REGONIB® (REGORAFENIB) F.C. TABLET

REGONIB®
REGORAFENIB

REGONIB ® (REGORAFENIB) F.C. TABLET FOR ORAL USE

Read this patient information carefully before you start taking Regonib® because it answers some common questions about Regonib®. 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 Regonib® 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 F.C. Tablet Contains: Regorafenib 40 mg.

Mechanism of action

Regonib® is a small molecule inhibitor of multiple kinases involved in normal cellular functions and in pathologic processes such as oncogenesis, tumor angiogenesis, and metastasis.

Pharmacokinetic

Absorption

Following a single 160 mg dose of Regonib® in patients with advanced solid tumors, Regonib® reaches a geometric mean peak plasma level (Cmax) of 2.5 µg/mL at a median time of 4 hours.

Distribution

Regonib® undergoes enterohepatic circulation with multiple plasma concentration peaks observed across the 24-hour dosing interval. Regonib® is highly bound (99.5%) to human plasma proteins.

Metabolism

Regonib® is metabolized by CYP3A4 and UGT1A9.

Excretion

71.0% feces (47% as parent compound, 24% as metabolites); 19.0% urine (17% as glucuronides).

INDICATION

Regonib® is prescribed for:

- Metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type, and anti-EGFR therapy.
- Locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.
- Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Dosage and administration

Recommended dose: 160 mg orally, once daily for the first 21 days of each 28-day cycle. Take Regonib® after a low-fat meal. It is not known if Regonib® is safe and effective in children less than 18 years of age.

Side effects / Adverse reactions

It should be noted that these side effects do not occur in all patient. **These are not all the possible side effects of Regonib®. For more information, ask your healthcare provider or pharmacist.**

Regonib® may cause serious side effects including:

- **Liver problem.** Regonib® can cause liver problems which can be serious and sometimes lead to death. The healthcare provider will do blood tests to check liver function before the patient start taking Regonib® and during your treatment with Regonib® to check for liver problems. Symptoms of liver problems during treatment include: yellowing of skin or the white part of eyes (jaundice), nausea or vomiting, dark "tea-colored" urine, change in sleep pattern.
- **Infection.** Regonib® may lead to a higher risk of infections especially of the urinary tract, nose, throat and lung. Regonib® may also lead to a higher risk of fungal infections of the mucous membrane, skin or the body. Infection may have symptoms such as fever, burning or pain when urinating, severe cough with or without an increase in mucus (sputum) production, unusual vaginal discharge or irritation, redness, swelling or pain in any part of the body, severe sore throat, shortness of breath.
- **Severe bleeding.** Regonib® can cause bleeding which can be serious and sometimes lead to death. Signs of bleeding during treatment with Regonib® include: vomiting blood or if your vomit looks like coffee-grounds, unusual vaginal bleeding, pink or brown urine, nose bleeds that happen often, red or black (looks like tar) stools, bruising, coughing up blood or blood clots, lightheadedness, menstrual bleeding that is heavier than normal.
- **A tear in stomach or intestinal wall (bowel perforation).** Regonib® may cause a tear in patient's stomach or intestinal wall (bowel perforation) that can be serious and sometimes lead to death. The symptoms may include: severe pain in your stomach-area (abdomen), nausea, swelling of the abdomen, vomiting, fever, dehydration, chills.
- **A skin problem called hand-foot skin reaction and severe skin rash.** Hand-foot skin reactions are common and sometimes can be severe. Patients who take Regonib® may get redness, pain, blisters, bleeding, or swelling on the palms of hands or soles of feet, or a severe rash.
- **High blood pressure.** The patient's blood pressure should be checked every week for the first 6 weeks of starting Regonib®. The patient's blood pressure should be checked regularly and any high blood pressure should be treated during treatment with Regonib®. Severe headaches, lightheadedness, or changes in vision may be the symptoms of high blood pressure.
- **Decreased blood flow to the heart and heart attack.** Emergency help is needed if the patient gets symptoms such as chest pain, shortness of breath, feel dizzy or feel like passing out.
- **A condition called Reversible Posterior Leukoencephalopathy Syndrome (RPLS).** The symptoms include: severe headaches, seizure, confusion, change in vision, or problems thinking.
- **Risk of wound healing problems.** Wounds may not heal properly during Regonib® treatment. Healthcare provider should be informed if the patient plan to have any surgery before starting or during treatment with Regonib®. Taking Regonib® should be stopped at least 2 weeks before planned surgery. Healthcare provider should tell when the patient may start taking Regonib® again after surgery.

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

The most common side effects

The most common side effects in patiens who take Regonib® include: • Pain, including stomach-area (abdomen) • Voice changes or hoarseness • Tiredness, weakness, fatigue • Increase in certain liver function test • Frequent or loose bowel movements (diarrhea) • Fever • Decreased appetite • Swelling, pain and redness of the lining in your mouth, throat, stomach and bowel (mucositis) • Weight loss • Infection.

Drug interaction

- Strong CYP3A4 inducers: Avoid strong CYP3A4 inducers.
- Strong CYP3A4 inhibitors: Avoid strong CYP3A4 inhibitors.
- BCRP substrates: Monitor patients closely for symptoms of increased exposure to BCRP substrates.
- Avoid eating grapefruit and drinking grapefruit juice and taking St. John's Wort during treatment with Regonib®. These can affect the way Regonib® works.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Regonib® may affect the way other medicines work, and other medicines may affect how Regonib® works.

Warnings

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

- have liver problems in addition to liver cancer
- have bleeding problems
- have high blood pressure
- have heart problems or chest pain
- plan to have surgery or have had a recent surgery. You should stop taking Regonib® at least 2 weeks before planned surgery.
- are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed.
- Regonib® can cause liver problems which can be serious and sometimes lead to death. Your healthcare provider will do blood tests to check your liver function before you start taking Regonib® and during your treatment with Regonib® to check for liver problems.
- Severe and sometimes fatal hepatotoxicity has occurred in clinical trials. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue Regonib® for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence.
- Regonib® can cause Infections, Hemorrhage, Gastrointestinal perforation or fistula, Dermatologic toxicity, Hypertension, Cardiac ischemia and infraction, Reversible posterior leukoencephalopathy syndrome (RPLS), Risk of impaired wound healing, Embryo-fetal toxicity.

Missed dose

If you miss a dose, take it as soon as you remember on that day. Do not take two doses on the same day to make up for a missed dose.

OVERDOSE

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

Pregnancy and lactation

- Regonib® can harm your unborn baby. Females should use effective birth control during treatment with Regonib® and for 2 months after your final dose of Regonib®. Tell your healthcare provider right away if you become pregnant during treatment with Regonib® or within 2 months after your final dose of Regonib®.
- Males with female partners who can become pregnant should use effective birth control during treatment with Regonib® and for 2 months after your final dose of Regonib®.
- It is not known if Regonib® passes into your breast milk. Do not breastfeed during treatment with Regonib® and for 2 weeks after your final dose of Regonib®.
- Instruct women of reproductive potential to immediately contact her healthcare provider if pregnancy is suspected or confirmed during or within 2 months of completing treatment with Regonib®.

Patient information

- Take Regonib® exactly as your healthcare provider tells you.
- You will usually take Regonib® 1 time a day for 21 days (3 weeks) and then stop for 7 days (1 week). This is 1 cycle of treatment. Repeat this cycle for as long as your healthcare provider tells you to.
- Swallow Regonib® tablets whole with water following a low-fat meal.
- Take Regonib® at the same time each day following a low-fat meal that contains less than 600 calories and less than 30% fat.
- Do not take Regonib® if you are allergic to Regorafenib or any of the other ingredients of this medicine.
- Driving and using machines: It is not known whether Regonib® alters the ability to drive or use machines. Do not drive or use any tools or machines if you experience treatment-related symptoms that affect your ability to concentrate and react.

Storage

- Store Regonib® tablets below 30°C.
- Keep Regonib® in the original container with the lid tightly closed. Do not put tablets in a daily or weekly pill box.
- The Regonib® bottle contains a desiccant to help keep your medicine dry. Keep the desiccant in the bottle.
- Keep the bottle of Regonib® tightly closed.
- Safely throw away (discard) any unused Regonib® tablets after 7 weeks of opening the bottle.
- Keep out of the reach of children.
- Keep away from light and moisture.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging

Bottle of 28 F.C. Tablets.

References

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/203085s011lbl.pdf

Manufactured By

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www.kimia-pharma.co