TLPH

Information for the user
Molotinib100mg 150 mg 200mg film-coated tablets
momelotinib

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 Molotinibis and what it is used for

What Molotinib is
Momelotinib is an inhibitor of wild type Janus Kinase 1 and 2 (JAK1/JAK2) and mutant JAK2V617F, which contribute to signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function.Molotinib is a prescription medicine used to treat adults with certain types of myelofibrosis (MF) who have anemia. It is not known if Molotinib is safe and effective in children.

What Molotinib is used for
Molotinib is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF [post-polycythemia vera (PV) and post-essential thrombocythemia (ET)], in adults with anemia.

How Molotinib works
This medicine is thought to work by blocking some enzymes known as Janus kinases (JAKs). These enzymes can be found in some receptors on the surface of cells and are involved in the reproduction and growth of blood cells. In myelofibrosis, JAKs are more active than normal. By blocking these enzymes, this medicine is expected to slow down the abnormal growth of blood cells, reducing the symptoms of the disease.

2.What you need to know before you take Molotinib

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

Before taking Molotinib, tell your healthcare provider about all of your medical conditions, including if you:
- have or have had hepatitis B
- have or have had liver problems
- have had a heart attack, or have or have had other heart problems, or stroke
- have or have had a blood clot
- smoke or were a smoker in the past
- have or have had any other cancers
- are pregnant or plan to become pregnant. Molotinib may harm your unborn baby.

Females who are able to become pregnant:
- You should use effective birth control (contraception) during treatment and for 1 week after the last dose of Molotinib.
- Tell your healthcare provider right away if you think you are pregnant or become pregnant during treatment with Molotinib.
- are breastfeeding or plan to breastfeed. It is not known if Molotinib passes into your breast milk. You should not breastfeed during treatment and for 1 week after the last dose of Molotinib. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking Molotinib with certain other medicines may affect the amount of Molotinib or the other medicines in your blood and may increase your risk of side effects. Know the medicines you take. Keep a list of the medicines you take to show your healthcare provider and pharmacist when you get a new medicine.

Drug Interactions

- **Effect of Other Drugs on Molotinib**

Organic Anion Transporting Polypeptide (OATP)1B1/B3 Inhibitors
Momelotinib is an OATP1B1/B3 substrate. Concomitant use with an OATP1B1/B3 inhibitor increases momelotinib maximal concentrations (Cmax) and area under the concentration-time curve (AUC) , which may increase the risk of adverse reactions with Molotinib. Monitor patients concomitantly receiving an OATP1B1/B3 inhibitor for adverse reactions and consider Molotinib dose modifications .

- **Effect of Molotinib on Other Drugs**

Breast Cancer Resistance Protein (BCRP) Substrates
Momelotinib is a BCRP inhibitor. Molotinib may increase exposure of BCRP substrates, which may increase the risk of BCRP substrate adverse reactions . When administered concomitantly with Molotinib, initiate rosuvastatin (BCRP substrate) at 5 mg and do not increase to more than 10 mg once daily. Dose adjustment of other BCRP substrates may also be needed. Follow approved product information recommendations for other BCRP substrates.

Use in Special Populations
- **Pregnancy and Lactation:** Molotinib should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the fetus.patients should not breastfeed during treatment with Molotinib, and for at least 1 week after the last dose of Molotinib.

- **Females and Males of Reproductive Potential:** Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for at least 1 week after the last dose of Molotinib.
- **Hepatic Impairment:** The recommended starting dose of Molotinib in patients with severe hepatic impairment (ChildPugh C) is 150 mg orally once daily . No dose modification is recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B). Momelotinib is extensively metabolized . Momelotinib exposure increased with severe hepatic impairment (Child-Pugh C). No clinically significant changes in momelotinib exposure were observed in subjects with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B)

3.How to take Molotinib

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 Molotinibto 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 Molotinib exactly as your healthcare provider tells you to take it.
- Take Molotinib by mouth 1 time each day.
- Take Molotinib with or without food.
- Swallow tablets whole. Do not cut, crush or chew tablets.
- If you miss a dose of Molotinib, skip the missed dose and take your next dose the following day at your regularly scheduled time. Do not take 2 doses at the same time to make up for the missed dose.
- Your healthcare provider will do blood tests before you start taking Molotinib and during treatment.
- Do not change your dose or stop taking Molotinib without first talking to your healthcare provider.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with Molotinib if you have certain side effects.
- If you take too much Molotinib, call your healthcare provider or go to the nearest emergency room right away and take your bottle of Molotinib with you.

4.Possible side effects

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

Molotinib may cause serious side effects, including:
- **Risk of Infections.** People who take Molotinib may develop serious infections that can lead to death, such as bacterial and viral infections, including COVID-19. If you have an active infection, your healthcare provider should not start treatment with Molotinib until your infection is gone. If you have had hepatitis B for a long time (chronic), Molotinib may cause your hepatitis B to become active again, and your healthcare provider will check your blood for active hepatitis B before starting treatment.

Your healthcare provider will monitor you and treat you for any infections that you get during treatment with Molotinib.

Tell your healthcare provider right away if you develop any of the following symptoms of infection:

o fever
o diarrhea
o chills
o vomiting
o cough
o pain or burning feeling when passing urine
o breathing problems

▪ **Low platelet and white blood cell counts.** Molotinib may cause new or worsening low platelet and white blood cell counts. Low platelet counts may increase your risk for bleeding and low white blood cell counts may increase your risk for infection. Your healthcare provider will do blood tests to check your blood counts before you start taking Molotinib and during treatment. Tell your healthcare provider right away if you have any signs of bleeding during treatment with Molotinib, including:

o unusual bleeding
o bruising
o black or tarry stools

▪ **Liver problems.** Molotinib may cause new or worsening increased liver enzymes and bilirubin in your blood. Your healthcare provider will check your liver enzymes before starting treatment, every month for the first 6 months of treatment, and then as needed during treatment with Molotinib. Your healthcare provider may stop treatment with Molotinib if your liver enzymes increase. Tell your healthcare provider if you develop any of the following signs or symptoms of liver problems:

o tiredness
o dark urine
o loss of appetite
o yellowing of your skin or the white part of your eyes
o pain in your right upper stomach area (abdomen)

▪ **Major cardiovascular events such as heart attack,** stroke, and death. Major cardiac events have happened, especially in people with cardiac risk factors and who are current or past smokers, taking another Janus kinase (JAK) inhibitor to treat rheumatoid arthritis. Molotinib is in the JAK family of medicines.

Get emergency help right away if you have any symptoms of a heart attack or stroke while taking Molotinib, including:

o discomfort in your chest that lasts for more than a few minutes, or that goes away and comes back
o severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
o pain or discomfort in your arms, back, neck, jaw, or stomach
o shortness of breath with or without chest discomfort
o breaking out in a cold sweat
o nausea or vomiting
o feeling lightheaded
o weakness in one part or on one side of your body
o slurred speech

▪ **Blood clots.** Blood clots in the veins of the legs (deep vein thrombosis, DVT) or lungs (pulmonary embolism, PE) have happened in some people taking another JAK inhibitor to treat rheumatoid arthritis, and may be life-threatening. Tell your healthcare provider if you have had blood clots in the veins of your legs or lungs in the past.

Tell your healthcare provider right away if you have any signs and symptoms of blood clots during treatment with Molotinib, including:

o swelling, pain, or tenderness in one or both legs
o sudden, unexplained chest pain
o shortness of breath or difficulty breathing

▪ **New cancers.** New cancers, including lymphoma and other cancers, except non-melanoma skin cancer, have happened in some people taking another JAK inhibitor to treat rheumatoid arthritis. The risk of new cancers is further increased in people who smoke or who smoked in the past.

The most common side effects of Molotinib include:

▪ low platelet count
▪ dizziness
▪ bleeding
▪ diarrhea
▪ bacterial infection
▪ nausea
▪ tiredness

These are not all of the possible side effects of Molotinib.

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 Molotinib

Keep this medicine out of the sight and reach of children.

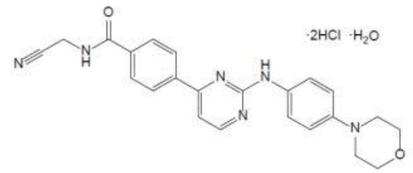
Do not use this medicine after the expiry date which is stated on the carton and the blister after EXP. The expiry date refers to the last day of that month.
Store in original bottle to protect from moisture. Replace cap securely each time after opening. Do not discard desiccant.

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 Molotinib contains

Molotinib contains momelotinib dihydrochloride monohydrate, which is a kinase inhibitor with the chemical name N-(Cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide dihydrochloride monohydrate. It has a molecular formula of $C_{23}H_{22}N_6O_2.2HCl.H_2O$, molecular weight of 505.40 and the following structural formula:



Momelotinib free base has a molecular formula of $C_{23}H_{22}N_6O_2$ and a molecular weight of 414.47.

Each 100mg film-coated tablet contains 121.94 mg of momelotinib dihydrochloride monohydrate.
Each 150mg film-coated tablet contains 182.91 mg of momelotinib dihydrochloride monohydrate.
Each 200mg film-coated tablet contains 243.88 mg of momelotinib dihydrochloride monohydrate.

Inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, propyl gallate, silicon dioxide, and sodium starch glycolate

What Molotinib looks like and contents of the pack

Momelotinib 100 mg tablet is round-shaped film-coated tablet with "TLPH" on one side
The tablets are provided in bottles and are available in packs containing 30 film-coated tablets .
Momelotinib 150 mg tablet is capsule--shaped film-coated tablet with "TLPH" on one side
The tablets are provided in bottles and are available in packs containing 30 film-coated tablets .
Momelotinib 200 mg tablet is capsule--shaped film-coated tablet with "TLPH" on one side
The tablets are provided in bottles and are available in packs containing 30 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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