensure there has been **no temperature excursion** during transport.

  - 3 temperature excursions up to -80 °C are permittable [5].
- Bring the shipper with the product inside to the place of storage.
- Unload EBVALLO from the shipper.
- Check the correspondance between the **patient identifier** and the information on the **Lot Information Sheet (LIS).**

The shipper will be picked up the same day or the next working day.
If different collection arrangements are required regarding the pick-up of the shipper, please contact your Pierre Fabre Representative through the Go Cell Therapy portal.

D • STORAGE AND PRESERVATION UNTIL PRODUCT USE [5]

- The EBVALLO carton must be stored **in the vapour phase of liquid nitrogen at ≤ -150 °C** until immediately prior to preparation for administration.
- Once the product is safely stored, please confirm product receipt and patient identity in the Go Cell Therapy platform.

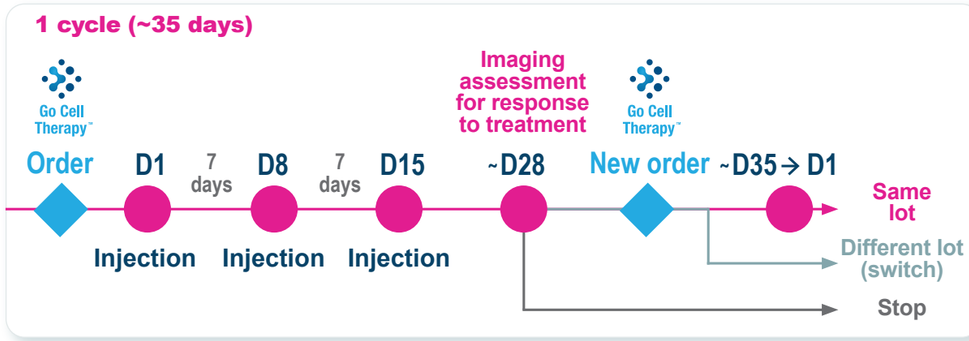
4 years

4 years shelf life when stored in the vapour phase of liquid nitrogen at ≤ -150 °C

The drug product lot manufacturing date (MFD) is provided on the vial. The expiry date is provided on the Lot Information Sheet (LIS) and carton.

4. EBVALLO PREPARATION & ADMINISTRATION [5]

A • POSOLOGY [5]



- EBVALLO is administered over multiple 35-day cycles, during which patients receive EBVALLO on **days 1, 8 and 15,** followed by **observation through day 35.**
- A response is assessed at approximately day 28.
- The **number of cycles** of the medicinal product to be administered is determined by the response to treatment. For more information, please refer to Annex 2.

B • EBVALLO DOSE CALCULATION [5]

- The recommended dose of EBVALLO to administer to your patient is **2 × 10^6 viable T-cells per kg** of body weight.
- **Each lot of EBVALLO has a different concentration, provided in the LIS** (Lot Information Sheet) included with the shipper, within the range of 2.8 × 10^7 to 7.3 × 10^7 viable T-cells/mL.

To define the volume of EBVALLO that you need to administer to your patient, you need to take into account :
- Your patient's weight
- The actual concentration of the lot provided in the LIS

The calculation is as follows :

Patient weight in kg	×	(2 x 10^6) viable T-cells/kg (recommended dose of EBVALLO)	=	Total viable T-cells to be administered	÷	Actual concentration (viable T-cells / mL) per LIS and carton	=	Volume of thawed cell suspension required (mL)
_____	×		=	_____	÷	_____	=	_____

EXAMPLE

60 kg	×	(2 x 10^6) viable T-cells/kg (recommended dose of EBVALLO)	=	12 × 10^7	÷	4 × 10^7	=	3 mL
Patient weight in kg				Total viable T-cells to be administered		Actual concentration (viable T-cells mL) per LIS and carton		Volume of thawed cell suspension required (mL)

Where do I find the actual concentration of the lot ?

The viable T-cell concentration on the LIS and carton is the actual concentration of each vial.

LOT INFORMATION SHEET

EBVALLO®
2.8 x 10^7 - 7.3 x 10^7 cells/mL
dispersion for injection
tabelecleucel (EBV-specific viable T cells)

An allogeneic Epstein-Barr virus (EBV)-specific T-cell immunotherapy.
Each vial contains 1 mL deliverable volume at a concentration of 2.8 x 10^7 - 7.3 x 10^7 viable T cells/mL dispersion for injection. This medicine contains cells of human origin.
The actual concentration noted below should be used to calculate the patient dose.

PATIENT INFORMATION

Pierre Fabre Patient Identification Number (PFPIN)
Institution Patient Identification | Patient Weight (kg) 1
Single European Code (SEC)

INFORMATION ON SUPPLIED LOT
The following lot was manufactured and included in this shipment:

Lot Number
Donor ID
Finished Drug Product (FDP) Number
Number of Vials
Actual Concentration (viable T cells/mL) **4 × 10^7**
Expiry Date

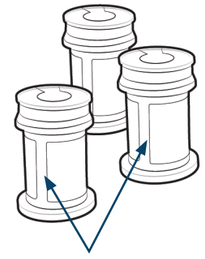
Donor/Donated Cells Cytomegalovirus (CMV) Markers	IgM Antibodies	
	IgG Antibodies	
	Nucleic Acid Testing (NAT)	

PRODUCT LOT HLA PROFILE
(restrictions in **bold red**)

HLA	ALLELE 1	ALLELE 2
A		
B		
C		
DRB1		
DQB1		

Page 1 of 2

This may be different than the nominal concentration listed on the vial label, which should not be used for dose preparation calculations.



Nominal concentration indicated on the vial label

Dose calculations for special populations [5] :

Elderly

No dose adjustment

Hepatic and renal impairment

No dose adjustment

Pediatric population

Same posology and administration in paediatric patients 2 years of age and older as for adult patients

- **If a patient misses a dose,** the missed dose should be given as soon as reasonably possible
- There are **no data regarding overdose** with EBVALLO.

C • WARNINGS AND PRECAUTIONS [5]

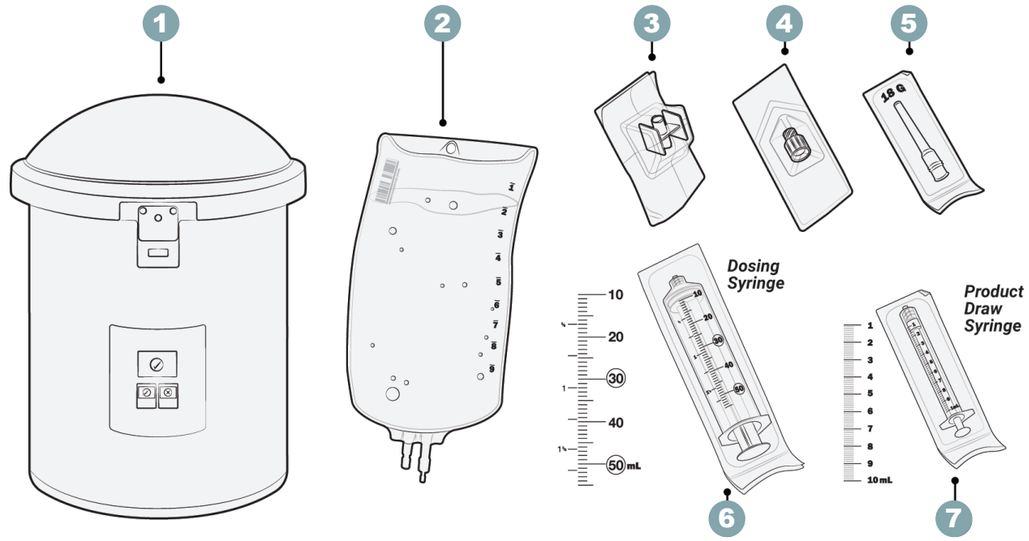
EBVALLO contains human blood cells.

Healthcare professionals handling EBVALLO should take appropriate precautions (wearing gloves and glasses) to avoid potential transmission of infectious diseases.

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

D • EBVALLO PREPARATION

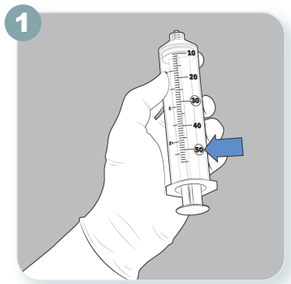
I • Gathering supplies [5]



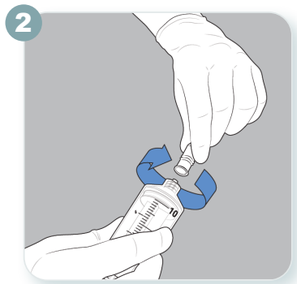
1. Confirm EBVALLO is **on site**
2. Gather the **diluent :** sterile, non-pyrogenic multiple electrolytes solution for injection Type 1 pH 7.4
3. Gather a **Luer Lock adapter**
4. Gather a **Luer Lock cap**
5. Gather sterile **18-gauge unfiltered needles** to transfer the diluent to the Product Draw Syringe, and to transfer cell suspension
6. Select the **Dosing Syringe :** a sterile needle that can accommodate the required diluent volume (up to 50 mL), and calculated volume of cell suspension needed based on patient's dose calculation (up to 6 mL)
7. Select the **Product Draw Syringe :** a sterile dosing syringe, with 1/10 mL graduation marks, that can accommodate the calculated volume of cell suspension needed based on patient's dose calculation (up to 6 mL)

- **Please also make sure that you have available :**
  - Thawing system supplies
  - Sterile bags
  - IV Flush : normal saline
  - Nylon gloves (for handling frozen material)

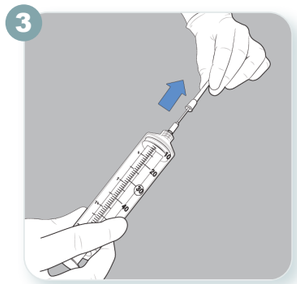
II • Diluent preparation [5]



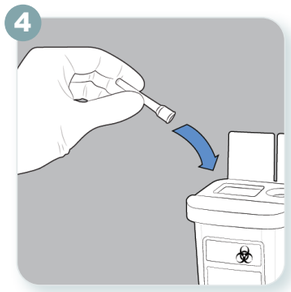
Select the appropriate diluent volume:
• 30 mL for patient weight ≤ 40 kg
• 50 mL for patient weight > 40 kg



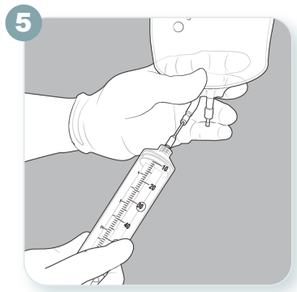
Attach needle to dosing syringe.



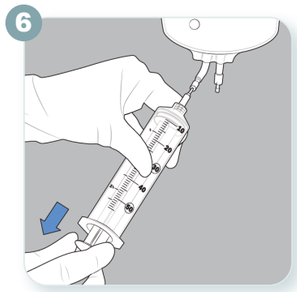
Remove needle cap from attached needle on dosing syringe.



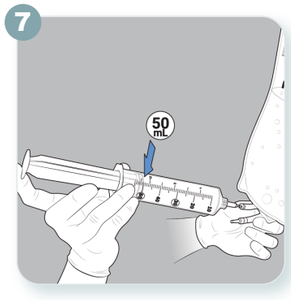
Dispose of needle cap in Sharps biohazard disposal container.



Pierce diluent bag with dosing syringe needle.

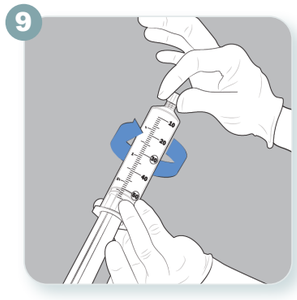


Aseptically draw the required diluent volume based on the patient's weight into a dosing syringe.



Draw correct amount into dosing syringe.

Dispose of dosing syringe needle in Sharps biohazard disposal container.



Place Luer Lock cap on syringe. Keep the diluent syringe ready under sterile conditions.

III • Pre-thawing checking and preparation [5]

- **Patient identity :** must match the patient identifiers (PFPIN and Institution Patient ID) on the accompanying EBVALLO LIS and carton.
- **Product-patient reconciliation :** must be performed by matching information on the LIS against
  1. The carton (matching PFPIN, Lot Number and Donor ID)
  2. The vial label (matching Lot Number and Donor ID).

Do not prepare or administer EBVALLO if the patient's identity or the product-patient reconciliation cannot be confirmed.

- Before starting thawing procedures, confirm that the patient is **on site** and has been **clinically evaluated.**

- Ensure that the required **dose calculations** are complete.

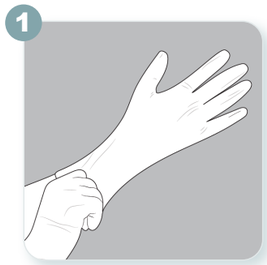
- Ensure that all **materials** needed to prepare the dose are available.

- **Inspect** EBVALLO vials for any cracks or tears in the vials before thawing.

If any vials appear to be leaking or damaged, the content should not be administered and should be eliminated according to local biological waste disposal procedures.

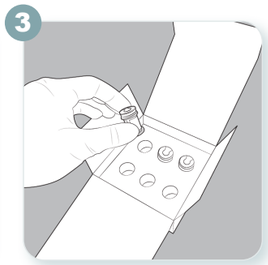
- Prepare the **water bath** or the **dry thawing chamber** by setting it to 37°C

IV • Thawing [5]



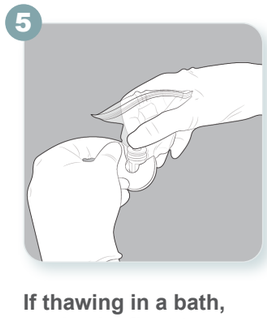
Put on insulated gloves prior to opening shipper.

Remove the carton from the vapour phase of liquid nitrogen at ≤ 150°C.



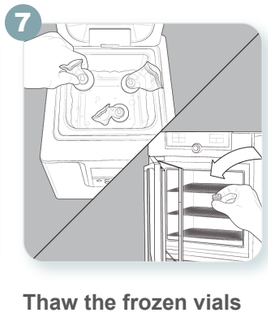
Remove frozen vial(s) from carton to prepare dose.

Place each vial inside a sterile bag during thawing to protect from contamination.



If thawing in a bath, apply vial float to outside of sterile bag where the frozen vial has been placed.

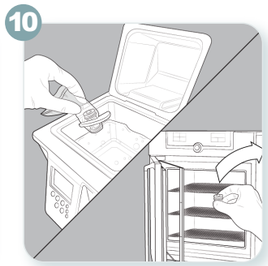
Ensure the vial is upright.



Thaw the frozen vials upright in a 37°C water bath or dry thawing chamber

Record the “start of thaw” time.

While the medicinal product thaws, swirl the product vial(s) gently until fully thawed by inspection (approximately 2.5 to 15 minutes)

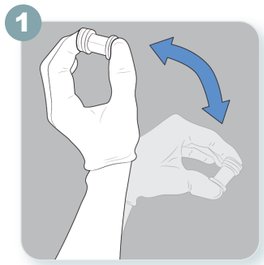


Remove the vial(s) from the water bath or thawing chamber immediately upon completion of thaw.

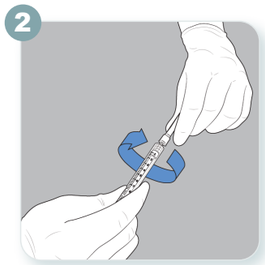
Inspect vial(s). If not fully thawed, return vial(s) to water bath or thawing chamber & continue thawing the solution

Record « use by » time on dosing syringe label: administration must be completed as early as possible and no later than 3 hours from the start of the thaw

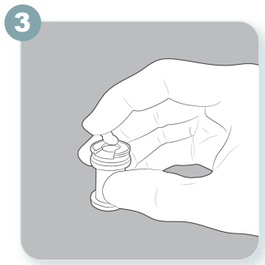
V • Dilution and dose preparation [5]



Gently invert the vial(s) until the cell dispersion is mixed

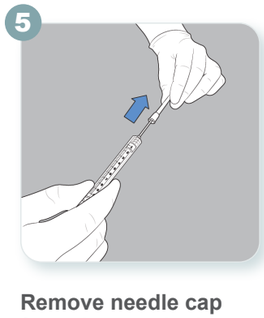


Attach 18-gauge unfiltered needle to product draw syringe.

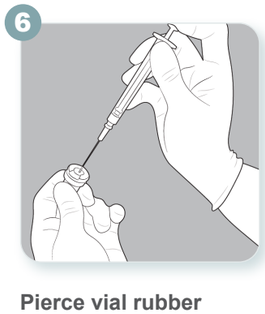


Remove protective cap to reveal septum of vial(s).

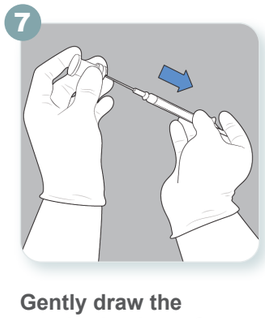
Sanitize all vial septums (e.g., wipe with alcohol prep pad).



Remove needle cap from the attached needle on product draw syringe.



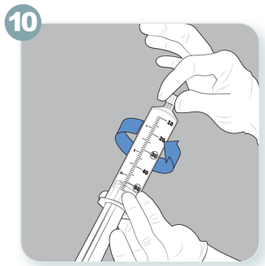
Pierce vial rubber septum of the thawed vial(s) with the product draw syringe.



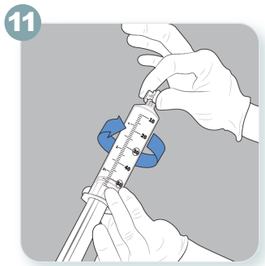
Gently draw the required volume from the vial(s) into the product draw syringe.

Repeat steps 1-7 with remaining vials until required volume of cell suspension obtained.

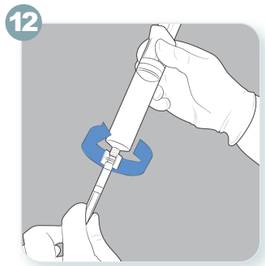
Dispose of product draw syringe needle and Luer Lock adapter in Sharps biohazard disposal container.



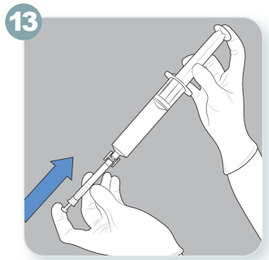
Remove Luer Lock cap from dosing syringe.



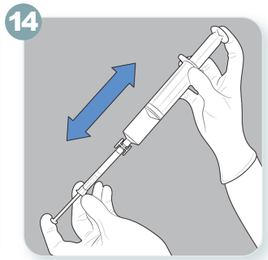
Attach Luer Lock adapter to dosing syringe.



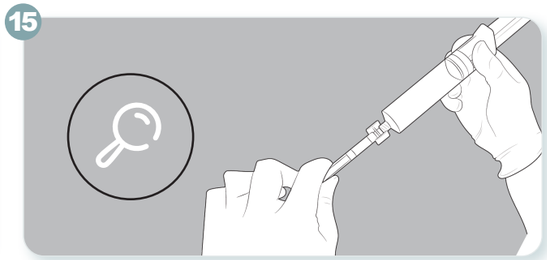
Attach product draw syringe with Luer Lock adapter to dosing syringe.



Gently aseptically transfer the product from the product draw syringe to the dosing syringe to create the diluted cell suspension.



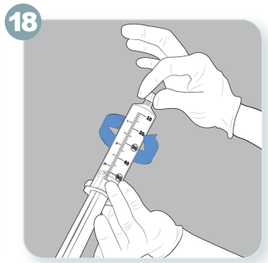
Ensure entire contents are transferred from the product draw syringe to the dosing syringe with a rinse step.



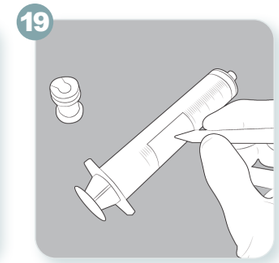
- Inspect the diluted Ebvallo in the dosing syringe: cell dispersion should appear as a translucent, hazy solution.
- If visible clumps appear, continue to gently mix the solution.
- Small clumps of cellular material should disperse with gentle manual mixing.

Detach the Luer Lock adapter from the dosing syringe and the product draw syringe.

Dispose of product draw syringe and Luer Lock adapter in Sharps biohazard disposal container.



Close dosing syringe with sterile Luer Lock cap for administration.



Label the dosing syringe according to institution practice.

15-25°C

once solution is thawed

Maintain EBVALLO between 15 °C to 25 °C during dose preparation and administration.

1 hour maximum

time limit to complete dose preparation

The cell suspension must be thawed and diluted as early as possible and no later than 1 hour of the start of thaw.

3 hours maximum

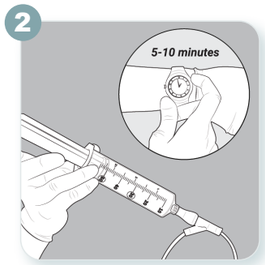
to administer once thawed

Administration must be completed within 3 hours from the start of thaw.

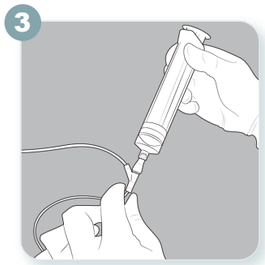
E • ADMINISTRATION [5]

- EBVALLO should be administered **under the supervision of a physician** experienced in the treatment of cancer in a controlled setting where adequate facilities for handling of adverse reactions, including those requiring urgent measures, are available.
- EBVALLO is for **intravenous use** only.
- Prior to administration, verify the **patient's identity** matches the patient identifiers on the EBVALLO dosing syringe according to institution practice.

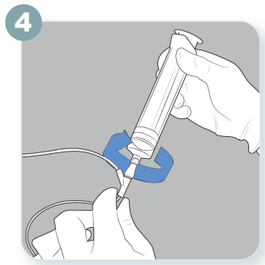
Once patient's IV catheter is prepared, attach the dosing syringe with cell suspension to the patient's giving set.



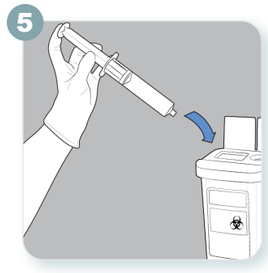
Connect the final medicinal product syringe to the patient's giving set and inject over 5 to 10 minutes.



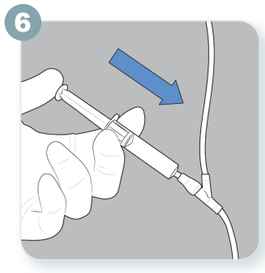
Ensure that the entire dose of cell suspension has been administered.



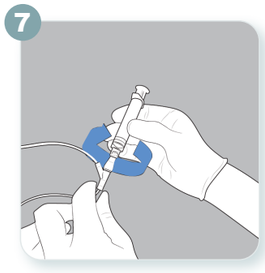
Remove dosing syringe from the patient's giving set.



Dispose of dosing syringe Sharps biohazard disposal container.



Once EBVALLO is fully dispensed from the syringe, flush the intravenous line with ≥ 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection.



Remove flush syringe from the patient's giving set.

Dispose of flush syringe in Sharps biohazard disposal container.

I • Monitoring after injection [5]

- It is recommended to **monitor vital signs :**
  - Immediately prior to each EBVALLO injection
  - Within 10 minutes following the conclusion of the injection
  - 1 hour after the initiation of the injection.

II • Precautions to be taken for the disposal of the medicinal product [5]

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

III • Accidental exposure [5]

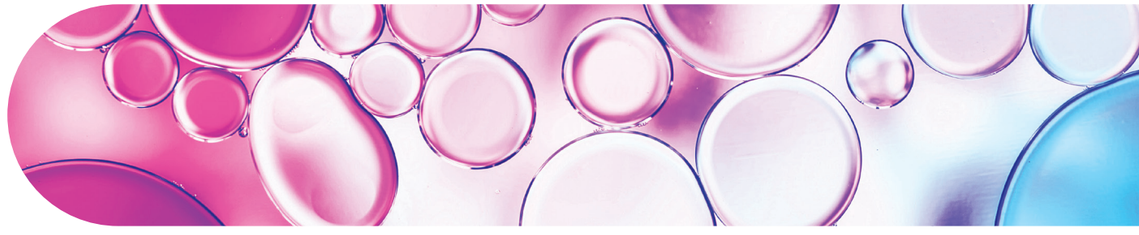
- In case of **accidental exposure,** local guidelines on handling of human-derived material should be followed, which may include washing of the contaminated skin and removal of contaminated clothes.
- Work surfaces and materials which have potentially been in contact with EBVALLO must be **decontaminated** with appropriate disinfectant.

5. QUALITY COMPLAINT

Go Cell Therapy™

For any quality complaint, please go to the Go Cell Therapy portal and click on **« Quality complaints ».**

Examples :
- The tamper seal of the shipper is not intact
- Temperature variation
- Vials appear to be leaking or damaged



EBVALLO® tabelecleucel

6. SUMMARY OF KEY STEPS TO ORDER, RECEIVE, PREPARE & ADMINISTER EBVALLO [5]

EBVALLO Ordering & Delivery

- Place order and discuss timing of delivery through the Go Cell Therapy platform.
- Upon reception, check the integrity of the shipper, the temperature history, the product-patient reconciliation, and the integrity of the product.

EBVALLO Storage

- Store in the vapour phase of liquid nitrogen at ≤ -150 °C until immediately prior to preparation for administration.

EBVALLO Preparation

- Calculate the volume of product to be administered.
- Gather supplies.
- Confirm that the patient is on site and has been clinically evaluated.
- Confirm the product-patient reconciliation : patient identity must match the information on the LIS and the carton.
- Prepare the diluent into the dosing syringe.
- Remove EBVALLO from the storage place.
- Thaw the cells at 37°C and record the start of thaw time :

15-25°C

once solution is thawed

1 hour maximum

time limit to complete dose preparation

3 hours maximum

to administer once thawed

- Transfer the cells from the unfrozen vials to the product draw syringe.
- Transfer the cells from the product draw syringe to the dosing syringe dilution.
- Label the EBVALLO dosing syringe.

EBVALLO Administration

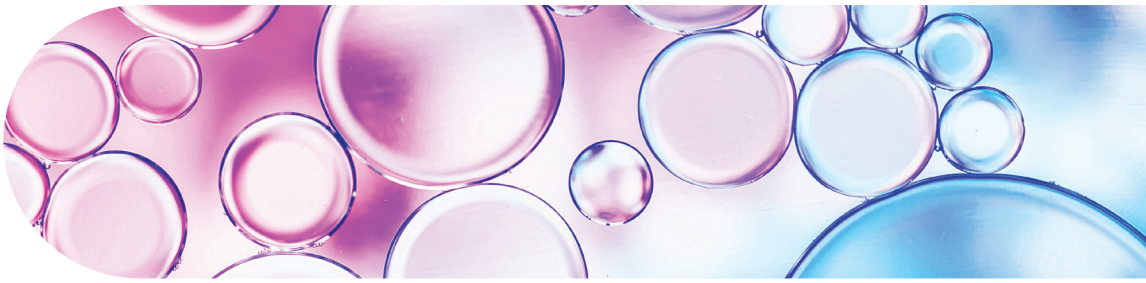
- Transport the EBVALLO dosing syringe to the patient's room.
- Verify the patient's identity matches the EBVALLO dosing syringe.
- Administrate as a single dose intravenously after dilution.
- Once fully dispensed, flush the intravenous line with ≥ 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection.
- Monitor vital signs immediately prior to injection, within 10 minutes following the conclusion of the injection, and 1 hour after initiation of the injection.

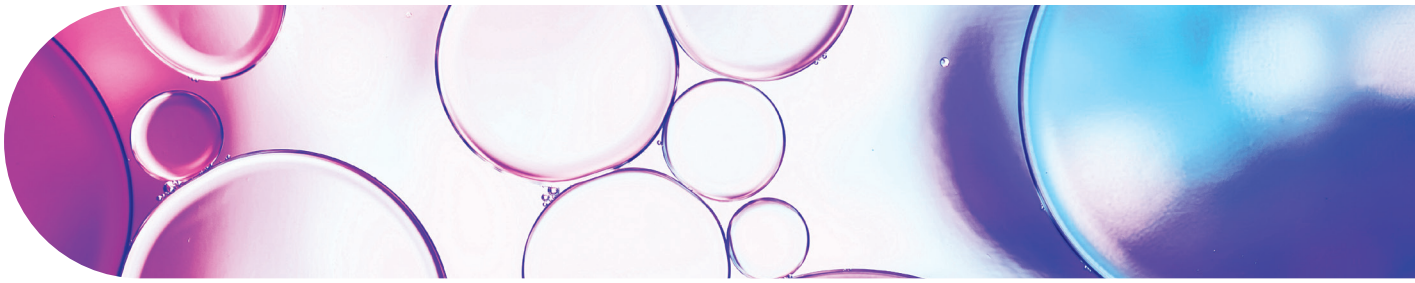
In case of any questions, please contact your Pierre Fabre representative through the Go Cell Therapy platform.

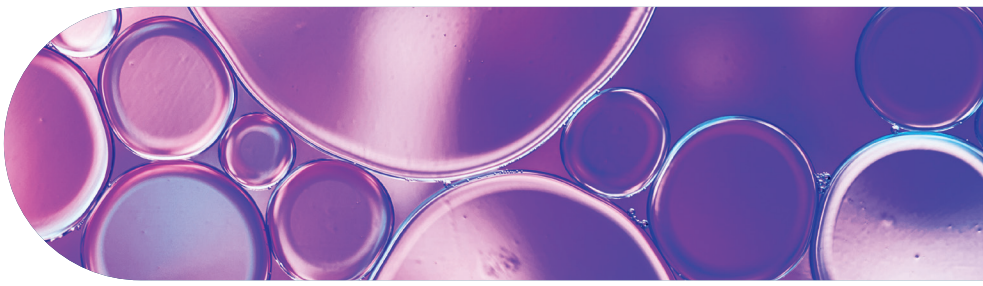
Go Cell Therapy™

EBVALLO®
tabelecleucel

ANNEXES

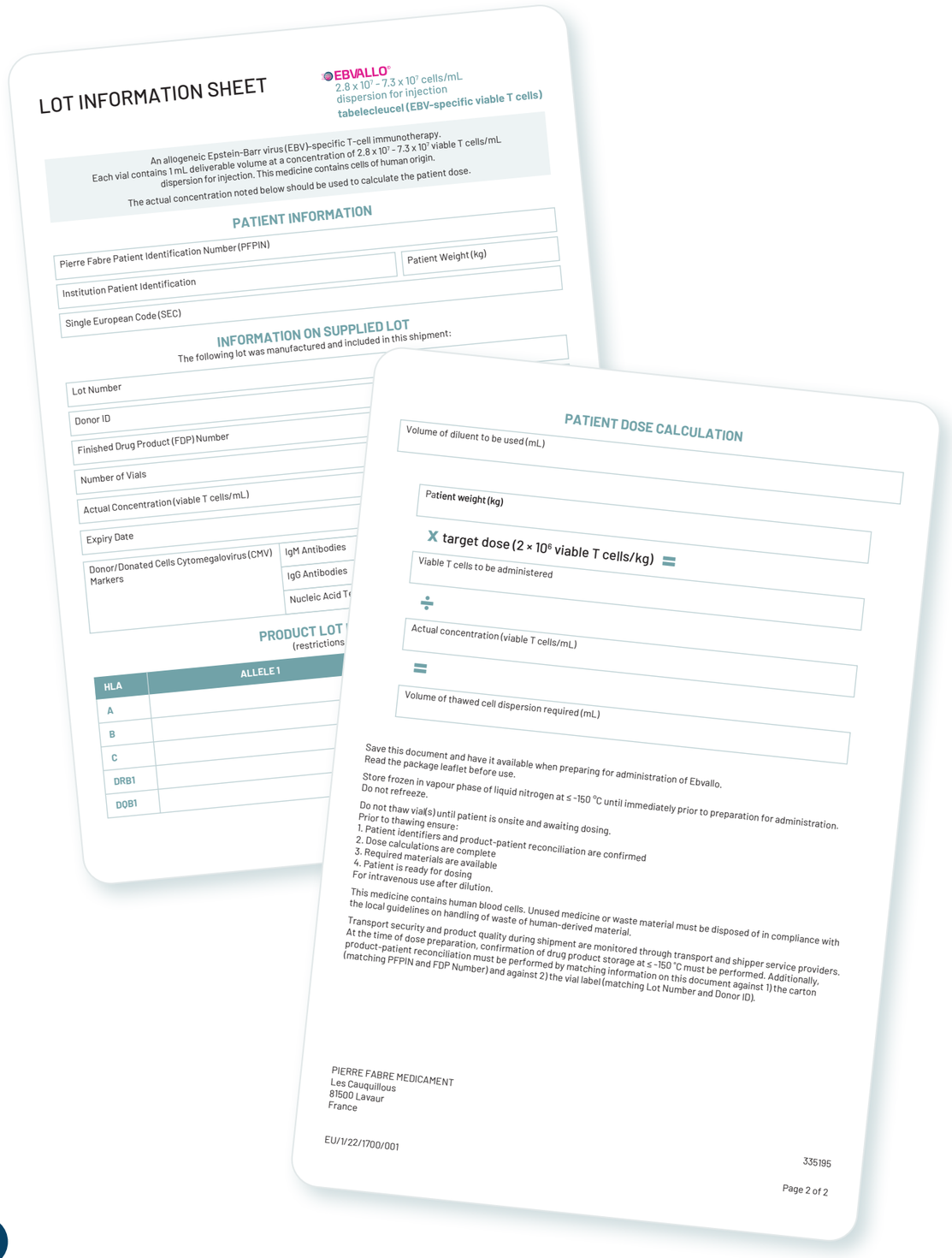






Pierre Fabre

7. ANNEX 1 – LOT INFORMATION SHEET [5]



LOT INFORMATION SHEET

EBVALLO®
2.8 x 10^7 – 7.3 x 10^7 cells/mL
dispersion for injection
tabelecleucel (EBV-specific viable T cells)

An allogeneic Epstein-Barr virus (EBV)-specific T-cell immunotherapy.
Each vial contains 1 mL deliverable volume at a concentration of 2.8 x 10^7 – 7.3 x 10^7 viable T cells/mL dispersion for injection. This medicine contains cells of human origin.
The actual concentration noted below should be used to calculate the patient dose.

PATIENT INFORMATION

Pierre Fabre Patient Identification Number (PFPIN)

Institution Patient Identification

Patient Weight (kg)

Single European Code (SEC)

INFORMATION ON SUPPLIED LOT

The following lot was manufactured and included in this shipment:

Lot Number

Donor ID

Finished Drug Product (FDP) Number

Number of Vials

Actual Concentration (viable T cells/mL)

Expiry Date

Donor/Donated Cells Cytomegalovirus (CMV) Markers

IgM Antibodies

IgG Antibodies

Nucleic Acid Te

PRODUCT LOT
(restrictions

HLA	ALLELE 1
A	
B	
C	
DRB1	
DQB1	

PATIENT DOSE CALCULATION

Volume of diluent to be used (mL)

Patient weight (kg)

X target dose (2 × 10^6 viable T cells/kg) =

Viable T cells to be administered

÷

Actual concentration (viable T cells/mL)

=

Volume of thawed cell dispersion required (mL)

Save this document and have it available when preparing for administration of Ebvallo.
Read the package leaflet before use.

Store frozen in vapour phase of liquid nitrogen at ≤ -150 °C until immediately prior to preparation for administration.
Do not refreeze.

Do not thaw vial(s) until patient is onsite and awaiting dosing.
Prior to thawing ensure:
1. Patient identifiers and product-patient reconciliation are confirmed
2. Dose calculations are complete
3. Required materials are available
4. Patient is ready for dosing

For intravenous use after dilution.

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.

Transport security and product quality during shipment are monitored through transport and shipper service providers. At the time of dose preparation, confirmation of drug product storage at ≤ -150 °C must be performed. Additionally, product-patient reconciliation must be performed by matching information on this document against 1) the carton (matching PFPIN and FDP Number) and against 2) the vial label (matching Lot Number and Donor ID).

PIERRE FABRE MEDICAMENT
Les Cauquillous
81500 Lavaur
France

EU/1/22/1700/001

335195

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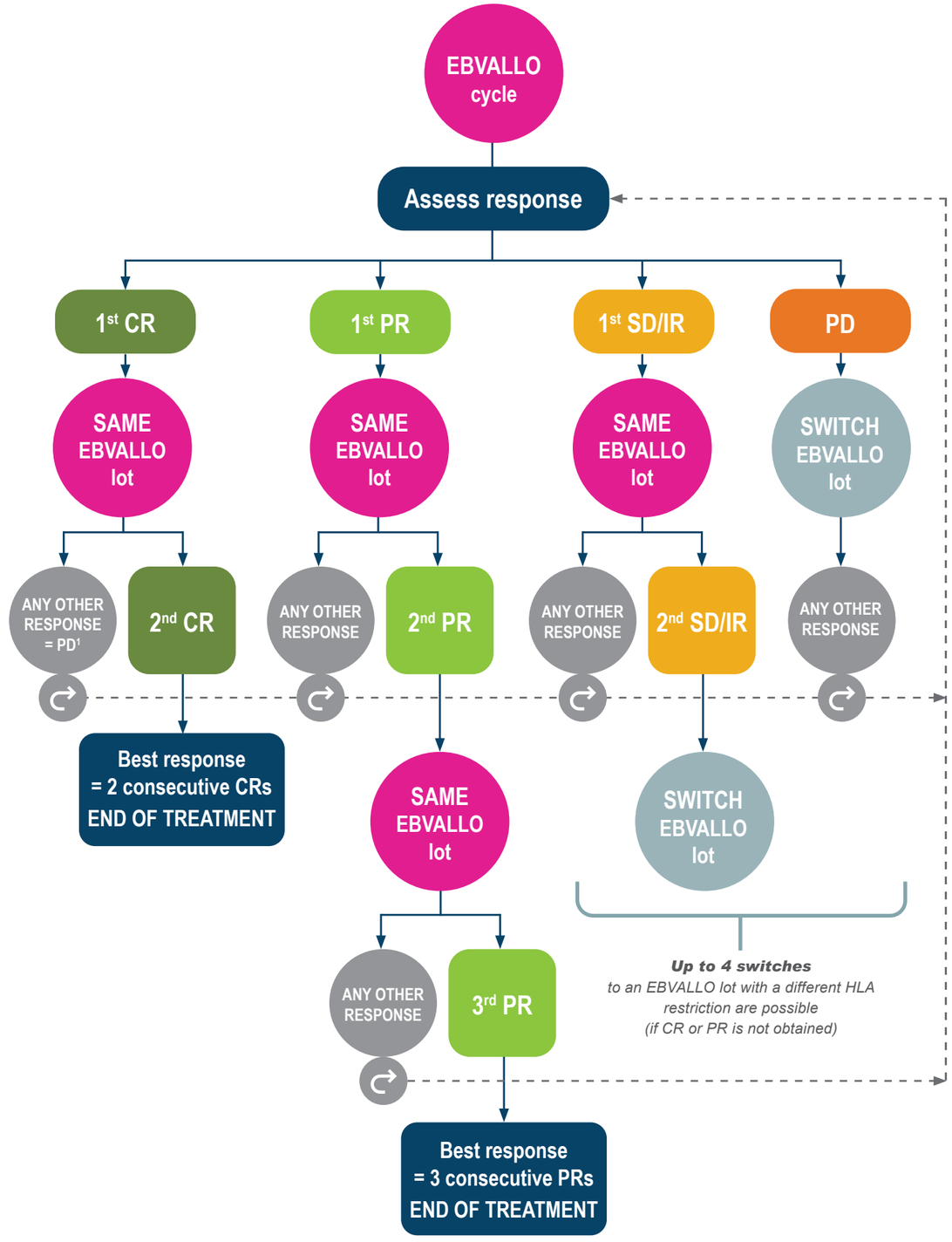
ANNEX 2 – TREATMENT ALGORITHM [5]



1. CR at the end of a cycle followed by PR or other response at any subsequent cycle is considered PD
***CR:** complete response; **PR:** partial response; **SD:** stable disease; **ID:** indeterminate response; **PD:** progressive disease*

EBVALLO®▼
tabelecleucel

Key information to keep in mind while handling EBVALLO[5]:

-150°C
Until immediately prior to preparation for administration

15-25°C
once solution is thawed

1 hour maximum
time limit to complete dose preparation

3 hours maximum
to administer once thawed

Summary SmPC

EBVALLO ABBREVIATED PRESCRIBING INFORMATION

▼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 below for how to report any adverse events.

NAME OF THE MEDICINAL PRODUCT: Ebvallo $2.8 \times 10^7 – 7.3 \times 10^7$ cells/mL dispersion for injection

CLINICAL PARTICULARS:

Therapeutic indications: Ebvallo is indicated as monotherapy for treatment of adult and paediatric patients 2 years of age and older with relapse and refractory Epstein-Barr virus post-transplant lymphoproliferative disease. (EBV+ PTLD) who have received at least one prior therapy. For solid organ transplant patients, prior therapy includes chemotherapy unless chemotherapy is inappropriate.

Posology and method of administration: Ebvallo should be administered under the supervision of a physician experienced in the treatment of cancer in a controlled setting where adequate facilities for handling of adverse reactions, including those requiring urgent measures, are available.

Posology: The recommended dose of Ebvallo contains 2×10^6 viable T-cells per kg of patient's body weight. Treatment consists of multiple doses for injection containing a dispersion of viable T-cells in one or more vials. Ebvallo is administered over multiple 35-day cycles, during which patients receive it on days 1, 8 and 15, followed by observation through day 35. A response is assessed at approximately day 28. (see SmPC Section 4.2).

Method of administration: Ebvallo should be administered under the supervision of a physician experienced in the treatment of cancer in a control setting where adequate facilities for handling of adverse reactions, including those for required urgent measures, are available. Ebvallo is for intravenous use only. Administer Ebvallo as a single dose intravenously after dilution. Connect the final medicinal product syringe to the patient's intravenous catheter and inject over 5 to 10 minutes. Once Ebvallo is fully dispensed from the syringe, flush the IV line with ≥ 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. For detailed instructions on preparation, accidental exposure and disposal of the medicinal product, see SMPC section 6.6

Contraindications: Hypersensitivity to the active substance or to any of the excipients: Dimethyl sulfoxide, Human serum albumin, Phosphate buffered saline.

Interaction with other medicinal products and other forms of interaction: No interaction studies have been performed. Ebvallo should only be administered after an adequate washout period of certain concomitant or recently administered medicinal products including chemotherapy (systemic or intrathecal), anti T-cell antibody-based therapies, extracorporeal photopheresis or brentuximab vedotin. They could potentially impact the efficacy of Ebvallo. For patients receiving chronic corticosteroid therapy, the dose of these drugs should be reduced; recommended no greater than 1 mg/kg per day of prednisone or equivalent. For complete information, please refer to SmPC Section 4.5

Contraceptives and breastfeeding: Ebvallo is not recommended during pregnancy and in women of childbearing potential not using contraception. Pregnant women should be advised on potential risks for the foetus. Breast-feeding women should be advised of potential risks to the breast-fed child. There are no data on the effect of Ebvallo on fertility. For complete information, please refer to SmPC Section 4.6

Undesirable effects: Summary of safety profile: The most common adverse reactions were pyrexia (31.1%), diarrhoea (26.2%), fatigue (23.3%), nausea (18.4%), anaemia (16.5%), decreased appetite (15.5%), hyponatraemia (15.5%), abdominal pain (14.6%), neutrophil count decreased (14.6%), white blood cell count decreased (14.6%), aspartate aminotransferase increased (13.6%), constipation (12.6%), alanine aminotransferase increased (11.7%), blood alkaline phosphatase increased (11.7%), hypoxia (11.7%), dehydration (10.7%), hypotension (10.7%), nasal congestion (10.7%) and rash (10.7%). For complete information, please refer to SmPC Section 4.8.

MARKETING AUTHORISATION HOLDER :

Pierre Fabre Médicament - Les Cauquillous, 81500 Lavaur, France.

DATE OF REVISION OF THE TEXT:

February 2023. Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu. For complete information, please refer to SmPC. Latest review of EU SmPC: 2023.

REPORTING OF SUSPECTED ADVERSE REACTIONS:

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions via the national reporting system (Appendix V - European Medicines Agency - Europa EU) and/or to the Pharmacovigilance department of Pierre Fabre laboratories (www.pierre-fabre.com/en/pharmacovigilance).

For complete information, please refer to:
EBVALLO Summary of Product Characteristics
https://www.ema.europa.eu/en/documents/product-information/ebvallo-epar-product-information_en.pdf

Pierre Fabre