

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

INREBIC®

fedratinib capsules

Read this carefully before you start taking **INREBIC** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **INREBIC**.

Serious Warnings and Precautions

Encephalopathy including Wernicke's encephalopathy has happened in some people who took INREBIC. This is a serious disease of the brain and can lead to death.

Wernicke's encephalopathy is a neurological problem that requires emergency care. It can happen if you do not have enough vitamin B1 (thiamine) in your body. Your doctor will do a blood test to check your vitamin B1 level before starting INREBIC and during treatment. Your doctor may tell you to stop taking INREBIC and take a vitamin B1 supplement if you develop side effects during treatment. Wernicke's encephalopathy can appear suddenly. You will need treatment right away.

Get medical help right away if you experience the following signs of Wernicke's encephalopathy:

- problems with balance and movement, such as difficulty walking
- confusion, memory problems or drowsiness
- eye problems, such as double or blurred vision or eye movements that you cannot control

What is INREBIC used for?

INREBIC is a prescription medicine. It is used to treat adults with an enlarged spleen and/or associated symptoms caused by certain types of myelofibrosis. Myelofibrosis is a rare form of blood cancer.

How does INREBIC work?

INREBIC is a medicine called a Janus kinase (JAK) inhibitor. Myelofibrosis is a cancer that disrupts the blood-forming tissues in the body. It often causes an enlarged spleen. By blocking the activity of a certain type of enzymes (called Janus Associated Kinases), INREBIC can reduce the size of your spleen and improve your symptoms.

What are the ingredients in INREBIC?

Medicinal ingredients: fedratinib, as fedratinib hydrochloride

Non-medicinal ingredients: gelatin, red iron oxide, silicified microcrystalline cellulose, sodium

stearyl fumarate, titanium dioxide, white ink.

INREBIC comes in the following dosage forms:

Capsules: 100 mg

Do not use INREBIC if:

- you are allergic to fedratinib or any of the other ingredients of INREBIC.
- you are receiving treatment with ruxolitinib.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take INREBIC. Talk about any health conditions or problems you may have, including if you:

- have or have had kidney or liver problems
- smoke or have ever smoked.
- have had a blood clot, heart attack, other heart problems, or stroke
- are pregnant, think you might be pregnant, or are planning on becoming pregnant. INREBIC may harm your unborn baby. If you are able to become pregnant, use an effective birth control while taking INREBIC. Continue using birth control for at least 1 month after stopping INREBIC. Ask your healthcare professional about options of effective birth control. If you become pregnant while taking INREBIC, tell your healthcare professional right away. You and your healthcare professional will decide what is best for you and your baby.
- are breastfeeding or planning to breastfeed. It is not known if INREBIC passes into your breast milk. You should not breastfeed while taking INREBIC and for at least 1 month after your last dose. Talk to your healthcare professional about the best way to feed your baby during treatment with INREBIC.
- have any type of cancer

Other warnings you should know about:

Diarrhea, Nausea and Vomiting: INREBIC can cause diarrhea, nausea and vomiting. The most common time to start having these side effects is during the first 2 months of treatment. Taking INREBIC with a high-fat large evening meal may help to reduce nausea and vomiting. To prevent nausea and vomiting your healthcare professional may prescribe another medicine (such as ondansetron). If you have loose or liquid stools, tell your healthcare professional right away. Start taking an antidiarrheal medicine (such as loperamide) and drink more fluids.

If you experience diarrhea, nausea or vomiting that does not respond to treatment or experience rapid weight loss, contact your health care provider immediately. This may lower the thiamine levels in your body. This can result in Wernicke's encephalopathy, which is serious and can lead to death.

Anemia (low red blood cell counts) and Thrombocytopenia (low platelet counts): Low red blood cell and platelet counts are common while taking INREBIC. You may need a blood transfusion if your blood counts drop too low. Tell your doctor if you develop any bleeding or bruising during treatment with INREBIC.

Major heart problems: You may be at an even greater risk of major heart problems if you are 65 years of age or older, a smoker or were a smoker in the past, or have any heart problems.

Risk of cancer: You may be at an even greater risk of cancer if you are 65 years of age or older, a smoker or were a smoker in the past, or had other cancers before.

Fertility: It is not known if INREBIC has an effect on fertility. Talk to your doctor if this is a concern for you.

Children and adolescents: INREBIC is not for use in patients under the age of 18 years.

Driving and using machines: While using INREBIC you may feel weak, tired, dizzy, or confused. You may have blurred vision. Before driving a vehicle or using machinery wait to see how you feel after taking INREBIC.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with INREBIC:

- Some medicines for fungal infections, such as ketoconazole, fluconazole, itraconazole, voriconazole, and posaconazole;
- HIV medicines, such as ritonavir and efavirenz;
- Some high blood pressure medicines such as diltiazem and metoprolol;
- Some medicines for infections (antibiotics) such as erythromycin and rifampicin;
- Some medicines for acid reflux such as cimetidine;
- The antidepressant fluvoxamine;
- The epilepsy medicine phenytoin;
- St John's Wort (*Hypericum perforatum*) an herbal product used to treat depression and other conditions;
- The anti-anxiety medicine midazolam;
- Some medicines used to treat gastroesophageal reflux disease (conditions where there is too much acid in the stomach) such as omeprazole;
- Products or juices containing grapefruit. Avoid eating or drinking any products or juices containing grapefruit while taking INREBIC.
- Some medicines used to lower blood glucose such as metformin. If you take these medicines you may need blood sugar levels to be monitored regularly.

How to take INREBIC:

- Take INREBIC exactly as your healthcare professional tells you. Check with your healthcare professional if you are not sure.
- Your healthcare professional will tell you how many INREBIC capsules to take.
- Take INREBIC with or without food. Taking INREBIC with a high-fat large evening meal may help to reduce nausea and vomiting. Examples of foods that are high in fat include salmon, eggs, cheese, beef, lamb and pork.
- Swallow the capsules whole. Do not open, break, or chew your capsules.
- Do not change your dose or stop taking INREBIC unless your healthcare professional tells you.

Usual dose: 400 mg (four 100 mg capsules) once a day.

Your healthcare professional may interrupt or change your dose or tell you to stop taking INREBIC. This may happen if you:

- have problems with your kidneys.
- experience certain side effects while taking INREBIC.
- are taking medicines that may interact with INREBIC.

Overdose:

If you think you, or a person you are caring for, have taken too much INREBIC, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of INREBIC, skip the dose. Take your next dose at the regular time. Do NOT take 2 doses of INREBIC at the same time to make up for the missed dose.

What are possible side effects from using INREBIC?

These are not all the possible side effects you may have when taking INREBIC. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Headache
- Dizziness
- Constipation
- Muscle spasms
- Itch

INREBIC can cause abnormal blood test results. This includes low blood cell counts and increased creatinine, bilirubin, lipase, amylase and liver enzymes. Your healthcare professional will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Anemia (low red blood cells): Being short of breath, feeling very tired, loss of energy, weakness, irregular heartbeats, pale complexion		✓	
Thrombocytopenia (low blood platelets): Bruising or bleeding for longer than usual if you hurt yourself, fatigue, weakness		✓	
Neutropenia (low white blood cells): infections, fatigue, fever, aches, pains and flu-like symptoms		✓	
Diarrhea : severe, at least 3 loose or liquid bowel movements in a day		✓	
Nausea : feeling the need to vomit		✓	

Vomiting		✓	
COMMON			
Acute kidney injury (severe kidney problems): very little or no urine, swelling in legs and ankles, puffiness in your face and hands, confusion, fatigue, weakness, nausea, weight gain (from retaining fluids)		✓	
Atrial fibrillation (abnormal heart rhythm which is rapid and irregular): chest discomfort with unpleasant awareness of your heartbeat, fatigue, weakness, dizziness, shortness of breath, feeling faint		✓	
Encephalopathy including Wernicke's encephalopathy (a rare neurological disorder): confusion, memory impairment or drowsiness, problems with balance such as difficulty walking, eye problems such as double or blurred vision, eye movements that you cannot control			✓
Heart failure (heart does not pump blood as well as it should): shortness of breath, fatigue, weakness, swelling in legs, ankles and feet, cough, fluid retention, lack of appetite, rapid or irregular heartbeat, reduced ability to exercise		✓	
Pleural effusion (fluid around the lungs): shortness of breath, dry cough, chest pain		✓	
Pneumonia (infection of the lungs): cough with or without mucus, fatigue, fever, sweating and shaking, chills, confusion, shortness of breath, difficult and painful breathing		✓	
Sepsis (infection of the blood): fever, dizziness, chills, little or no urine, low blood pressure, palpitations, fast heart rate, rapid breathing, high or very low body temperature		✓	
Urinary tract infection (infection in urinary system including kidneys, ureters, bladder and urethra): frequent urination, pain or burning sensation while urinating, blood in the urine, pain in the pelvis, strong smelling urine, cloudy urine		✓	

UNCOMMON			
Cardiogenic shock (heart is not able to pump enough blood to the organs of the body): rapid breathing and severe shortness of breath, fast heartbeat, bulging of large veins in neck, loss of consciousness, swelling of feet, sweating, pale skin, cold hands or feet			✓
Cardiorespiratory arrest (heart has stopped pumping blood caused by an electrical problem in the heart): chest pain, rapid or irregular heartbeats, shortness of breath, fainting, dizziness, sudden collapse, unresponsive to touch or sound, not breathing or making gasping sounds			✓
Hemorrhagic shock (shock from severe blood loss): rapid breathing and heartbeat, dizziness, confusion, weakness, low blood pressure, less urine than normal, cold clammy skin, thirst and dry mouth, blue lips and fingertips			✓
Hemorrhagic stroke (bleeding in the brain): loss of consciousness, nausea, vomiting, severe sudden headache, seizures, weakness on one side of body (face, leg or arm), dizziness, difficulty speaking or understanding others			✓
Pancreatitis (inflammation of the pancreas): upper abdominal pain, nausea, vomiting, fever, rapid pulse, tenderness when touching abdomen		✓	
Rectal hemorrhage (bleeding from the rectum): abdominal pain, blood in your bowel movement, dizziness, fainting, rectal pain		✓	
UNKNOWN			
Cancers including lymphoma (cancer of the lymphatic system)		✓	
Deep vein thrombosis (blood clot in the deep veins of the leg or arm): swelling, pain, arm or leg may be warm to the touch and may appear red which is caused by a blood clot in the deep veins of the leg or arm		✓	
Pulmonary embolism (blood clot in the lung): chest pain that may increase with deep breathing, cough, coughing up bloody sputum, shortness of breath		✓	
Myocardial infarction (heart attack): pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen,		✓	

shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat.			
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If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store at room temperature (between 15 to 30°C).
- **Keep out of reach and sight of children.**

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of any unused INREBIC.

If you want more information about INREBIC:

- Talk to your healthcare professional
 - Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website <https://www.bms.com/ca/en>, or by contacting the sponsor, Bristol-Myers Squibb Canada at: 1-866-463-6267.
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