Package leaflet: Information for the user

LENVIMA 4 mg hard capsules
LENVIMA 10 mg hard capsules
lenvatinib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What LENVIMA is and what it is used for

What LENVIMA is
LENVIMA is a medicine that contains the active substance lenvatinib. It is used on its own to treat progressive or advanced thyroid cancer in adults when radioactive iodine treatment has not helped to stop the disease.

LENVIMA can also be used on its own to treat liver cancer (*hepatocellular carcinoma*) in adults who have not previously been treated with another anticancer medicine that travels through the bloodstream. People get LENVIMA when their liver cancer has spread or cannot be taken out by surgery.

LENVIMA can also be used together with another anticancer medicine called pembrolizumab to treat advanced cancer of the lining of the uterus (*endometrial carcinoma*) in adults whose cancer has spread after being previously treated with another anticancer medicine that travels through the bloodstream and cannot be taken out by surgery or radiation treatment.

How LENVIMA works
LENVIMA blocks the action of proteins called receptor tyrosine kinases (RTKs), which are involved in the development of new blood vessels that supply oxygen and nutrients to cells and help them to grow. These proteins can be present in high amounts in cancer cells, and by blocking their action LENVIMA may slow the rate at which the cancer cells multiply and the tumour grows and help to cut off the blood supply that the cancer needs.

2. What you need to know before you take LENVIMA

Do not take LENVIMA if:
- you are allergic to lenvatinib or any of the other ingredients of this medicine (listed in section 6).
- you are breast-feeding (see the section below on Contraception, pregnancy and breast-feeding).

Warnings and precautions
Talk to your doctor before taking LENVIMA if you:
- have high blood pressure
- are a woman able to become pregnant (see the section below on Contraception, pregnancy and breast-feeding)
- have a history of heart problems or stroke
- have liver or kidney problems
- have had recent surgery or radiotherapy
- need to have a surgical procedure. Your doctor may consider stopping LENVIMA if you will be undergoing a major surgical procedure as LENVIMA may affect wound healing. LENVIMA may be restarted once adequate wound healing is established.
- are over 75 years
- belong to an ethnic group other than White or Asian
- weigh less than 60 kg
- have a history of abnormal connections (known as a fistula) between different organs in the body or from an organ to the skin
- If you have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.
- have or have had pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. You may be advised to have a dental check-up before starting LENVIMA as bone damage in the jaw (osteonecrosis) has been reported in patients treated with LENVIMA. If you need to undergo an invasive dental treatment or dental surgery, tell your dentist that you are being treated with LENVIMA, particularly when you are also receiving or have received injections of bisphosphonates (used to treat or prevent bone disorders).
- are receiving or have received some medicines used to treat osteoporosis (antiresorptive medicines) or cancer medicines which alter formation of blood vessels (so called angiogenesis inhibitors), as the risk of bone damage in the jaw may be increased.

Before taking LENVIMA, your doctor may carry out some tests, for example to check your blood pressure and your liver or kidney function and to see if you have low levels of salt and high levels of thyroid stimulating hormone in your blood. Your doctor will discuss the results of these tests with you and decide whether you can be given LENVIMA. You may need to have additional treatment with other medicines, to take a lower dose of LENVIMA, or to take extra care due to an increased risk of side effects.

If you are not sure talk to your doctor before taking LENVIMA.

Children and adolescents
LENVIMA is not currently recommended for use in children and adolescents younger than 18 years old.

Other medicines and LENVIMA
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes herbal preparations and medicines without a prescription.

Contraception, pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
- If you could become pregnant, use highly effective contraception while taking this medicine, and for at least one month after you finish treatment. Because it is not known if LENVIMA can reduce the effect of the oral contraceptive pill, if this is your normal method of contraception you should ensure you also add a barrier method such as the cap or condoms if you have sex during treatment with LENVIMA.
- Do not take LENVIMA if you are planning to become pregnant during your treatment. This is because it may seriously harm your baby.

- If you become pregnant while being treated with LENVIMA, tell your doctor immediately. Your doctor will help you decide whether the treatment should be continued.
- Do not breast-feed if you are taking LENVIMA. This is because the medicine passes into breast milk and may seriously harm your breastfed baby.

Driving and using machines
LENVIMA may cause side effects that can affect your ability to drive or use machines. Avoid driving or using machines if you feel dizzy or tired.

3. How to take LENVIMA

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How much to take
Thyroid cancer
- The recommended dose of LENVIMA is usually 24 mg once a day (2 capsules of 10 mg and 1 capsule of 4 mg).
- If you have severe liver or kidney problems the recommended dose is 14 mg once a day (1 capsule of 10 mg and 1 capsule of 4 mg).
- Your doctor may reduce your dose if you have problems with side effects.

Liver cancer
- The recommended dose of LENVIMA depends on your body weight when you first start treatment. The dose is usually 12 mg once a day (3 capsules of 4 mg) if you weigh 60 kg or more and 8 mg once a day (2 capsules of 4 mg) if you weigh less than 60 kg.
- Your doctor may reduce your dose if you have problems with side effects.

Uterine cancer
- The recommended dose of LENVIMA is 20 mg once a day (2 capsules of 10 mg), in combination with pembrolizumab. The pembrolizumab is given by your doctor as an injection in your vein, either 200 mg every 3 weeks or 400 mg every 6 weeks.
- Your doctor may reduce your dose if you have problems with side effects.

Taking this medicine
- You can take the capsules with or without food.
- Do not open the capsules to avoid exposure to the contents of the capsule
- Swallow the capsules whole with water. If you cannot swallow the capsules whole, a liquid mixture can be prepared using water, apple juice, or milk. The liquid mixture may be given by mouth or through a feeding tube. If given through a feeding tube, then the liquid mixture should be prepared using water. If not used at the time of preparation, the liquid mixture may be stored in a covered container and must be refrigerated at 2ºC to 8ºC for a maximum of 24 hours. Shake the liquid mixture for 30 seconds after removing from the refrigerator. If the liquid mixture is not used within 24 hours of preparation, it should be thrown away. Preparation and administration of the liquid mixture:
    - Place the whole capsule(s) corresponding to the prescribed dose (up to 5 capsules) in a small container (approximately 20 mL (4 tsp) capacity) or oral syringe (20 mL); do not break or crush capsules.
    - Add 3 mL of liquid to the container or oral syringe. Wait 10 minutes for the capsule shell (outer surface) to dissolve, then stir or shake the mixture for 3 minutes until the capsules are fully dissolved.
        - If liquid mixture is prepared in an oral syringe, cap the syringe, remove plunger and use a second syringe or medicine dropper to add the liquid to the first syringe, then replace plunger prior to mixing.

    - Drink the liquid mixture from the container or use an oral syringe to take directly into the mouth or through a feeding tube.
    - Next, add an additional 2 mL of liquid to the container, or oral syringe using a second syringe or dropper, swirl or shake and take the liquid mixture. Repeat this step at least twice and until there is no visible sign of the mixture to make sure all of the medication is taken.
- Take the capsules at about the same time each day.

How long to take LENVIMA
You will usually carry on taking this medicine as long as you are getting benefit.

If you take more LENVIMA than you should
If you take more LENVIMA than you should, talk to a doctor or pharmacist straight away. Take the medicine pack with you.

If you forget to take LENVIMA
Do not take a double dose (two doses at the same time) to make up for a forgotten dose.

What to do if you forget to take your dose depends on how long it is until your next dose.
- If it is 12 hours or more until your next dose: take the missed dose as soon as you remember. Then take the next dose at the normal time.
- If it is less than 12 hours until your next dose: skip the missed dose. Then take the next dose at the normal time.

4. Possible side effects

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

Tell your doctor straight away if you notice any of the following side effects - you may need urgent medical treatment:
- feeling numb or weak on one side of your body, severe headache, seizure, confusion, difficulty talking, vision changes or feeling dizzy - these may be signs of a stroke, bleeding on your brain, or the effect on your brain of a severe increase in blood pressure.
- chest pain or pressure, pain in your arms, back, neck or jaw, being short of breath, rapid or irregular heart rate, coughing, bluish colour to lips or fingers, feeling very tired – these may be signs of a heart problem, a blood clot in your lung or a leak of air from your lung into your chest so your lung cannot inflate.
- severe pain in your belly (abdomen) - this may be due to a hole in the wall of your gut or a fistula (a hole in your gut which links through a tube-like passage to another part of your body or skin).
- black, tarry, or bloody stools, or coughing up of blood - these may be signs of bleeding inside your body.
- yellow skin or yellowing of the whites of the eyes (jaundice) or drowsiness, confusion, poor concentration – these may be signs of liver problems.
- diarrhoea, feeling and being sick (nausea and vomiting) - these are very common side effects that can become serious if they cause you to become dehydrated, which can lead to kidney failure. Your doctor can give you medicine to reduce these side effects.
- pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth - these could be signs of bone damage in the jaw (osteonecrosis).

Tell your doctor straight away if you notice any of the side effects above.

The following side effects may happen with this medicine when given alone:

Very common (may affect more than 1 in 10 people)
- high or low blood pressure
- loss of appetite or weight loss
- feeling sick (nausea) and being sick (vomiting), constipation, diarrhoea, abdominal pain, indigestion
- feeling very tired or weak
- hoarse voice
- swelling of the legs
- rash
- dry, sore, or inflamed mouth, odd taste sensation
- joint or muscle pain
- feeling dizzy
- hair loss
- bleeding (most commonly nose bleeds, but also other types of bleeding such as blood in the urine, bruising, bleeding from the gums or gut wall)
- trouble sleeping
- changes in urine tests for protein (high) and urinary infections (increased frequency in urination and pain in passing urine)
- headache
- back pain
- redness, soreness and swelling of the skin on the hands and feet (palmar-plantar erythrodysaesthesia)
- underactive thyroid (tiredness, weight gain, constipation, feeling cold, dry skin)
- changes in blood test results for potassium levels (low) and calcium levels (low)
- decrease in the number of white blood cells
- changes in blood test results for liver function
- low levels of platelets in the blood which may lead to bruising and difficulty in wound healing
- changes in blood test results for magnesium (low), cholesterol (high) and thyroid stimulating hormone (high)
- changes in blood test results for kidney function and kidney failure
- increase in lipase and amylase (enzymes involved in digestion)

Common (may affect up to 1 in 10 people)
- loss of body fluids (dehydration)
- heart palpitations
- dry skin, thickening and itching of the skin
- feeling bloated or having excess wind
- heart problems or blood clots in the lungs (difficulty breathing, chest pain) or other organs
- liver failure
- drowsiness, confusion, poor concentration, loss of consciousness that may be signs of liver failure
- feeling unwell
- inflammation of the gallbladder
- stroke
- anal fistula (a small channel that forms between the anus and the surrounding skin)
- a hole (perforation) in the stomach or intestines

Uncommon (may affect up to 1 in 100 people)
- painful infection or irritation near the anus
- mini-stroke
- liver damage
- severe pain in the upper left part of the belly (abdomen) which may be associated with fever, chills, nausea and vomiting (splenic infarction)
- inflammation of the pancreas

- wound healing problems
- bone damage in the jaw (osteonecrosis)
- inflammation of the colon (colitis)
- decreased secretion of hormones produced by adrenal glands

Not Known (the following side effects have been reported since the marketing of LENVIMA but the frequency for them to occur is not known)
- other types of fistulae (an abnormal connection between different organs in the body or between the skin and an underlying structure such as throat and windpipe). Symptoms depend on where the fistula is located. Talk to your doctor if you experience any new or unsual symptoms such as coughing when swallowing.
- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections).

The following side effects may happen with this medicine when given in combination with pembrolizumab:

Very common (may affect more than 1 in 10 people)
- changes in urine tests for protein (high) and urinary infections (increased frequency in urination and pain in passing urine)
- low levels of platelets in the blood which may lead to bruising and difficulty in wound healing
- decrease in the number of white blood cells
- decrease in the number of red blood cells
- underactive thyroid (tiredness, weight gain, constipation, feeling cold, dry skin) and changes in blood test results for thyroid stimulating hormone (high)
- overactive thyroid (symptoms can include rapid heart rate, sweating and weight loss)
- changes in blood test results for calcium levels (low)
- changes in blood test results for potassium levels (low)
- changes in blood test results for cholesterol levels (high)
- changes in blood test results for magnesium levels (low)
- loss of appetite or weight loss
- feeling dizzy
- headache
- back pain
- dry, sore, or inflamed mouth, odd taste sensation
- bleeding (most commonly nose bleeds, but also other types of bleeding such as blood in the urine, bruising, bleeding from the gums or gut wall)
- high blood pressure
- hoarse voice
- feeling sick (nausea) and being sick (vomiting), constipation, diarrhoea, abdominal pain
- increase in amylase (enzyme involved in digestion)
- increase in lipase (enzyme involved in digestion)
- changes in blood test results for liver function
- changes in blood test results for kidney function
- redness, soreness and swelling of the skin on the hands and feet (palmar-plantar erythrodysaesthesia)
- rash
- joint or muscle pain
- feeling very tired or weak
- swelling of the legs

Common (may affect up to 1 in 10 people)
- loss of body fluids (dehydration)
- trouble sleeping
- heart palpitations

- low blood pressure
- blood clots in the lungs (difficulty breathing, chest pain)
- inflammation of the pancreas
- feeling bloated or having excess wind
- indigestion
- inflammation of the gallbladder
- hair loss
- kidney failure
- feeling unwell
- inflammation of the colon (colitis)
- decreased secretion of hormones produced by adrenal glands
- a hole (perforation) in the stomach or intestines

Uncommon (may affect up to 1 in 100 people)
- headache, feeling confused, seizure, and changes in vision
- signs of a stroke, including feeling numb or weak on one side of your body, severe headache, seizure, confusion, difficulty talking, vision changes or feeling dizzy
- mini-stroke
- 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 colour to lips or fingers, and feeling very tired
- severe difficulty breathing and chest pain, caused by a leak of air from your lung into your chest so your lung cannot inflate
- painful infection or irritation near the anus
- anal fistula (a small channel that forms between the anus and the surrounding skin)
- liver failure or signs of liver damage, including yellow skin or yellowing of the whites of the eyes (jaundice) or drowsiness, confusion, poor concentration
- dry skin, thickening and itching of the skin
- wound healing problems

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 LENVIMA

- 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 on each blister after 'EXP'. The expiry date refers to the last day of that month.
- Do not store above 25°C. Store in the original blister in order to protect from moisture.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What LENVIMA contains
- The active substance is lenvatinib.
  - LENVIMA 4 mg hard capsules: - Each hard capsule contains 4 mg of lenvatinib (as mesilate).

– LENVIMA 10 mg hard capsules: - Each hard capsule contains 10 mg of lenvatinib (as mesilate).

- The other ingredients are calcium carbonate, mannitol, microcrystalline cellulose, hydroxypropylcellulose, low-substituted hydroxypropyl cellulose, talc. The capsule shell contains hypromellose, titanium dioxide (E171), yellow iron oxide (E172), red iron oxide (E172). The printing ink contains shellac, black iron oxide (E172), potassium hydroxide, propylene glycol.

What LENVIMA looks like and contents of the pack

- The 4 mg capsule is a yellowish red body and yellowish red cap, approximately 14.3 mm in length, marked in black ink with "Є" on the cap, and "LENV 4 mg" on the body.
- The 10 mg capsule is a yellow body and yellowish red cap, approximately 14.3 mm in length, marked in black ink with "Є" on the cap, and "LENV 10 mg" on the body.
- The capsules come in blisters of polyamide/aluminium/PVC with a push through aluminium foil lidding in cartons of 30, 60 or 90 hard capsules. Not all pack sizes may be marketed.

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