KEYTRUDA® 50 mg powder for concentrate for solution for infusion
pembrolizumab

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- It is important that you keep the Alert Card with you during treatment.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What KEYTRUDA is and what it is used for
2. What you need to know before you are given KEYTRUDA
3. How you are given KEYTRUDA
4. Possible side effects
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1. What KEYTRUDA is and what it is used for

KEYTRUDA contains the active substance pembrolizumab, which is a monoclonal antibody. KEYTRUDA works by helping your immune system fight your cancer.

KEYTRUDA is used in adults to treat:
- a kind of skin cancer called melanoma
- a kind of lung cancer called non-small cell lung cancer
- a kind of cancer called classical Hodgkin lymphoma
- a kind of cancer called bladder cancer (urothelial carcinoma).

People get KEYTRUDA when their cancer has spread or cannot be taken out by surgery.

2. What you need to know before you are given KEYTRUDA

You should not be given KEYTRUDA:
- if you are allergic to pembrolizumab or any of the other ingredients of this medicine (listed in section 6 “Contents of the pack and other information”). Talk to your doctor if you are not sure.

Warnings and precautions

Talk to your doctor or nurse before receiving KEYTRUDA.

Before you get KEYTRUDA, tell your doctor if you:
- have an autoimmune disease (a condition where the body attacks its own cells)
- 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
- have kidney damage
- have had a solid organ transplant or a bone marrow (stem cell) transplant that used donor stem cells (allogeneic)

When you get KEYTRUDA, you can have some serious side effects. You may experience more than one side effect at the same time.
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.

- inflammation of the lungs, which may include shortness of breath, chest pain or coughing (possibly fatal)
- inflammation of the intestines, which may include diarrhoea 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 liver, which may include nausea or vomiting, feeling less hungry, pain on the right side of stomach, yellowing of skin or whites of eyes, dark urine or bleeding or bruising more easily than normal
- inflammation of the kidneys, which may include changes in the amount or colour of your urine
- inflammation of hormone glands (especially the thyroid, pituitary and adrenal glands), which may include rapid heartbeat, weight loss, increased sweating, weight gain, hair loss, feeling cold, constipation, deeper voice, muscle aches, dizziness or fainting, headaches that will not go away or unusual headache
- type 1 diabetes, which may include feeling more hungry or thirsty than usual, need to urinate more often or weight loss
- inflammation of the eyes, which may include changes in eyesight
- inflammation in the muscles, which may include muscle pain or weakness
- inflammation of the heart muscle, which may include shortness of breath, irregular heartbeat, feeling tired, or chest pain
- inflammation of the pancreas, which may include abdominal pain, nausea and vomiting
- inflammation of the skin, which may include rash, itching, skin blistering, peeling or sores, and/or ulcers in mouth or in lining of nose, throat, or genital area (possibly fatal)
- an immune disorder that can affect the lungs, skin, eyes and/or lymph nodes (sarcoidosis)
- inflammation of the brain, which may include confusion, fever, memory problems or seizures (encephalitis)
- infusion reactions, which may include shortness of breath, itching or rash, dizziness or fever

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 signs and symptoms, which may include skin rash, liver inflammation, abdominal pain, or diarrhoea.

Children and adolescents
KEYTRUDA should not be used in children and adolescents below 18 years of age.
Other medicines and KEYTRUDA
Tell your doctor
- If you are taking other medicines that make your immune system weak. Examples of these may include corticosteroids, such as prednisone. These medicines may interfere with the effect of KEYTRUDA. However, once you are treated with KEYTRUDA, your doctor may give you corticosteroids to reduce the side-effects that you may have with KEYTRUDA.
- If you are taking, have recently taken or might take any other medicines.

Pregnancy
- You must not use KEYTRUDA if you are pregnant unless your doctor specifically recommends it.
- 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.
- If you are a woman who could become pregnant, you must use adequate birth control while you are being treated with KEYTRUDA and for at least 4 months after your last dose.

Breast-feeding
- If you are breast-feeding, tell your doctor.
- Do not breast-feed while taking KEYTRUDA.
- It is not known if KEYTRUDA passes into your breast milk.

Driving and using machines
Do not drive or use machines after you have been given KEYTRUDA unless you are sure you are feeling well. Feeling tired or weak is a very common side effect of KEYTRUDA. This can affect your ability to drive or to use machines.

3. How you are given KEYTRUDA
KEYTRUDA will be given to you in a hospital or clinic under the supervision of a doctor experienced in cancer treatment.
- Your doctor will give you KEYTRUDA through an infusion into your vein (IV) for about 30 minutes, every 3 weeks.
- Your doctor will decide how many treatments you need.

The recommended dose is:
- 200 mg of pembrolizumab if you have non-small cell lung cancer that has not been previously treated with chemotherapy, classical Hodgkin lymphoma or if you have bladder cancer.
- 2 mg of pembrolizumab per kilogram of your body weight if you have melanoma or if you have non-small cell lung cancer that has been previously treated with chemotherapy.

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.

If you stop receiving KEYTRUDA
Stopping your treatment may stop the effect of the medicine. Do not stop treatment with KEYTRUDA unless you have discussed this with your doctor. If you have any further questions about your treatment, ask your doctor.

You will also find this information in the Patient Alert Card you have been given by your doctor. It is important that you keep this Alert Card and show it to your partner or caregivers.
4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

When you get KEYTRUDA, you can have some serious side effects. See section 2.

The following side effects have been reported:

**Very common (may affect more than 1 in 10 people)**
- diarrhoea; nausea
- itching; skin rash
- feeling tired

**Common (may affect up to 1 in 10 people)**
- joint pain
- decrease in the number of red blood cells
- thyroid gland problems; hot flush
- feeling less hungry
- headache; dizziness; change in your sense of taste
- inflammation of the lungs; shortness of breath; cough
- inflammation of the intestines; dry mouth
- stomach pain; constipation; vomiting
- red raised rash sometimes with blisters; patches of skin which have lost colour
- muscle pain, aches or tenderness; pain in the muscles and bones; pain in arms or legs; joint pain with swelling
- swelling; unusual tiredness or weakness; chills; flu-like illness; fever
- increased liver enzyme levels in the blood; abnormal kidney function test
- reaction related to the infusion of the medicine

**Uncommon (may affect up to 1 in 100 people)**
- lung infection
- a decreased number of white blood cells (neutrophils, leukocytes, lymphocytes and eosinophils); decrease in the number of platelets (bruising or bleeding more easily)
- inflammation of the pituitary gland situated at the base of the brain; decreased secretion of hormones produced by the adrenal glands; inflammation of the thyroid
- type 1 diabetes; decreased sodium, potassium and calcium in the blood
- trouble sleeping
- seizure; lack of energy; inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs
- dry eye; inflammation of the eyes; eye pain, irritation, itchiness or redness; uncomfortable sensitivity to light; seeing spots
- inflammation of the heart muscle, which may present as shortness of breath, irregular heartbeat, feeling tired, or chest pain
- high blood pressure
- inflammation of the pancreas
- inflammation of the liver
- dry, itchy skin; thickened, sometimes scaly, skin growth; hair loss; inflammation of the skin; acne-like skin problem; hair colour changes; small skin bumps, lumps or sores
- inflammation of the sheath that surrounds tendons
- inflammation of the kidneys
- increased level of amylase, an enzyme that breaks down starch; increased calcium in the blood

**Rare (may affect up to 1 in 1,000 people)**
- inflammation response against platelets or red blood cells
- an immune disorder that can affect the lungs, skin, eyes and/or lymph nodes (sarcoidosis)
- a temporary inflammation of the nerves that causes pain, weakness, and paralysis in the extremities; a condition in which the muscles become weak and tire easily
- inflammation of the brain, which may present as confusion, fever, memory problems or seizures (encephalitis)
- a hole in the small intestines
- tender red bumps under the skin
- itching, skin blistering, peeling or sores, and/or ulcers in mouth or in lining of nose, throat, or genital area (toxic epidermal necrolysis or Stevens-Johnson syndrome)

**Reporting of side effects**

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

**United Kingdom:** Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

**Ireland:** HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

**Malta:** ADR Reporting at: www.medicinesauthority.gov.mt/adrportal

5. **How to store KEYTRUDA**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).

From a microbiological point of view, the reconstituted or diluted solution should be used immediately. The reconstituted or diluted solution must not be frozen. If not used immediately, chemical and physical in-use stability of KEYTRUDA has been demonstrated for 24 hours at 2°C to 8°C. This 24 hour total hold from reconstitution may include up to 6 hours at room temperature (at or below 25°C). If refrigerated, the vials and/or intravenous bags must be allowed to come to room temperature prior to use.

Do not store any unused portion of the infusion solution for reuse. Any unused medicine or waste material should be disposed of in accordance with local requirements.

6. **Contents of the pack and other information**

**What KEYTRUDA contains**

The active substance is pembrolizumab. One vial contains 50 mg of pembrolizumab.

After reconstitution, 1 mL of concentrate contains 25 mg of pembrolizumab.

The other ingredients are L-histidine, L-histidine hydrochloride monohydrate, sucrose and polysorbate 80.

**What KEYTRUDA looks like and contents of the pack**

KEYTRUDA is a white to off-white lyophilised powder.

It is available in cartons containing one glass vial.
**Preparation and administration**

- Prior to reconstitution, the vial of lyophilised powder can be out of refrigeration (temperatures at or below 25°C) for up to 24 hours.
- Aseptically add 2.3 mL of water for injections to yield a 25 mg/mL (pH 5.2-5.8) solution of KEYTRUDA. Each vial contains an excess fill of 10 mg (0.4 mL) to ensure the recovery of 50 mg of KEYTRUDA per vial. After reconstitution, 1 mL of concentrate contains 25 mg of pembrolizumab.
- To avoid foaming, deliver the water along the walls of the vial and not directly on the lyophilised powder.
- Slowly swirl the vial to allow reconstitution of the lyophilised powder. Allow up to 5 minutes for the bubbles to clear. Do not shake the vial.
• Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. Reconstituted KEYTRUDA is a clear to slightly opalescent, colourless to slightly yellow solution. Discard the vial if visible particles are observed.

• Withdraw the required volume up to 2 mL (50 mg) of KEYTRUDA and transfer into an intravenous bag containing sodium chloride 9 mg/mL (0.9%) or glucose 50 mg/mL (5%) to prepare a diluted solution with a final concentration ranging from 1 to 10 mg/mL. Mix diluted solution by gentle inversion.

• From a microbiological point of view, the reconstituted or diluted solution should be used immediately. The reconstituted or diluted solution must not be frozen. If not used immediately, chemical and physical in-use stability of KEYTRUDA has been demonstrated for 24 hours at 2°C to 8°C. This 24 hour total hold from reconstitution may include up to 6 hours at room temperature (at or below 25°C). If refrigerated, the vials and/or intravenous bags must be allowed to come to room temperature prior to use. Administer the infusion solution intravenously over 30 minutes using a sterile, non-pyrogenic, low-protein binding 0.2 to 5 µm in-line or add-on filter.

• Do not co-administer other medicinal products through the same infusion line.

• KEYTRUDA is for single use only. Discard any unused portion left in the vial.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

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