Applicant: MSD (Pty) Ltd
APPROVED PATIENT INFORMATION LEAFLET
Keytruda Solution for Infusion

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

KEYTRUDA® Solution for Infusion

Pembrolizumab

Contains 280 mg sucrose

Read all of this leaflet carefully before you are given KEYTRUDA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

1. What KEYTRUDA is and what it is used for
2. What you need to know before you use KEYTRUDA
3. How to use 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 to treat:

- a kind of skin cancer called melanoma in adults and children.

- a kind of lung cancer called non-small cell lung cancer in adults.
- a kind of cancer called classical Hodgkin lymphoma in adults and children.
- a kind of cancer called urothelial carcinoma, including bladder cancer, in adults.
- a kind of head and neck cancer called head and neck squamous cell carcinoma in adults.
- a kind of kidney cancer called renal cell carcinoma in adults.
- a kind of cancer in adults that can occur in any part of the body and is shown by a laboratory test to be microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR).
- a kind of cancer called colon or rectal cancer in adults that is shown by a laboratory test to be MSI-H or dMMR.
- a kind of cancer called oesophageal carcinoma in adults.
- a kind of breast cancer called triple-negative breast cancer in adults.
- a kind of uterine cancer called endometrial carcinoma in adult women.
- a kind of cancer called cervical cancer in adult women.
- a kind of stomach cancer called gastric or gastro-oesophageal junction adenocarcinoma in adults.
- a kind of bile duct or gallbladder cancer called biliary tract carcinoma in adults.

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

People get KEYTRUDA after they had surgery to remove melanoma, non-small cell lung cancer, or renal cell carcinoma to help prevent their cancer from coming back (adjuvant therapy).

People get KEYTRUDA before surgery (neoadjuvant therapy) to treat non-small cell lung cancer or triple-negative breast cancer and then continue getting KEYTRUDA after surgery (adjuvant therapy) to help prevent their cancer from coming back.

KEYTRUDA may be given in combination with other anti-cancer medicines with or without radiation therapy. 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.

2. What you need to know before you use KEYTRUDA

You should not be given KEYTRUDA:

- if you are hypersensitive (allergic) to pembrolizumab or any of the other ingredients of KEYTRUDA (listed in section 6 “Contents of the pack and other information”).
- if you are pregnant.
- do not breastfeed your baby while receiving KEYTRUDA or within 4 months of your last dose.

Warnings and precautions

Tell your doctor or healthcare provider before being given KEYTRUDA if you:

- have a disease of your immune system like Crohn’s, 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.
- have kidney damage.
- had an organ transplant (like a kidney transplant) or had a bone marrow (stem cell) transplant that used donor stem cells (allogeneic).

If you have any of the following conditions, call or tell your doctor right away:

- 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, including diabetic ketoacidosis (acid in the blood produced from diabetes), symptoms may include feeling more hungry or thirsty than usual, need to urinate more often or weight loss, feeling tired or feeling sick, stomach pain, fast and deep breathing, confusion, unusual sleepiness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat.
- 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 (myocarditis).
- 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).

- inflammation and scarring of the bile ducts, which may include 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 (cholangitis sclerosing).
- inflammation of the stomach (gastritis).
- decreased function of the parathyroid gland, which may include muscle cramps or spasms, fatigue and weakness (hypoparathyroidism).
- infusion reactions, which may include shortness of breath, itching or rash, dizziness or fever.
- destruction of red blood cells, which may include dark urine, pale or yellow skin/eyes, lightheadedness, feeling tired, rapid heartbeat, or shortness of breath (hemolytic anemia)
- decreased ability of the pancreas to make digestive enzymes, which may include diarrhoea with loose and oily stools, weight loss, metabolic bone disease, and vitamin or mineral deficiencies (exocrine pancreatic insufficiency).
- inflammation of the covering of the heart, which may include chest pain, shortness of breath or feeling tired (pericarditis).

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

Children and adolescents

Do not give KEYTRUDA to children under 18 years of age, except for children:

- with classical Hodgkin lymphoma aged 3 years and older
- with melanoma aged 12 years and older.

Other medicines and KEYTRUDA

- Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)
- Tell your doctor if you take other medicines that make your immune system weak e.g. steroids, such as prednisone.

Pregnancy, breastfeeding and fertility

- You should not receive KEYTRUDA while you are pregnant or breastfeeding your baby.
- If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before receiving this medicine.
- 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.
- If you are breastfeeding your baby tell your doctor.

- Do not breastfeed your baby while being given KEYTRUDA or for 4 months after the last dose.

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.

KEYTRUDA contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before receiving KEYTRUDA. KEYTRUDA contains sucrose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

3. How to use KEYTRUDA

You will not be expected to give yourself KEYTRUDA. It will be given to you by a person who is qualified to do so. KEYTRUDA should be administered by slow intravenous infusion of approximately 30 minutes at the usual dose every 3 weeks or 6 weeks, depending on the dose you are given. Your doctor will tell you how long your treatment with KEYTRUDA will last.

If you miss your appointment to receive 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 use more KEYTRUDA than you should

Since a healthcare provider will administer KEYTRUDA he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to use KEYTRUDA

Since a healthcare provider will administer KEYTRUDA, it is unlikely that the dose will be missed.

4. Possible side effects

KEYTRUDA can have serious side effects. These side effects can become life-threatening and 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. Not all side effects reported for KEYTRUDA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using KEYTRUDA, please consult your healthcare provider for advice.

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 cells (neutrophils, lymphocytes)
- reactions related to the infusion of the medicine
- overactive thyroid gland; 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
- inflammation of the liver
- red raised rash sometimes with blisters; inflammation of the skin; 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
- flu-like illness; chills

- 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 (leukocytes); inflammation response against platelets; an increased number of white blood cells (eosinophils)
- an immune disorder that can affect the lungs, skin, eyes and/or lymph nodes (sarcoidosis)
- decreased secretion of hormones produced by the adrenal glands; inflammation of the pituitary gland situated at the base of the brain; inflammation of the thyroid
- type 1 diabetes, including diabetic ketoacidosis
- a condition in which the muscles become weak and tire easily; seizure
- 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 (myocarditis); inflammation of the covering of the heart, which may present as chest pain, shortness of breath or feeling tired (pericarditis), accumulation of fluid around the heart
- inflammation of the pancreas; inflammation of the stomach; a sore that develops on the inside lining of your stomach or upper part of your small intestine
- thickened, sometimes scaly, skin growth; small skin bumps, lumps or sores; hair colour changes
- 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 red blood cells; a condition called haemophagocytic lymphohistiocytosis, where the immune system makes too many infection fighting cells called histiocytes and lymphocytes that may cause various symptoms; 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)
- decreased function of the parathyroid gland, which may present as muscle cramps or spasms, fatigue and weakness
- a temporary inflammation of the nerves that causes pain, weakness and paralysis in the extremities (Guillain-Barré syndrome); inflammation of the brain, which may present as 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); swelling of the optic nerve that may result in vision loss in one or both eyes, pain with eye movement, and/or loss of colour vision (optic neuritis); 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 blood vessels
- lack or reduction of digestive enzymes made by the pancreas (exocrine pancreatic insufficiency); a hole in the small intestines; coeliac disease (characterised by symptoms such as stomach pain, diarrhoea, and bloating after consuming gluten-containing foods)
- inflammation of the bile ducts

- itching, skin blistering, peeling or sores and/or ulcers in mouth or in lining of nose, throat or genital area (Stevens-Johnson syndrome or toxic epidermal necrolysis); tender red bumps under the skin
- disease in which the immune system attacks the glands that make moisture for the body, such as tears and saliva (Sjogren's syndrome)
- inflammation of the bladder, which may present as frequent and/or painful urination, urge to pass urine, blood in urine, pain or pressure in lower abdomen.

The following side effects have been reported in clinical studies with pembrolizumab in combination with chemotherapy or chemotherapy with radiation therapy:

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

- decrease in the number of red blood cells; decreased number of white blood cells (neutrophils); decrease in the number of platelets (bruising or bleeding more easily)
- reduced thyroid gland activity
- decreased potassium in the blood; feeling less hungry
- trouble sleeping
- inflammation of the nerves causing numbness, weakness, tingling or burning pain of the arms and legs; headache; dizziness
- shortness of breath; cough
- diarrhoea; nausea; vomiting; stomach pain; constipation
- hair loss; itching; skin rash
- pain in the muscles and bones; joint pain
- feeling tired; unusual tiredness or weakness; fever; swelling

- increased blood level of the liver enzyme alanine aminotransferase; increased blood level of the liver enzyme aspartate aminotransferase; 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; decreased number of white blood cells (leukocytes, lymphocytes)
- reaction related to the infusion of the medicine
- decreased secretion of hormones produced by the adrenal glands; overactive thyroid gland; inflammation of the thyroid
- decreased sodium or calcium in the blood
- change in your sense of taste; lack of energy
- dry eye
- abnormal heart rhythm
- high blood pressure
- inflammation of the lungs
- inflammation of the intestines; inflammation of the stomach; dry mouth
- inflammation of the liver
- red raised rash, sometimes with blisters; inflammation of the skin; acne-like skin problem; dry, itchy skin
- muscle pain; aches or tenderness; pain in arms or legs; joint pain with swelling
- sudden kidney damage
- flu-like illness; chills

- increased bilirubin in the blood; increased blood level of the liver enzyme alkaline phosphatase; increased calcium in the blood.

Uncommon (may affect up to 1 in 100 people)

- inflammation response against red blood cells; an increased number of white blood cells (eosinophils)
- inflammation of the pituitary gland situated at the base of the brain
- type 1 diabetes, including diabetic ketoacidosis
- inflammation of the brain, which may present as confusion, fever, memory problems or seizures (encephalitis); seizure
- 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 (myocarditis); inflammation of the covering of the heart, which may present as chest pain, shortness of breath or feeling tired (pericarditis); accumulation of fluid around the heart
- inflammation of the blood vessels
- inflammation of the pancreas; a sore that develops on the inside lining of your stomach or upper part of your small intestine
- thickened, sometimes scaly, skin growth; patches of skin that have lost colour; small skin bumps, lumps or sores
- inflammation of the sheath that surrounds tendons

- inflammation of the kidneys; inflammation of the bladder, which may present as frequent and/or painful urination, urge to pass urine, blood in urine, pain or pressure in lower abdomen
- increased level of amylase, an enzyme that breaks down starch.

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

- inflammation response against platelets
- an immune disorder that can affect the lungs, skin, eyes and/or lymph nodes (sarcoidosis)
- decreased function of the parathyroid gland, which may present as muscle cramps or spasms, fatigue and weakness
- a condition in which the muscles become weak and tire easily; a temporary inflammation of the nerves that causes pain, weakness, and paralysis in the extremities (Guillain-Barré syndrome); swelling of the optic nerve that may result in vision loss in one or both eyes, pain with eye movement, and/or loss of colour vision (optic neuritis); 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)
- lack or reduction of digestive enzymes made by the pancreas (exocrine pancreatic insufficiency); a hole in the small intestines; coeliac disease (characterised by symptoms such as stomach pain, diarrhoea, and bloating after consuming gluten-containing foods)
- inflammation of the bile ducts
- itching, skin blistering, peeling or sores and/or ulcers in mouth or in lining of nose, throat, or genital area (Stevens-Johnson syndrome); tender red bumps under the skin; hair colour changes

- 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 or lenvatinib:

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

- urinary infections (increased frequency in urination and pain in passing urine)
- decrease in the number of red blood cells
- reduced thyroid gland activity
- feeling less hungry
- headache; change in your sense of taste
- high blood pressure
- shortness of breath; cough
- diarrhoea; stomach pain; nausea; vomiting; constipation
- skin rash; itching
- joint pain; pain in the muscles and bones; muscle pain, aches or tenderness; pain in arms or legs
- feeling tired; unusual tiredness or weakness; swelling; fever
- increased levels of lipase, an enzyme that breaks down fats; increased liver enzyme levels in the blood; abnormal kidney function test.

Common (may affect up to 1 in 10 people)

- lung infection

- decreased number of white blood cells (neutrophils, lymphocytes, leukocytes); decrease in the number of platelets (bruising or bleeding more easily)
- reaction related to the infusion of the medicine
- decreased secretion of hormones produced by the adrenal glands; overactive thyroid gland; inflammation of the thyroid
- 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
- dry eye
- abnormal heart rhythm
- inflammation of the lungs
- inflammation of the intestines; inflammation of the pancreas; inflammation of the stomach; dry mouth
- inflammation of the liver
- red raised rash, sometimes with blisters; inflammation of the skin; dry skin; acne-like skin problem; hair loss
- joint pain with swelling
- inflammation of the kidneys
- flu-like illness; chills
- increased levels of amylase, an enzyme that breaks down starch; increased bilirubin in the blood; increased blood levels of a liver enzyme known as alkaline phosphatase; increased calcium in the blood.

Uncommon (may affect up to 1 in 100 people)

- an increased number of white blood cells (eosinophils)
- inflammation of the pituitary gland situated at the base of the brain
- type 1 diabetes, including diabetic ketoacidosis
- 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)
- 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 (myocarditis); accumulation of fluid around the heart
- inflammation of the blood vessels
- a sore that develops on the inside lining of your stomach or upper part of your small intestine
- dry, itchy skin; thickened, sometimes scaly, skin growth; patches of skin which have lost colour; small skin bumps, lumps or sores; hair colour changes
- inflammation of the sheath that surrounds tendons.

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

- decreased function of the parathyroid gland, which may present as muscle cramps or spasms, fatigue and weakness
- swelling of the optic nerve that may result in vision loss in one or both eyes, pain with eye movement, and/or loss of colour vision (optic neuritis)
- a hole in the small intestines

- 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)
- inflammation of the bladder, which may present as frequent and/or painful urination, urge to pass urine, blood in urine, pain or pressure in lower abdomen.

Other side effects that have been reported with frequency not known (cannot be estimated from the available data)

- lack or reduction of digestive enzymes made by the pancreas (exocrine pancreatic insufficiency); coeliac disease (characterised by symptoms such as stomach pain, diarrhoea, and bloating after consuming gluten-containing foods)

If you have any side effect that bothers you or that does not go away, tell your doctor.
If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of KEYTRUDA.

5. How to store KEYTRUDA

Store vials in a refrigerator at 2 to 8 °C in the original carton to protect from light. Do not freeze. Do not shake.

Prior to dilution, the vial of liquid can be out of refrigeration (at or below 25 °C) for up to 24 hours.

The product does not contain a preservative. The diluted product should be used immediately. If not used immediately, diluted solutions of KEYTRUDA may be stored at room temperature for a cumulative time of up to 6 hours. Diluted solutions of KEYTRUDA may also be stored under refrigeration at 2 to 8 °C; however, the total time from dilution of KEYTRUDA to completion of infusion should not exceed 96 hours. If refrigerated, allow the vials and/or IV bags to come to room temperature prior to use. Translucent to white proteinaceous particles may be seen in the diluted solution. Do not freeze the infusion solution. Discard any unused portion left in the vial.

Do not use after the expiry date stated on the label.

Store all medicines out of reach of children.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What KEYTRUDA contains

Each vial contains 100 mg pembrolizumab in 4 mL solution (25 mg/mL).

The other ingredients are: L-histidine, L-histidine hydrochloride monohydrate, sucrose, polysorbate 80 (EA433) and water for injection.

What KEYTRUDA looks like and contents of the pack

KEYTRUDA is supplied in a 10 mL clear type 1 glass vial with a grey rubber stopper and an aluminium seal with a dark blue coloured flip-off cap as a single vial in a carton.

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Holder of Certificate of Registration

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Access to the corresponding Professional Information

https://pi-pil-repository.sahpra.org.za/