TLPH

Package leaflet: Information for the user
Pitobrunib 50 mg /100mg film-coated tablets
pirtobrutinib

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.

What is in this leaflet

1.What Pitobrunibis and what it is used for

What Pitobrunib is
Pitobrunib is a kinase inhibitor indicated for the treatment of
▪Adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor.
▪Adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor.

What Pitobrunibis used for
Pitobrunib for the treatment of adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a Bruton's tyrosine kinase (BTK) inhibitor and a BCL-2 inhibitor.

How Pitobrunib works
Pirtobrutinib is a small molecule, noncovalent inhibitor of BTK. BTK is a signaling protein of the B-cell antigen receptor (BCR) and cytokine receptor pathways. In B-cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. Pirtobrutinib binds to wild type BTK and BTK harboring C481 mutations, leading to inhibition of BTK kinase activity. In nonclinical studies, pirtobrutinib inhibited BTK-mediated B-cell CD69 expression and inhibited malignant B-cell proliferation. Pirtobrutinib showed dose-dependent anti-tumor activities in BTK wild type and BTK C481S mutant mouse xenograft models.

2.What you need to know before you take Pitobrunib

Do not take Pitobrunib
- if you are allergic to Pirtobrutinib or any of the other ingredients of this medicine (listed in section 6).

Before taking Pitobrunib, tell your healthcare provider about all of your medical conditions, including if you:
▪have an infection or have been advised that you are at increased risk of infection
▪have had recent surgery or plan to have surgery.Your healthcare provider may stop Pitobrunib for any planned medical, surgical, or dental procedure.
▪have bleeding problems or are taking a blood thinner medicine
▪have or had heart rhythm problems
▪have high blood pressure
▪have a history of other cancers including skin cancer
▪have kidney problems
▪are pregnant or plan to become pregnant. Pitobrunib can harm your unborn baby.
Females who are able to become pregnant:
Your healthcare provider will do a pregnancy test before starting treatment with Pitobrunib.
You should use effective birth control (contraception) during treatment with Pitobrunib and for 1 week after your last dose of Pitobrunib.
Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with Pitobrunib.
▪are breastfeeding or plan to breastfeed. It is not known if Pitobrunib passes into your breast milk. Do not breastfeed during treatment with Pitobrunib and for 1 week after your last dose of Pitobrunib.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking Pitobrunib with certain other medicines may affect how Pitobrunib or the other medicines work and can cause side effects.

Drug Interactions
▪ **Strong CYP3A Inhibitors:** Concomitant use with Pitobrunib increased pirtobrutinib systemic exposure, which may increase risk of Pitobrunib ARs. Avoid use of strong CYP3A inhibitors with Pitobrunib. If concomitant use is unavoidable, reduce Pitobrunib dosage according to approved labeling.
▪ **Strong or Moderate CYP3A Inducers:** Concomitant use with Pitobrunib decreased pirtobrutinib systemic exposure, which may reduce Pitobrunib efficacy. Avoid concomitant use of Pitobrunib with strong or moderate CYP3A inducers. If concomitant use with moderate CYP3A inducers is unavoidable, increase Pitobrunib dosage according to approved labeling.
▪ **Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP Substrates:** Concomitant use with Pitobrunib increased their plasma concentrations, which may increase risk of adverse reactions related to these substrates for drugs that are sensitive to minimal concentration changes. Follow recommendations for these sensitive substrates in their approved labeling.

Use in Special Populations
▪ **Pregnancy and Lactation:** Due to potential for Pitobrunib to cause fetal harm, verify pregnancy status in females of reproductive potential prior to starting Pitobrunib and advise use of effective contraception during treatment and for one week after last dose. Presence of pirtobrutinib in human milk is unknown. Advise women not to breastfeed while taking Pitobrunib and for one week after last dose.
▪ **Geriatric Use:** In the pooled safety population of patients with hematologic malignancies, patients aged ≥65 years experienced higher rates of Grade ≥3 ARs and serious ARs compared to patients<65 years of age.
▪ **Renal Impairment:** Severe renal impairment increases pirtobrutinib exposure. Reduce Pitobrunib dosage in patients with severe renal impairment according to approved labeling.

3.How to take Pitobrunib

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
Your doctor will tell you what dose of Pitobrunibto take.Your doctor may decide to increase or lower your dose or temporarily interrupt treatment. Continue treatment at the dose prescribed by your doctor.

▪Take Pitobrunib exactly as your healthcare provider tells you.
▪Do not change your dose or stop taking Pitobrunib unless your healthcare provider tells you to do so.
▪Take Pitobrunib tablets 1 time each day at about the same time each day.
▪Take Pitobrunib with or without food.
▪Swallow Pitobrunib tablets whole with water. Do not cut, crush, or chew the tablets.
▪If you miss a dose of Pitobrunib, take it as soon as you remember on the same day. If it has been more than 12 hours from the time you usually take Pitobrunib, skip the missed dose, and take your next dose on the next day at your usual time.

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

Pitobrunib can cause serious side effects, including:
Infections can happen during treatment with Pitobrunib. These infections can be serious and may lead to death. Your healthcare provider may prescribe vaccines and certain medicines if you have an increased risk of getting infections. Tell your healthcare

provider right away if you develop fever, chills, weakness, flu-like symptoms, or any other signs of infection during treatment with Pitobrunib.
Bleeding problems (hemorrhage) can happen during treatment with Pitobrunib and can be serious and may lead to death. Your risk of severe bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you develop any signs or symptoms of bleeding, including:
▪blood in your stools or black stools (looks like tar)
▪pink or brown urine
▪increased bruising
▪unexpected bleeding, or bleeding that is severe or you cannot control
▪dizziness
▪vomit blood or vomit blood that looks like coffee grinds
▪weakness
▪cough up blood or blood clots
▪confusion
▪changes in your speech
▪headache that lasts a long time
Decrease in blood cell counts. Decrease in blood cell counts (white blood cells, platelets, and red blood cells) are common with Pitobrunib, but can also be severe. This may increase your risk of infection, bleeding, and anemia. Your healthcare provider should do blood tests to check your blood counts regularly during treatment with Pitobrunib.
Heart rhythm problems. Heart rhythm problems including atrial fibrillation and atrial flutter have happened in people treated with Pitobrunib. Your risk for heart rhythm problems may be increased if you have high blood pressure or have had heart rhythm problems in the past. Tell your healthcare provider if you develop any of the following signs or symptoms:
▪ fast or irregular heartbeat (palpitations)
▪ chest discomfort
▪ dizziness
▪ shortness of breath
▪ fainting
Second primary cancers. New cancers have happened in people during treatment with Pitobrunib, including cancers of the skin or other organs. Your healthcare provider will check you for other cancers during treatment with Pitobrunib. Use sun protection when you are outside in sunlight.

Your healthcare provider may decrease your dose, temporarily stop, or permanently stop treatment with Pitobrunib if you develop severe side effects.
The most common side effects of Pitobrunib include:
▪ tiredness
▪ muscle, joint, and bone pain
▪ diarrhea
▪ cough
▪ COVID-19
▪ bruising
These are not all the possible side effects of Pitobrunib.

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. By reporting side effects you can help provide more information on the safety of this medicine.

5.How to store Pitobrunib
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 blister after EXP. The expiry date refers to the last day of that month.

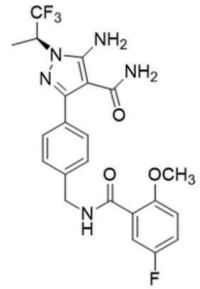
Store in the original package in order to protect from light.

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 Pitobrunib contains

Pirtobrutinib is a kinase inhibitor. It is an orally available, small molecule ATP-competitive inhibitor of BTK. The active pharmaceutical ingredient is pirtobrutinib with the molecular formula C22H21F4N5O3 and a molecular weight of 479.44 g/mol. The chemical name for pirtobrutinib is 5-amino-3-{4-[(5-fluoro-2-methoxybenzamido)methyl]phenyl}-1-[(2S)-1,1,1-trifluoropropan-2-yl]-1H-pyrazole-4-carboxamide.



Each 50mg film-coated tablet contains 50 mg (Pirtobrutinib).
Each 100mg film-coated tablet contains 100 mg (Pirtobrutinib).

Inactive ingredients: croscarmellose sodium, hypromellose acetate succinate, lactose monohydrate, magnesium stearate, microcrystalline cellulo and silicon dioxide.

What Pitobruniblooks like and contents of the pack

Pitobrunib 50 mg tablet is blue oval-shaped film-coated tablet
The tablets are provided in bottles and are available in packs containing 30 film-coated tablets .
Pitobrunib 100 mg tablet is blue round-shaped film-coated tablet
The tablets are provided in bottles and are available in packs containing 60 film-coated tablets .

Manufacturer
Tongmeng(Lao) Pharmaceutical and Food Co., Ltd
Rd13 South,31km,Ban Naphasuk,Saithany District
Vientiane Lao PDR

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

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