PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS (PREPARATIONS) - 1986

This medicine is marketed upon physician's prescription only

KEYTRUDA® 100 mg/4 mL

Concentrate for Solution for intravenous Infusion

Each 1 mL of concentrated solution contains:
Pembrolizumab 25 mg

For a list of inactive ingredients see section 6.1 "What **KEYTRUDA** contains".

Read the entire leaflet carefully before you start using this medicine.

- This leaflet contains concise information about **KEYTRUDA.** If you have any further questions, refer to your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

In addition to the leaflet, **KEYTRUDA** has a Patient Card. This card contains important safety information, that you need to know before starting and during the treatment with **KEYTRUDA** and act accordingly. Read the Patient Card and the patient leaflet before you start using this medicine. Keep the Card for further reference if needed.

1. WHAT KEYTRUDA IS INTENDED FOR?

KEYTRUDA is a prescription medicine used to treat:

- skin cancer called melanoma. **KEYTRUDA** may be used in adults and children 12 years of age and older:
  - when your melanoma has spread or cannot be removed by surgery (advanced melanoma), **or**
  - with Stage IIB, Stage IIC, or Stage III melanoma, to help prevent melanoma from coming back after it and lymph nodes that contain cancer have been removed by surgery.
- lung cancer called non-small cell lung cancer (NSCLC).
  - **KEYTRUDA** may be used with the chemotherapy medicines pemetrexed and carboplatin as your first treatment when your lung cancer:
    - has spread (advanced NSCLC), **and**
    - is a type of lung cancer called "nonsquamous", **and**
    - your tumor does not have an abnormal "EGFR" or "ALK" gene.
  - **KEYTRUDA** may be used with the chemotherapy medicines carboplatin and either paclitaxel or paclitaxel protein-bound as your first treatment when your lung cancer:
    - has spread (advanced NSCLC), **and**
    - is a type called "squamous".
  - **KEYTRUDA** may be used alone when your lung cancer:
    - has spread (advanced NSCLC), **and**
    - tests positive for "PD-L1", **and**
    - as your first treatment if you have not received chemotherapy to treat your advanced NSCLC and your tumor does not have an abnormal "EGFR" or "ALK" gene,

      or
    - you have received chemotherapy that contains platinum to treat your advanced NSCLC, and it did not work or it is no longer working, **and**

        - if your tumor has an abnormal “EGFR” or “ALK” gene, you have also received an EGFR or ALK inhibitor medicine and it did not work or is no longer working.
    - **KEYTRUDA** may be used in combination with chemotherapy that contains platinum and another chemotherapy medicine:
        - before surgery when you have early-stage NSCLC which can be removed by surgery, **and**
        - then continued alone after surgery to help prevent your lung cancer from coming back.
    - **KEYTRUDA** may be used alone as a treatment in adults for your lung cancer:
        - to help prevent your lung cancer from coming back after your tumor(s) has been removed by surgery and you have received platinum-based chemotherapy, **and**
        - you have stage IB and your tumor(s) is 4 cm or greater in size, stage II, or stage IIIA NSCLC.
- head and neck squamous cell cancer (HNSCC):
    - **KEYTRUDA** may be used with the chemotherapy medicines fluorouracil and a platinum as your first treatment when your head and neck cancer has spread or returned and cannot be removed by surgery.
    - **KEYTRUDA** may be used alone as your first treatment when your head and neck cancer:
        - has spread or returned and cannot be removed by surgery, **and**
        - your tumor tests positive for “PD-L1”.
    - **KEYTRUDA** may be used alone when your head and neck cancer:
        - has spread or returned, **and**
        - you have received chemotherapy that contains platinum, and it did not work or is no longer working.
- classical Hodgkin lymphoma (cHL):
    - in adults when:
        - your cHL has returned **or**
        - you have tried a treatment and it did not work, **or**
    - in children when:
        - you have tried a treatment and it did not work **or**
        - your cHL has returned after you received 2 or more types of treatment.
- primary mediastinal B-cell lymphoma (PMBCL) in adults and children when:
    - you have tried a treatment and it did not work **or**
    - your PMBCL has returned after you received 2 or more types of treatment.
- bladder and urinary tract cancer called urothelial cancer.
    - **KEYTRUDA** may be used with the medicine enfortumab vedotin in adults when your bladder or urinary tract cancer has spread or cannot be removed by surgery (advanced urothelial cancer).
    - **KEYTRUDA** may be used alone 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 tumor tests positive for “PD-L1”, **or**
        - you are not able to receive a medicine called cisplatin or carboplatin (regardless of “PD-L1” status), **or**
        - the disease has progressed during or after you have received chemotherapy that contains platinum.
    - **KEYTRUDA** may be used alone 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 tumor 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.
- cancer that is shown by a laboratory test to be a microsatellite instability-high (MSI-H) or a mismatch repair deficient (dMMR) solid tumor. **KEYTRUDA** may be used in adults and children to treat:

- cancer that has spread or cannot be removed by surgery (advanced cancer), **and**
- has progressed following systemic treatment, and you have no satisfactory treatment options, **or**
- you have colon or rectal cancer, that has progressed although you have received chemotherapy treatment with fluoropyrimidine, oxaliplatin, and irinotecan.

It is not known if **KEYTRUDA** is safe and effective in children with MSI-H cancers of the brain or spinal cord (central nervous system cancers).

- colon or rectal cancer. **KEYTRUDA** may be used as your first treatment when your cancer:
  - has spread or cannot be removed by surgery (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 stomach cancer called gastric or gastroesophageal junction (GEJ) adenocarcinoma.
  - **KEYTRUDA** may be used in adults in combination with the medicine trastuzumab along with fluoropyrimidine and platinum chemotherapy as your first treatment when your stomach cancer:
    - is HER2-positive, **and** your tumor tests positive for "PD-L1", **and**
    - has spread or cannot be removed by surgery (advanced gastric cancer).
  - **KEYTRUDA** may be used in adults in combination with fluoropyrimidine and platinum chemotherapy as your first treatment when your stomach cancer:
    - is HER2-negative, **and** your tumor tests positive for "PD-L1", **and**
    - has spread or cannot be removed by surgery (advanced gastric cancer).
- cancer called esophageal or certain gastroesophageal junction (GEJ) carcinomas. **KEYTRUDA** may be used with platinum- and fluoropyrimidine- based chemotherapy medicines when:
  - your cancer cannot be cured by surgery or a combination of chemotherapy and radiation therapy.
- cancer called squamous cell carcinoma of the esophagus. **KEYTRUDA** may be used when:
  - your cancer has returned or spread (advanced esophageal cancer), **and**
  - your tumor tests positive for "PD-L1" and you have received one or more types of treatment and it did not work or is no longer working.
- cervical cancer.
  - **KEYTRUDA** may be used with chemotherapy and radiation therapy when your cervical cancer has spread to nearby tissue or organs or has affected your kidneys (Stage III to IVA cervical cancer based on FIGO 2014 classification).
  - **KEYTRUDA** may be used with chemotherapy medicines, with or without the medicine bevacizumab, when:
    - your cervical cancer does not go away (persistent), has returned, or has spread (advanced cervical cancer), **and**
    - your tumor tests positive for "PD-L1".
  - **KEYTRUDA** may be used alone when your cervical cancer:
    - has returned, or has spread (advanced cervical cancer), **and**
    - you have received chemotherapy, and it did not work or is no longer working, **and**
    - your tumor tests positive for "PD-L1".
- bile duct or gallbladder cancer called biliary tract cancer (BTC). **KEYTRUDA** may be used with chemotherapy medicines gemcitabine and cisplatin when your biliary tract cancer has spread or cannot be removed by surgery.
- a kind of skin cancer called Merkel cell carcinoma (MCC) in adults and children. **KEYTRUDA** may be used to treat your skin cancer when it has spread or returned.
- kidney cancer called renal cell carcinoma (RCC).
  - **KEYTRUDA** may be used in adults 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 in adults 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 if you are intermediate-high or high risk for your kidney cancer (RCC) coming back after surgery to:

        - remove all or part of your kidney, **or**
        - remove all or part of your kidney and also surgery to remove cancer that has spread to other parts of the body (metastatic lesions).
- a kind of uterine cancer called advanced or recurrent endometrial carcinoma.
    - **KEYTRUDA** may be used with the chemotherapy medicines carboplatin and paclitaxel, and then
    - **KEYTRUDA** may be used alone, in adults:
        - when your cancer has spread (advanced) **or** if your cancer has returned (recurrent), **and**
            - if a laboratory test shows that your tumor is mismatch repair proficient (pMMR) and at least 12 months have passed after you have received chemotherapy medicines after surgery, **or**
            - if a laboratory test shows that your tumor is mismatch repair deficient (dMMR).
    - **KEYTRUDA** may be used with the medicine lenvatinib in adults:
        - when you have received chemotherapy that contains platinum, and it is no longer working, **and**
        - your cancer cannot be cured by surgery or radiation.
- a kind of cancer that is shown by a test to be tumor mutational burden-high (TMB-H). **KEYTRUDA** may be used in adults and children to treat:
    - solid tumors that have spread or cannot be removed by surgery (advanced cancer), **and**
    - you have received anti-cancer treatment, and it did not work or is no longer working, **and**
    - you have no satisfactory treatment options.

  It is not known if **KEYTRUDA** is safe and effective in children with TMB-H cancers of the brain or spinal cord (central nervous system cancers).
- skin cancer called cutaneous squamous cell carcinoma (cSCC). **KEYTRUDA** may be used when your skin cancer:
    - has returned or spread, **and**
    - cannot be cured by surgery or radiation.
- cancer called triple-negative breast cancer (TNBC).
    - **KEYTRUDA** 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.
    - **KEYTRUDA** may be used with chemotherapy medicines when your breast cancer:
        - has returned and cannot be removed by surgery or has spread, **and**
        - tests positive for “PD-L1”.

Therapeutic group: Antineoplastic agents, humanized monoclonal antibody.

2. BEFORE USING KEYTRUDA

You should not be given KEYTRUDA:

if you are allergic to the active ingredient (pembrolizumab) or any of the other ingredients of this medicine (for a list of inactive ingredients, see section 6).

2.1 Special warnings regarding the use of KEYTRUDA

Before starting treatment with KEYTRUDA, tell your doctor if you:

- have immune system problems such as Crohn’s disease, ulcerative colitis, or lupus
- have received an organ (such as a kidney or a liver) or tissue transplant, including corneal transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have lung or breathing problems
- have liver problems
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- have any other medical problems

- are pregnant or plan to become pregnant, breastfeeding or plan to breastfeed (please refer to section 2.5 “pregnancy, breast-feeding and fertility”)

2.2 Children and Adolescents
KEYTRUDA is intended for children and adolescents under 18 years for melanoma, classical Hodgkin lymphoma (cHL), primary mediastinal B-cell lymphoma (PMBCL), Merkel Cell Cancer (MCC), MSI-H or dMMR cancer, or TMB-H cancer, as safety and efficacy have been established in pediatric patients for use in these indications.

2.3 Tests and follow-up
During treatment with **KEYTRUDA** your doctor will do blood tests to check you for side effects.

2.4 Interactions with other medicines
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, you should tell the doctor or pharmacist.

2.5 Pregnancy, breast-feeding and fertility
- **Pregnancy**
  Before you receive **KEYTRUDA**, tell your doctor if you are pregnant or plan to become pregnant.
  - **KEYTRUDA** can harm your unborn baby.

  Females who are able to become pregnant:
  - Your doctor will give you a pregnancy test before you start treatment with **KEYTRUDA**.
  - You should use an effective method of birth control during treatment with **KEYTRUDA** and for 4 months after the last dose of **KEYTRUDA**. Talk to your doctor about birth control methods that you can use during this time.
  - Tell your doctor right away if you think you may be pregnant or if you become pregnant during treatment with **KEYTRUDA**.
- **Breastfeeding**
  Before you receive **KEYTRUDA**, tell your doctor if you are breastfeeding or plan to breastfeed.
  - It is not known if **KEYTRUDA** passes into your breast milk.
  - Do not breastfeed during treatment with **KEYTRUDA** and for 4 months after your last dose of **KEYTRUDA**.

3. HOW SHOULD YOU USE KEYTRUDA?
Always use **KEYTRUDA** as instructed by the doctor. You should check with your doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.
The dosage and duration of treatment will be determined by the doctor only.
- Your doctor will give you **KEYTRUDA** into your vein through an intravenous (IV) line over 30 minutes.
- In adults, **KEYTRUDA** is usually given every 3 weeks or 6 weeks depending on the dose of **KEYTRUDA** that you are receiving.
- In children, **KEYTRUDA** is usually given every 3 weeks.
- Your doctor will decide how many treatments you need.

Do not exceed the recommended dose.

If you miss an appointment to get KEYTRUDA
If you miss any appointments, call your doctor as soon as possible to reschedule your appointment.

If you stop receiving KEYTRUDA
Stopping your treatment may stop the effect of the medicine. Do not stop your treatment with **KEYTRUDA** unless you have discussed this with your doctor.

If you have further questions on the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, **KEYTRUDA** may cause side effects, in some users.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

KEYTRUDA is a medicine that may treat certain cancers by working with your immune system.
KEYTRUDA can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.
Call or see your doctor right away if you develop any new or worsening signs or symptoms including:

- **Lung problems.** Symptoms of lung problems may include:
  - cough
  - shortness of breath
  - chest pain
- **Intestinal problems that can lead to tears or holes in your intestine.** Signs and symptoms of intestinal problems may include:
  - diarrhea (loose stools) or more frequent bowel movements than usual
  - stools that are black, tarry, sticky, or have blood or mucus
  - severe stomach-area (abdomen) pain or tenderness
- **Liver problems.** Signs and symptoms of liver problems may include:
  - yellowing of your skin or the whites of your eyes
  - severe nausea or vomiting
  - pain on the right side of your stomach area (abdomen)
  - dark urine (tea colored
  - bleeding or bruising more easily than normal
  - feeling less hungry than usual
- **Hormone gland problems.** Signs and symptoms that your hormone glands are not working properly may include:
  - headaches that will not go away or unusual headache
  - eye sensitivity to light
  - eye problems
  - rapid heartbeat
  - increased sweating
  - extreme tiredness
  - weight gain or weight loss
  - feeling more hungry or thirsty than usual
  - urinating more often than usual
  - hair loss
  - feeling cold
  - constipation
  - your voice gets deeper
  - dizziness or fainting
  - changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness
  - muscle aches
  - feeling very weak
- **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
  - 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
    - a different odour to your urine or sweat
- **Kidney problems, including nephritis and kidney failure.** Signs of kidney problems may include:
    - changes in the amount or color of your urine
    - swelling of your ankles
    - loss of appetite
- **Skin problems.** Signs of skin problems may include:
    - rash
    - itching
    - blisters, peeling or skin sores
    - painful sores or ulcers in your mouth or in your nose, throat, or genital area
    - fever or flu-like symptoms
    - swollen lymph nodes
- **Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with KEYTRUDA. Call or see your doctor right away for any new or worsening signs or symptoms, which may include:**
    - *Cardiac/Vascular:* chest pain, irregular heartbeat, shortness of breath, swelling of ankles, feeling tired, and inflammation of blood vessels, which may present as fever, pain, skin rashes or weight loss
    - *Nervous System:* confusion, sleepiness, memory problems, seizures, fever, changes in mood or behavior, stiff neck, muscle weakness, balance problems, tingling, or numbness of the arms or legs, bladder or bowel problems, need to urinate more often, leaking of urine, trouble urinating, constipation, pain, paralysis in the extremities
    - *Ocular:* changes in eyesight, vision changes, eye pain, irritation, itchiness or redness, uncomfortable sensitivity to light, seeing spots, headache
    - *Gastrointestinal:* nausea, vomiting, stomach pain or tenderness, digestive issues
    - *Musculoskeletal and Connective Tissue*: severe or persistent muscle or joint pains, severe muscle weakness, muscle cramps, numbness, muscle stiffness, dark-colored urine
    - *Endocrine:* muscle spasms, fatigue and weakness
    - *Hematologic/Immune:* low red blood cells, bruising, pale or yellow skin/eyes, lightheadedness, rapid heartbeat, difficulty breathing, swollen lymph nodes, rash or tender lumps on skin, tiny red spots on the skin, cough, bleeding
- **Infusion (IV) reactions that can sometimes be severe and life-threatening.** Signs and symptoms of infusion reactions may include:
    - chills or shaking
    - itching or rash
    - flushing
    - shortness of breath or wheezing
    - dizziness
    - feeling like passing out
    - fever
    - back pain

Rejection of a transplanted organ or tissue. People who have had an organ or tissue transplant may have an increased risk of organ or tissue transplant rejection. Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ or tissue transplant that you have had.

Complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with **KEYTRUDA**. Your doctor will monitor you for the following signs and symptoms: skin rash, liver inflammation, stomach-area (abdominal) pain, and diarrhea.

Getting medical treatment right away may help keep these problems from becoming more serious. Your doctor will check you for these problems during treatment with **KEYTRUDA**. Your doctor may treat you with corticosteroid or hormone replacement medicines. Your doctor may also need to delay or completely stop treatment with **KEYTRUDA**, if you have severe side effects.

The following side effects have been reported with KEYTRUDA alone:

Very common side effects (reported in 10% or more of patients)

- low red blood cell count
- irregular heartbeat
- low levels of thyroid hormone
- high levels of thyroid hormone
- constipation
- diarrhea
- nausea
- stomach area (abdominal) pain
- vomiting
- fever
- feeling tired or weak
- pain
- flu-like illness
- liver problems
- increased liver enzymes in the blood
- upper respiratory tract infection
- lung infection
- urinary tract infection
- other infections
- decreased appetite
- decreased blood sodium
- weight loss
- back pain
- pain in muscles, bone or joints
- headache
- tingling, or numbness of the arms or legs
- cough
- shortness of breath
- inflammation of the lungs, which may present with cough, shortness of breath, chest pain, fever and chills, fatigue, or wheezing
- increased blood creatinine
- blood in urine
- sudden kidney injury
- rash
- skin discoloration
- itching

- swelling of arms or legs
- swelling of face
- bleeding
- common cold
- abnormal laboratory test results

Common side effects (reported in 1% to less than 10% of patients)
- infusion reactions
- inflammation of the eyes; eye pain, irritation, itchiness or redness; uncomfortable sensitivity to light; seeing spots
- inflammation of the heart muscle or lining of the heart, which may present as shortness of breath, irregular heartbeat, feeling tired, or chest pain
- inflammation of the thyroid, which may present as fatigue, swelling at the base of the neck, pain in front of the throat
- accumulation of fluid around the heart, which may present with chest pain, shortness of breath, cough, or swelling
- inflammation of the joints, which may present as joint pain, stiffness, swelling, or reduced range of motion
- muscle pain, aches or tenderness
- neck pain
- dizziness
- trouble sleeping
- altered mental state
- decreased number of white blood cells (neutrophils) with a fever
- infection of the blood
- swallowing difficulties
- throat pain
- mouth sores or swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina
- allergic reaction with signs that may include wheezing, difficulty breathing, rashes or hives, itchiness, swelling
- painful sores or ulcers in your mouth or in your nose, throat, or genital area
- temporary increase in the size of a tumor or the symptoms associated with it

Uncommon side effects (reported in less than 1% of patients)
- inflammation of the spinal cord, which may present as pain, numbness, tingling, or weakness in the arms or legs; bladder or bowel problems including need to urinate more often, leaking of urine, trouble urinating, and constipation

Side effects of KEYTRUDA when used alone that are more common in children than in adults include:
- fever
- vomiting
- headache
- stomach area (abdominal) pain
- low levels of white blood cells, platelets, or red blood cells (anemia)

The following side effects have been reported when KEYTRUDA is administered in combination with chemotherapy or chemotherapy with radiation therapy:

Very common side effects (reported in 20% or more of patients)

- nausea
- constipation
- diarrhea
- vomiting
- stomach area (abdominal) pain
- urinary tract infections
- feeling tired
- fever
- weight loss
- decreased appetite
- joint and muscle pain
- tingling or numbness of the arms or legs
- headache
- trouble sleeping
- cough
- shortness of breath
- rash
- hair loss
- mouth sores or swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina
- high blood pressure
- low levels of thyroid hormone
- abnormal laboratory test results
- blisters or rash on the palms of your hands and soles of your feet

Very common side effects (reported in 10% to less than 20% of patients)

- high levels of thyroid hormone
- swallowing difficulties
- lung infection
- itching
- pain or burning on urination
- pain of the pelvic area
- neck pain
- dizziness

The following side effects have been reported when KEYTRUDA is administered in combination with chemotherapy and bevacizumab:

Very common side effects (reported in 20% or more of patients)

- low red blood cell count
- low white blood cell count
- decreased platelet count
- low levels of thyroid hormone
- nausea
- diarrhea
- constipation
- vomiting
- feeling tired or weak
- urinary tract infection

- decreased appetite
- joint pain
- tingling or numbness of the arms or legs
- hair loss
- rash
- high blood pressure
- abnormal laboratory test results

The following side effects have been reported when KEYTRUDA is administered in combination with axitinib:

Very common side effects (reported in 20% or more of patients)
- low levels of thyroid hormone
- diarrhea
- nausea
- constipation
- feeling tired or weak
- liver problems
- decreased appetite
- hoarseness
- cough
- blisters or rash on the palms of your hands and soles of your feet
- mouth sores or swelling of the lining of the mouth, nose, eyes, throat, intestines, or vagina
- rash
- high blood pressure
- abnormal laboratory test results

Common side effects (reported in 1% to less than 10% of patients)
- irregular heartbeat

The following side effects have been reported when KEYTRUDA is administered in combination with lenvatinib:

Very common side effects (reported in 20% or more of patients)
- low levels of thyroid hormone
- diarrhea
- mouth sores
- nausea
- stomach area (abdominal) pain
- vomiting
- constipation
- feeling tired
- liver problems
- urinary tract infection
- decreased appetite
- weight loss
- joint and muscle pain
- headache
- protein in your urine

- kidney problems
- hoarseness
- rash
- blisters or rash on the palms of your hands and soles of your feet
- high blood pressure
- bleeding
- abnormal laboratory test results

Common side effects (reported in 1% to less than 10% of patients)
- signs of a heart problem, including chest pain or pressure, pain in your arms, back, neck or jaw, being short of breath, rapid or irregular heart rate, coughing, bluish color to lips or fingers, and feeling very tired

The following side effects have been reported when KEYTRUDA is administered in combination with enfortumab vedotin:

Very common side effects (reported in 20% or more of patients)
- rash
- itching
- hair loss
- feeling tired
- weight loss
- tingling or numbness of the arms or legs
- changes in sense of taste
- decreased appetite
- diarrhea
- nausea
- constipation
- dry eye
- urinary tract infection
- abnormal laboratory test results

Very common side effects (reported in 10% to less than 20% of patients)
- fever
- dry skin
- vomiting
- inflammation of the lungs, which may present with cough, shortness of breath, chest pain, fever and chills, fatigue, or wheezing
- low levels of thyroid hormone

Common side effects (reported in 1% to less than 10% of patients)
- blurred vision
- drug leakage from the infusion site

Uncommon side effects (reported in less than 1% of patients)
- muscle pain, aches or tenderness

The following side effects have been reported with unknown incidence (effects the incidence of which has not yet been determined):

- decreased ability of the pancreas to make digestive enzymes, which may include diarrhea with loose and oily stools, weight loss, metabolic bone disease, and vitamin or mineral deficiencies
- pain in the upper right part of the stomach (abdominal) area, swelling of the liver or spleen, feeling tired, itching, or yellowing of the skin or the whites of eyes

These are not all the possible side effects of **KEYTRUDA**. For more information, ask your doctor or pharmacist.
Tell your doctor if you have any side effect that bothers you or that does not go away.
If a side effect appears, if any of the side effects gets worse or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking the link "reporting side effects due to medical treatment" located in the home page of the Ministry of Health web site (www.health.gov.il) directing to the on line form for side effects reporting, or by logging on the following link:
https://sideeffects.health.gov.il

5. HOW TO STORE KEYTRUDA?

- Avoid Poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use **KEYTRUDA** after the expiry date (exp. date) that appears on the packaging. The expiry date refers to the last day of the indicated month.
- **Storage conditions**:
  Store vials under refrigeration at 2°C to 8°C in original carton to protect from light. Do not freeze. Do not shake.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, **KEYTRUDA** also contains:
Water for injection, sucrose, L-histidine, polysorbate 80.

What KEYTRUDA looks like and contents of the package
KEYTRUDA is a clear to slightly opalescent, colorless to slightly yellow solution.
KEYTRUDA is supplied in a carton containing one 100 mg/4 mL (25 mg/mL) single-use vial.

Marketing Authorization Holder and Importer
Merck Sharp & Dohme (Israel - 1996) Company Ltd., 34 Ha'charash St., Hod-Hasharon.

Revised in May 2025 according to MoH's guidelines.

Registration number of the medicine listed in the National Drug Registry of the Ministry of Health:
154.38.34448

Instructions for healthcare professionals

Preparation and Administration
Preparation for Intravenous Infusion

- Visually inspect the solution for particulate matter and discoloration prior to administration. The solution is clear to slightly opalescent, colorless to slightly yellow. Discard the vial if visible particles are observed.
- Dilute **KEYTRUDA 100 mg/4 mL** (concentrated solution) prior to intravenous administration.
- Withdraw the required volume from the vial(s) of **KEYTRUDA** and transfer into an intravenous (IV) bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. **Mix diluted solution by gentle inversion**. Do not shake. The final concentration of the diluted solution should be between 1 mg/mL to 10 mg/mL.
- Discard any unused portion left in the vial.

Storage of Diluted Solution

The product does not contain a preservative.
From a microbiological point of view, the product, once diluted, should be used immediately. If not used immediately, store the diluted solution from the **KEYTRUDA 100 mg/4 mL** vial either:

- At room temperature for no more than 6 hours from the time of dilution. This includes room temperature storage of the diluted solution, and the duration of infusion.
- Under refrigeration at 2°C to 8°C for no more than 96 hours from the time of dilution. If refrigerated, allow the diluted solution to come to room temperature prior to administration. Do not shake.

Discard after 6 hours at room temperature or after 96 hours under refrigeration.

Do not freeze.

Administration

- Administer diluted solution intravenously over 30 minutes through an intravenous line containing a sterile, non-pyrogenic, low-protein binding 0.2 micron to 5 micron in-line or add-on filter.
- Do not co-administer other drugs through the same infusion line.