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

Pharmacy/Cell Lab/Infusion Centre 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 indicated for the treatment of paediatric and young adult patients up to and including 25 years of age with B-cell acute lymphoblastic leukaemia and adult patients with relapsed or refractory diffuse large B-cell lymphoma, delivered in its final packaging of one or more infusion bags for a specific patient ("Kymriah") to mitigate a decrease in cell viability.

Arrival, Receipt and Storage of KYMRIAH

- Kymriah is supplied as a cell dispersion in one or more infusion bags ("Dose") labelled for the specific patient. Kymriah is shipped directly to the cryostorage facility associated with the infusion centre in a dry vapour shipper in the vapour phase of liquid nitrogen
- Verify the number of bag(s) received for the Dose of Kymriah with the QP Batch Certificate or 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)
- 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 and store the infusion bag(s) and store below –120°C in the cryostorage container
- Use closed, break-proof, leak-proof containers when transporting Kymriah 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.

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.

- One dose of tocilizumab and emergency equipment must be available per patient prior to infusion and during the recovery period. The treatment centre 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 prescribing information
  - In the exceptional case where tocilizumab is not available due to a shortage that is listed in the European Medicines Agency shortage catalogue, 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. Kymriah is for autologous use only

2. Thawing KYMRIAH

One Dose comprises one or more 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 Please call MyKymriah Service Center at (800 850 0774) or send an email to (my.kymriah@novartis.com). and contact Novartis Country Quality Organisation 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
  - 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.

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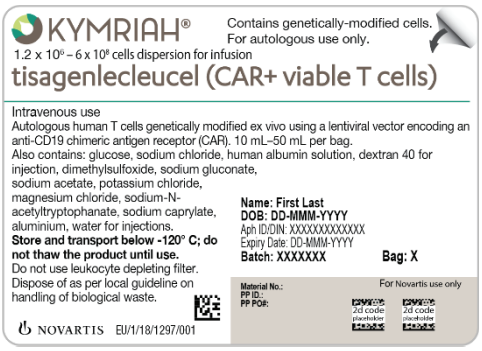
This guide can help you prepare for the arrival and receipt of KYMRIAH

KYMRIAH Packaging and Shipment

- Kymriah is supplied as a frozen dispersion of genetically modified autologous T cells in one or more 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 1)
- Kymriah is shipped from Novartis to the cryostorage facility associated with the infusion centre 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 1:
Example of KYMRIAH Product Label



Arrival, receipt and storage of KYMRIAH

After delivery of the dry vapour shipper, the cryostorage facility associated with the infusion centre 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
- Use closed, break-proof, leak-proof containers when transporting Kymriah 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 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 Please call MyKymriah Service Center at (800 850 0774) or send an email to (my.kymriah@novartis.com) and contacting the Novartis Country Quality Organisation
   - An exported PDF version of the temperature profile should be kept with the patient's medical records

(continued on the following page)

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 **CTL019 Service Centre** at **+800 100 10 100** and contact the Novartis Country Quality Organisation
   - 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 QP Batch Certificate or 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 Please call MyKymriah Service Center at (800 850 0774) or send an email to (my.kymriah@novartis.com)and contact the Novartis CountryQuality Organisation
   - 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-pickup arrangement, please call the Please call MyKymriah Service Center at (800 850 0774) or send an email to (my.kymriah@novartis.com).

Healthcare providers are encouraged to report AEs if causality to the Kymriah treatment is suspected
Adverse reactions associated with Kymriah can be reported to Novartis or local Health Authorities SFDA

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
Fax: 966112057662+
Email: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

When reporting adverse events, healthcare providers should always include the individual Kymriah Batch-identification number printed on the front of the Kymriah Patient Alert Card

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

Please see the full product labelling for Kymriah.

NOVARTIS
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KYMRIAH

Important note: Before prescribing, consult full prescribing information.

Presentation: Cell dispersion for infusion in one or more bags for intravenous use (tisagenlecleucel).

Indications: 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.**

Dosage and administration:

Dose in paediatric and young adult B-cell ALL patients:

For patients 50 kg and below: 0.2 to 5.0 x 106 CAR-positive viable T-cells/kg body weight.

For patients above 50 kg: 0.1 to 2.5 x 108 CAR-positive viable T-cells (non-weight based).

Dose in adult DLBCL patients:

0.6 to 6.0 × 108 CAR-positive viable T-cells (non-weight based).

Manufacture and release of Kymriah usually takes about 3 to 4 weeks.

Kymriah must be administered in a treatment center that has been qualified by the Marketing Authorization Holder (MAH). Therapy should be initiated under the direction of and supervised by a healthcare professional experienced in the treatment of hematological malignancies and trained for Kymriah administration and management of patients treated with Kymriah. A minimum of one dosesof tocilizumab per patient for use in the event of cytokine release syndrome and emergency equipment must be available on site prior to infusion. Treatment centers should have timely access to additional doses of tocilizumab with in 8 hours.

Pre-treatment conditioning (lymphodepleting chemotherapy)

Lymphodepleting chemotherapy is recommended to be administered before Kymriah infusion unless the white blood cell (WBC) count within one week prior to infusion is ≤1,000 cells/µL.

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

Chemotherapy. The availability of Kymriah must be confirmed prior to starting the lymphodepleting Regimen. If there is a delay of more than 4 weeks between completing lymphodepleting chemotherapy and the infusion and the WBC count is >1,000 cells/µL, then the patient should be re-treated with lymphodepleting chemotherapy prior to receiving Kymriah.

B-cell ALL

The recommended lymphodepleting chemotherapy regimen is:

Fludarabine (30 mg/m2 intravenous daily for 4 days) and cyclophosphamide (500 mg/m2 intravenous daily for 2 days starting with the first dose of fludarabine). If the patient experienced a previous Grade 4 haemorrhagic cystitis with cyclophosphamide, or demonstrated a chemorefractory state to a cyclophosphamide-containing regimen administered shortly before lymphodepleting chemotherapy, then the following should be used: Cytarabine (500 mg/m2 intravenous daily for 2 days) and etoposide (150 mg/m2 intravenous daily for 3 days starting with the first dose of cytarabine).

DLBCL

The recommended lymphodepleting chemotherapy regimen is:

Fludarabine (25 mg/m2 intravenous daily for 3 days) and cyclophosphamide (250 mg/m2 intravenous daily for 3 days starting with the first dose of fludarabine). If the patient experienced a previous Grade 4 haemorrhagic cystitis with cyclophosphamide, or demonstrated a chemorefractory state to a cyclophosphamide-containing regimen administered shortly before lymphodepleting chemotherapy, then the following should be used: Bendamustine (90 mg/m2 intravenous daily for 2 days).

Lymphodepleting chemotherapy may be omitted if a patient's white blood cell (WBC) count is ≤1,000 cells/µL within 1 week prior to Kymriah infusion.

Pre-medication

To minimise potential acute infusion reactions, it is recommended that patients be pre-medicated with paracetamol and diphenhydramine or another H1 antihistamine within approximately 30 to 60 minutes prior to Kymriah infusion. Corticosteroids should not be used at any time except in the case of a life-threatening emergency (Special warnings and precautions for use)

Method of administration

Kymriah is for intravenous use only.

Precautions to be taken before handling or administering the medicinal product.

This medicinal product contains genetically modified human blood cells. Healthcare professionals handling Kymriah should take appropriate precautions (wearing gloves and glasses) to avoid potential transmission of infectious diseases as for any human-derived material.

Preparation for infusion

Prior to Kymriah infusion, it must be confirmed that the patient's identity matches the essential unique patient information on the infusion bag(s).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.

Administration

Kymriah should be administered as an intravenous infusion through latex-free intravenous tubing without a leukocyte depleting filter, at approximately 10 to 20 mL per minute by gravity flow. All contents of the infusion bag(s) should be infused. 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. When the full volume of Kymriah has been infused, 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. If the volume of Kymriah to be administered is ≤20 mL, intravenous push may be used as an alternative.

Clinical assessment prior to infusion:

Kymriah treatment should be delayed in some patient groups at risk (see warnings and precautions).

Patients seropositive for hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV)

There is no experience with manufacturing Kymriah for patients with a positive test for HIV, active HBV, or active HCV infection. Leukaphersis material from these patients will not be accepted for Kymriah manufacturing. Screening for HBV, HCV, and HIV must be performed in accordance with clinical guidelines before collection of cells for manufacturing.

Active central nervous system (CNS) leukemia or lymphoma:

There is limited experience of use of Kymriah in patients with active CNS leukemia and active CNS lymphoma. Therefore, the risk/benefit of Kymriah has not been established in these populations.

Safety monitoring prior to infusion:

Due to the risks associated with Kymriah, the infusion should be withheld if a patient has any of the following conditions:

- **Active uncontrolled serious adverse reactions from preceding chemotherapies especially pulmonary, cardiac and hypotension.**
- **Active uncontrolled infection.**
- **Active chronic graft versus host disease (GvHD).**
- **Significant clinical worsening of leukemia burden or lymphoma following lymphodepleting chemotherapy.**

Monitoring after infusion:

- Patients should be monitored daily for the first 10 days following infusion for signs and symptoms of potential cytokine release syndrome (CRS), neurological events and other toxicities.Physicians should consider hospitalization for the first 10 days post infusion or at the first signs/symptoms of CRS and/or neurological events.
- After the first 10 days following the infusion, the patient should be monitored at the physician's discretion.
- Patients should be instructed to remain within proximity (2 hours' travel) of a qualified clinical facility for at least 4 weeks following infusion.

Special populations

Pediatric population

- B-cell ALL: No formal studies have been performed in pediatric patients below 3 years of age.
- DLBCL: The safety and efficacy of Kymriah in children and adolescents below 18 years of age have not yet been established. No data are available.

Elderly

- B-cell ALL: The safety and efficacy of Kymriah in this population have not been established.
- DLBCL: No dose adjustment is required in patients over 65 years of age.

Contraindications:

- Hypersensitivity to tisagenlecleucel or to any excipient including dimethyl sulfoxide (DMSO) or dextran 40.
- Contraindications of the lymphodepleting chemotherapy must be considered

Warnings and precautions:

- **Patient information:** Patients should be educated to inform their treating physician immediately when signs of CRS or neurological events are observed. Patients should stay within 2 hours distance from Kymriah infusion location for 4 weeks.
- Risk of CRS: Cytokine release syndrome, including fatal or life-threatening events, has been frequently observed after Kymriah infusion (see Undesirable effects) In almost all cases, development of cytokine release syndrome occurred between 1 to 10 days (median onset 3 days) after Kymriah infusion. The median time to resolution of cytokine release syndrome was 8 days.See full prescribing information for CRS management.
- **Risk of neurological toxicities:** Majority of severe or life-threatening events, in particular encephalopathy, confusional state or delirium, occurred within 8 weeks post infusion and were transient. The median time to onset of neurological events was 8 days and the median time to resolution was 7 days for B-cell ALL and 6 and 13 days for DLBCL, respectively.Neurological events can be concurrent with cytokine release syndrome, following resolution of cytokine release syndrome or in the absence of cytokine release syndrome. Patients should be monitored for neurological events.
- **Risk of infections:** Delay start of therapy with Kymriah until active uncontrolled infections have resolved. As appropriate, administer prophylactic antibiotics and employ surveillance testing prior to and during treatment with Kymriah. Serious infections were observed in patients, some of which were life threatening or fatal. After Kymriah administration observe patient and ensure prompt management in case of signs of infection.
- **Risk of febrile neutropenia:** Frequently observed after Kymriah infusion, may be concurrent with CRS. Appropriate management necessary.
- **Risk of low immunoglobulin levels**: Preemptive measures such as infection precautions, antibiotic prophylaxis and immunoglobulin replacement should be taken according to age and standard guidelines.
- **Risk of prolonged cytopenias**: Appropriate management necessary. Prolonged cytopenia associated with increased risk of infections. Myeloid growth factors particularly granulocyte macrophage-colony stimulating factor (GM-CSF), are not recommended until CRS resolved and typically not during the first 3 weeks after Kymriah infusion.
- **Risk of secondary malignancies:** Patients treated with Kymriah may develop secondary malignancies or recurrence of their cancer and should be monitored life-long for secondary malignancies.
- **Risk of hypogammaglobulinaemia or agammaglobulinemia:** Infection precautions, antibiotic prophylaxis and immunoglobulin replacement should be managed per age and standard guidelines.
- **Risks due to live vaccines:** The safety of immunization with live viral vaccines during or following Kymriah treatment was not studied. Vaccination with live virus vaccines is not recommended at least 6 weeks prior to the start of lymphodepleting chemotherapy, during Kymriah treatment, and until immune recovery following treatment with Kymriah.
- **Risk of tumor lysis syndrome (TLS):** Patients with elevated uric acid or high tumor burden should receive allopurinol or alternative prophylaxis prior to Kymriah infusion. Continued monitoring for TLS following Kymriah administration should also be performed.
- **Prior stem cell transplantation:** Kymriah infusion is not recommended within 4 months of undergoing an allogenic stem cell transplant (SCT) because of potential risk of worsening GVHD. Leukaphersis for Kymriah manufacturing should be performed at least 12 weeks after allogenic SCT.
- **Prior treatment with anti CD19 therapy:** There is limited experience with Kymriah in patients exposed to prior CD19 directed therapy. Kymriah is not recommended if the patient has relapsed with CD19-negative leukaemia after prior anti-CD19 therapy.
- **Fetal risk**: There is no preclinical or clinical data to assess whether Kymriah constitutes a risk to a pregnant woman or the fetus.
- **Risk of viral reactivation:** Not recommended in patients with hepatitis B because of potential risk of virus reactivation. Screening for HCV, HIV active HBV should be performed before collection of cells for manufacturing.
- **Risk of interference with serological testing:** Due to limited and short spans of identical genetic information between the lentiviral vector used to create Kymriah and HIV, some commercial HIV nucleic acid tests (NAT) may give a false positive result.
- **Risk due to content of dextran 40 and DMSO:** contains 11 mg dextran 40 and 82.5 mg DMSO per mL known to possibly cause anaphylactic reactions following parenteral administration. Patients not previously exposed to dextran and DMSO should be observed closely during the first minutes of the infusion period.
- **Risk of driving and engaging in hazardous activities:** in the 8 weeks following infusion these activities should be refrained due to risks for altered or decreased consciousness or coordination.

Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females

Pregnancy status for females of child-bearing age should be verified prior to starting treatment with Kymriah.

See the prescribing information for lymphodepleting chemotherapy for information on the need for effective contraception in patients who receive the lymphodepleting chemotherapy. There are insufficient exposure data to provide a recommendation concerning duration of contraception following treatment with Kymriah.

Pregnancy

There are no data from the use of Kymriah in pregnant women. No animal studies have been conducted with Kymriah to assess whether it can cause foetal harm when administered to a pregnant woman (see preclinical safety data). It is not known whether Kymriah has the potential to be transferred to the foetus via the placenta and could cause foetal toxicity, including B-cell lymphocytopenia. Kymriah is not recommended during pregnancy and in women of childbearing potential not using contraception. Pregnant women should be advised on the potential risks to the foetus. Pregnancy after Kymriah therapy should be discussed with the treating physician. Pregnant women who have received Kymriah may have hypogammaglobulinaemia. Assessment of immunoglobulin levels is indicated in newborns of mothers treated with Kymriah.

Breast-feeding

It is unknown whether Kymriah cells are excreted in human milk. A risk to the breast-fed infant cannot be excluded. Women who are breast-feeding should be advised of the potential risk to the breast-fed infant.

Following administration of Kymriah, breast-feeding should be discussed with the treating physician.

Fertility

There are no data on the effect of Kymriah on fertility. Effects of Kymriah on male and female fertility have not been evaluated in animal studies.

Adverse drug reactions:

Very common (≥10%): Anaemia, haemorrhage, febrile neutropenia, neutropenia, thrombocytopenia, arrhythmia, diarrhoea, nausea, vomiting, constipation, abdominal pain, pyrexia, fatigue, oedema, pain, chills, CRS, hypogammaglobulinaemia, infections (pathogen unspecified), viral-, bacterial- or fungal infections, neutrophil count decreased, platelet count decreased, aspartate aminotransferase increased, lymphocyte count decreased, white blood cell count decreased, haemoglobin decreased, decreased appetite, hypokalaemia, hypophosphataemia, hypomagnaesemia, hypocalcaemia, arthralgia, headache, encephalopathy, anxiety, delirium, sleep disorder, acute kidney injury, cough, dyspnoea, hypoxia, rash, hypotension, hypertension.

Common (≥1 to <10%): Haemophagocytic lymphohistiocytosis, leukopenia, pancytopenia, coagulopathy, lymphopenia, cardiac failure, cardiac arrest, visual impairment, stomatitis, abdominal distension, dry mouth, ascites, influenza like illness, asthenia, multiple organ dysfunction syndrome, hyperbiliburinaemia, infusion related reaction, GvHD, alanine aminotransferase increased, blood bilirubin increased, weight decreased, serum ferritin increased, blood fibrinogen decreased, international normalised ratio increased, fibrin D dimer increased, activated partial thromboplastin time prolonged, blood alkaline phosphatase increased, prothrombin time prolonged, hypoalbuminaemia, hyperglycaemia, hyponatraemia, hyperuricaemia, fluid overload, hypercalcaemia, TLS, hyperkalaemia, hyperphosphataemia, hypernatraemia, hypermagnesaemia, back pain, myalgia, musculoskeletal pain, dizziness, peripheral neuropathy, tremor, motor dysfunction, seizure, speech disorder, neuralgia, ataxia, oropharygeal pain, pulmonary oedema, nasal congestion, pleural effusion, tachypnoea, acute respiratory distress syndrome, pruritus, erythema, hyperhidrosis, night sweats, thrombosis, capillary leak syndrome.

Uncommon (≥0.1 to <1%): B-cell aplasia, ischemic cerebral infarction, lung infiltration, flushing.

Adverse reaction from spontaneous report (not known): anaphylactic reaction/infusion related reaction.

Interactions:

The co administration of agents known to inhibit T-cell function has not been formally studied. Administration of tocilizumab and steroids does not impact the expansion and persistence of CAR-T-cells as per the management of CRS treatment algorithm. The co administration of agents known to stimulate T-cell function has not been investigated and the effects are unknown.

Packs and prices: Country-specific.

Legal classification: Country-specific.

Version: V1.0

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