GUIDE FOR HANDLING AND METHOD OF ADMINISTRATION FOR

LIBMELDY®, dispersion for infusion

(atidarsagene autotemcel)

Healthcare professionals are asked to report any suspected adverse reactions. Reporting details are at the end of this guide.

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.

General Guidance

- Libmeldy must be administered in a qualified treatment centre (QTC) with experience in haematopoietic stem cell transplantation (HSCT).
- Libmeldy is intended solely for autologous use via intravenous infusion and should under no circumstances be administered to other patients.
- The dose of Libmeldy to be infused should be defined 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. For detailed guidance on the definition of the dose of Libmeldy to be infused, please refer to the Lot Information Sheet and Section 6.6 of the Summary of Product Characteristics (SPC), and the information intended for healthcare professionals provided at the end of the patient information leaflet (PIL).
- It is recommended that pre-medication with intravenous chlorpheniramine or an equivalent drug be used before the infusion of Libmeldy, to reduce the possibility of an allergic reaction to the infusion.
- A myeloablative conditioning is required before infusion of Libmeldy to promote efficient engraftment of the genetically modified autologous $CD34^+$ cells. Busulfan is the recommended conditioning agent.
- Libmeldy should only be administered once.

Precautions to be taken before handling or administering Libmeldy

- Libmeldy is prepared from mobilised peripheral blood and it consists of genetically modified human cells. It may carry a risk of transmitting infectious agents to healthcare professionals who handle the medicinal product.
- Healthcare professionals handling Libmeldy must take appropriate precautions (wearing gloves, protective clothing and eye protection) to avoid potential transmission of infectious diseases.

Instructions for receiving and storing Libmeldy

- Each infusion bag is provided inside an overwrap bag, which is contained in a metal cassette. The infusion bag(s) must be stored inside their cassette(s), in cryogenic storage, until ready to thaw for administration.
- The Lot Information Sheet will indicate the total number of bags supplied.
- Upon receipt of Libmeldy, verify that the temperature of the cryoshipper (liquid nitrogen [LN_2] dry vapour shipper) has been maintained throughout the shipment by checking the temperature live view link.
- If Libmeldy is shipped to the QTC in advance of treatment and is subsequently stored at the site, then a liquid nitrogen cryogenic storage/transport dewar (rather than the LN_2 cryoshipper) can be used to store and transport Libmeldy from QTC storage to infusion. During receipt and transfer to storage of the cassette(s) from the LN_2 cryoshipper to a cryogenic storage/transport dewar, check for any visible damage to the cassette and secondary overwrap bag. Verify that the information on the label of the cassette(s) and secondary overwrap bag(s) match the Lot Information Sheet. During the inspection of the labels, do not allow the cassette(s) to be exposed to ambient temperature for longer than 1 minute.
- Libmeldy is intended solely for autologous use.
- Libmeldy must remain at <-130°C at all times until it is thawed for administration.

NOTE: If storing with other cell therapy products that may have a slightly different storage temperature, the QTC should ensure that the storage temperature is maintained at <-130°C at all times.

Instructions to check Libmeldy prior to administration

- Do not remove the product from cryogenic storage until the patient is ready to be infused.
- Verify that the information on the label of the cassette matches the Lot Information Sheet.
- Prior to thawing Libmeldy, confirm that the cryopreserved product has been stored appropriately at <-130°C and that the patient identity matches the unique patient information reported on the Libmeldy secondary packaging label and on the accompanying Lot Information Sheet.
- Libmeldy is intended solely for autologous use. Do not thaw or infuse Libmeldy if the information on the patient specific labels does not match the intended patient.
- Inspect the overwrap bag for any visible breaks or cracks prior to thawing.

NOTE: If the overwrap bag is compromised, follow institutional guidelines for handling of waste of human-derived material and contact Orchard immediately at QTC@orchard-tx.com with complaints@orchard-tx.com in copy.

Instructions for the thawing of Libmeldy

- Do not thaw Libmeldy until the patient is ready to be infused.
- Do not remove the infusion bag from the overwrap bag until after the product has been thawed.
- Thaw Libmeldy in the sealed overwrap bag at 37°C using a controlled thawing device.
- Ensure that the controlled thawing device is functional and maintained in line with device manufacturers' guidance.
- Thaw until no visible ice remains
- Once thawing is complete, immediately remove the product, within the overwrap bag, from the thawing device.
- Do not continue to warm the product in the device after thawing is complete.
- Keep at room temperature (20°C - 25°C) and proceed immediately to infusion.
- Carefully open the sealed overwrap bag and remove the primary infusion bag.
- Gently massage the infusion bag between fingers and thumbs to resuspend the cells and disperse any potential cellular aggregates. Inspect the contents for any remaining visible cellular aggregates. If visible cellular aggregates remain, gently massage the infusion bag.
- Do not shake the bag. Small clumps of cellular material should disperse with gentle manual mixing.
- If more than one infusion bag is required for the patient treatment dose, the next bag should only be thawed after the content of the preceding bag has been infused.
- The infusion bag should not be washed, spun down, sampled and/or resuspended in new media prior to infusion.
- Libmeldy should not be irradiated as irradiation could lead to inactivation of the product.

NOTE: If the infusion bag is compromised, follow institutional guidelines for handling of waste of human-derived material and contact Orchard immediately at QTC@orchard-tx.com with complaints@orchard-tx.com in copy.

Instructions for administration of Libmeldy

- Do not administer Libmeldy after the expiry date (stated on the label).
- Confirm the patient's identity matches the unique patient identifiers on each infusion bag label prior to administration. Do not thaw or infuse Libmeldy if the information on the patient specific label does not match the intended patient.
- Libmeldy infusion must be completed within 2 hours of thawing each bag.
- Infuse Libmeldy intravenously using a transfusion administration set. The recommended administration set consists of a blood transfusion set equipped with a 200 µm filter. Do not use filters with finer mesh size as it may trap the drug product.
- Infuse by gravity. An infusion pump may be used to regulate infusion rate and maintain fluid balance.
- The maximum infusion rate is 5 mL/kg/h, and each bag of Libmeldy should be administered within approximately 30 minutes as an intravenous infusion via a central venous catheter.
- If more than one bag of Libmeldy is needed, only one bag of Libmeldy should be infused per hour, and the absence of any immediate hypersensitivity reaction should be confirmed before starting the infusion of the subsequent bag.
- Following administration, rinse the bag, infusion set and line at the same infusion rate with sodium chloride 9 mg/mL (0.9%) solution for injection to facilitate complete delivery of Libmeldy. The total volume of fluid administered should be in accordance with medical guidelines given the age and weight of the patient.
- Patients not previously exposed to dimethyl sulfoxide (DMSO) should be observed closely. 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, during the infusion and after the infusion of each Libmeldy bag as per institution guidelines.
- Standard procedures for patient management after HSPC transplantation should be followed after Libmeldy infusion.

Precautions to be taken for the disposal of Libmeldy

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

Accidental exposure to Libmeldy

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

Reporting of suspected adverse reactions

- Report any suspected adverse reactions via the National Pharmacovigilance Centre (NPC): SFDA Call Center: 19999, E-mail: npc.drug@sfda.gov.sa, Website: https://ade.sfda.gov.sa/
- Also report any suspected adverse reactions involving Libmeldy to Orchard Therapeutics by email to drugsafety@orchard-tx.com and Cigalah by email to drug-safety@cigalah.com.sa.
- When reporting possible adverse reactions, include the medicinal product lot number found on the patient alert card and Lot Information Sheet.