READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

KEYTRUDA® has been issued marketing authorization **with conditions** for the following patients, pending the results of studies to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for KEYTRUDA®, please refer to Health Canada's Notice of Compliance with conditions – drug products website: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/index-eng.php

KEYTRUDA® is indicated for the treatment of:

- adult patients with metastatic non-small cell lung carcinoma (NSCLC) as monotherapy, whose tumours express PD-L1 [(Tumour Proportion Score (TPS) ≥ 1%)] as determined by a validated test and who have disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have received authorized therapy for these aberrations prior to receiving KEYTRUDA®.

- adult patients with refractory or relapsed classical Hodgkin Lymphoma (cHL), as monotherapy, who have failed autologous stem cell transplant (ASCT) and brentuximab vedotin (BV) or who are not ASCT candidates and have failed BV.

- adult and pediatric patients with refractory Primary Mediastinal B-cell Lymphoma (PMBCL) or who have relapsed after 2 or more lines of therapy, as monotherapy.

KEYTRUDA® has been issued marketing authorization **without conditions** for the treatment of patients with:

- Unresectable or metastatic melanoma who have not received prior treatment with ipilimumab. Subjects with BRAF V600 mutant melanoma may have received prior BRAF inhibitor therapy.

- Unresectable or metastatic melanoma and disease progression following ipilimumab therapy and, if BRAF V600 mutation positive, following a BRAF or MEK inhibitor.

- Metastatic non-small cell lung carcinoma (NSCLC) as monotherapy, in adults whose tumours have high PD-L1 expression (TPS ≥50%) as determined by a validated test, with no EGFR or ALK genomic tumour aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC.

- Locally advanced or metastatic urothelial carcinoma who have disease

progression during or following platinum-containing chemotherapy or within 12 months of completing neoadjuvant or adjuvant platinum-containing chemotherapy.

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

An NOC/c is a form of market approval granted to a product on the basis of **promising** evidence of clinical effectiveness following review of the submission by Health Canada.

Products approved under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

℞ **KEYTRUDA®**
pembrolizumab

Read this carefully before you start taking KEYTRUDA® and each time you get an infusion. 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?**

KEYTRUDA® is a prescription medicine used to treat:

- a kind of skin cancer called melanoma in adults when it has spread or cannot be removed by surgery (advanced melanoma).
- a kind of lung cancer called non-small cell lung cancer in adults when it:
  - tests postive for PD-L1 and,
  - has spread or cannot be removed by surgery (advanced lung cancer) and,
  - if your tumour has an abnormal "EGFR" or "ALK" gene, and you have tried chemotherapy that contains platinum and an EGFR or ALK gene inhibitor medicine.
- a kind of cancer called classical Hodgkin lymphoma (cHL) in adults
  - that has come back after an authologous stem cell transplant (ASCT) and therapy with brentuximab vedotin (BV), or
  - that was not suitable for ASCT and has come back after treatment with BV
- 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 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.

KEYTRUDA® can be used only in children with primary mediastinal B-cell lymphoma. It is not known if KEYTRUDA® is safe and effective in children less than 18 years of age for other pediatric diseases.

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

What are the ingredients in KEYTRUDA®?
The active substance is pembrolizumab.
The other ingredients are L-histidine, polysorbate-80, L-histidine Monohydrochloride Monohydrate, sucrose, and water for infusion.

KEYTRUDA® comes in the following dosage forms:
Powder for solution for infusion, 50 mg per vial
Solution for infusion 100 mg/4mL 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)
- take other medicines that make your immune system weak. Examples of these may include steroids, such as prednisone.

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.
- 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.
- Do not breast-feed while taking KEYTRUDA®.

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.
- Your doctor will decide how many treatments you need.

Usual dose:

The recommended dose is 200 mg.

Overdose:

If you think you have taken too much KEYTRUDA®, contact your 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:

Very common (may affect more than 1 in 10 people)
- diarrhea, nausea
- itching, rash
- joint pain
- feeling unusually tired or weak
- fever
- feeling less hungry
- shortness of breath
- patches of skin which have lost colour (vitiligo)

Common (may affect more than 2 in 100 people and up to 1 in 10 people)
- flu-like illness
- dry mouth
- headache
- change in your sense of taste
- cough
- lack of white blood cells
- rapid heart beat
- cold sores
- upper respiratory tract infection
- stuffy nose
- stomach pain, constipation, vomiting, inflammation of the mucous membrane in the mouth dry skin, redness of the skin, red raised skin rash
- back pain, muscle aches
- chills
- swelling of the face, legs or arms
- changes in test results:
    - decrease in the number of red blood cells
    - decrease in the number of white blood cells
    - abnormal liver enzyme levels in the blood
    - decreased sodium levels in the blood
    - abnormal levels of thyroid stimulating hormone in the blood
    - weight loss
    - weight gain

The most common side effects when KEYTRUDA is given to children are:
- fever
- vomiting
- fatigue
- constipation

- abdominal pain
- nausea

If you 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 heart beat, 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; low red blood cell count (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		√

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
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.		√

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 help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Marketed Health Products Safety and Effectiveness Information Bureau
    Marketed Health Products Directorate
    Health Products and Food Branch
    Health Canada,
    Address Locator 1908C
    Ottawa, ON
    K1A 0K9

    Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html).

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.

Also, to report an adverse event related to KEYTRUDA®, please contact Merck Canada at 1-800-567-2594.

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 this medicine out of the sight and reach of children.

Powder for Solution for Infusion: Store in a refrigerator (2°C to 8°C).
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); or Merck Canada website www.merck.ca, or by calling Merck Canada at 1-800-567-2594.

To report an adverse event related to KEYTRUDA®, please contact 1-800-567-2594.

This leaflet was prepared by Merck Canada Inc.

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