LENRAFED Hard Capsules

Lenvatinib (4mg, 10mg)

What is in this leaflet

1. What LENRAFRED is used for
2. How LENRAFRED works
3. Before you use LENRAFRED
4. How to use LENRAFRED
5. While you are using it
6. Side effects
7. Storage and Disposal of LENRAFRED
8. Product Description
9. Manufacturer and Product Registration Holder
10. Date of revision

What LENRAFRED is used for

LENRAFRED is a medicine that contains the active substance lenvatinib. It is used to treat:

- progressive or advanced thyroid cancer in adults when radioactive iodine treatment has not helped to stop the disease.
- patients with cancer of the thymus gland (thymic carcinoma) that cannot be removed by surgery and has already been treated with other medicines.
- patients with advanced kidney cancer (advanced renal cell carcinoma) as first treatment when used in combination with pembrolizumab.
- patients with advanced kidney cancer (advanced renal cell carcinoma) where other treatments (so-called "VEGF-targeted therapy") have not helped stop the disease. It is used in combination with everolimus.
- liver cancer (*hepatocellular carcinoma*) in adults who have not previously been treated with another anticancer medicine that travels through the bloodstream. People get LENRAFRED when their liver cancer has spread or cannot be taken out by surgery.
- Advanced cancer of the lining of the uterus (endometrial carcinoma) in patients 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, when used together with another anticancer medicine called pembrolizumab.

How LENRAFRED works

LENRAFRED 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 LENRAFRED 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.

Before you use LENRAFRED

When you must not use it

Do not take LENRAFRED if:

- you are allergic to lenvatinib or any of the other ingredients of this medicine (listed in section product description).
- you are breastfeeding (see the section below on Contraception, pregnancy and breastfeeding).

Before you start use it

Talk to your doctor before taking LENRAFRED if you:

- have high blood pressure
- are a woman able to become pregnant (see the section below on Contraception, pregnancy and breastfeeding)
- 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 LENRAFRED if you will be undergoing a major surgical procedure as LENRAFRED may affect wound healing. LENRAFRED 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 60kg
- have a history of abnormal connection (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 LENRAFRED as bone damage in the jaw (osteonecrosis) has been reported in patients treated with LENRAFRED. If you need to undergo an invasive dental treatment or dental surgery, tell your dentist that you are being treated with LENRAFRED, 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 LENRAFRED, your doctor may carry out some blood 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 LENRAFRED. You may need to have additional treatment with other medicines, to take a lower dose of LENRAFRED, or to take extra care due to an increased risk of side effects.

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

Children and adolescents

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

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 LENRAFRED 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 of LENRAFRED.
- Do not take LENRAFRED 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 LENRAFRED, tell your doctor immediately. Your doctor will help you decide whether the treatment should be continued.
- Do not breast-feed if you are taking LENRAFRED. This is because the medicine passes into breast milk and may seriously harm your breastfed baby.

Taking other medicines
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.

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

The recommended dose of LENRAFRED is:
- 24 mg once a day (2 capsules of 10 mg and 1 capsule of 4 mg) for advanced thyroid cancer and thymus gland cancer.
- 20 mg once a day (two 10 mg capsules) in combination with pembrolizumab either 200 mg every 3 weeks or 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes for advanced kidney cancer.
- 18 mg once a day (1 capsule of 10 mg and 2 capsule of 4 mg) in combination with one 5 mg tablet of everolimus once a day for advanced kidney cancer.
- For liver cancer, the recommended dose 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 60kg.
- For endometrial cancer, the recommended dose is 20 mg (2 capsules of 10mg) once daily, in combination with pembrolizumab 200mg injection every 3 weeks.
- If you have severe liver or kidney problems, the recommended dose of LENRAFRED is:
  - 14 mg once a day (1 capsule of 10 mg and 1 capsule of 4 mg) for advanced thyroid cancer
  - 10 mg once a day (1 capsule of 10 mg) in combination with one 5 mg tablet of everolimus once a day for advanced kidney cancer. If you are receiving LENRAFRED in combination with pembrolizumab, your doctor or pharmacist will check to see how much pembrolizumab you should receive.
  - 10 mg once a day (1 capsule of 10 mg) in combination with pembrolizumab for endometrial cancer.
- Your doctor may reduce your dose if you have problems with side effects.

When to use it
- You can take the capsules with or without food.
- Swallow the capsules whole with water or dissolved. To dissolve them, pour a tablespoon of water or apple juice into a small glass and put the capsules into the liquid without breaking or crushing them. Leave for at least 10 minutes then stir for at least 3 minutes to dissolve the capsule shells. Drink the mixture. After drinking, add the same amount of water or apple juice, swirl and swallow.
- Take the capsules at about the same time each day.
- Caregivers should not open the capsules to avoid exposure to the contents of the capsule.

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

If you forget to use it
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.

If you use too much (overdose)
If you take more LENRAFRED than you should, talk to a doctor or pharmacist straight away. Take the medicine pack with you.

While you are using it
Things you must do
Take your medicine exactly as your doctor has told you.
Tell all the doctors, dentists and pharmacists treating you that you are taking LENRAFRED.
Tell your doctor immediately if you become pregnant while taking this medication.

Things you must not do
Do not stop taking the medicine unless advised by your doctor.
Do not take any new medicines without consulting your doctor.
Do not give LENRAFRED to anyone else, even if they have the same symptoms or condition as you.

Things to be careful of
Driving and using machines
LENRAFRED 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.

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 or in combination with everolimus:
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 (hand-foot syndrome)
- underactive thyroid (tiredness, weight gain, constipation, feeling cold, dry skin)
- changes in blood test results for potassium levels (low) and calcium levels (low), cholesterol (high) and thyroid stimulating hormone (high), high lipase and amylase levels (enzymes involved in digestion), high creatinine levels (blood test results for kidney function).
- decrease in 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

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
- inflammation of the pancreas
- stroke
- anal fistula (a small channel that forms between the anus and the surrounding skin)
- changes in blood test results for magnesium (low)
- changes in blood test results for kidney function and kidney failure
- 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
- would healing problems
- bone damage in the jaw (osteonecrosis)
- inflammation of the colon (colitis)
- 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 would depend on where the fistula is located. Talk to your doctor if you experience any new or unusual symptoms such as coughing when swallowing.

Not Known (the following side effects have been reported since the marketing of LENRAFRED but the frequency for them to occur is not known)
- 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), potassium levels (low), cholesterol levels (high) and 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 (hand-foot syndrome)
- 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)
- 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

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccine (AEFI)].

Storage and Disposal of LENRAFRED

Storage

Keep out of the reach and sight of children. Store below 30°C. Store in the original blister in order to protect from moisture.

Disposal

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.

Product Description

What it looks like

- The 4 mg capsule is Hard Hypromellose capsule with pink opaque body and pink opaque cap imprinted with SML on the cap and 18 on the body with black ink containing off white to pale yellow granular powder
- The 10 mg capsule is a Hard Hypromellose capsule with yellow opaque body and pink opaque cap imprinted with SML on the cap and 19 on the body with black ink containing off white to pale yellow granular powder.
- The capsules come in blisters of alu/alu of 10 capsules. Two or three such blisters in a carton with a pack insert.

Ingredients

- Active ingredient
  LENRAFRED 4 mg hard capsules: - Each hard capsule contains 4 mg of lenvatinib (as mesilate).
  LENRAFRED 10 mg hard capsules: - Each hard capsule contains 10 mg of lenvatinib (as mesilate).

- Inactive ingredients
- Excipients: Calcium hydroxide, Mannitol, Microcrystalline cellulose, Low-Substituted hydroxypropyl cellulose, Potassium Hydroxide, Hydroxy Propyl Cellulose & Talc

- Capsule: Titanium Dioxide, Red Iron Oxide, Hypromellose & Yellow Iron Oxide (10mg only).

- Imprinting Ink: Shellac, Dehydrated Alcohol, Isopropyl Alcohol, Butyl Alcohol, Propylene glycol, Ammonia, Black Iron Oxide, Potassium Hydroxide & Purified Water

MAL number(s):

MALXXXXXXAZ
MALXXXXXXAZ

Manufacturer

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