

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrIMBRUVICA® ibrutinib capsules

Read this carefully before you start taking **IMBRUVICA®** 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 **IMBRUVICA®**.

Serious Warnings and Precautions

IMBRUVICA® should only be prescribed by a qualified doctor who is experienced in the use of anti-cancer drugs.

- Major bleeding events, some fatal, have been reported (see below)
- **IMBRUVICA®** should not be used in patients with moderate or severe liver problems (see below)
- **IMBRUVICA®** should not be used with certain medications that can increase the blood level of **IMBRUVICA®** (see below)

What is **IMBRUVICA®** used for?

IMBRUVICA® is used in adults to treat:

- **Chronic Lymphocytic Leukemia (CLL):** **IMBRUVICA®** is used to treat patients with active CLL who have not had prior therapy, including those with a deletion of the “TP53” gene (17p deletion). **IMBRUVICA®** is also used to treat patients with CLL who have received at least one prior therapy, including those with a deletion of the “TP53” gene (17p deletion). In patients with CLL who have received at least one prior therapy, **IMBRUVICA®** can also be used in combination with bendamustine and rituximab.
- **Mantle Cell Lymphoma (MCL):** **IMBRUVICA®** is used to treat patients with previously treated MCL when the disease has come back or has not responded to treatment.
- **Marginal Zone Lymphoma (MZL):** **IMBRUVICA®** is used to treat patients with MZL. It is used when they need medicine and not radiation or surgery. It is for patients who have received at least one prior therapy including an antibody that acts against their cancer. This antibody is called anti-CD20.
- **Waldenström’s Macroglobulinemia (WM):** **IMBRUVICA®** is used to treat patients with WM, and can also be used in combination with rituximab.
- **Chronic graft versus host disease (cGVHD):** **IMBRUVICA®** is used to treat patients with cGVHD after failure of first line corticosteroid therapy and who need additional therapy.
- It is not known if **IMBRUVICA®** is safe and effective in children under the age of 18 years.

How does **IMBRUVICA®** work?

IMBRUVICA® blocks a specific protein in the body that helps cancer cells live and grow. This protein is called “Bruton’s Tyrosine Kinase.” By blocking this protein, **IMBRUVICA®** may help kill and reduce the number of cancer cells and slow the spread of the cancer.

What are the ingredients in IMBRUVICA®?

Medicinal ingredient: ibrutinib

Non-medicinal ingredients: croscarmellose sodium, gelatin, iron oxide black (E172), magnesium stearate, microcrystalline cellulose, shellac, sodium lauryl sulfate, titanium dioxide (E171)

IMBRUVICA® comes in the following dosage form:

140 mg capsules

Do not use IMBRUVICA® if you:

- are allergic to ibrutinib or any of the other ingredients in this medicine or components of the container. If you are not sure about this, talk to your healthcare professional before taking IMBRUVICA®.

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

- have ever had unusual bleeding or bruising or are on any medicines that increase your risk of bleeding such as aspirin, anti-inflammatories (e.g., ibuprofen, naproxen, and others), warfarin, heparin, other medications to prevent or treat blood clots (e.g., dabigatran, rivaroxaban, apixaban), or any supplements that increase your risk of bleeding such as fish oil, flaxseed, or vitamin E. You should not take warfarin (COUMADIN®) with IMBRUVICA®.
- have or have had heart rhythm problems or severe heart failure, or if you have any of the following: fast and irregular heartbeat, lightheadedness, dizziness, shortness of breath, chest discomfort, swollen legs, or if you faint.
- have or are at increased risk of heart disease.
- have high blood pressure.
- have any infection.
- have had a hepatitis B infection (a viral infection of the liver).
- have liver or kidney problems. You should not take this drug if you have certain liver problems.
- are planning to have any medical, surgical or dental procedure. Your doctor may ask you to stop taking IMBRUVICA® for a short time.

Other warnings you should know about:

Tests and check-ups before and during treatment

Laboratory tests may show that your blood count contains more white blood cells (called “lymphocytes”) in the first few weeks of treatment. This is expected and may last for a few weeks or months. This does not necessarily mean that your blood cancer is getting worse. Your doctor will check your blood counts before and during the treatment. In rare cases your doctor may need to give you another medicine. Talk to your doctor about what your test results mean.

Your doctor will check your blood pressure during treatment and may need to give you another medicine to control your blood pressure.

Children and adolescents

IMBRUVICA® is not recommended for use in patients under 18 years of age.

IMBRUVICA® with food

Do not take IMBRUVICA® with grapefruit or Seville oranges; this includes eating them, drinking the juice, or taking supplements that might contain them. These products may increase the amount of IMBRUVICA® in your blood.

Pregnancy, breast-feeding and fertility

IMBRUVICA® can harm your unborn baby.

Do not get pregnant while you are taking IMBRUVICA®. Women of childbearing age must use two forms of effective birth control methods together during treatment with IMBRUVICA® and for at least 3 months after the last dose of IMBRUVICA®.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your healthcare professional for advice before taking IMBRUVICA®.

Tell your healthcare professional immediately if you become pregnant.

Do not breast-feed while you are taking IMBRUVICA®.

Do not father a child while taking IMBRUVICA® and for 3 months after stopping treatment. Use condoms and do not donate sperm during treatment and for 3 months after your treatment has finished. If you plan to father a child, talk to your healthcare professional before taking IMBRUVICA®.

Men who are sexually active with a pregnant woman must use a condom during and for 3 months after treatment with IMBRUVICA®.

Driving and using machines

You may feel tired or dizzy after taking IMBRUVICA®, which may affect your ability to drive and use tools or machines. Ask your healthcare professional about your ability to drive and use tools or machines while taking IMBRUVICA®.

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

The following may interact with IMBRUVICA®:

- medicines called antibiotics used to treat bacterial infections (clarithromycin, ciprofloxacin, erythromycin, rifampin).
- medicines for fungal infections (ketoconazole, itraconazole, fluconazole, voriconazole, posaconazole).
- medicines for HIV infection (indinavir, nelfinavir, ritonavir, saquinavir, atazanavir, darunavir/ritonavir, cobicistat, fosamprenavir).
- medicine to prevent nausea and vomiting (aprepitant).
- medicines called kinase inhibitors for treatment of other cancers (crizotinib, imatinib).
- medicines called calcium channel blockers for high blood pressure, chest pain, irregular heartbeat and other heart problems (diltiazem, verapamil).
- medicines called statins to treat high cholesterol (rosuvastatin).

- heart medicines/anti-arrhythmics (amiodarone, dronedarone).
- medicines that may increase your risk of bleeding, including:
 - aspirin and anti-inflammatories such as ibuprofen or naproxen.
 - blood thinners such as warfarin, heparin or other medicines for blood clots such as dabigatran, rivaroxaban, apixaban.
 - supplements such as fish oil, vitamin E and flaxseed.
- medicines used to prevent seizures or to treat epilepsy or medicines used to treat a painful condition of the face called trigeminal neuralgia (carbamazepine and phenytoin).
- an herbal medicine used for depression (St. John's Wort).

If you are taking digoxin, a medicine used for heart problems, or methotrexate, a medicine used to treat other cancers or to reduce the activity of the immune system (e.g., for rheumatoid arthritis or psoriasis), it should be taken at least 6 hours before or after IMBRUVICA®.

How to take IMBRUVICA®:

Take IMBRUVICA® as prescribed by your doctor.

Swallow IMBRUVICA® capsules whole, with a glass of water. Do not open, break or chew them. Do not take IMBRUVICA® with grapefruit juice.

Take IMBRUVICA® at about the same time each day.

Drink plenty of fluids to stay hydrated while taking IMBRUVICA®. This will help your kidneys continue to function properly.

Usual adult dose:

- **Chronic Lymphocytic Leukemia (CLL):** 3 capsules once a day
- **Waldenström's Macroglobulinemia (WM):** 3 capsules once a day
- **Chronic graft versus host disease (cGVHD):** 3 capsules once a day
- **Mantle Cell Lymphoma (MCL):** 4 capsules once a day
- **Marginal Zone Lymphoma (MZL):** 4 capsules once a day

Your doctor may decide that you should take a lower dose if you get side effects.

For the treatment of CLL and WM, your doctor may prescribe IMBRUVICA® alone or in combination with other treatments.

IMBRUVICA® is given as a continuous daily therapy, which means you need to take it every day until your disease no longer responds to treatment or you experience unacceptable side effects. Do not change your dose or stop taking IMBRUVICA® unless your doctor tells you to.

Overdose:

If you think you have taken too much IMBRUVICA® contact your 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 IMBRUVICA® take it as soon as you remember on the same day. Take your next dose of IMBRUVICA® at your regular time on the next day. Do not take extra capsules of IMBRUVICA® to make up for a missed dose. Call your healthcare professional if you are not sure of what to do.

What are possible side effects from using IMBRUVICA®?

These are not all the possible side effects you may feel when taking IMBRUVICA®. If you experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.

- Lymphocytosis: An increase in the number of white blood cells, specifically lymphocytes may be reported in your blood test results (see **Other warnings you should know about**). This increase in white blood cells is expected in the first few weeks of treatment and may last for 3 or more months. Uncommonly, this increase may be severe, causing cells to clump together (leukostasis). Your doctor will monitor your blood counts. Talk to your doctor about what your blood test results mean.
- Diarrhea: You may experience an increase in frequency of loose or watery stools. If you have diarrhea that lasts for more than a week, your doctor may need to give you treatment to manage your diarrhea such as a fluid and salt replacement or another medicine. Contact your doctor if your diarrhea persists.
- Viral, bacterial, or fungal infections: Infections can be serious and may lead to death. Contact your doctor if you have fever, chills, weakness, confusion, body aches, cold or flu symptoms, feel tired or feel short of breath, or have any other signs or symptoms of a possible infection.
- Fatigue, lack of energy, anxiety, difficulty falling or staying asleep
- Common cold
- Muscle aches, muscle spasm, joint aches
- Headache, dizziness, weakness
- Rash, skin infection
- Inflammation of the fatty tissue underneath the skin
- Nausea, sore mouth, constipation, vomiting, loss of appetite, stomach pain, indigestion
- Nail changes such as brittle fingernails and toenails
- Types of skin cancers that are not melanoma, most frequently squamous cell or basal cell skin cancers, have happened in people taking IMBRUVICA®. Other cancers that are not skin cancer have happened in people taking IMBRUVICA®. Talk to your doctor about monitoring for new skin cancer symptoms.

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			
Low red blood cells (anemia) (symptoms like fatigue, loss of energy, weakness, shortness of breath)		✓	

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	
Low white blood cells (neutrophils) (symptoms like fever, chills or sweating or any signs of infection)		✓	
Low platelets (symptoms like bruising, bleeding, fatigue and weakness)		✓	
Edema (symptoms like swollen hands, ankles or feet)		✓	
Being short of breath		✓	
Fever		✓	
Pneumonia (symptoms like cough with or without mucus, fever, chills, shortness of breath)		✓	
Sinus infection (symptoms like thick, yellow, smelly discharge from the nose, pressure or pain in the face and eyes, congestion, headache)		✓	
Bruising, small red or purple spots caused by bleeding under the skin	✓		
High blood pressure		✓	
Common			
Urinary tract infection (symptoms like pain or burning when urinating, bloody or cloudy urine, foul smelling urine)		✓	
Hypokalemia (low potassium levels in the blood): muscle weakness, cramps, twitches, abnormal heart rhythms		✓	
Nose bleeds		✓	
Severe diarrhea (symptoms like increased number of bowel movements, watery or bloody stool, stomach pain and/or cramps)		✓	

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	
Irregular heart rhythm (arrhythmic symptoms may include palpitations, lightheadedness, dizziness, shortness of breath, chest discomfort, fainting)		✓	
Blurred vision	✓		
Infection of the blood (symptoms like feeling dizzy or faint, confusion or disorientation, diarrhea, nausea, vomiting, slurred speech, severe muscle pain)			✓
Serious bleeding problems sometimes resulting in death (symptoms like blood in your stool or urine, bleeding that lasts for a long time or that you cannot control, coughing up blood or blood clots, increased bruising, feel dizzy or weak, confusion, change in your speech, or a headache that lasts a long time)			✓
Inflammation within the lungs (symptoms like difficulty breathing or persistent cough)		✓	
Tumour Lysis Syndrome (symptoms like nausea, vomiting, decreased urination, irregular heartbeat, confusion, delirium, seizures)			✓
Elevated levels of uric acid in the blood (symptoms like red, warm, and swollen joints, flank pain, blood in urine, or cream-colored skin nodules)		✓	
Peripheral Neuropathy (symptoms like weakness, numbness, tingling, pain, or hot or cold sensation in hands, feet or other parts of the body)	✓		

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	
Uncommon			
Severe increase in white blood cells (symptoms like fever, fainting, bleeding, bruising, weight loss, general pain, lack of energy, severe headache, trouble walking)		✓	
Severe allergic reactions (symptoms like swelling of face, eyes, lips, mouth, or tongue, trouble swallowing or breathing, itchy skin rash, redness of the skin)			✓
Severe rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome)			✓
Kidney failure (symptoms like decreased or lack of urination, nausea, swelling of the ankles, legs or feet, fatigue, confusion, seizures or coma)			✓
Severe liver problems (symptoms like nausea, loss of appetite, fatigue, yellowing of your skin and eyes (jaundice), pain in your upper right abdomen, dark urine, disorientation, or confusion)		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect® (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, Ontario
K1A 0K9Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect® (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>).

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 IMBRUVICA® at room temperature between 15°C and 30°C.

Keep out of the reach and sight of children.

If you want more information about IMBRUVICA®:

- Talk to your healthcare professional.
- For questions or concerns, contact the manufacturer, Janssen Inc. (www.janssen.com/canada).
- 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.html>), the manufacturer's website www.janssen.com/canada, or by contacting the manufacturer at: 1-800-567-3331 or 1-800-387-8781.

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