205 mm

278 mm

LOKEMIDE®(IBRUTINIB) CAPSULE

LOKEMIDE®
IBRUTINIB

LOKEMIDE® (IBRUTINIB) CAPSULE FOR ORAL USE
Read this patient information carefully before you start taking LOKEMIDE® because it answers some common questions about LOKEMIDE®. This medication is prescribed for your current condition, therefore do not use it, in similar cases and do not recommend it to others.
To report SUSPECTED ADVERSE REACTIONS, contact Noavaran Daroui Kimia Co. at +982188012946 or send email to medical@kimia-pharma.co

Read this patient information carefully before you start taking LOKEMIDE® because it contains important information for you. This leaflet does not take the place of talking with your healthcare provider about your medical condition or treatment.

COMPOSITION
Each capsule Lokemide® 70 mg contains: Ibrutinib 70 mg.
Each capsule Lokemide® 140 mg contains: Ibrutinib 140 mg.

Mechanism of action
Lokemide® is a small molecule that works by inhibiting a type of enzyme, called a protein kinase that controls the rate at which certain cells multiply.

Pharmacokinetic
Absorption
Absolute bioavailability of Lokemide® in fasted condition was 2.9% (90% CI: 2.1, 3.9) in healthy subjects. Lokemide® is absorbed after oral administration with a median Tmax of 1 hour to 2 hours.
Distribution
Reversible binding of Lokemide® to human plasma protein in vitro was 97.3% with no concentration dependence in the range of 50 ng/mL to 1000 ng/mL.
Metabolism
Metabolism is the main route of elimination for Lokemide®. It is metabolized to several metabolites primarily by cytochrome P450 (CYP) 3A and to a minor extent by CYP2D6.
Excretion
Lokemide®, mainly in the form of metabolites, is eliminated primarily via feces.

INDICATION
Lokemide® is a prescription medicine used to treat adults with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy.
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL).
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion.
- Waldenström's macroglobulinemia (WM).
- Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy.
- Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

It is not known if Lokemide® is safe and effective in children.

Dosage and administration

- MCL and MZL: 560 mg taken orally once daily.
- CLL/SLL, WM, and cGVHD: 420 mg taken orally once daily.

Dose should be taken orally with a glass of water. Do not open, break, or chew the capsules.

Side effects / Adverse reactions

The most common side effects in people who take Lokemide® include:

- The most common side effects of Lokemide® in adults with B-cell malignancies (MCL, CLL/SLL, WM and MZL) include: diarrhea, muscle and bone pain, rash, nausea, bruising, tiredness, fever.
- The most common side effects of Lokemide® in adults with cGVHD include: tiredness, bruising, diarrhea, mouth sores (stomatitis), muscle spasms, nausea, and pneumonia.
- **Decrease in blood cell counts.** Decreased blood counts (white blood cells, platelets, and red blood cells) are common with Lokemide®, but can also be severe. Your healthcare provider should do monthly blood tests to check your blood counts.
- **Heart rhythm problems** (ventricular arrhythmias, atrial fibrillation and atrial flutter). Serious heart rhythm problems and death have happened in people treated with Lokemide®, especially in people who have an increased risk for heart disease, have an infection, or who have had heart rhythm problems in the past. Tell your healthcare provider if you get any symptoms of heart rhythm problems, such as feeling as if your heart is beating fast and irregular, lightheadedness, dizziness, shortness of breath, chest discomfort, or you faint. If you develop any of these symptoms, your healthcare provider may do a test to check your heart (ECG) and may change your Lokemide® dose.
- **High blood pressure (hypertension).** New or worsening high blood pressure has happened in people treated with Lokemide®. Your healthcare provider may start you on blood pressure medicine or change current medicines to treat your blood pressure.
- **Second primary cancers.** New cancers have happened during treatment with Lokemide®, including cancers of the skin or other organs.
- **Tumor lysis syndrome (TLS).** TLS is caused by the fast breakdown of cancer cells. TLS can cause kidney failure and the need for dialysis treatment, abnormal heart rhythm, seizure, and sometimes death. Your healthcare provider may do blood tests to check you for TLS.
- **Bleeding problems (hemorrhage) are common** during treatment with Lokemide®, and can also be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs of bleeding, including:
  blood in your stools or black stools (looks like tar), increased bruising, pink or brown urine, dizziness, unexpected bleeding, or bleeding that is severe or that you cannot control, weakness, confusion, vomit blood or vomit looks like coffee grounds, cough up blood or blood clots, change in your speech, headache that lasts a long time.
- **Infections** can happen during treatment with Lokemide®. These infections can be serious and may lead to death. Tell your healthcare provider right away if you have fever, chills, weakness, confusion, or other signs or symptoms of an infection during treatment with Lokemide ®.

Diarrhea is a common side effect in people who take Lokemide®. Drink plenty of fluids during treatment with Lokemide® to help reduce your risk of losing too much fluid (dehydration) due to diarrhea. Tell your healthcare provider if you have diarrhea that dose not go away.
These are not all the possible side effects of Lokemide®. Call your doctor for medical advice about side effects.

Drug interaction

- Strong CYP3A4 Inhibitors: Dose reduction may be necessary.
- Strong CYP3A4 Inducers (e.g., carbamazepine, rifampin, phenytoin): Dose increase may be necessary.
- Avoid grapefruit and Seville oranges (often used in marmalades) during Lokemide® treatment.

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

Warnings

Before taking Lokemide®, tell your healthcare provider about all of your medical conditions, including if you:

- Have had recent surgery or plan to have surgery. Your healthcare provider may stop Lokemide® for any planned medical, surgical, or dental procedure.
- Have bleeding problems.
- Have or had heart rhythm problems, smoke, or have a medical condition that increases your risk of heart disease, such as high blood pressure, high cholesterol, or diabetes.
- Have an infection.
- Have liver problems.
- If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.
- Are breastfeeding or plan to breastfeed.

Do not use Lokemide® if: It is not recommended to administer Lokemide® to patients with moderate or severe hepatic impairment.

Missed dose
If you miss a dose of Lokemide® take it as soon as you remember on the same day. Take your next dose of Lokemide® at your regular time on the next day. Do not take extra doses of Lokemide® to make up for a missed dose.

OVERDOSE
If you take too much Lokemide® call your healthcare provider or go to the nearest hospital emergency room right away.

Pregnancy and lactation

- Embryo-fetal toxicity: Lokemide® can harm your unborn baby. If you are able to become pregnant, your healthcare provider will do a pregnancy test before starting treatment with Lokemide®. Tell your healthcare provider if you are pregnant or think you may be pregnant during treatment with Lokemide®.
- Females who are able to become pregnant should use effective birth control (contraception) during treatment with Lokemide® and for 3 months after the last dose.
- Males with female partners who are able to become pregnant should use effective birth control, such as condoms, during treatment with Lokemide® and for 3 months after the last dose.
- There is no information regarding the presence of Ibrutinib or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. You and your healthcare provider should decide if you will take Lokemide® or breastfeed.

Patient information

- Take Lokemide® exactly as your healthcare provider tells you to take it.
- Take Lokemide® 1 time a day.
- Swallow Lokemide® capsules whole with a glass of water.
- Do not open, break, or chew Lokemide® capsules.
- Take Lokemide® at about the same time each day.
- You should not drink grapefruit juice, eat grapefruit, or eat Seville oranges (often used in marmalades) during treatment with Lokemide®. These products may increase the amount of Lokemide® in your blood.
- If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

Storage

- Store Lokemide® capsules below 30°C.
- Keep Lokemide® capsules in the original container with the lid tightly closed.
- Keep Lokemide® and all medicines out of the reach of children.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging

Lokemide® 70 mg:Bottle of 28 Capsules.

Lokemide® 140 mg:Bottle of 90 Capsules.

References
1-https://www.accessdata.fda.gov/drugsatfda_docs/label /2020/205552s030, 210563s006lbl. pdf
2-British National Formulary 73, March-September 2017, Section Maligned Disease, Ibrutinib, Page 867-868

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