

Advanced Kidney Cancer

KEYTRUDA and LENVIMA are prescription medicines used together to treat a kind of kidney cancer called advanced renal cell carcinoma (RCC) in adults as your first treatment when your kidney cancer has spread or cannot be removed by surgery.

Advanced Endometrial Cancer

KEYTRUDA and LENVIMA are prescription medicines used together to treat a kind of uterine cancer called advanced endometrial carcinoma in adults:

- when a laboratory test shows that your tumor is mismatch repair proficient (pMMR) or not microsatellite instability-high (MSI-H), **and**
- · you have received anti-cancer treatment, and it is no longer working, and
- your cancer cannot be cured by surgery or radiation.

The safety and efficacy of LENVIMA have not been established in children.



How tracking your symptoms may help you

Having cancer and receiving treatment may affect how you feel and your day-to-day activities. For example, you may feel more tired or nauseous, or you may not feel like eating much. By tracking how you are feeling and sharing any symptoms you develop, you can help your health care team better address your needs. Symptoms should be reported to your health care team and managed as early as possible.

Remember, if you start to feel any new or worsening symptoms or side effects or have any questions, contact your health care team right away.

Important Safety Information for KEYTRUDA® (pembrolizumab)

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 any time during treatment or even after your treatment has ended.

Important Safety Information for LENVIMA® (lenvatinib)

LENVIMA may cause serious side effects, including: High blood pressure (hypertension): High blood pressure is a common side effect of LENVIMA and can be serious. Your blood pressure should be well controlled before you start taking LENVIMA. Your healthcare provider should check your blood pressure regularly during treatment with LENVIMA. If you develop blood pressure problems, your healthcare provider may prescribe medicine to treat your high blood pressure.



Side effects of KEYTRUDA

Listed below are some serious side effects for KEYTRUDA. If you start having any of these symptoms or if they get worse, call or see your health care team right away. These are not all the possible side effects of KEYTRUDA. Tell your health care team if you experience any side effects that bother you or that do not go away.



Lung problems

- Cough
- · Shortness of breath
- Chest pain



Intestinal problems

- Diarrhea (loose stools) or more bowel movements than usual
- Stools that are black, tarry, sticky, or have blood or mucus
- Severe stomach-area (abdomen) pain or tenderness



Liver problems

- 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



Hormone gland problems

- Headaches that will not go away or unusual headaches
- 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



Kidney problems

- Decrease in the amount of your urine
- · Blood in your urine
- Swelling of your ankles
- Loss of appetite



Skin problems

- Rash
- Itching
- Skin blistering or peeling
- 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

- Chest pain, irregular heartbeat, shortness of breath, swelling of ankles
- Confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- Double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- Persistent or severe muscle pain or weakness, muscle cramps
- · Low red blood cells, bruising



Infusion reactions that can sometimes be severe or life-threatening

- · 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. Your health care provider should tell you what signs and symptoms you should report and they will 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 health care provider will monitor you for these complications.

See page 6 for Symptom Tracker.



Side effects of KEYTRUDA (continued)

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

Before you receive KEYTRUDA, tell your health care provider if you:

Have immune system problems such as Crohn's disease, ulcerative colitis, or lupus; have had an organ or tissue transplant, including corneal transplant, or have had or plan to have a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic); have had radiation treatment in your chest area; have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome.

If you are pregnant or plan to become pregnant, tell your health care provider. KEYTRUDA can harm your unborn baby. If you are able to become pregnant, you will be given a pregnancy test before you start treatment. Use effective birth control during treatment with KEYTRUDA and for 4 months after your last dose of KEYTRUDA. Talk to your health care provider about birth control methods that you can use during this time. Tell them right away if you think you may be pregnant or you become pregnant during treatment with KEYTRUDA.

Tell your health care provider 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.

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Common side effects of KEYTRUDA when given with LENVIMA include low levels of thyroid hormone; high blood pressure; feeling tired; diarrhea; joint and muscle pain; nausea; decreased appetite; vomiting; mouth sores; weight loss; stomach-area (abdominal) pain; urinary tract infection; protein in your urine; constipation; headache; bleeding; blisters or rash on the palms of your hands and soles of your feet; hoarseness; rash; liver problems; and kidney problems.

These are not all the possible side effects of KEYTRUDA. Talk to your health care provider for medical advice about side effects.

Before you take LENVIMA, tell your health care provider about all of your medical conditions, including if you:

- · have high blood pressure
- · have heart problems
- have a history of blood clots in your arteries (type of blood vessel), including stroke, heart attack, or change in vision
- have or have had liver or kidney problems
- have a history of a tear (perforation) in your stomach or intestine, or an abnormal connection between two or more body parts (fistula)
- have headaches, seizures, or vision problems
- · have any bleeding problems
- plan to have surgery, a dental procedure, or have had a recent surgery. You should stop taking LENVIMA at least 1 week before planned surgery.
- are pregnant or plan to become pregnant. LENVIMA can harm your unborn baby.

Females who are able to become pregnant:

- Your health care provider should do a pregnancy test before you start treatment with LENVIMA.
- You should use an effective method of birth control (contraception) during treatment with LENVIMA and for 30 days after the last dose of LENVIMA. Talk with your health care provider about birth control methods you can use during this time. Tell your health care provider right away if you become pregnant or think you are pregnant during treatment with LENVIMA.
- are breastfeeding or plan to breastfeed. It is not known if LENVIMA passes into your breast milk. Do not breastfeed during treatment with LENVIMA and for 1 week after the last dose.

See page 6 for Symptom Tracker.



Before you take LENVIMA, tell your health care provider about all of your medical conditions, including if you: (continued)

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your health care provider if you are taking, or have taken, an osteoporosis medicine.

Know the medicines you take. Keep a list of your medicines to show your health care provider and pharmacist when you get a new medicine.

Side effects of LENVIMA

Listed below are some serious side effects for LENVIMA. If you start having any of these symptoms or if they get worse, call or see your health care provider right away. These are not all the possible side effects of LENVIMA. Tell your health care provider if you experience any side effects.



High blood pressure (hypertension)

- High blood pressure is a common side effect of LENVIMA and can be serious. Your blood pressure should be well controlled before you start taking LENVIMA.
- Your health care provider should check your blood pressure regularly during treatment with I FNVIMA
- If you develop blood pressure problems, your health care provider may prescribe medicine to treat your high blood pressure.



Heart problems

 LENVIMA can cause serious heart problems that may lead to death. Call your health care provider right away if you get symptoms of heart problems, such as shortness of breath or swelling of your ankles.



Problem with blood clots in your blood vessels (arteries)

- Get emergency medical help right away if you get any of the following symptoms:
 - severe chest pain or pressure
 - o pain in your arms, back, neck, or jaw
 - shortness of breath
 - numbness or weakness on one side of your body
 - · trouble talking
 - sudden severe headache
 - sudden vision changes



Liver problems

- LENVIMA may cause liver problems that may lead to liver failure and death. Your health care provider will check your liver function before and during treatment with LENVIMA. Tell your health care provider right away if you develop any of the following symptoms:
 - your skin or the white part of your eyes turns yellow (jaundice)



- light-colored bowel movements (stools)
- feeling drowsy, confused or loss of consciousness



Kidney problems

 Kidney failure, which can lead to death, has happened with LENVIMA treatment. Your health care provider should do regular blood tests to check your kidneys.



Increased protein in your urine (proteinuria)

 Proteinuria is a common side effect of LENVIMA and can be serious. Your health care provider should check your urine for protein before and during your treatment with LENVIMA.



Diarrhea

- Diarrhea is a common side effect of LENVIMA and can be serious.
- If you get diarrhea, ask your health care provider about what medicines you can take to treat your diarrhea.
- It is important to drink more water when you get diarrhea.
- Tell your health care provider or go to the emergency room, if you are unable to drink enough liquids and your diarrhea is not able to be controlled.



An opening in the wall of your stomach or intestines (perforation) or an abnormal connection between two or more body parts (fistula)

 Get emergency medical help right away if you develop severe stomach (abdomen) pain.

See page 6 for Symptom Tracker.

Side effects of LENVIMA (continued)



Changes in the electrical activity of your heart called QT prolongation

- QT prolongation can cause irregular heartbeats that can be life threatening.
- Your health care provider will do blood tests during your treatment with LENVIMA to check the levels of potassium, magnesium, and calcium in your blood, and may check the electrical activity of your heart with an electrocardiogram (ECG).



Low levels of blood calcium (hypocalcemia)

 Your health care provider will check your blood calcium levels during treatment with LENVIMA and may tell you to take a calcium supplement if your calcium levels are low.



A condition called Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

 Call your health care provider right away if you get severe headache, seizures, weakness, confusion, or blindness or change in vision.



Bleeding

- LENVIMA may cause serious bleeding problems that may lead to death. Tell your health care provider if you develop any signs or symptoms of bleeding during treatment with LENVIMA, including:
 - severe and persistent nose bleeds
 - vomiting blood
 - red or black (looks like tar) stools
 - blood in your urine
 - coughing up blood or blood clots
 - heavy or new onset vaginal bleeding



Change in thyroid hormone levels

 Your health care provider should check your thyroid hormone levels before starting and every month during treatment with LENVIMA.



Wound healing problems

 Wound healing problems have happened in some people who take LENVIMA. Tell



ENVIMA

(lenvatinib) capsules | 10 mg and 4 mg

your health care provider if you plan to have any surgery before or during treatment with LENVIMA.

(pembrolizumab) Injection 100 mg

- You should stop taking LENVIMA at least 1 week before planned surgery.
- Your health care provider should tell you when you may start taking LENVIMA again after surgery.



Severe jawbone problems (osteonecrosis)

- Severe jawbone problems have happened in some people who take LENVIMA. Certain risk factors such as taking a bisphosphonate medicine or the medicine denosumab, having dental disease, or an invasive dental procedure may increase your risk of getting jawbone problems. Your health care provider should examine your mouth before you start and during treatment with LENVIMA. Tell your dentist that you are taking LENVIMA. It is important for you to practice good mouth care during treatment with LENVIMA. Tell your health care provider right away if you have any signs or symptoms of jawbone problems during treatment with LENVIMA, including jaw pain, toothache, or sores on your gums, and if you plan to have any dental procedures before or during treatment with LENVIMA. You should avoid having invasive dental procedures if possible, during treatment with LENVIMA. Stopping your bisphosphonate medicine before an invasive dental procedure may help decrease your risk of getting these jaw problems.
 - You should stop taking LENVIMA at least 1 week before planned dental surgery or invasive dental procedures.
 - Your health care provider should tell you when you may start taking LENVIMA again after dental procedures.

The most common side effects of LENVIMA when given in combination with KEYTRUDA include decrease in thyroid hormone levels; tiredness; joint and muscle pain; nausea; decreased appetite; vomiting; mouth sores; weight loss; stomach-area (abdomen) pain; urinary tract infection; constipation; headache; bleeding; rash, redness, itching, or peeling of your skin on your hands and feet; hoarseness; and rash.

LENVIMA may cause fertility problems in males and females. Talk to your health care provider if this is a concern for you.

Your health care provider may need to reduce your dose of LENVIMA, or delay or completely stop treatment if you have certain side effects.

These are not all the possible side effects of LENVIMA. Call your doctor for medical advice about side effects.

See page 6 for Symptom Tracker.

What and How to Track



Use this page to track any symptoms you are experiencing and how severe they are. **Don't forget to contact your health care team right away if you start to feel any new or worsening symptoms or side effects or have any questions.** Write suggestions from your health care team that may help manage your symptoms. Print or copy as many pages as you need. Have them handy when you talk to your health care team.

Date	Describe any symptoms you're experiencing	Health care team's suggestions	Additional notes
	How severe? (circle one) 1 mild 2 moderate 3 severe 4 very severe		
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You are encouraged to report negative side effects of prescription drugs to the FDA at <u>1-800-FDA-1088</u> or visit www.fda.gov/medwatch.