

Package leaflet: Information for the patient

KEYTRUDA® 25 mg/mL concentrate for solution for infusion pembrolizumab

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
5. How to store KEYTRUDA
6. Contents of the pack and other information

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)
- a kind of head and neck cancer called head and neck squamous cell carcinoma.
- a kind of kidney cancer called renal cell carcinoma.

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

People get KEYTRUDA after they have had surgery to remove melanoma to help prevent their cancer from coming back (adjuvant therapy).

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, ask your doctor.

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. 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.

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
- 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
- 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)
- 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)
- 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. Corticosteroids may also be given to you before receiving KEYTRUDA in combination with chemotherapy to prevent and/or treat nausea, vomiting, and other side effects caused by chemotherapy.
- 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

KEYTRUDA has a minor effect on your ability to drive or use machines. Feeling dizzy, tired or weak are possible side effects of KEYTRUDA. Do not drive or use machines after you have been given KEYTRUDA unless you are sure you are feeling well.

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.

- The recommended dose of KEYTRUDA is either 200 mg every 3 weeks or 400 mg every 6 weeks.
- Your doctor will give you KEYTRUDA through an infusion into your vein (intravenous) for about 30 minutes.
- Your doctor will decide how many treatments you need.

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 with pembrolizumab alone:

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

- decrease in the number of red blood cells
- reduced thyroid gland activity
- feeling less hungry
- headache
- shortness of breath; cough
- diarrhoea; stomach pain; nausea; vomiting; constipation
- itching; skin rash
- pain in muscle and bones; joint pain
- feeling tired; unusual tiredness or weakness; swelling; fever

Common (may affect up to 1 in 10 people)

- lung infection
- decrease in the number of platelets (bruising or bleeding more easily); decrease in the number of white blood cell (lymphocytes)
- reactions related to the infusion of the medicine
- overactive thyroid gland activity; hot flush
- decreased sodium, potassium, or calcium in the blood
- trouble sleeping
- dizziness; inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; lack of energy; change in your sense of taste
- dry eye
- abnormal heart rhythm
- high blood pressure
- inflammation of the lungs
- inflammation of the intestines; dry mouth
- red raised rash sometimes with blisters; patches of skin which have lost colour; dry, itchy skin; hair loss; acne-like skin problem
- muscle pain, aches or tenderness; pain in arms or legs; joint pain with swelling
- chills; flu-like illness
- increased liver enzyme levels in the blood; increased calcium in the blood; abnormal kidney function test

Uncommon (may affect up to 1 in 100 people)

- a decreased number of white blood cells (neutrophils, leukocytes, and eosinophils)
- an immune disorder that can affect the lungs, skin, eyes and/or lymph nodes (sarcoidosis)
- 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
- seizure
- inflammation of the eyes; eye pain, irritation, itchiness or redness; uncomfortable sensitivity to light; seeing spots
- inflammation of the covering of the heart; accumulation of fluid around the heart

- inflammation of the pancreas
- a sore that develops on the inside lining of your stomach or upper part of your small intestine
- inflammation of the liver
- thickened, sometimes scaly, skin growth; inflammation of the skin; 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

Rare (may affect up to 1 in 1,000 people)

- inflammation response against platelets or red blood cells; feeling weak, lightheaded, short of breath or if your skin looks pale (signs of low level of red blood cells, possibly due to a type of anaemia called pure red cell aplasia); a condition called haemophagocytic lymphohistiocytosis, where the immune system makes too many infection fighting cells called histiocytes and lymphocytes that may cause various symptoms
- inflammation of the brain, which may present as confusion, fever, memory problems or seizures (encephalitis)
- 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
- 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 the membrane around the spinal cord and brain, which may present as neck stiffness, headache, fever, eye sensitivity to light, nausea or vomiting (meningitis)
- inflammation of the heart muscle, which may present as shortness of breath, irregular heartbeat, feeling tired, or chest pain
- 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)
- disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's syndrome)
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The following side effects have been reported in clinical studies with pembrolizumab in combination with chemotherapy:

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

- decrease in the number of red blood cells
- decreased number of white blood cells; decrease in the number of platelets (bruising or bleeding more easily)
- decreased potassium in the blood; feeling less hungry
- dizziness; headache; inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; change in your sense of taste
- shortness of breath; cough
- diarrhoea; nausea; vomiting; constipation; stomach pain
- skin rash; itching; hair loss
- pain in the muscles and bones; joint pain
- unusual tiredness or weakness; swelling; fever
- abnormal kidney function test

Common (may affect up to 1 in 10 people)

- lung infection
- decreased number of white blood cells (neutrophils) with a fever
- reaction related to the infusion of the medicine

- thyroid gland problems
- decreased sodium or calcium in the blood
- trouble sleeping
- dry eye
- abnormal heart rhythm
- high blood pressure
- inflammation of the lungs
- inflammation of the intestines; dry mouth
- red raised rash, sometimes with blisters
- muscle pain, aches or tenderness; joint pain with swelling; pain in arms or legs
- inflammation of the kidneys; sudden kidney damage
- chills; flu-like illness
- increased calcium in the blood; increased liver enzyme levels in the blood

Uncommon (may affect up to 1 in 100 people)

- inflammation of the pituitary gland situated at the base of the brain; inflammation of the thyroid; decreased secretion of hormones produced by the adrenal glands
- type 1 diabetes
- seizure
- accumulation of fluid around the heart
- inflammation of the pancreas
- a sore that develops on the inside lining of your stomach or upper part of your small intestine
- inflammation of the liver
- thickened, sometimes scaly, skin growth; acne-like skin problem; inflammation of the skin; patches of skin that have lost colour
- inflammation of the sheath that surrounds tendons
- increased level of amylase, an enzyme that breaks down starch; increased bilirubin in the blood

Rare (may affect up to 1 in 1,000 people)

- a decreased number of white blood cells (eosinophils)
- inflammation of the heart muscle, which may present as shortness of breath, irregular heartbeat, feeling tired, or chest pain; inflammation of the covering of the heart
- hair colour changes; dry, itchy skin; small skin bumps, lumps or sores
- disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's syndrome)

The following side effects have been reported in clinical studies with pembrolizumab in combination with axitinib:

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

- thyroid gland problems
- feeling less hungry
- headache; change in your sense of taste
- high blood pressure
- shortness of breath; cough; hoarseness
- diarrhoea; stomach pain; nausea; vomiting; constipation
- blisters or rash on palms of hands or soles of feet; skin rash; itching
- feeling tired; unusual tiredness or weakness; fever
- increased liver enzyme levels in the blood; abnormal kidney function test
- pain in the muscles and bones; joint or muscle pain, aches or tenderness; pain in arms or legs

Common (may affect up to 1 in 10 people)

- lung infection
- decrease in the number of red blood cells; decreased number of white blood cells (neutrophils, leukocytes); decrease in the number of platelets (bruising or bleeding more easily)

- reaction related to the infusion of the medicine
- inflammation of the pituitary gland situated at the base of the brain; inflammation of the thyroid; decreased secretion of hormones produced by the adrenal glands
- decreased potassium, sodium or calcium in the blood
- trouble sleeping
- dizziness; lack of energy; inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs
- dry eye
- abnormal heart rhythm
- inflammation of the lungs
- inflammation of the intestines; dry mouth
- red raised rash, sometimes with blisters; acne-like skin problem; inflammation of the skin; dry, itchy skin; hair loss
- inflammation of the liver
- muscle pain, aches or tenderness; joint or muscle pain with swelling; inflammation of the sheath that surrounds tendons
- sudden kidney damage; inflammation of the kidneys
- swelling; flu-like illness; chills
- increased calcium in the blood; increased liver enzyme levels in the blood

Uncommon (may affect up to 1 in 100 people)

- decreased number of white blood cells (lymphocytes and eosinophils)
- type 1 diabetes
- a condition in which the muscles become weak and tire easily
- inflammation of the heart muscle, which may present as shortness of breath, irregular heartbeat, feeling tired, or chest pain
- inflammation of the eyes; eye pain, irritation, itchiness or redness; uncomfortable sensitivity to light; seeing spots
- inflammation of the pancreas
- a sore that develops on the inside lining of your stomach or upper part of your small intestine
- hair colour changes; thickened, sometimes scaly, skin growth; small skin bumps, lumps or sores; patches of skin that have lost colour
- increased level of amylase, an enzyme that breaks down starch
- disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's 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 via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

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).

Do not freeze.

Store in the original carton in order to protect from light.

From a microbiological point of view, the product, once diluted, should be used immediately. The diluted solution must not be frozen. If not used immediately, chemical and physical in-use stability of KEYTRUDA has been demonstrated for 96 hours at 2°C to 8°C. This 96-hour hold 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 of 4 mL contains 100 mg of pembrolizumab.
Each mL of concentrate contains 25 mg of pembrolizumab.

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

What KEYTRUDA looks like and contents of the pack

KEYTRUDA is a clear to slightly opalescent, colourless to slightly yellow solution, pH 5.2 – 5.8. It is available in cartons containing one glass vial.

Marketing Authorisation Holder

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Manufacturer

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.

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The following information is intended for healthcare professionals only:

Preparation and administration of the infusion

- Do not shake the vial.
- Equilibrate the vial to room temperature (at or below 25°C).
- Prior to dilution, the vial of liquid can be out of refrigeration (temperatures at or below 25°C) for up to 24 hours.
- Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. The concentrate 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 4 mL (100 mg) of concentrate 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. Each vial contains an excess fill of 0.25 mL (total content per vial 4.25 mL) to ensure the recovery of 4 mL of concentrate. Mix diluted solution by gentle inversion.
- From a microbiological point of view, the product, once diluted, should be used immediately. The diluted solution must not be frozen. If not used immediately, chemical and physical in-use stability of KEYTRUDA has been demonstrated for 96 hours at 2°C to 8°C. This 96-hour hold 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. Translucent to white proteinaceous particles may be seen in diluted solution. 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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