Pharmacy/Cell Lab/Infusion Center Training Material

Novartis Oncology

This material can help you follow the steps for reception, storage, handling, thawing, administration, and preparation for infusion of a CD19-directed genetically modified autologous T cell immunotherapy delivered in its final packaging of one to three infusion bags for a specific patient ("Kymriah") to mitigate a decrease in cell viability.

Kymriah is indicated for the treatment of:

- Paediatric and young adult patients up to and including 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse.
- Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy.
- Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Process Overview

Arrival, Receipt and Storage of KYMRIAH

- Kymriah is supplied as a cell dispersion in one to three infusion bags ("Dose") labelled for the specific patient
- Kymriah is shipped directly to the cryostorage facility associated with the infusion center in a dry vapour shipper in the vapour phase of liquid nitrogen
- Each CS50 (50 ml) infusion bag contains 10 to 30 ml of dispersion and each CS250 (250 ml) infusion bag contains 30 to 50 ml of dispersion
- Verify the number of bag(s) received for the Dose of Kymriah with the Certificate of Conformance
- Confirm that there were no temperature excursions during transport
- Unload Kymriah from the dry vapour shipper
- Open the secondary packaging, inspect the product and note the Donation Identification Number (DIN) or apheresis ID (in accordance with your institutional procedures)
- Store the Kymriah infusion bag(s) below -120°C, e.g., in a container for cryogenic storage in the vapour phase of liquid nitrogen. Ensure that Kymriah is stored in a protective packaging that has been validated in the cryostorage tank, following the institutional procedures to avoid a bag integrity risk

Handling KYMRIAH

- Kymriah is prepared from autologous blood of the patient collected by leukapheresis and contains genetically modified human blood cells. Patient leukapheresis material and Kymriah may carry a risk of transmitting infectious viruses to healthcare professionals handling the product
- Healthcare professionals should employ appropriate precautions (wearing gloves and glasses) when handling leukapheresis material or Kymriah to avoid potential transmission of infectious diseases when handling the product
- Kymriah should be transported within the facility in closed, break-proof, leak-proof containers. Do not irradiate
- All material that has been in contact with Kymriah (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling of biological waste

Kymriah is recommended to be infused 2 to 14 days after completion of the lymphodepleting chemotherapy for B-cell ALL and DLBCL indications. Kymriah is recommended to be infused 2 to 6 days after completion of the lymphodepleting chemotherapy for FL indication. There must be a confirmation that the patient can receive Kymriah.

1. Preparation for Infusion

The timing of thaw of Kymriah and infusion should be coordinated. The infusion start time should be confirmed in advance and adjusted for thaw so that Kymriah is available for infusion when the recipient is ready.

Once a Kymriah infusion bag has been thawed and is at room temperature (20°C - 25°C), it should be infused within 30 minutes to maintain maximum product viability, including any interruption during the infusion.

- Two doses of tocilizumab and emergency equipment must be available per patient prior to infusion and during the recovery period. The treatment center must have access to additional doses of tocilizumab within 8 hours to manage cytokine release syndrome (CRS) according to the CRS management algorithm per local package insert.
  - In the exceptional case where tocilizumab is not available due to a shortage, the treatment centre must have access to suitable alternative measures instead of tocilizumab to treat CRS
- Confirm patient identity: Prior to Kymriah preparation, match the patient's identity with the patient identifiers on the Kymriah infusion bag(s). Kymriah is for autologous use only

2. Thawing Kymriah

One Dose comprises one to three infusion bags. If more than one infusion bag has been received for the Dose, the next bag should only be thawed after the contents of the preceding bag have been infused.

Do not thaw Kymriah until it is ready to use.

- Examine the Kymriah infusion bag for any breaks or cracks prior to thawing. Place the Kymriah infusion bag inside a second sterile bag during thawing to protect ports from contamination and avoid spills in the unlikely event of the bag leaking
- If the Kymriah infusion bag appears to have been damaged or to be leaking, it should not be infused and should be disposed of according to local procedures on handling of biological waste. Call the **Novartis Customer Service Center (Kymriah Care®) at 1800-407-5614/ +65 6722 6126/ email: kymriahcares.ap@novartis.com)** and contact Novartis Country Quality Organization to notify them of the product issue
- Thaw Kymriah at 37°C using either a water bath or dry thaw method until there is no visible ice in the infusion bag. Inspect the contents of the thawed infusion bag for any visible cell clumps. If visible cell clumps remain, gently mix the contents of the bag. Small clumps of cellular material should disperse with gentle manual mixing. Do not infuse Kymriah if clumps are not dispersed.
  - Remove infusion bag from the thawing device immediately and keep at room temperature (20°C - 25°C) until infusion
  - Once an infusion bag has been thawed and is at room temperature (20°C - 25°C), it should be infused within 30 minutes, including any interruption during the infusion, to maintain maximum product viability
  - Kymriah should not be manipulated. Do not wash, spin down, and/or resuspend Kymriah in new media prior to infusion
  - There may be a decrease in cell viability of Kymriah due to inappropriate handling of the manufactured product, including transport and storage, in addition to thawing and standing time prior to infusion. This may impact the efficacy and safety profile of Kymriah.

3. Administration of KYMRIAH

- The patient's identity must be confirmed with the patient identifiers on the Kymriah infusion bag
- Kymriah is infused by intravenous infusion through latex-free intravenous tubing without a leukocyte depleting filter at approximately 10-20 mL per minute by gravity flow
- If the volume of Kymriah to be administered is ≤ 20 mL, intravenous push may be used as an alternative method of administration
- Sterile sodium chloride 9 mg/mL (0.9%) solution for injection should be used to prime the tubing prior to infusion and to rinse it after infusion
- Infuse all contents of the Kymriah infusion bag. The Kymriah infusion bag should be rinsed with 10 to 30 mL sodium chloride 9 mg/mL (0.9%) solution for injection by back priming to ensure as many cells as possible are infused into the patient

Repeat sections 2-3 above, sequentially, for any additional Kymriah infusion bag(s) received.

This guide can help you prepare for the arrival and receipt of Kymriah.

APPENDIX

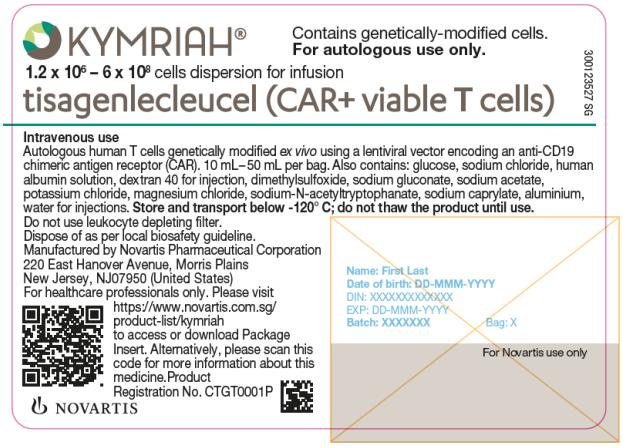
Supplemental Information

KYMRIAH Packaging and Shipment

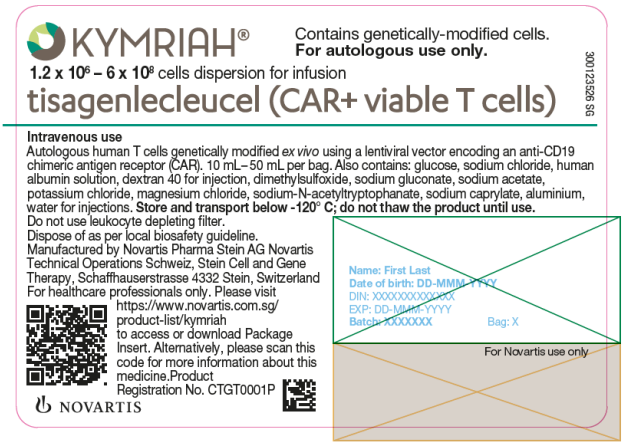
- Kymriah is supplied as a frozen dispersion of genetically modified autologous T cells in one to three infusion bags labelled for the specific recipient
  - Kymriah infusion bag(s) have an affixed product label containing unique patient identifiers, including patient name, patient date of birth (DOB), and either patient Donation Identification Number (DIN) or apheresis ID (Figure i and ii)
- Kymriah is shipped from Novartis to the cryostorage facility associated with the infusion center in a dry vapour shipper in the vapour phase of liquid nitrogen
  - During transport, Kymriah is maintained below -120°C
  - Temperature is continuously monitored and recorded using an online data log viewer
- A shipping notification e-mail containing a tracking link is sent to all registered Novartis ordering platform users when Kymriah is shipped from the Novartis manufacturing facility
  - A shipment tracking link can also be found within the Novartis ordering platform

Figure (i) and (ii):
Example of KYMRIAH Product Label manufactured by:

(i) Novartis Pharmaceutical Corporation



(ii) Novartis Pharma Stein AG Novartis Technical Operations Schweiz, Stein Cell and Gene Therapy



Arrival, receipt and storage of KYMRIAH

After delivery of the dry vapour shipper, the cryostorage facility associated with the infusion center must:

- Confirm that there were no temperature excursions during transport by viewing temperature data in the online data log viewer
- Unload Kymriah from the dry vapour shipper
- Confirm patient identity and receipt of Kymriah in the Novartis ordering platform
- Transfer Kymriah to on-site storage below -120°C, e.g., in a container for cryogenic storage in the vapour phase of liquid nitrogen
- Store the Kymriah infusion bag(s) in a protective packaging that has been validated in the cryostorage tank, following institutional procedures to avoid a bag integrity risk

The following steps provide details on how to complete these requirements:

While performing these steps, follow institutional standard operating procedures to ensure that Kymriah is kept below -120°C.

Follow local guidelines on handling of biological waste and employ appropriate precautions (wearing gloves and glasses) when handling Kymriah to avoid potential transmission of infectious diseases.

Use closed, break-proof, leak-proof containers when transporting Kymriah within the facility.

1. Access the temperature recordings for the shipment through the online data log viewer
   - Access the online data log viewer via the tracking link in either the shipping notification e-mail or the link found within the Novartis ordering platform
   - To ensure the most updated temperature recordings are displayed, refresh in the online data log viewer
2. Check the temperature recordings to ensure there were no temperature excursions during transport
   - Note: A temperature reading above -120°C represents a temperature excursion; however, a brief spike above -120°C is normal and acceptable at the time Kymriah was loaded into the dry vapour shipper
   - Report any temperature excursions by calling the **Novartis Customer Service Center (Kymriah Cares®) at 1800-407-5614/ +65 6722 6126/ email: kymriahcares.ap@novartis.com)** and contacting the Novartis Country Quality Organization
   - An exported PDF version of the temperature profile should be kept with the patient's medical records
3. Unload Kymriah and accompanying documentation from the dry vapour shipper
   - Upon delivery, ensure that the dry vapour shipper is sealed with an intact uniquely identifiable tamper-proof zip tie. If the zip tie is not intact, call the **Novartis Customer Service Center (Kymriah Cares®) at 1800-407-5614/ +65 6722 6126/ email: kymriahcares.ap@novartis.com)** and contact the Novartis Country Quality Organization
   - Follow institutional standard operating procedures for liquid nitrogen handling when unloading the dry vapour shipper
   - Verify the number of bags received for the Dose of Kymriah with the Certificate of Conformance
4. Carefully examine the Kymriah infusion bag(s) and ensure that the bag(s) is/are intact and free from any damage, including cracks, leaks, etc. Confirm that the patient identifiers on the Kymriah infusion bag label(s) match those in institutional records. If damage is noted, or patient identifiers do not match, call the **Novartis Customer Service Center (Kymriah Cares®) at 1800-407-5614/ +65 6722 6126/ email: kymriahcares.ap@novartis.com)** and contact the Novartis Country Quality Organization

(continued on the following page)

- Follow institutional standard operating procedures to ensure that Kymriah is kept below-120°C

5. Log in to the Novartis ordering platform and document the receipt of Kymriah
6. Transfer Kymriah to on-site storage
   - Store and transport frozen product below -120°C, e.g., in a container for cryogenic storage in the vapour phase of liquid nitrogen. Store the Kymriah infusion bag(s) in a protective packaging that has been validated in the cryostorage tank, following institutional procedures to avoid a bag integrity risk
7. The empty dry vapour shipper will be picked up the next business day. If you need a different pick-up arrangement, please call the **Novartis Customer Service Center (Kymriah Cares® at 1800-407-5614/+65 6722 6126/ email: kymriahcares.ap@novartis.com)**

For questions, please contact your Novartis Customer Liaison Manager or call the Novartis Customer Service Center (Kymriah Cares®) at 1800-407-5614/ +65 6722 6126/ email: kymriahcares.ap@novartis.com)

Please see the full product labeling for Kymriah.

For Healthcare Professionals only

Please visit https://www.novartis.com.sg/product-list/kymriah to access or download Package Insert. Alternatively, please scan this code for more information about this medicine

NOVARTIS

Novartis (Singapore) Pte Ltd
20 Pasir Panjang Rd #10-25/28 Mapletree Business City Singapore 117439

This document has been approved by HSA as of 14 Mar 2025.