

KYMRIAH (tisagenlecleucel) dispersion for intravenous infusion Patient Information Brochure

Important Information for You (the Patient), Guardians, and Caregivers

Study the Patient leaflet before beginning use of the product.

Your doctor will give you a copy of the Patient Leaflet for Kymriah® (also known as tisagenlecleucel), a Kymriah Patient Alert Card, and the Kymriah Patient Information Brochure (this document).

Please read and keep the Patient Leaflet.

Please read the Kymriah Patient Alert Card in its entirety, carry the card with you at all times and show it to all healthcare providers.

Please read and keep this Kymriah Patient Information Brochure to remind you of the signs and symptoms of CRS (cytokine release syndrome), neurological events, and infections that require immediate medical attention.

If you have any questions about Kymriah, please speak to your doctors or nurses.

What is Kymriah?

Kymriah is a medicine made from some of your own white blood cells, and is used to treat:

- Children and young adults, up to and including the age of 25 years, with B cell acute lymphoblastic leukaemia, expressing CD19 (CD19+), that is resistant, recurrent after a transplant or recurring for the second time or more.
- Adults with diffuse large B cell lymphoma, that is resistant or recurrent after at least two lines of systemic treatment.

Limitation of Use: Kymriah is not indicated for treatment of patients with primary or secondary central nervous system lymphoma.

- Adults with follicular lymphoma, that is resistant or recurrent after at least two lines of systemic treatment

What should I expect before getting Kymriah?

Collection of blood to manufacture Kymriah

- Since Kymriah is made from your own white blood cells, some of your blood will be taken using a catheter (a small tube) placed in your vein; this procedure is called "leukapheresis".
- Some of your white blood cells are separated from your blood and the rest of your blood is returned to your vein. This can take 3 to 6 hours and may need to be repeated.
- Your collected white blood cells are frozen and sent away to the manufacturing site to make Kymriah.

Manufacturing Kymriah

- Kymriah is a treatment that is manufactured specifically for you. Manufacturing time may vary and typically takes several weeks.
- There are situations where Kymriah cannot be successfully manufactured and be given to you. In some cases, a second manufacturing of Kymriah may be attempted.
- There are also instances where the final product obtained in the production process falls outside the pre-specified criteria for Kymriah (i.e., the product is out-of-specification). However, if your treating physician assesses that the anticipated benefit outweighs the risks, the final product may still be provided for infusion at your physician's request.

Bridging therapy / potential disease worsening

- While Kymriah is being manufactured, additional therapy (known as 'bridging therapy') may be needed to stabilize your cancer. This may induce side effects which can be severe or life-threatening. The treating physician will inform you about potential side effects of this therapy
- While awaiting Kymriah manufacture, the underlying disease may worsen and progress.

Lymphodepleting chemotherapy

- Shortly before you are administered Kymriah, your doctor may give you a type of treatment called lymphodepleting chemotherapy (also called conditioning chemotherapy) over a few days to prepare your body for Kymriah infusion.

Possible side effects that may occur after Kymriah infusion

- **Tell your doctor immediately** if you get any of the following side effects after the Kymriah infusion. They usually happen in the first 8 weeks after the infusion, but can also develop later:
 - High fever and chills. These may be symptoms of a serious condition called cytokine release syndrome. Other symptoms of cytokine release syndrome are difficulty breathing, nausea, vomiting, diarrhoea, loss of appetite, fatigue, muscle pain, joint pain, swelling, low blood pressure, fast heartbeat, headache, heart, lung and kidney failure and liver injury. These symptoms almost always occur within the first 14 days after infusion.
 - Neurological events such as altered thinking or decreased consciousness, loss of contact with reality, confusion, agitation, seizures, difficulty speaking and understanding speech, and difficulty walking. These may be symptoms of a condition called immune effector cell-associated neurotoxicity syndrome (ICANS)
 - Feeling warm, fever, chills, or shivering, sore throat or mouth ulcers, which may be signs of an infection. Some infections may be life-threatening or fatal.
 - After treatment with Kymriah and complete recovery, you may suffer from hypogammaglobulinemia (a deficiency of the gamma-globulin protein in the blood) and agammaglobulinemia (a condition in which there is complete deficiency of immunoglobulins, proteins produced by immune system cells).

Effect on blood cells

- Kymriah can lower one or more types of your blood cells (red blood cells, white blood cells, or platelets). After treatment, your doctor will test your blood to check for this. Tell your doctor right away if you get a fever, are feeling tired, or have bruising or bleeding.

These are not all the possible side effects of Kymriah. For other potential side effects, refer to the Patient Leaflet. You may need to be hospitalized for side effects

Reporting Adverse Reactions

Adverse reactions may be reported to the Ministry of Health by means of the online form for reporting adverse reactions located at: <https://sideeffects.health.gov.il>

You may also report to the Registration Holder Novartis Israel LTD. at: safetydesk.israel@novartis.com

Monitoring / possible hospitalization

- Plan to stay within 2 hours travel from the hospital where you were treated for at least 4 weeks after you have been given Kymriah.
- Your doctor will recommend that you return to the hospital daily for at least 10 days and will consider whether you need to stay at the hospital as an in-patient for the first 10 days after infusion. This is so your doctor can check if your treatment is working and help you if you have any side effects, such as potential cytokine release syndrome, neurological events and other toxicities.
- After the first 10 days following Kymriah infusion, you will be monitored as per your doctor's discretion.

Additional important instructions for you (and/or your caregiver) about using Kymriah

- Take temperature twice a day for 3-4 weeks after administration of Kymriah. If temperature is elevated, see your doctor immediately.
- Due to the potential of Kymriah to cause problems such as altered or decreased consciousness, confusion, and seizures in the 8 weeks following infusion, you should not drive, use machines, or take part in activities that require alertness.
- Do not donate blood, organs, tissues or cells.

Effect on HIV testing

- There may be an effect on the results of some types of HIV test: treatment with Kymriah may result in a false positive test result; ask your doctor about this.

Important information for healthcare professionals:

- This patient has received an infusion of Kymriah (tisagenlecleucel), a CAR-T cell therapy for: _____ [please fill in indication as appropriate].
- Following Kymriah treatment, development of cytokine release syndrome, neurological events, infections, prolonged cytopenias and prolonged depletion of normal B-cells/ agammaglobulinemic can occur, typically within the first few weeks after infusion; however, later occurrence might happen.
- Please contact his/her treating oncologist before giving steroids or cytotoxic medications. Consult with his/her treating oncologist for the treatment of the patient.

Contact details for Kymriah treating physician

- Name:
- Telephone number(s):
- Centre / City

This document has been determined by the Ministry of Health and the content therefore has been checked and approved on November 2022.

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