PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

℞KEYTRUDA®

Pembrolizumab

Read this carefully before you start taking **KEYTRUDA®** and each time you get a refill. 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 **KEYTRUDA®**.

What is KEYTRUDA® (key-true-duh) **used for?**

- **See the following boxed text**

For the following indication(s) KEYTRUDA® 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.

KEYTRUDA® is a prescription medicine used to treat:

- a kind of cancer called classical Hodgkin lymphoma (cHL) in adults and children:
  - that has come back after an autologous stem cell transplant (ASCT), or
  - that was not suitable for ASCT

- a kind of cancer called primary mediastinal B-cell lymphoma in adults and children
  - that was not responsive to other treatments, or
  - that has come back after you have tried at least 2 other treatments

- a kind of bladder and urinary tract cancer called urothelial carcinoma, in adults
  - KEYTRUDA® may be used when your cancer has not spread to nearby tissue in the bladder, but is at high-risk for spreading (high-risk non-muscle-invasive bladder cancer [NMIBC]) when:
    - your tumour is a type called "carcinoma in situ" (CIS), and
    - you have tried treatment with Bacillus Calmette-Guerin (BCG) and it did not work, and
    - you are not able to or have decided not to have surgery to remove your bladder
  - KEYTRUDA® may be used when your bladder or urinary tract cancer:
    - has spread or cannot be removed by surgery (advanced urothelial cancer), and
      - you are not able to receive chemotherapy that contains a medicine called cisplatin, and your tumour tests positive for PD-L1, or
      - you are not able to receive a medicine called cisplatin or carboplatin

- a kind of colon, rectal, or endometrial cancer in adults that is shown by a laboratory test to be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
  - when you have received prior anti-cancer medicine and it did not work or is no longer working

- a kind of uterine cancer in adults called endometrial carcinoma. KEYTRUDA® is used with the

medicine lenvatinib when your endometrial carcinoma:
    - has worsened after anti-cancer treatment that contained platinum;
    - cannot be cured by surgery or radiation;
    - is not microsatellite instability high (MSI-H); or
    - is not mismatch repair deficient (dMMR).

- a kind of cancer called triple negative breast cancer in adults:
    - tests positive for "PD-L1", and
    - has returned and cannot be removed by surgery or has spread

For the following indications KEYTRUDA® has been approved ***without conditions***. This means it has passed Health Canada's review and can be bought and sold in Canada.

KEYTRUDA® is a prescription medicine used to treat:

- a kind of skin cancer called melanoma in adults
    - KEYTRUDA® may be used alone as your first treatment when your skin cancer:
        - has spread or cannot be removed by surgery (advanced melanoma)
    - KEYTRUDA® may be used alone when your skin cancer:
        - has spread or cannot be removed by surgery (advanced melanoma), and
        - after you have tried a medicine called ipilimumab and it did not work or is no longer working, and
        - if your tumour has an abnormal "BRAF" gene, and you also have tried a different medicine called a BRAF or MEK inhibitor, and it did not work or is no longer working
    - KEYTRUDA® may be used alone when your skin cancer:
        - has been removed by surgery to help prevent the cancer from coming back
- a kind of skin cancer called melanoma in children (12 years of age or older)
    - KEYTRUDA® may be used alone when your skin cancer:
        - has been removed by surgery to help prevent the cancer from coming back
- a kind of lung cancer called non-small cell lung cancer in adults
    - KEYTRUDA® may be used alone as your first treatment when your lung cancer:
        - has spread (advanced lung cancer), or
        - has not spread outside your chest (stage III) and you cannot have surgery or chemotherapy with radiation, and
        - tests positive for "PD-L1", and
        - if your tumour does not have an abnormal "EGFR" or "ALK" gene
    - KEYTRUDA® may be used with the medicine pemetrexed and chemotherapy that contains platinum as your first treatment when your lung cancer:
        - has spread (advanced lung cancer), and
        - is a type called "non-squamous", and
        - if your tumour does not have an abnormal "EGFR" or "ALK" gene
    - KEYTRUDA® may be used with the chemotherapy medicines carboplatin and either

paclitaxel or nab-paclitaxel as your first treatment when your lung cancer:
    - has spread (advanced lung cancer), and
    - is a type called "squamous"
  - KEYTRUDA® may be used alone when your lung cancer:
    - has worsened on or after chemotherapy that contains platinum, and
    - has spread (advanced lung cancer), and
    - tests positive for "PD-L1", and
    - if your tumour has an abnormal "EGFR" or "ALK" gene, you have tried an EGFR or ALK inhibitor medicine.

- a kind of bladder and urinary tract cancer called urothelial carcinoma, in adults when
  - it has spread or cannot be removed by surgery (advanced urothelial cancer); and
  - you have received chemotherapy that contains platinum, and it did not work or is no longer working

- a kind of kidney cancer in adults called renal cell carcinoma
  - KEYTRUDA® may be used with the medicine axitinib as your first treatment when your kidney cancer has spread or cannot be removed by surgery (advanced RCC).
  - KEYTRUDA® may be used with the medicine lenvatinib as your first treatment when your kidney cancer has spread or cannot be removed by surgery (advanced RCC).
  - KEYTRUDA® may be used alone to help prevent kidney cancer from coming back after surgery.

- a kind of head and neck cancer called head and neck squamous cell carcinoma in adults:
  - may be used alone as your first treatment when your head and neck cancer:
    - has spread
    - has come back after previous therapy and
    - test positive for "PD-L1"

- a kind of head and neck cancer called head and neck squamous cell carcinoma in adults:
  - may be used with the chemotherapy medicines platinum and fluorouracil (FU) as your first treatment when your head and neck cancer:
    - has spread
    - has come back after previous therapy

- a kind of cancer called colon or rectal cancer. KEYTRUDA® may be used as your first treatment when your cancer:
    - has spread (advanced colon or rectal cancer), **and**
    - has been shown by a laboratory test to be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).

- a kind of cancer called esophageal carcinoma or esophagogastric junction (EGJ) adenocarcinoma
  - may be used with the chemotheapy medicines platinum and fluorouracil (FU) as your first treatment when your esophageal cancer:
    - has spread (advanced esophageal cancer), or
    - your tumor cannot be removed by surgery.

- a kind of cancer called cervical cancer in adult women
    - may be used with the chemotheapy medicines, with or without the medicine bevacizumab, when your cervical cancer:
        - does not go away, has returned, or has spread,

      and
        - tests positive for "PD-L1"
- a kind of cancer called triple-negative breast cancer in adults
    - may be used with chemotherapy medicines as treatment before surgery and then continued alone after surgery when you:
        - have early-stage breast cancer, **and**
        - are at high risk of your breast cancer coming back.

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.

KEYTRUDA® may be given in combination with other anti-cancer medicines. It is important that you also read the package leaflets for these other medicines. If you have any questions about these medicines, please ask your doctor.

KEYTRUDA® can be used only in children with classical Hodgkin lymphoma or primary mediastinal B-cell lymphoma less than 18 years of age, or in children 12 years and older with melanoma. It is not known if KEYTRUDA® is safe and effective in children less than 18 years of age for other pediatric diseases.
People get KEYTRUDA® when their cancer has spread or cannot be taken out by surgery.
People get KEYTRUDA® before surgery to treat triple-negative breast cancer and then continued after surgery to help prevent their cancer from coming back.

How does KEYTRUDA® work?
KEYTRUDA® works by helping your immune system fight your cancer.

What are the ingredients in KEYTRUDA®?
Medicinal ingredients: pembrolizumab
Non-medicinal ingredients: L-histidine; L-histidine monohydrochloride monohydrate; polysorbate-80; sucrose; and water for infusion.

KEYTRUDA® comes in the following dosage forms:
Solution for infusion 100 mg/4 mL vial

Do not use KEYTRUDA® if:

- you have had a severe allergic reaction to pembrolizumab or any other ingredients in KEYTRUDA®

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take KEYTRUDA®. Talk about any health conditions or problems you may have, including if you:

- have an autoimmune disease (a condition where the body attacks its own cells), such as Crohn's disease, Ulcerative Colitis or Lupus;
- have pneumonia or inflammation of your lungs (called pneumonitis);
- were previously given ipilimumab, another medicine for treating melanoma, and experienced serious side effects because of that medicine;
- had an allergic reaction to other monoclonal antibody therapies;
- have or have had chronic viral infection of the liver, including hepatitis B (HBV) or hepatitis C (HCV);
- have human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS);
- have liver damage or have had a liver transplant;
- have kidney damage or have had a kidney transplant;
- have had a solid organ transplant or a bone marrow (stem cell) transplant that used donor stem cells (allogeneic); or
- take other medicines that make your immune system weak. Examples of these may include steroids, such as prednisone.

Other warnings you should know about:

There are possible side effects of KEYTRUDA® treatment in people who have received a transplant.

- **Rejection of a transplanted organ.** People who have had an organ transplant may have an increased risk of organ transplant rejection. Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.
- **Complications, including graft-versus-host-disease (GVHD) in people with bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be severe and can lead to death. They may occur if you had this kind of transplant in the past or if you get it in the future. Your doctor will monitor you for the following signs and symptoms: skin rash; liver inflammation; abdominal pain; and diarrhea.

Pregnancy

- If you are pregnant, think you may be pregnant or are planning to have a baby, tell your doctor. Your healthcare provider should do a pregnancy test before you start treatment with KEYTRUDA®.
- Tell your healthcare provider right away if you become pregnant during treatment with KEYTRUDA®.
- KEYTRUDA® can cause harm or death to your unborn baby.
- You must use effective contraception while you are being treated with KEYTRUDA® and for at least 4 months after the last dose of KEYTRUDA® if you are a woman who could become pregnant.

Breast-feeding

- If you are breast-feeding, tell your doctor. You and your doctor should decide whether you will breast-feed or take KEYTRUDA®. You should not do both.
- KEYTRUDA® may pass into your breast milk. You should not breast-feed for at least 4 months after the last dose

- **Females of Childbearing Potential:** KEYTRUDA® may cause fertility problems, which may affect the

ability to have children. Talk to your healthcare provider if you have concerns about fertility.

Driving and using machines
If you experience side effects affecting your ability to concentrate or react, do not drive or use machines until you feel better.

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

How you are given KEYTRUDA®:
- Your doctor will give you KEYTRUDA® through an infusion into your vein (IV) for about 30 minutes.
- Most people get KEYTRUDA® every 3 weeks or every 6 weeks, depending on the dose you are given.
- Your doctor will decide how many treatments you need.

Usual dose:
The recommended dose is 200 mg or 400 mg in adults, depending on how often you are given a dose.

The recommended dose is 2 mg/kg (up to a maximum of 200 mg) in children treated for melanoma (12 years of age and older), classical Hodgkin lymphoma or primary mediastinal B-cell lymphoma.

Overdose:

If you think you, or a person you are caring for, have taken too much KEYTRUDA®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

If you miss an appointment to get KEYTRUDA®:
- Call your doctor right away to reschedule your appointment.
- It is very important that you do not miss a dose of this medicine.

What are possible side effects from using KEYTRUDA®?
When you get KEYTRUDA®, you can have some serious side effects. These side effects can sometimes become life-threatening and can lead to death. These side effects may happen anytime during treatment or even after your treatment has ended. You may experience more than one side effect at the same time. The following lists do not include all the possible side effects you may feel when taking KEYTRUDA®. If you experience any side effects not listed here, contact your healthcare professional.

The following side effects have been reported in clinical trials when KEYTRUDA® is given alone:

Very common (may affect more than 1 in 10 people)
- diarrhea, nausea;
- itching, rash;
- joint pain;
- feeling unusually tired or weak;
- low levels of thyroid hormone;
- high levels of thyroid hormone;
- fever;
- feeling less hungry;

- shortness of breath;
- patches of skin which have lost colour (vitiligo);
- increase in liver enzyme levels.

Common (may affect more than 2 in 100 people and up to 1 in 10 people)
- flu-like illness;
- dry mouth;
- dry eyes;
- headache;
- change in your sense of taste;
- cough;
- dehydration;
- feeling dizzy;
- excessive sweating;
- joint disorder;
- hair loss;
- lack of white blood cells;
- rapid heartbeat;
- cold sores;
- upper respiratory tract infection;
- stuffy nose;
- loss of appetite;
- stomach pain, constipation, vomiting, inflammation of the mucous membrane in the mouth;
- dry skin, redness of the skin, red raised skin rash; itchy patches of thick red skin with silvery scales (psoriasis); skin conditions resembling acne;
- back pain, muscle aches; pain in the upper and lower extremities;
- chills;
- swelling of the face, legs or arms;
- numbness, prickling, tingling or pain in the feet or hands;
- changes in test results:
    - decrease in the number of red blood cells
    - decrease in the number of white blood cells
    - decrease in hemoglobin
    - abnormal liver enzyme levels in the blood
    - decreased in bilirubin levels in the blood
    - decreased sodium levels in the blood
    - abnormal levels of thyroid stimulating hormone in the blood
    - increased level of sugar in the blood
    - decreased level of potassium in the blood
    - increased creatinine levels in the blood
    - weight loss
    - weight gain.

The most common (may affect more than 1 in 10 children) side effects when KEYTRUDA® is given to children are:
- fever;

- vomiting;
- headache;
- abdominal pain;
- decrease in number of red blood cells;
- cough;
- constipation;
- feeling tired;
- nausea;
- diarrhea;
- decreased appetite;
- abnormal liver enzyme levels in the blood;
- joint pain;
- feeling unusually tired or weak;
- back pain;
- pain in arms or legs;
- rash;
- decrease in white blood cell count;
- shortness of breath.

The following side effects have been reported in clinical trials when KEYTRUDA® is given in combination with chemotherapy. Ask your doctor for more information regarding side effects of your chemotherapy.

Very common (may affect more than 1 in 10 people)
- decrease in red blood cell count;
- nausea;
- hair loss;
- decrease in neutrophils (a type of white blood cell);
- decrease in white blood cell count;
- fatigue;
- decrease in platelet count;
- swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina;
- vomiting;
- mouth sores;
- diarrhea;
- decreased appetite;
- increased liver enzyme levels in the blood;
- inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs;
- constipation;
- weakness;
- rash;
- low levels of thyroid hormone;
- joint pain;
- headache;
- eye tearing;

- weight loss;
- muscle pain;
- hiccups;
- increased creatinine levels in the blood;
- fever;
- change in your sense of taste;
- itching;
- decreased magnesium levels in the blood;
- high blood pressure;
- protein in urine.

The following side effects of KEYTRUDA® have been reported in clinical trials when given with lenvatinib. If you are taking KEYTRUDA® in combination with lenvatinib, then you should also read the Patient Medication Information for lenvatinib. It contains more information on the side-effects of lenvatinib.

Very common (may affect more than 1 in 10 people)

• feeling tired or weak • high blood pressure • diarrhea • joint and muscle pain • decreased appetite • low levels of thyroid hormone • nausea • vomiting • mouth sores • weight loss • stomach-area (abdominal) pain • headache • constipation • hoarseness • urinary tract infection • bleeding • fever • swelling of legs or arms • upper respiratory tract infection	• low magnesium level • blisters or rash on the palms of your hands and soles of your feet • shortness of breath • cough • rash • protein in your urine • voice change • high level of amylase or lipase in your blood • itching • abnormal levels of thyroid stimulating hormone in the blood • change in your sense of taste • liver problems • kidney problems • indigestion • dry mouth • trouble sleeping

The most common side effects when KEYTRUDA® is given in combination with axitinib are:
- low or high levels of thyroid hormone;
- diarrhea;
- nausea;
- inflammation of the mucous membranes including in the mouth;
- feeling unusually tired or weak;
- fatigue;
- increase in liver enzyme levels;

- decreased appetite;
- joint pain;
- protein in urine;
- voice change;
- blisters or rash on the palms of your hands and soles of your feet;
- itching;
- rash;
- high blood pressure.

If you are being treated with KEYTRUDA® either alone or in combination with chemotherapy and have any of the following conditions, call or see your doctor right away. Your doctor may give you other medicines in order to prevent more severe complications and reduce your symptoms. Your doctor may withhold the next dose of KEYTRUDA® or stop your treatment with KEYTRUDA®.

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional**	
	Only if severe	**In all cases**
COMMON		
Inflammation of the lungs (pneumonitis) which can cause shortness of breath, chest pain, or coughing		√
Inflammation of the intestines (colitis) which can cause diarrhea or more bowel movements than usual, black, tarry, sticky stools or stools with blood or mucus, severe stomach pain or tenderness, nausea, vomiting		√
Inflammation of the pituitary or thyroid gland (hypophysitis, hypopituitarism, including secondary adrenal insufficiency; hyperthyroidism, hypothyroidism) which can cause rapid heartbeat, weight loss, increased sweating, weight gain, hair loss, feeling cold, constipation, voice getting deeper, muscle aches, dizziness or fainting, headaches that will not go away or unusual headache, feeling more hungry or thirsty, urinating more often than usual		√
Skin problems which can cause rash, itching; skin blistering, peeling, or sores; ulcers in mouth or in lining of nose, throat, or genital area		√
UNCOMMON		
Inflammation of the liver (hepatitis) which can cause nausea or vomiting, feeling less hungry, pain on the right side of stomach, yellowing of skin or whites of eyes, dark urine, bleeding or bruising more easily than normal		√
Inflammation of the kidneys (nephritis) which can cause changes in the amount or colour of your urine		√
Muscle problems, which can cause muscle pain or weakness, severe or persistent muscle or joint pains (myositis)		√

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional**	
	Only if severe	**In all cases**
Muscle problems, which can cause weakness and rapid fatigue of muscles or weakness and tingling in arms and legs (myasthenia gravis or Guillain-Barré syndrome)		√
Low red blood cell count (anemia/hemolytic anemia)		√
Eye problems, which can cause changes in eyesight		√
Shortness of breath, irregular heartbeat, feeling tired, or chest pain (myocarditis)		√
Blood sugar problems (type 1 diabetes mellitus) which can cause hunger or thirst, a need to urinate more often, or weight loss		√
Confusion, fever, memory problems, or seizures (encephalitis)		√
Swollen lymph nodes, rash or tender lumps on skin, cough, or eye pain (sarcoidosis)		√
Inflammation of the pancreas (pancreatitis), which can cause abdominal pain, nausea, and vomiting		√
Reactions related to the infusion such as shortness of breath, itching or rash, dizziness, or fever, wheezing, flushing, feeling like passing out		√
Pain, numbness, tingling, or weakness in the arms or legs; bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating and constipation (myelitis)		√
Inflammation of blood vessels (vasculitis), symptoms include red skin lesions, numbness and weakness		√
Decreased function of the parathyroid gland, which may include muscle cramps or spasms, fatigue and weakness (hypoparathyroidism)		√
Pain in the upper right part of the stomach, swelling of the liver or spleen, fatigue, itching, or yellowing of the skin or the whites of eyes (sclerosing cholangitis)		√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell 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 (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) 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.

Storage:
It is unlikely that you will be asked to store KEYTRUDA® yourself. It will be stored in the hospital or clinic where it is given to you.

Keep out of reach and sight of children.

Solution for Infusion: Store in a refrigerator (2°C to 8°C). Protect from light.

If you want more information about KEYTRUDA®:

- 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 Health Canada website: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the Merck Canada website www.merck.ca or by calling Merck Canada at 1-800-567-2594.

This leaflet was prepared by Merck Canada Inc.

Last Revised: SEPTEMBER 14, 2022