

# Kymriah<sup>®</sup> (tisagenlecleucel) suspension for intravenous infusion

## FACT SHEET

Kymriah<sup>®</sup> (pronounced: Kim-RYE-ah) is the first CAR-T cell therapy approved by the FDA for two distinct indications – in non-Hodgkin lymphoma and B-cell acute lymphoblastic leukemia.

## Indications<sup>1</sup>

Kymriah<sup>®</sup> (tisagenlecleucel) suspension for intravenous infusion, formerly CTL019, is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

- patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse
- adult patients with relapsed or refractory (*r/r*) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLCL), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. Kymriah is not indicated for the treatment of patients with primary central nervous system lymphoma

## Product Description<sup>1</sup>

Kymriah is a type of treatment called chimeric antigen receptor T cell (CAR-T) therapy, which uses the patient's own T cells to fight cancer.

Kymriah is a one-time treatment with a dose range based on patient weight.

- ALL patients who weigh 50 kg or less receive a weight-based dosing
- ALL patients who weigh above 50 kg receive a fixed dose ( $0.1$  to  $2.5 \times 10^8$  total CAR-positive viable T cells)
- DLBCL patients receive a fixed dose ( $0.6$  to  $6.0 \times 10^8$  CAR-positive viable T cells)

## About Kymriah

Manufacturing Kymriah involves extracting T cells from a patient's own blood through a specialized blood filtration system called leukapheresis, which is done intravenously. The T cells are then sent to the Novartis manufacturing facility and genetically reprogrammed to recognize cancer cells and other cells expressing a specific antigen. After the CAR-T cells undergo expansion and strict quality testing, they are shipped to the treatment center and infused into the patient.

Kymriah uses the 4-1BB costimulatory domain in its chimeric antigen receptor, which enhances expansion and persistence of the cancer fighting cells.<sup>2</sup>

Kymriah is manufactured for each individual patient at the Novartis Morris Plains, New Jersey facility, which has manufactured CAR-T cells for hundreds of patients. Novartis has a reproducible, flexible and validated manufacturing process which builds on years of global clinical trial experience. In the US, the target turnaround time for manufacturing Kymriah in the commercial setting is 22 days.

During Kymriah manufacturing, Novartis uses cryopreservation of a patient's harvested (or leukapheresed) cells and after manufacturing of the CAR-T cells, which supports treatment of patients in clinical trials from around the world and gives treating physicians and centers flexibility

to schedule apheresis at a time that's in the best interest for their patients and initiate therapy with Kymriah based on the individual patient's condition.

### About ALL

- There has been a need for new treatment options for patients with relapsed or refractory B-cell ALL, whose prognosis is poor<sup>3,4</sup>.
- Patients often must undergo multiple treatments, including chemotherapy, radiation, targeted therapy or stem cell transplant, yet less than 10% of patients survive five years<sup>5,6</sup>.

**~60%**

**of ALL cases occur in patients less than 20 years of age<sup>7</sup>.**

**If left untreated, relapsed or refractory DLBCL has a life expectancy of**

**3 to 4 months<sup>8</sup>.**

### About DLBCL

- DLBCL is the most common form of NHL, accounting for up to 40% of all NHL cases globally<sup>9</sup>.
- Approximately 10% of patients with DLBCL have refractory disease, meaning they do not respond to initial treatment, and about 75% of patients with relapsed or refractory disease are ineligible for autologous stem cell transplant (ASCT) or do not respond to salvage therapy, and therefore cannot proceed to ASCT<sup>8,10</sup>.
- There has been a critical need for new treatment options for patients with relapsed or refractory DLBCL. Options are limited, and survival rates are low for patients who are ineligible for ASCT or for whom salvage chemotherapy and ASCT have failed<sup>11</sup>.

### Development

In 2012, Novartis and the University of Pennsylvania (Penn) entered into a global collaboration to further research, develop and commercialize CAR-T cell therapies, including Kymriah, for the investigational treatment of cancers. Children's Hospital of Philadelphia (CHOP) was the first institution to investigate Kymriah in the treatment of pediatric patients and led a single site trial.

### Novartis Commitment

Novartis is a leader in next-generation immuno-oncology (IO). Novartis is at the forefront of investigational immunocellular therapy as the first pharmaceutical company to initiate global CAR-T trials, and has significantly invested in CAR-T research and worked with pioneers in the field. Novartis is committed to helping eligible patients have access to Kymriah.

To address the unique aspects of the therapy, Novartis has developed various patient access programs to support safe and timely access for patients. Novartis is also providing traditional support to patients by helping them navigate insurance coverage, and by providing financial assistance for those who are uninsured or those experiencing a delay in coverage.

### Important Safety Information

The full prescribing information, including Boxed WARNING, for Kymriah can be found at: <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/kymriah.pdf>

Kymriah may cause side effects that are severe or life-threatening, such as Cytokine Release Syndrome (CRS) or Neurological Toxicities. Patients with CRS may experience symptoms including difficulty breathing, fever (100.4°F/38°C or higher), chills/shaking chills, severe nausea, vomiting and diarrhea, severe muscle or joint pain, very low blood pressure, or dizziness/lightheadedness. Patients may be admitted to the hospital for CRS and treated with other medications.

Patients with neurological toxicities may experience symptoms such as altered or decreased consciousness, headaches, delirium, confusion, agitation, anxiety, seizures, difficulty speaking and understanding, or loss of balance. Patients should be advised to call their healthcare provider or get emergency help right away if they experience any of these signs and symptoms of CRS or neurological toxicities.

Because of the risk of CRS and neurological toxicities, Kymriah is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Kymriah REMS.

Serious allergic reactions, including anaphylaxis, may occur after Kymriah infusion. Kymriah can increase the risk of life-threatening infections that may lead to death. Patients should be advised to tell their healthcare provider right away if they develop fever, chills, or any signs or symptoms of an infection.

Patients may experience prolonged low blood cell counts (cytopenia), where one or more types of blood cells (red blood cells, white blood cells, or platelets) are decreased. The patient's healthcare provider will do blood tests to check all of their blood cell counts after treatment with Kymriah. Patients should be advised to tell their healthcare provider right away if they get a fever, are feeling tired, or have bruising or bleeding.

Patients may experience hypogammaglobulinemia, a condition in which the level of immunoglobulins (antibodies) in the blood is low and the risk of infection is increased. It is expected that patients may develop hypogammaglobulinemia with Kymriah, and may need to receive immunoglobulin replacement for an indefinite amount of time following treatment with Kymriah. Patients should tell their healthcare provider about their treatment with Kymriah before receiving a live virus vaccine.

After treatment with Kymriah, patients will be monitored lifelong by their healthcare provider, as they may develop secondary cancers or recurrence of their cancer.

Patients should not drive, operate heavy machinery, or do other dangerous activities for eight weeks after receiving Kymriah because the treatment can cause temporary memory and coordination problems, including sleepiness, confusion, weakness, dizziness, and seizures.

Some of the most common side effects of Kymriah are difficulty breathing, fever (100.4°F/38°C or higher), chills/shaking chills, confusion, severe nausea, vomiting and diarrhea, severe muscle or joint pain, very low blood pressure, dizziness/lightheadedness, and headache. However, these are not all of the possible side effects of Kymriah. Patients should talk to their healthcare provider for medical advice about side effects.

Prior to a female patient starting treatment with Kymriah, their healthcare provider may do a pregnancy test. There is no information available for Kymriah use in pregnant or breast-feeding women. Therefore, Kymriah is not recommended for women who are pregnant or breast feeding. Patients should talk to their healthcare provider about birth control and pregnancy.

Patients should tell their healthcare provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

After receiving Kymriah, patients should be advised that some commercial HIV tests may cause a false-positive test result. Patients should also be advised not to donate blood, organs, or tissues and cells for transplantation after receiving Kymriah.

Please see the full Prescribing Information for Kymriah, including Boxed WARNING, and Medication Guide at [www.Kymriah.com](http://www.Kymriah.com)

#### References:

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