Package leaflet: Information for the patient

Inrebic 100 mg hard capsules
fedratinib

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Inrebic is and what it is used for
2. What you need to know before you take Inrebic
3. How to take Inrebic
4. Possible side effects
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1. What Inrebic is and what it is used for

What Inrebic is
Inrebic contains the active substance fedratinib. It is a type of medicine known as 'protein kinase inhibitors'.

What Inrebic is used for
Inrebic is used to treat adult patients with an enlarged spleen or with symptoms related to myelofibrosis, a rare form of blood cancer.

How Inrebic works
An enlarged spleen is one of the characteristics of myelofibrosis. Myelofibrosis is a disorder of the bone marrow, in which the marrow is replaced by scar tissue. The abnormal marrow can no longer produce enough normal blood cells and as a result the spleen becomes significantly enlarged. By blocking the action of certain enzymes (called Janus Associated Kinases), Inrebic can reduce the size of the spleen in patients with myelofibrosis and relieve symptoms such as fever, night sweats, bone pain and weight loss in patients with myelofibrosis.

2. What you need to know before you take Inrebic

Do not take Inrebic
- if you are allergic to fedratinib or any of the other ingredients of this medicine (listed in section 6).
- if you are pregnant or think you may be pregnant.

Warnings and precautions
Talk to your doctor or pharmacist before taking these capsules and during treatment, if you have any of the following signs or symptoms:

Condition affecting the brain called encephalopathy, including Wernicke's encephalopathy

- Confusion, memory loss, or difficulty thinking; loss of balance or difficulty walking.
- Eye problems such as random eye movement, double-vision, blurred vision and loss of vision.
  These maybe signs of a brain condition called encephalopathy, including Wernicke's encephalopathy which may lead to death.
  Contact your doctor immediately if you get any of these signs or symptoms.

Talk to your doctor or pharmacist during your treatment

- if you are feeling very tired, being short of breath, pale skin or fast heartbeat – these may be signs of a low red blood cell count.
- if you have unusual bleeding or bruising under the skin, longer than usual bleeding after your blood has been drawn, or bleeding from your gums – these may be signs of a low blood platelet count.
- if you have frequent or re-occurring of infections which may be a sign of a low white blood cell count.
- if you have nausea, vomiting or diarrhoea.
- if you have or ever had any kidney problems.
- if you have or ever had any liver problems.
- if you have or ever had any problems with your pancreas.
- if you have eye problems – especially an inflammation of the eye called uveitis.

The following has been observed in another similar type of medicine used for the treatment of rheumatoid arthritis: heart problems, blood clots and cancer. Talk to your doctor or pharmacist before or during treatment if you:

- are older than 65. Patients aged 65 years and older may be at increased risk of heart problems including heart attack and some types of cancer.
- have or have had heart problems.
- have or have had cancer.
- are a smoker or have smoked in the past.
- have previously had blood clots in the veins of your legs (deep vein thrombosis) or lungs (pulmonary embolism).
- get sudden shortness of breath or difficulty breathing, chest pain or pain in upper back, swelling of the leg or arm, leg pain or tenderness, or redness or discoloration in the leg or arm as these can be signs of blood clots in the veins.
- notice any new growths on the skin or changes in existing growths. Your doctor may recommend that you have regular skin examinations while taking Inrebic.

Your doctor will discuss with you if Inrebic is appropriate for you.

<u>Blood tests</u>
Before and during treatment, you will have blood tests to check your blood cell levels (red blood cells, white blood cells and platelets), and your liver and pancreatic function.

Before treatment, you will have a blood test to check your vitamin B1 level. Your doctor will also tell you to take a daily dose of 100 mg vitamin B1 supplement during treatment. Your doctor may also request additional blood tests to check your vitamin B1 level during treatment.

Your doctor may adjust the dose or stop treatment based on the results of the blood tests.

Children and adolescents
Inrebic should not be used in children or young people under 18 years of age because this medicine has not been studied in this age group.

Other medicines and Inrebic
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Inrebic can affect the way some other medicines work. Also some other medicines can affect the way Inrebic works.

The following may increase the risk of side effects with Inrebic:
- Ketoconazole, fluconazole (used to treat fungal infections);
- Fluvoxamine (used to treat depression);
- Ritonavir (used to treat HIV infections/AIDS).

The following may reduce the effectiveness of Inrebic:
- Rifampicin (used to treat tuberculosis (TB) and some other infections);
- Phenytoin (used to treat epilepsy and control fits or convulsions);
- Efavirenz (used to treat HIV infections/ AIDS).

Inrebic may affect other medicines:
- Midazolam (used to help you sleep or relieve anxiety);
- Omeprazole (used to treat stomach problems);
- Metoprolol (used to treat angina or high blood pressure);
- Metformin (used to lower blood sugar levels);
- Also simvastatin, S-mephenytoin and dextromethorphan.

Your doctor will decide if the dose needs to be changed.

Also tell your doctor if you recently had an operation or if you are going to have an operation or a procedure as Inrebic may interact with some sedatives.

Inrebic with food and drink
You should not eat grapefruit or drink grapefruit juice during your treatment with Inrebic, as they may increase the amount of the medicine that passes into your blood. Taking Inrebic with a high fat meal may reduce the likelihood of feeling sick (nausea) or being sick (vomiting). (See section 3 for more information on how to take Inrebic)

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Do not take Inrebic during pregnancy. If you are able to become pregnant, you must use effective contraception whilst taking these capsules and avoid becoming pregnant for at least one month after the last dose.

Do not breast-feed while taking Inrebic and for at least one month after the last dose as it is not known if this medicine passes into breast milk.

Driving and using machines
If you feel dizzy, do not drive or operate machines until these side effects have gone away.

Inrebic contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take Inrebic

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is 400 mg (four 100 mg capsules) taken by mouth once daily.

You will have blood tests before and while you take this medicine to monitor your progress. Your doctor will also tell you to take a daily dose of 100 mg vitamin B1 supplement during treatment (see section 2 "Blood tests").

If you get certain side effects while you are taking Inrebic (see section 4) your doctor may lower your dose or pause or stop treatment.

Taking these capsules
- swallow the capsules whole, preferably with water.
- do not open, break or chew the capsules.
- the capsules can be taken either with or without food but it is preferable to take them with food to avoid feeling or being sick (vomiting).

You should continue taking Inrebic for as long as your doctor tells you to. This is a long-term treatment.

If you take more Inrebic than you should
If you accidentally take too many Inrebic capsules or a higher dose than you should, contact your doctor or pharmacist straight away.

If you forget to take Inrebic
If you miss a dose or vomit after taking a capsule, skip the missed dose and take your next scheduled dose at your regular time the next day. Do not take a double dose to make up for a forgotten or vomited capsule.

If you stop taking Inrebic
Do not stop taking Inrebic unless your doctor tells you to.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Tell your doctor immediately if you notice any of the following symptoms which could be a sign of a serious condition which affects the brain called encephalopathy (including Wernicke's encephalopathy):
- Confusion, memory loss or difficulty thinking,
- Loss of balance or difficulty walking,
- Eye problems such as double-vision, blurred vision loss of vision or random eye movements.

Talk to your doctor if you get any other side effects. These can include:

Very common side effects (may affect more than 1 in 10 people)
- Low levels of red blood cells which may cause tiredness, shortness of breath, pale skin or a fast heartbeat *(anaemia)*.
- Reduction in blood platelets, which can make you bleed or bruise easily *(thrombocytopenia)*.
- Reduction in white blood cells (*neutropenia*), sometimes with fever. Low level of white blood cells can reduce your ability to fight off infections.
- Feeling sick *(nausea)* or being sick *(vomiting)*.
- Diarrhoea.
- Constipation.
- Bleeding.
- Urinary tract infection.
- Headache.
- Muscle spasms.
- Tiredness *(fatigue)* or weakness *(asthenia)*.
- Changes in blood test results (*alanine amino transferase increased*, *aspartate aminotransferase increased*, *increase in blood creatinine*, increase in *amylase* and *lipase* levels). These may be signs of liver, kidney or pancreas problems.

Common side effects (may affect up to 1 in 10 people)
- Dizziness.
- Increase in blood pressure (*hypertension*).
- Indigestion *(dyspepsia)*.
- Bone pain.
- Pain in limbs, hands or feet (*pain in extremity)*.
- Weight gain.
- Painful passing of urine.
- Inflammation of the eye (which causes pain and redness, vision problems or blurry vision).

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. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Inrebic

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 bottle after EXP. The expiry date refers to the last day of that month.

Keep the bottle tightly closed in order to protect from moisture.

This medicine does not require any special temperature storage conditions.

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 Inrebic contains

- The active substance is fedratinib. Each hard capsule contains fedratinib dihydrochloride monohydrate equivalent to 100 mg fedratinib.
- The other ingredients are:
  - The capsule content contains silicified microcrystalline cellulose (contains microcrystalline cellulose (E460) and silica colloidal anhydrous (E551)) and sodium stearyl fumarate (see section 2, "Inrebic contains sodium").
  - The capsule shell contains gelatin (E441), titanium dioxide (E171) and red iron oxide (E172).
  - The white printing ink is composed of shellac (E904), titanium dioxide (E171) and propylene glycol (E1520).

What Inrebic looks like and contents of the pack

- Inrebic are 21.4 -22.0 mm, reddish-brown capsules, printed with "FEDR" on the cap and "100 mg" on the body in white ink.
- The capsules are packaged in a high-density polyethylene (HDPE) bottle with a seal and polypropylene child resistant cap. Each bottle contains 120 capsules and is packed in a cardboard carton.

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