TLPH

Information for the user
Ensidnib 50 mg、100mg film-coated tablets
Enasidenib

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 Ensidnib and what it is used for

Ensidnib was developed as a cancer medicine for the treatment of AML in adult patients whose cancer cells have a mutation (change) in the gene for a protein called IDH2 and who cannot receive intensive cancer treatment. Ensidnib was to be used in patients whose disease did not respond to treatment (refractory) or had come back (relapsed) after previous treatments including a haematopoietic stem cell transplant (a transplant of cells that can develop into different types of blood cells)

Idihifa contains the active substance enasidenib and was to be available as tablets.

How Ensidnib works

The active substance in Ensidnib, enasidenib, works by blocking the action of mutated forms of IDH2, a protein that plays an important role in generating energy for cells. Mutated IDH2 produces high levels of a substance called D-2-HG, which contributes to the growth of cancer cells. By blocking the action of mutated IDH2, enasidenib is expected to reduce production of D-2-HG and so slow down the
progression of the disease.

2.What you need to know before you take Ensidnib

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

Before taking Ensidnib, tell your healthcare provider about all of your medical conditions, including if you:
- Are pregnant, plan to become pregnant, or think you might be pregnant during treatment with Ensidnib. Ensidnib can cause harm to your unborn baby if taken during pregnancy
- If you are able to become pregnant, your healthcare provider will do a pregnancy test before you start taking Ensidnib
- **Females** who are able to become pregnant and who take Ensidnib should use effective birth control (contraception) during treatment with Ensidnib and for at least 2 months after your last dose of Ensidnib
- **Males** who have female partners that are able to become pregnant should use effective birth control during treatment with Ensidnib and for at least 2 months after your last dose of Ensidnib
- Ensidnib may affect how hormonal contraceptives work and may cause them to not work as well
- Talk to your healthcare provider about birth control methods that may be right for you while taking Ensidnib
- Ensidnib may cause fertility problems in females and males, which may affect your ability to have children. Talk to your healthcare provider if you have concerns about fertility
- Are breastfeeding or plan to breastfeed. It is not known if Ensidnib passes into your breast milk. You should not breastfeed during your treatment with Ensidnib and for at least 2 months after your last dose of Ensidnib

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

WARNINGS AND PRECAUTIONS

Differentiation Syndrome: In the clinical trial, 14% of patients treated with Ensidnib experienced differentiation syndrome, which may be life-threatening or fatal if not treated. Differentiation syndrome has been observed with and without concomitant hyperleukocytosis, in as early as 1 day and up to 5 months after Ensidnib initiation. Symptoms in patients treated with Ensidnib included acute respiratory distress represented by dyspnea and/or hypoxia and need for supplemental oxygen; pulmonary infiltrates and pleural effusion; renal impairment; fever; lymphadenopathy; bone pain; peripheral edema with rapid weight gain; and pericardial effusion. Hepatic, renal, and multi-organ dysfunction have also been observed. If differentiation syndrome is suspected, initiate systemic corticosteroids and hemodynamic monitoring until improvement. Taper corticosteroids only after resolution of symptoms. Differentiation syndrome symptoms may recur with premature discontinuation of corticosteroids. If severe pulmonary symptoms requiring intubation or ventilator support and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids, interrupt Ensidnib until signs and symptoms are no longer severe. Hospitalization for close observation and monitoring of patients with pulmonary and/or renal manifestation is recommended.
Embryo-Fetal Toxicity: Based on animal embryo-fetal toxicity studies, Ensidnib can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Ensidnib and for at least 2 months after the last dose. Advise pregnant women, of the potential risk to the fetus.

DRUG INTERACTIONS

Coadministration of Ensidnib increases the exposure of OATP1B1, OATP1B3, BCRP, and P-glycoprotein (P-gp) substrates, which may increase the incidence and severity of adverse reactions of these substrates. If coadministered, decrease the dosage of the substrate as recommended in the respective prescribing information and as clinically indicated.

LACTATION

Because of the potential for adverse reactions in the breastfed child, advise women not to breastfeed during treatment with Ensidnib and for at least 2 months after the last dose.

3.How to take Ensidnib

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 Ensidnibto 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 Ensidnib exactly as your healthcare provider tells you to
▪Take Ensidnib 1 time a day at the same time each day. Ensidnib can be taken with or without food
▪Swallow Ensidnib tablets whole with 8 ounces (one cup) of water. Do not chew or split the tablet
▪If you miss a dose of Ensidnib or vomit after taking a dose of Ensidnib, take the dose of Ensidnib as soon as possible on the same day. Then take your next dose the next 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 should do blood tests to check your blood counts before you start Ensidnib treatment and at a minimum of every 2 weeks for at least the first 3 months during treatment to check for side effects

4.Possible side effects

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

Ensidnib may cause serious side effects, including:

▪**Differentiation Syndrome**. Differentiation syndrome is a condition that affects your blood cells which may be life-threatening or lead to death if not treated. Differentiation syndrome has happened within 1 day and up to 5 months after starting Ensidnib. Call your healthcare provider or go to the nearest hospital emergency room right away if you develop any of the following symptoms of differentiation syndrome while taking Ensidnib:
▪fever
▪cough
▪shortness of breath
▪swelling of arms and legs
▪swelling around neck, groin, or underarm area
ofast weight gain (greater than 10 pounds within a week)
obone pain
If you develop any of these symptoms of differentiation syndrome, your healthcare provider may start you on a medicine taken by mouth or given through a vein (intravenous) called corticosteroids and may monitor you in the hospital.

The most common side effects of Ensidnib include:

▪nausea
▪vomiting
▪diarrhea
▪jaundice
▪decreased appetite
Tell your healthcare provider if you have any changes to the color of your skin or the whites of your eyes.

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 Ensidnib

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.

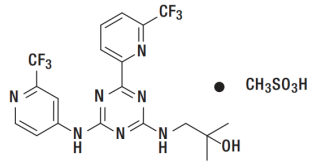
▪Store Ensidnib at room temperature from 68°F to 77°F (20°C to 25°C).
▪Keep Ensidnib in the original container.
▪Keep the container tightly closed with desiccant canister inside to protect the tablets from moisture.

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 Ensidnib contains

Enasidenib is an inhibitor of isocitrate dehydrogenase-2 (IDH2) enzyme. Enasidenib is available as the mesylate salt with the chemical name: 2-methyl-1-[(4-[6-(trifluoromethyl)pyridin-2-yl]-6-{[2-(trifluoromethyl)pyridin-4-yl]amino}- 1,3,5-triazin-2-yl)amino]propan-2-ol methanesulfonate. Or 2-Propanol, 2-methyl-1-[[4-[6-(trifluoromethyl)-2-pyridinyl]-6-[[2-(trifluoromethyl)-4- pyridinyl]amino-1,3,5-triazin-2-yl]amino]-, methanesulfonate (1:1). The chemical structure is:



The empirical formula is C19H17F6N7O ▪ CH3SO3H (C20H21F6N7O4S), and the molecular weight is 569.48 g/mol. Enasidenib is practically insoluble (solubility ≤74 mcg/mL) in aqueous solutions across physiological pH range (pH 1.2 and 7.4).
Ensidnib (enasidenib) is available as a 50mg tablet (equivalent to 60 mg enasidenib mesylate) and a 100mg tablet (equivalent to 120 mg enasidenib mesylate) for oral administration. Each tablet contains inactive ingredients of colloidal silicon dioxide, hydroxypropyl cellulose, hypromellose acetate succinate, iron oxide yellow, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, sodium lauryl sulfate, sodium starch glycolate, talc, and titanium dioxide.

What Ensidniblooks like and contents of the pack

▪50mg tablet: Pale yellow to yellow oval-shaped film-coated tablet debossed “THPL” on one side
▪30-count bottles of 50mg tablets with a desiccant canister
▪100-mg tablet: Pale yellow to yellow capsule-shaped film-coated tablet debossed “TLPH” on one side
▪30-count bottles of 100-mg tablets with a desiccant canister .

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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