RIZOLUNG® CAPSULE

RIZOLUNG®
CRIZOTINIB

RIZOLUNG® (CRIZOTINIB) CAPSULE FOR ORAL USE
Read this patient information carefully before you start taking Rizolung® because it answers some common questions about Rizolung®. 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 +982166433514 or send email to medical@kimia-pharma.co

Read this patient information carefully before you start taking Rizolung® 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 Rizolung® 200 mg contains: Crizotinib 200 mg.
Each capsule Rizolung® 250 mg contains: Crizotinib 250 mg.

Mechanism of action
Crizotinib is an inhibitor of receptor tyrosine kinases including ALK, HGFR, c-Met, ROS1, and RON.

Pharmacokinetic
Absorption
The median time to achieve peak concentration is 4 to 6 hours, and the mean absolute bioavailability of Rizolung® was 43%.
Distribution
The geometric mean volume of distribution (Vss) of Rizolung® was 1772 L. Protein binding of Rizolung® is 91%.
Metabolism
Rizolung® is predominantly metabolized by CYP3A.
Elimination
The mean apparent plasma terminal half-life of Rizolung® is 42 hours.
Excretion
Following administration of a single oral 250 mg dose of radiolabeled Rizolung® dose to healthy subjects, 63% (53% as unchanged) of the administered dose was recovered in feces and 22% (2.3% as unchanged) in urine.

Indication
Rizolung® is a kinase inhibitor indicated for the treatment of:

- patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.
- pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK-positive.
    - Limitations of Use: The safety and efficacy of Rizolung® have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL.
- adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK-positive.

It is not known if Rizolung® is safe and effective in older adults with ALCL or in children younger than 1 year of age with ALCL or IMT.

Dosage and Administration
- Metastatic NSCLC: The recommended dosage is 250 mg orally twice daily.
- Systemic ALCL: The recommended dosage is 280 mg/m^2 orally twice daily based on body surface area.
- Unresectable IMT:
    - Adult: The recommended dosage is 250 mg orally twice daily.
    - Pediatric: The recommended dosage is 280 mg/m^2 orally twice daily based on body surface area.

Side effects / Adverse reactions
It should be noted that these side effects do not occur in all patients. These are not all the possible side effects of Rizolung®. For more information, ask your healthcare provider or pharmacist.

Rizolung® may cause serious side effects including:

- **Liver problems.** Rizolung® may cause life-threatening liver injury. Your healthcare provider should do blood tests to check your liver every 2 weeks during the first 2 months of treatment with Rizolung®, then once a month and as recommended by your healthcare provider during treatment. Tell your healthcare provider right away if you develop any of the following new or worsening symptoms:
    - yellowing of your skin or the white part of your eyes
    - dark or brown (tea color) urine
    - pain on the right side of your stomach
    - bleed or bruise more easily than normal
    - severe tiredness
    - nausea or vomiting
    - decreased appetite
    - itching
- **Lung problems (pneumonitis).** Rizolung® may cause life-threatening lung problems. Symptoms may be similar to those symptoms from lung cancer. Tell your healthcare provider right away if you have any new or worsening symptoms, including:
    - trouble breathing or shortness of breath
    - fever
    - cough with or without mucous
- **Heart problems.** Rizolung® may cause very slow, very fast, or abnormal heartbeats. Your healthcare provider may check your pulse rate and blood pressure regularly during treatment with Rizolung®. Tell your healthcare provider right away if you feel dizzy or faint or have abnormal heartbeats. Tell your healthcare provider if you take any heart or blood pressure medicines.
- **Severe vision problems.** Vision problems are common with Rizolung®. These problems usually happen within 1 week of starting treatment with Rizolung®. Vision problems with Rizolung® can be severe and may cause partial or complete loss of vision in one or both eyes. Your healthcare provider may hold or permanently stop your treatment with Rizolung® and refer you to an eye specialist if any vision problems develop during treatment with Rizolung®. Tell your healthcare provider right away if you have any new vision problems, loss of vision or any change in vision, including:
    - double vision
    - new or increased floaters
    - light hurting your eyes
    - blurry vision
    - seeing flashes of light

  In addition, for children or young adults taking Rizolung® to treat anaplastic large cell lymphoma (ALCL) or children taking Rizolung® to treat inflammatory myofibroblastic tumor (IMT): Your healthcare provider may refer you to an eye specialist before starting Rizolung®, and within 1 month of starting Rizolung® to check for vision problems. You should have an eye examination every 3 months during treatment with Rizolung® and more often if there are any new vision problems.
- **Severe stomach, intestine, and mouth (gastrointestinal) problems in children or young adults with ALCL or children with IMT.** Rizolung® may cause severe diarrhea, nausea, vomiting, or mouth sores. Tell your healthcare provider right away if problems with swallowing, vomiting, or diarrhea develop during treatment with Rizolung®.
    - Your healthcare provider may give medicines as needed to prevent or treat diarrhea, nausea, and vomiting.
    - Your healthcare provider may recommend drinking more fluids or may prescribe electrolyte supplements or other kinds of nutritional support if severe symptoms develop.

Call your healthcare provider right away if you have any of aforementioned symptoms.

The most common side effects of Rizolung® in people with NSCLC include:

- vision problems
- swelling of your hands, feet, face, and eyes
- nausea, diarrhea, or vomiting
- constipation
- increased liver function blood tests
- decreased appetite
- feeling of numbness or tingling in your arms or legs
- tiredness
- upper respiratory infection
- dizziness

The most common side effects of Rizolung® in people with ALCL include:

- diarrhea, vomiting, or nausea
- stomach-area (abdominal) pain
- muscle and joint pain
- decreased appetite
- vision problems
- cough
- mouth sores
- fever
- headache
- itchy skin
- tiredness
- low blood counts

The most common side effects of Rizolung® in adults with IMT include:

- vision problems
- nausea
- swelling of your hands, feet, face, or eyes

The most common side effects of Rizolung® in children with IMT include:

- diarrhea, vomiting, or nausea
- vision problems
- fever
- swelling of your hands, feet, face, or eyes
- stomach-area (abdominal) pain
- upper respiratory infection
- muscle and joint pain
- constipation
- rash
- cough
- tiredness
- headache

Call your doctor for medical advice about side effects.

Drug interaction
- **Strong or Moderate CYP3A Inhibitors**
  Concomitant use of Rizolung® with strong CYP3A inhibitors may increase the risk of adverse reactions of Rizolung®. Avoid concomitant use of strong CYP3A inhibitors. If concomitant use of strong CYP3A inhibitors is unavoidable, reduce the Rizolung® dosage. Avoid grapefruit or grapefruit juice which may also increase plasma concentrations of Rizolung®. Use caution with concomitant use of moderate CYP3A inhibitors.
- **Strong CYP3A Inducers**
  Concomitant use of Rizolung® with strong CYP3A inducers may decrease the efficacy of Rizolung®. Avoid concomitant use of strong CYP3A inducers. The concurrent use of strong CYP3A inducers, including but not limited to carbamazepine, phenobarbital, phenytoin, rifampicin, and St. John's wort, should be avoided.
- **CYP3A Substrates**
  Concomitant use of Rizolung® increases the risk of adverse reactions of CYP3A substrates. Avoid concomitant use where minimal concentration changes may lead to serious adverse reactions. If concomitant use of Rizolung® is unavoidable, decrease the CYP3A substrate dosage in accordance with approved product labeling.
- **Drugs That Prolong the QT Interval**
  Rizolung® can prolong the QT/QTc interval. Avoid concomitant use of Rizolung® with drugs that prolong the QT interval.
- **Drugs That Cause Bradycardia**
  Rizolung® can cause bradycardia. Avoid concomitant use of Rizolung® with drugs that cause bradycardia (e.g., beta-blockers, non-dihydropyridine calcium channel blockers, clonidine, and digoxin).

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

- have liver or kidney problems
- have vision or eye problems
- have heart problems, including a condition called long QT syndrome
- are pregnant or plan to become pregnant. Rizolung® can harm your unborn baby.
- have lung problems
- are breastfeeding or plan to breastfeed.

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

Missed dose
If a dose of Rizolung® is missed, it should be taken as soon as you remember. If it is close to the time of the next dose (within 6 hours), the missed dose should be skipped, and the next dose should be taken at the regular time.

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

Pregnancy and lactation
Rizolung® can cause fetal harm when administered to a pregnant woman.

Females who are able to become pregnant:

- Your healthcare provider will check to see if you are pregnant before starting treatment with Rizolung®.
- Effective birth control (contraception) should be used during treatment with Rizolung® and for at least 90 days after the final dose of Rizolung®.
- Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with Rizolung®.

Males who have female partners who can become pregnant:

- You should use condoms during treatment with Rizolung® and for at least 90 days after the final dose of Rizolung®.

It is not known if Rizolung® passes into the breast milk. Do not breastfeed during treatment with Rizolung® and for 45 days after the final dose. Talk to your healthcare provider about the best way to feed the baby during this time.

Patient information
- Rizolung® should be taken exactly as prescribed by your healthcare provider.
- Rizolung® capsules should be swallowed whole.
- Rizolung® may be taken with or without food.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with Rizolung® if you have certain side effects. Do not change the dose or stop treatment with Rizolung® unless your healthcare provider tells you to.
- If you vomit after taking a dose of Rizolung®, do not take an extra dose. The next dose should be taken at the regular time.
- Rizolung® should be given to children under adult supervision.
- Rizolung® can cause changes in vision, dizziness, and tiredness. Do not drive or operate machinery if you have any of these symptoms.
- Avoid spending prolonged time in sunlight. Rizolung® can make your skin sensitive to the sun (photosensitivity), and you may burn more easily. You should use sunscreen and wear protective clothing that covers your skin to help protect against sunburn if you have to be in the sunlight during treatment with Rizolung®.

Storage
- Keep away from light and moisture. Store below 30°C.
- Keep out of the reach of children.
- Keep the desiccant in the bottle. Do not eat or throw away desiccant pack.
- Keep in the original container.
- Safely throw away medicine that is out of date or that you no longer need. Ask your pharmacist how to safely throw away Rizolung® capsules.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging
Bottle of 60 capsules

MANUFACTURED BY:
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www.kimia-pharma.co

References
https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/202570s033lbl.pdf
https://www.ema.europa.eu/en/documents/product-information/xalkori-epar-product-information_en.pdf
BNF 83 (British National Formulary) March 2022