

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

**PrKYMRIAH™
(Tisagenlecleucel)**

Read this carefully before you start taking KYMRIAH™. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about KYMRIAH.

Serious Warnings and Precautions

The following serious side effects have been seen in people taking KYMRIAH:

- High fever and chills which may be symptoms of a serious condition called Cytokine Release Syndrome (CRS). Other symptoms of CRS are difficulty breathing, nausea, vomiting, diarrhea, muscle pain, joint pain, low blood pressure, or dizziness/light-headedness.
- Neurological problems like altered or decreased consciousness, delirium, confusion, agitation, seizures, difficulty speaking and understanding speech, loss of balance

KYMRIAH should only be administered by an experienced healthcare professional at specialized treatment centres

What KYMRIAH is

KYMRIAH is made from some of your own normal white blood cells:

- These cells are called 'T-cells'
- They are important for your immune system and for fighting your cancer.
- It comes in infusion bags.

What is KYMRIAH used for?

KYMRIAH is used to treat:

- B-cell Acute lymphoblastic leukaemia (B-cell ALL) - a form of cancer composed of some types of white blood cells that have become malignant. It can be used in children and young adults from 3 to 25 years of age with this cancer.
- Diffuse large B-cell lymphoma (DLBCL) – a form of cancer composed of some types of white blood cells that have become malignant, mostly in the lymph nodes. KYMRIAH can be used in adults (18 years of age or older) for whom DLBCL has returned after other treatments or when other treatments did not work.

How does KYMRIAH work?

The normal T-cells are taken from your blood and are genetically modified so that they can find and kill the cancer cells more effectively. When you have an infusion of KYMRIAH into your blood, the modified T-cells will stick to the cancer cells and cause them to die.

If you have any questions about how KYMRIAH works or why this medicine has been prescribed for you, ask your doctor.

What are the ingredients in KYMRIA[®]H?

Medicinal ingredients: tisagenlecleucel

Non-medicinal ingredients: Dextran, dextrose, dimethylsulfoxide (DMSO), human serum albumin, plasma-Lyte A (multiple electrolytes for injection, Type 1, pH 7.4), and sodium chloride.

KYMRIA[®]H comes in the following dosage forms:

KYMRIA[®]H is provided as a cell suspension in one or more infusion bags. KYMRIA[®]H is administered as an intravenous infusion for one time only.

What KYMRIA[®]H looks like:

KYMRIA[®]H is supplied as an infusion bag containing a cloudy to clear, colorless to slightly yellow suspension of cells (tisagenlecleucel).

Do not use KYMRIA[®]H:

If you are allergic (hypersensitive) to tisagenlecleucel or any of the other ingredients of KYMRIA[®]H

If you think you may be allergic, ask your doctor for advice.

To help avoid side effects and ensure proper use, talk to your healthcare professional before receiving KYMRIA[®]H. Talk about any health conditions or problems you may have, including:

- If you have had a stem cell transplantation in the last 6 months.
- If you have any lung or heart or blood pressure problems.
- If you have a sign or symptom of a serious graft versus host disease (GVHD), i.e. when transplanted cells attack your body, such as rashes, nausea, vomiting, diarrhea, including bloody stools.
- If you notice the symptoms of your leukemia worsening, such as fever, weakness, bleeding at the gums, bruising.
- If you notice the symptoms of your lymphoma worsening, such as unexplained fever, weakness, night sweats, sudden weight loss.
- If you have any infections. Your infection will be treated before KYMRIA[®]H infusion.
- If you have ever had viral hepatitis B or C or HIV.
- If you have recently been vaccinated.
- If you are pregnant, think you may be pregnant, or plan to become pregnant (see section Pregnancy and breast-feeding).

Other warnings you should know about:

Tell your doctor immediately if you get any of these symptoms after administration of KYMRIA[®]H:

- If you experience feeling warm, fever, chills or shivering. These can be symptoms of an infection.
- If you develop frequent infections with sore throat or mouth ulcers, these may be symptoms of a low level of white blood cells (neutropenia with high fever).
- High fever and chills may also be symptoms of a serious condition called Cytokine Release Syndrome (CRS). Other symptoms of CRS are difficulty breathing, nausea, vomiting, diarrhea, muscle pain, joint pain, low blood pressure, or dizziness/light-headedness. When occurring, these symptoms are almost always noticed within the first 9 or 10 days after infusion and last for about 7 or 8 days.
- If you experience neurological problems like altered or decreased consciousness, delirium, confusion, agitation, seizure, difficulty speaking and understanding, and loss of

balance. When occurring, these symptoms usually begin in the first 8 weeks after the infusion, but some of these symptoms can occur weeks or months later as well.

Monitoring before and after your treatment with KYMRIA[®]

Before receiving KYMRIA[®]

Before you are given KYMRIA[®] infusion, your doctor will:

- Check your lung, heart and blood pressure functions.
- Check to see if you are pregnant.
- Look for any signs of infection. Any active infection will be treated before administration of KYMRIA[®].
- Check if your cancer is getting worse.
- Check for signs of a medical complication called “Graft versus Host Disease” that may occur usually after a prior transplant.
- Check your blood for something called uric acid and how many cancer cells there are in the blood. This will show if you are likely to have ‘tumor lysis syndrome’ - if needed, you will be given medicines to help reduce the chance of this.
- Check if you have any antibodies to hepatitis B or C or HIV in the blood.

After receiving KYMRIA[®]

- Your doctor will regularly monitor your blood counts after you receive KYMRIA[®] as you may experience a reduction in the number of blood cells and blood components such as decreases in different types of normal white blood cells and/or a reduction on your normal antibodies that help fight infection.
- Your doctor will regularly check for signs of Cytokine Release Syndrome or neurological problems
- Some types of HIV testing may be affected – ask your doctor about this.
- Do not donate blood, organs, tissues and cells for transplants.

Children

KYMRIA[®] has not been studied in children and adolescents below 18 years of age with diffuse large B-cell lymphoma and should not be administered in this age group for diffuse large B-cell lymphoma.

Older people (above 65 years of age)

Patients aged 65 years or older with diffuse large B-cell lymphoma can be administered KYMRIA[®] in the same way as younger adults.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with KYMRIA[®]:

- ‘Live’ vaccines – in particular, do not receive ‘live’ vaccines:
 - In the 6 weeks before being given a short course of chemotherapy (“lymphodepleting” chemotherapy) to prepare your body for the KYMRIA[®] cells
 - During KYMRIA[®] treatment
 - After treatment while the immune system is recovering.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Your doctor will discuss with you the potential risk(s) of receiving KYMRIATM during pregnancy or breast-feeding.

Women of child-bearing potential and male patients

The effects of KYMRIATM in pregnant women are not known, but it may harm your unborn baby.

Pregnancy status should be verified before starting treatment. KYMRIATM should only be used if the result is negative. Women who could become pregnant should use effective birth control after being given KYMRIATM. Ask your doctor about options of effective birth control.

If you become pregnant or think you are pregnant after treatment with KYMRIATM, tell your doctor right away.

Sexually active males treated with KYMRIATM should use a condom for intercourse.

Driving and using machines

Do not drive, use heavy machines, or engage in hazardous activities for 8 weeks following the KYMRIATM infusion. KYMRIATM can cause neurological problems such as altered or decreased consciousness, confusion and seizures.

How you will receive KYMRIATM:

Your doctor or a physician will always give KYMRIATM to you.

Giving blood to make KYMRIATM

KYMRIATM is made from your own white blood cells.

- Your doctor will take some of your blood using a tube placed in your vein - this is called 'leukapheresis'. This can take 3 to 6 hours and may need to be repeated.
- Your blood cells are frozen and sent away to manufacture KYMRIATM. It takes about 3 to 4 weeks to make KYMRIATM, but the time may vary.
- Before you are given KYMRIATM, your doctor may give you chemotherapy for a few days to prepare your body and possibly to control your cancer.

Medicines given before KYMRIATM administration

During the 30 to 60 minutes before being given KYMRIATM you may receive other medicines to help to reduce infusion reactions and/or fever. These may include acetaminophen and an H1 antihistamine such as diphenhydramine.

How you are given KYMRIATM

- Prior to KYMRIATM infusion, your doctor will check that your identity is matching with the patient identifiers on the KYMRIATM infusion bag.
- Your doctor will give KYMRIATM through a tube in your vein. This usually takes less than 1 hour.
- Plan to stay within 2 hours distance of where you were given your treatment for at least 3 to 4 weeks after you have been given KYMRIATM. Your doctor will check to see if your treatment is working and help you with any side effects.

KYMRIAH is given to you only once.

What are possible side effects from using KYMRIAH?

Listed below are the most common (but not all) possible side effects you may feel when taking KYMRIAH. If you experience any side effects not listed here, contact your healthcare professional

Very common:

- Loss of appetite, Weight loss
- Fast heart beat (tachycardia)
- Headache
- Dizziness
- Cough
- Shortness of breath, labored breathing, breathlessness, rapid breathing
- Abdominal pain, Constipation, Diarrhea
- Nausea, Vomiting
- Fever
- Tiredness (fatigue)
- Chills
- Altered state of consciousness
- Nose bleeding
- Reduced level of calcium in the blood, sometimes leading to cramps
- Thirst, low urine output, dark urine, dry flushed skin, irritability (possible symptoms of high level of sugar in blood)
- Headache, dizziness (possible symptoms of hypertension)
- Excessive emotional distress (anxiety)
- Pain in muscles, bones or joints (musculoskeletal pain, myalgia, arthralgia), Pain in extremity, Back pain

Common:

- Yellow skin and eyes (possible symptoms of high level of bilirubin in the blood)
- Decreased immunoglobulins in your blood that will lead to frequent and persistent infections
- Involuntary shaking of the body (tremor)
- Difficulty in speaking or understanding speech (dysphasia)
- Tingling or numbness (paresthesia)
- Bloating (abdominal distension)
- Dry mouth
- Mouth sores (stomatitis)
- Weakness (asthenia)
- Itching (pruritus)
- Skin reddening (erythema)
- Excessive sweating (hyperhidrosis)
- Red or purple, flat, pinhead spots under the skin (petechiae)
- Night sweats
- Tiredness, chills, sore throat, joint or muscles aching (possible symptoms of influenza-like)

illness)

- Hot flushes
- Blood in urine (haematuria)
- Difficulty and pain when passing urine (dysuria)

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
VERY COMMON		
Feeling warm, fever, chills or shivering (possible symptoms of an unspecified pathogen)		√
Spontaneous bleeding or bruising (Low levels of blood platelets)		√
Frequent infections, weakness, fever, chills, sore throat or mouth ulcers due to infections (possible symptoms of low level of white blood cells or febrile neutropenia)		√
Weakness, spontaneous bleeding or bruising and frequent infections, fever, chills, and sore throat (possible symptoms of low level of red blood cells)		√
High fever, chills, difficulty breathing, nausea, vomiting, diarrhea, muscle pain, joint pain, low blood pressure, or dizziness/light-headedness. (possible symptom of CRS)		√
Personality changes, headache, confusion, paralysis of part or all of the body, stiff neck, abnormal speech and eye movement (possible symptoms of encephalopathy or metabolic encephalopathy)		√
Muscle weakness, muscle spasms, abnormal heart rhythm (possible symptoms of low levels of potassium in the blood)		√
Dizziness, light headedness (possible symptom of hypotension)		√
Swelling of limbs (edema peripheral)		√
COMMON		
Viral or bacterial or fungal infections		√
Blood clotting, internal and external bleeding (possible symptom of disseminated intravascular coagulation)		√
Swollen ankles (possible symptom of low levels of albumin in the blood)		√
Tiredness, confusion, muscle twitching, convulsions (possible symptom of low level of sodium in blood)		√
A syndrome of pathologic immune activation characterized by clinical signs and symptoms of		√

extreme inflammation (histiocytosis hematophagic)		
Producing less urine than normal and/or muscle spasms, possible symptom of an increase in potassium, phosphate and uric acid in the blood that can cause kidney problems (possible symptom of tumor lysis syndrome)		√
State of severe confusion (delirium)		√
Weakness or paralysis of limbs or face, difficulty speaking (possible symptom of ischemic cerebral infarction)		√
Convulsions, fits (Seizures)		√
Severe nerve pain (neuralgia)		√
Irregular heart beat (possible symptom of atrial fibrillation)		√
Breathlessness, difficulty breathing when lying down, swelling of the feet or legs (possible symptom of heart failure)		√
Blue discoloration of lips or extremities (hypoxia)		√
Swelling and edema (possible symptom of capillary leak syndrome in context of CRS)		√
Severely decrease urine output (possible symptom of acute kidney injury)		√
High fever, chills, difficulty to breath, yellow skin and eyes, bloody stools, severely decreased urine output (possible symptom of multiple organ dysfunction syndrome)		√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reporting Suspected Side Effects

For the general public: Should you experience a side effect following immunization, please report it to your doctor, nurse, or pharmacist.

Should you require information related to the management of the side effect, please contact your healthcare provider. The Public Health Agency of Canada, Health Canada and Novartis Pharmaceuticals Canada Inc. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (<http://www.phac-aspc.gc.ca/im/ae-fi-essi-form-eng.php>) and send it to your local Health Unit.

If you want more information about KYMRIA[®]:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the <http://hc-sc.gc.ca/index-eng.php>; the manufacturer's website <http://www.novartis.ca>, or by calling 1-800-363-8883.

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