This document has been approved by Saudi Food and Drug Authority (SFDA)

Pharmacy/Cell Lab/Infusion Center Training Material

Novartis Oncology

This material can help you follow the steps for reception, storage, handling, thawing and preparation for infusion of Kymriah to mitigate a decrease in cell viability.

Arrival, Receipt and Storage of KYMRIAH

- Kymriah is supplied as a cell dispersion in 1 or more infusion bags labelled for the specific patient. Kymriah is shipped directly to the cryostorage facility associated with the infusion centre in a Dewar in the vapour phase of liquid nitrogen
- Verify the number of bags received for the dose of Kymriah with the QP Batch Certificate
- Confirm that there were no temperature excursions during transport
- Unload Kymriah from the dry vapour shipper Dewar
- Open the Tyvek bag, open the protective polybag and cassette, inspect the product and note the DIN or apheresis ID (in accordance with your institutional procedures)
- Repack the cassette into the Tyvek bag and store below –120°C in the cryostorage container

  *Note: If the size of the repacked Kymriah cassette is too big to allow storage in your cryotank due to the rack configuration, the alternative Novartis recommendation for storage is for the site to:

  — Ensure that the Kymriah Cryobag is stored in a protective cassette that has been validated in the cryostorage tank, following institutional procedures to avoid a bag integrity risk

  — Ensure that a secondary overwrap is protecting the cassette protecting the bag (ideally a sealed polybag) and that the Batch ID traceability in the secondary overwrap is maintained (sticker, hangtag or markers can be used)
- Use closed, break-proof, leak-proof containers when transporting infusion bags within the facility

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

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Kymriah is recommended to be infused 2 to 14 days after completion of the lymphodepleting chemotherapy. 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 Kymriah 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.

- One dose 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 CRS according to the CRS management algorithm per local prescribing information
- Confirm patient identity: Prior to Kymriah preparation, match the patient's identity with the patient identifiers on the Kymriah infusion bag. Kymriah is for autologous use only

2. Thawing KYMRIAH

One individual treatment dose comprises 1 or more infusion bags. If more than one infusion bag has been received for the treatment dose, the next bag should only be thawed after the contents of the preceding bag have been infused.

Do not thaw the product until it is ready to use.

- Examine the infusion bag(s) for any breaks or cracks prior to thawing. Place the 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 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. Please call **MyKymriah Service Center** at **(800 850 0774)** or send an email to **(my.kymriah@novartis.com)**.
- Thaw Kymriah at 37°C using either a water bath or dry thaw method until there is no visible ice in the infusion bag
  - — Remove infusion bag from the thawing device immediately and keep at room temperature (20°C - 25°C) until infusion
  - — Once Kymriah 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, 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 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 infusion bag. The 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 bags received.

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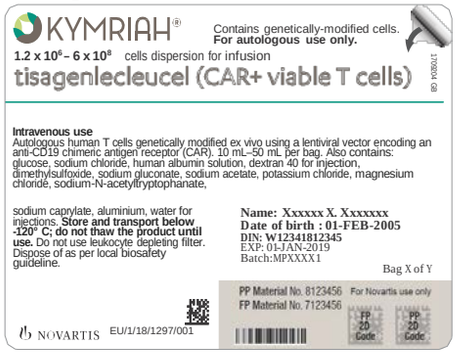
This guide can help you prepare for the arrival and receipt of KYMRIAH.

KYMRIAH Packaging and Shipment

- Kymriah is supplied as a frozen dispersion of genetically modified autologous T cells in 1 or more infusion bags labeled for the specific recipient
  - — Infusion bags 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 1)

Figure 1:
Example of KYMRIAH Product Label



- Kymriah is shipped from Novartis to the cryostorage facility associated with the infusion center in a Dewar 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 is also found in the patient's Finished Product Delivery Appointment page within the Novartis ordering platform

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 Dewar
- — Confirm patient identity and receipt of Kymriah in the Novartis ordering platform
- — Transfer Kymriah to on-site storage below -120°C in a Dewar in the vapour phase of liquid nitrogen
- — Where possible, store in the original Tyvek bag containing the cassette protecting the bag. Note instructions on Page 1 for alternate recommendations
- — Use closed, break-proof, leak-proof containers when transporting infusion bags within the facility

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 patient's Finished Product Delivery Appointment page 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 **MyKymriah Service Center** at **(800 850 0774)** or send an email to **(my.kymriah@novartis.com)**.
   - — An exported PDF version of the temperature profile should be kept with the patient's medical records

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3. Unload Kymriah and accompanying documentation from the dry vapour shipper Dewar
   - Upon delivery, ensure that the Dewar is sealed with an intact uniquely identifiable tamper-proof zip tie. If the zip tie is not intact, please call **MyKymriah Service Center** at **(800 850 0774)** or send an email to **(my.kymriah@novartis.com)**.
   - Follow institutional standard operating procedures for liquid nitrogen handling when unloading the Dewar
   - Verify the number of bags received for the dose of Kymriah with the QP Batch Certificate
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, please call **MyKymriah Service Center** at **(800 850 0774)** or send an email to **(my.kymriah@novartis.com)**.
   - Follow institutional standard operating procedures to ensure that Kymriah is kept below -120°C
5. Log in to the Novartis ordering platform and navigate to the patient's Finished Product Delivery Appointment page
   - Access the patient's Finished Product Delivery Appointment page in the Novartis ordering platform via the link provided in the shipping notification e-mail
   - Login credentials should have been received via e-mail after completion of the Novartis ordering platform Access Form and completion of system training with Novartis
6. On the bottom of the page, click "View" to display the Certificate of Conformance (this is the same as the QP Batch Certificate). Confirm that the details listed on the QP Batch Certificate exactly match the details in your institutional records.
7. Return to the patient's Finished Product Delivery Appointment page, and click "Update Details." Enter the number of infusion bags received for the treatment dose, and click "Save"
8. When the confirmation prompt appears on the screen, read it carefully and click "Confirm" if the qualifications in the prompt are met
9. In the next prompt that appears, rekey the patient's DIN/apheresis ID directly from a Kymriah infusion bag label. Click "Proceed"
   - When entering the DIN/apheresis ID, do not include spaces or special characters
   - Note: Rekeying the DIN/apheresis ID directly from a Kymriah infusion bag label into the Novartis ordering platform is critical in maintaining Chain of Identity
10. Return to the patient's Finished Product Delivery Appointment page, and enter the date and time of product receipt where requested. Click "Save Changes." After the prompt appears indicating that changes have been successfully saved, click "OK"
    - Note: Receipt of the final product has now been documented
11. Transfer Kymriah to on-site storage
    - Store and transport frozen product below -120°C, e.g. in a Dewar in the vapour phase of liquid nitrogen. Where possible, store in the original Tyvek bag containing the cassette protecting the bag. Note instructions on Page 1 for alternate recommendations
12. The empty dry vapour shipper will be picked up the next business day. If you need a different pick-up arrangement, please call **MyKymriah Service Center** at **(800 850 0774)** or send an email to **(my.kymriah@novartis.com)**.

- For questions, please contact your Novartis Cell Therapy Network Manager or call **MyKymriah Service Center** at **(800 850 0774)** or send an email to **(my.kymriah@novartis.com)**.

Please see the full product labeling for Kymriah.
You can report any problem or adverse events or request additional copies of the materials through

Patient Safety Department Novartis Saudi Limited - Saudi Arabia.
Toll Free Number: 8001240078
Phone: +966112658100
Fax: +966112658107
Email: adverse.events@novartis.com
Website: http://report.novartis.com/

Saudi Food and Drug Authority National Pharmacovigilance Center
Unified Contact Center: 19999
Toll Free Number: 80024900000
Fax: +966112057662
Email: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

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