READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrKYMRIAH®

[Kim-RAH-ya]

(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, dizziness and light-headedness which may be symptoms of a serious condition called Cytokine Release Syndrome (CRS). Other symptoms of CRS are fast heartbeat, chills, difficulty breathing, nausea, vomiting, diarrhea, muscle pain, joint pain, or low blood pressure.
- 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 called T-cells. T-cells are important for your immune system (the body's defences) to work properly. Kymriah comes in infusion bags.

What is Kymriah used for?

Kymriah is used to treat:

- B-cell acute lymphoblastic leukemia (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 up to and including 25 years of age.
- 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.

For the following indication, Kymriah has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

- Kymriah is used to treat follicular Lymphoma (FL) - a form of cancer that affects types of white blood cells, called lymphocytes mostly in the lymph nodes. It is called 'follicular' lymphoma because the abnormal white blood cells usually develop in clumps called 'follicles' inside lymph nodes. Kymriah can be used in adults (18 years of age or older).

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does Kymriah work?

The normal T-cells are taken from your blood and a new gene is put into the T-cells so that they can target the cancer cells more effectively. When Kymriah is infused into your blood, the modified T-cells find and kill the cancer cells.

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 Kymriah?

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.

Kymriah comes in the following dosage forms:

Kymriah is provided as a cell suspension in one or more infusion bags. Kymriah is administered as an intravenous infusion for one time only.

What Kymriah looks like:

Kymriah is supplied as an infusion bag containing a cloudy to clear, colourless to slightly yellow suspension of cells (tisagenlecleucel).

Do not use Kymriah:

If you are allergic (hypersensitive) to tisagenlecleucel or any of the other ingredients of Kymriah.

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 Kymriah. Talk about any health conditions or problems you may have, including:

- If you have had a stem cell transplantation in the last 4 months. Your doctor will check if you have signs or symptoms of graft versus host disease (GvHD). This happens when transplanted cells attack your body, causing symptoms such as rash, nausea, vomiting, diarrhea and bloody stools.
- If you have any lung or heart or blood pressure problems.
- If you notice that the symptoms of your lymphoma or leukemia are getting worse. If you have leukemia this might include fever, feeling weak, bleeding gums, bruising. If you have lymphoma, this might included unexplained fever, feeling weak, night sweats, and/or sudden weight loss.
- If you have had hepatitis B (HPV), hepatitis C (HBC) or human immunodeficiency virus (HIV) infection.
- If you had a vaccination in the previous 6 weeks or are planning to have one in the next few months.
- If you are pregnant, think you may be pregnant, or plan to become pregnant (see section Pregnancy and breast-feeding and Contraception for women and men).
- If you have an infection. The infection will be treated before the Kymriah infusion.

Monitoring before and after your treatment with Kymriah

Before receiving Kymriah

Before you are given Kymriah 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 Kymriah.
- Check if your lymphoma or leukemia is getting worse.
- Check for signs of a medical complication called “graft versus host disease (GvHD)” that may occur usually after a prior transplant.
- Check your blood for uric acid and how many cancer cells there are in the blood. This will show if you are likely to have ‘tumour lysis syndrome (TLS)’ - 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 Kymriah

- Your doctor will regularly monitor your blood counts after you receive Kymriah 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 CRS or neurological problems
- Some types of HIV testing may be affected – ask your doctor about this.

- Do not donate blood, organs, tissues, sperms, oocytes and other cells.
- You should be monitored life-long to check if your lymphoma or leukemia returns or a new cancer occurs. In the event that a new cancer occurs, your doctor or you should contact Novartis (mykymriah.cart@novartis.com or 1-833-395-2278).
- You should be monitored for neurological events.
- You should be monitored for signs and symptoms of infection.
- You should be monitored for signs and symptoms of TLS.

Children

Kymriah has not been studied in children and adolescents below 18 years of age with diffuse large B-cell lymphoma or follicular lymphoma and should not be administered in this age group for diffuse large B-cell or follicular lymphoma.

Older people (65 years of age or above)

Patients aged 65 years or above with diffuse large B-cell or follicular lymphoma can be administered Kymriah 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 Kymriah:

- '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 Kymriah cells
  - During Kymriah 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 Kymriah. This is because the effects of Kymriah in pregnant or breast feeding women are not known, and it may harm your unborn baby or your newborn/infant.

Your doctor will check with you if you are pregnant.

If you become pregnant or think you may be pregnant after treatment with Kymriah, talk to your doctor immediately.

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

Contraception for women and men

Women of child-bearing potential should use effective birth control after being given Kymriah. Ask your doctor about options of effective birth control.

Sexually active males receiving Kymriah should use a condom for intercourse.

Discuss pregnancy or fathering a child with your doctor if you have received Kymriah.

Driving and using machines

Do not drive, use machines, or take part in activities that need you to be alert. Kymriah can cause problems such as altered or decreased consciousness, confusion and seizures (fits) in the 8 weeks following infusion.

How you will receive Kymriah:

Kymriah will always be given to you by a qualified health care professional in a qualified treatment center.

Kymriah contains human blood cells. Your doctor handling Kymriah will therefore take appropriate precautions (wearing gloves and glasses for example) to avoid potential transmission of infectious diseases.

Collection of blood to manufacture Kymriah

Kymriah 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 Kymriah. It takes about 3 to 4 weeks to make Kymriah, but the time may vary.
- While awaiting Kymriah manufacture, the underlying disease may worsen and progress and your healthcare provider may give you therapy 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.
- In addition, before you get Kymriah, your healthcare provider may give you chemotherapy for a few days to prepare your body.
- Kymriah is a treatment that is manufactured specifically for you. 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.

Medicines given before Kymriah administration

During the 30 to 60 minutes before being given Kymriah 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 Kymriah

- Your doctor will check that the individual patient identifiers on the Kymriah infusion bag match up to you.
- Your doctor will give Kymriah by infusion, which means it will be given as a drip through a tube in your vein. This usually takes less than 1 hour. During the infusion, your doctor will check if you have difficulty breathing or dizziness (possible symptoms of allergic reactions).

Kymriah is a one-time treatment.

After you are given Kymriah

Plan to stay within proximity (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 2 to 3 times a week for at least the first week and will consider whether you need to stay at the hospital as an in-patient after infusion. This is so your doctor can check if your treatment is working and help you if you have any side effects.

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, including those not listed here, contact your healthcare professional.

Very common:

- Abdominal pain, constipation, weight loss
- Muscle weakness, muscle spasms
- Symptoms of high blood sugar like thirst, low urine output, dark urine, dry flushed skin, irritability
- Swelling of the arms or legs

Common:

- Swelling of the belly
- Changes or loss of vision
- Sore throat, stuffy nose, flu-like symptoms
- Bloating, mouth sores, dry mouth
- Skin reactions such as rash, hot flushes, night sweats, itching (pruritus), skin reddening (erythema), excessive sweating (hyperhidrosis)
- Muscle cramps
- Excessive emotional distress (anxiety)
- Sleep disturbances

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
VERY COMMON		
Fever, chills, shivering, nausea, vomiting, tiredness, dizziness, pain where the infusion needle is inserted,		√

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
blisters, itching, and/or shortness of breath or wheezing during or shortly after infusion (possible infusion reaction)		
Feeling warm, fever, chills or shivering, coughing (possible symptoms of an infection)		√
Bleeding or bruising more easily (possible symptoms of low levels of cells in the blood known as platelets)		√
Frequent infections, weakness, fatigue, fever, chills and/or shivering, sore throat, mouth ulcers, rash, swelling, yellow or pale skin, yellow eyes, uncontrolled internal or external bleeding, blood in the urine, breathlessness, abnormal body movement, irritability (possible symptoms of blood disorders)		√
Extreme tiredness, weakness and shortness of breath (may be symptoms of a lack of red blood cells)		√
High fever, chills, muscle pain, joint pain, nausea, vomiting, diarrhea, excessive sweating, rash, loss of appetite, fatigue, headache, dizziness/light-headedness, shortness of breath, heavy breathing, rapid breathing, blue discolouration of lips or extremities (possible symptoms of CRS)		√
Side effects affecting the respiratory organs, like, coughing, rapid breathing, painful breathing, shortness of breath or labored breathing, breathlessness (possible symptom of pulmonary oedema, a build-up of fluid in the alveoli (air spaces) in the lungs, which keeps oxygen from getting into the blood)		√
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)		√
Dizziness, light-headedness (possible symptoms of hypotension)		√
Viral or bacterial or fungal infections		√
Swollen ankles (possible symptoms of low levels of albumin in the blood)		√
Blue discolouration of lips or extremities (hypoxia)		√

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
Severely decreased urine output (possible symptoms of acute kidney injury)		√
COMMON		
Tiredness, confusion, muscle twitching, convulsions (possible symptoms of low level of sodium in blood)		√
Side effects affecting the nervous system, including involuntary shaking of the body (tremor), tingling or numbness (paresthesia), impaired memory or thinking (cognitive disorders), sensation of numbness or tingling in finger and toes (peripheral neuropathy), uncontrollable movements or actions of the body including tremors, jerks, twitches, spasms, contractions, or gait problems (motor dysfunction), difficulty in speaking or understanding speech (speech disorders)		√
Fever, malaise, yellow colour of your skin and eyes (possible symptoms of hemophagocytic lymphohistiocytosis)		√
Producing less urine than normal and/or muscle spasms (possible symptoms of tumour lysis syndrome)		√
Weakness or paralysis of limbs or face, difficulty speaking (possible symptoms of a stroke)		√
Convulsions, fits (seizures)		√
Severe nerve pain (neuralgia)		√
Fast and/or irregular heartbeat, breathlessness, difficulty breathing when lying down, swelling of the feet or legs, stopped heartbeat (possible symptoms of heart failure, worsening of heart failure or cardiac arrest)		√
Swelling and oedema (possible symptoms of capillary leak syndrome in context of CRS)		√
High fever, chills, difficulty to breath, yellow skin and eyes, bloody stools, severely decreased urine output (possible symptoms of multiple organ dysfunction syndrome)		√
Involuntary shaking of the body, difficulty writing, difficulty expressing thoughts verbally, impaired attention, sleepiness (*possible symptoms of Immune*		√

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
Effector Cell-Associated Neurotoxicity Syndrome - ICANS)		
State of severe confusion *(delirium)*		√
UNCOMMON		
Difficulty of control of movements *(ataxia)*		√
UNKNOWN		
Difficulty breathing, dizziness (possible symptoms of allergic reactions)		√
Weakness or numbness in the arms or legs, worsening of or loss of vision, having fixed and irrational thoughts that are not shared by others, headache, impaired memory or thinking, unusual behaviors (possible symptoms of neurotoxicity)		√

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:

a. 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

b. 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/aefi-essi-form-eng.php) and send it to your local Health Unit.

If you want more information about Kymriah:

1 Talk to your healthcare professional

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

This leaflet was prepared by:

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