



Information for the patient

Larotreni 25 mg / 100 mg hard capsules

Larotrectinib

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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, pharmacist or nurse.
- 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.
- This leaflet has been written as though the person taking the medicine is reading it. If you are giving this medicine to your child, please replace "you" with "your child" throughout.

What is in this leaflet:

1. What Larotreni is and what it is used for
2. What you need to know before you take Larotreni
3. How to take Larotreni
4. Possible side effects
5. How to store Larotreni
6. Contents of the pack and other information

1. What Larotreni is and what it is used for

What Larotreni is used for

Larotreni contains the active substance larotrectinib.

It is used in adults, adolescents and children to treat solid tumours (cancer) in various parts of the body that are caused by a change in the NTRK gene (neurotrophic tyrosine receptor kinase).

Larotreni is only used when

- these cancers are advanced or have spread to other parts of the body or if a surgery to remove the cancer is likely to cause severe complications and

- there are no satisfactory treatment options.

Before you are given Larotreni, your doctor will do a test to check if you have the change in the NTRK gene.

How Larotreni works

In patients whose cancer is due to an altered NTRK gene, the change in the gene causes the body to make an abnormal protein called TRK fusion protein, which can lead to uncontrolled cell growth and cancer. Larotrectinib blocks the action of TRK fusion proteins and so may slow or stop the growth of the cancer. It may also help to shrink the cancer.

If you have any questions on how Larotreni works or why it has been prescribed for you, ask your doctor, pharmacist or nurse.

2. What you need to know before you take Larotreni

Do not take Larotreni if

- you are allergic to larotrectinib or any of the other ingredients of this medicine (listed in section 6).

Tests and checks

Larotrectinib can increase the amount of the liver enzymes ALT and AST in your blood. Your doctor will do blood tests before and during treatment to check the level of ALT and AST and check how well your liver is working.

Other medicines and Larotreni

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This is because some medicines may affect the way Larotreni works or Larotreni may affect how other medicines work.

In particular, tell your doctor, pharmacist or nurse if you are taking any of the following medicines:

- medicines used to treat fungal or bacterial infections called itraconazole, voriconazole, clarithromycin, telithromycin, troleandomycin
- a medicine used to treat Cushing's syndrome called ketoconazole
- medicines used to treat HIV infection called atazanavir, indinavir, nelfinavir, ritonavir, saquinavir, rifabutin, efavirenz
- a medicine used to treat depression called nefazodone
- medicines used to treat epilepsy called phenytoin, carbamazepine, phenobarbital
- a herbal medicine used to treat depression called St. John's wort
- a medicine used to treat tuberculosis called rifampicin
- a medicine used for strong pain relief called alfentanil
- medicines used to prevent organ rejection after an organ transplant called ciclosporin, sirolimus, tacrolimus
- a medicine used to treat an abnormal heart rhythm called quinidine
- medicines used to treat migraines called dihydroergotamine, ergotamine
- a medicine used to treat long-term pain called fentanyl
- a medicine used to control involuntary movements or sounds called pimizide
- a medicine to help you stop smoking called bupropion
- medicines to reduce blood sugar levels called repaglinide, tolbutamide
- a medicine that prevents blood clots called warfarin
- a medicine used to reduce the amount of acid produced in the stomach called omeprazole
- a medicine used to help control high blood pressure called valsartan
- a group of medicines used to help lower cholesterol called statins - hormonal medicines used for contraception, see section "contraception - for men and women" below.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse.

Taking Larotreni with food and drink

Do not eat grapefruit or drink grapefruit juice while taking Larotreni. This is because it may increase the amount of Larotreni in your body.

Pregnancy and breast-feeding

Pregnancy

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You should not use Larotreni during pregnancy since the effect of Larotreni on the unborn is not known.

Breast-feeding

Do not breast-feed while taking this medicine and for 3 days after the last dose. This is because it is not known if Larotreni passes into breast milk.

Contraception - for men and women

You should avoid getting pregnant while taking this medicine. If you are able to become pregnant, your doctor should do a pregnancy test before you start treatment. You must use effective methods of contraception while taking Larotreni and for at least 1 month after the last dose, if

- you are able to become pregnant. If you use hormonal contraceptives, you should also use a barrier method, such as a condom.

- you have sex with a woman able to become pregnant. Ask your doctor about the best method of contraception for you.

Driving, cycling and using machines

Larotreni may make you feel dizzy or tired. If this happens, do not drive, cycle or use any tools or machines.

3. How to take Larotreni

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

How much to take

Adults (from 18 years)

- The recommended dose of Larotreni is 100 mg (1 capsule of 100 mg or 4 capsules of 25 mg), two times a day.

- Your doctor will review your dose and change it as needed.

Children and adolescents

- Your child's doctor will work out the right dose for your child based on their height and weight.
- The maximum recommended dose is 100 mg (1 capsule of 100 mg or 4 capsules of 25 mg), two times a day.
- Your child's doctor will review the dose and change it as needed.

An oral solution of Larotrectinib is available for patients who cannot swallow the capsules.

How to take this medicine

- Larotreni can be taken with or without food.
- Do not eat grapefruit or drink grapefruit juice while taking this medicine.
- Swallow the Larotrectinib capsules whole with a glass of water. Do not open, chew or crush the capsule as it has a very bitter taste.

If you take more Larotreni than you should

Talk to your doctor, pharmacist or nurse or go to a hospital straight away. Take the medicine pack and this leaflet with you.

If you miss a dose of Larotreni

Do not take a double dose to make up for a forgotten dose or if you vomit after taking this medicine. Take your next dose at the usual time.

If you stop taking Larotreni

Do not stop taking this medicine without talking to your doctor first. It is important to take Larotreni for as long as your doctor tells you.

If you are not able to take the medicine as your doctor prescribed talk to your doctor straight away.

If you have further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

You should immediately contact your doctor if you experience any of the following serious side effects:

- feeling dizzy (very common side effect, may affect more than 1 in 10 people), tingling, feeling numb, or a burning feeling in your hands and feet, difficulty walking normally (common side effect, may affect up to 1 in 10 people). This could be symptoms of nervous system problems. Your doctor may decide to lower the dose, or pause or stop the treatment.

Tell your doctor, pharmacist or nurse if you notice any of the following side effects:

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

- you may look pale and feel your heart pumping, which could be symptoms of low red blood cells (anaemia)
- flu like symptoms including fever, which could be symptoms of low white blood cells (neutropenia, leukopenia)
- feeling or being sick (nausea or vomiting)
- constipation
- muscle pain (myalgia)
- feeling tired (fatigue)
- increased amount of liver enzymes in blood tests
- weight increase.

Common (may affect up to 1 in 10 people):

- change in how things taste (dysgeusia)
- muscle weakness
- increased amount of "alkaline phosphatase" in blood tests (very common in children).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Larotreni

- 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 the bottle label after EXP. The expiry date refers to the last day of that month.

- This medicine does not require any special storage conditions.

- Do not use this medicine if you notice that capsules look damaged.

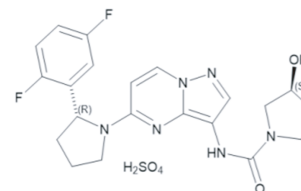
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use.

These measures will help to protect the environment.

6. Contents of the pack and other information

What Larotreni contains

The active substance is larotrectinib. Larotrectinib is a kinase inhibitor. Larotrectinib (larotrectinib) capsules and oral solution are formulated using larotrectinib sulfate. The molecular formula for larotrectinib sulfate is $C_{21}H_{26}F_2NaO_5S$ and the molecular weight is 526.51 g/mol for the sulfate salt and 428.44 g/mol for the free base. The chemical name is (3S)-N-({[2R]-2-(2,5-difluorophenyl)-1-pyrrolidinyl]pyrazolo[1,5-a]pyrimidin-3-yl}-3-hydroxy-1-pyrrolidinecarboxamide sulfate. Larotrectinib sulfate has the following chemical structure:



Each Larotreni 25 mg capsule contains 25 mg of larotrectinib (as sulfate).

Each Larotreni 100 mg capsule contains 100 mg of larotrectinib (as sulfate).

The other ingredients are:

Capsule shell:

- Gelatin
- Titanium dioxide

What Larotreni looks like and the contents of the bottle

- Larotreni 25 mg is supplied as white opaque hard gelatine capsule, (18 mm long x 6 mm wide)

- Larotreni 100 mg is supplied as white opaque hard gelatine capsule, (22 mm long x 7 mm wide)

Each carton contains 1 child-resistant plastic bottle containing 56 or 60 hard gelatine capsules.

Marketing Authorisation Holder

Tongmeng(Lao) Pharmaceutical and Food Co., Ltd
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Manufacturer

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:



TLPH