

Package leaflet: Information for the patient

IMBRUVICA® 140 mg hard capsules

ibrutinib

Ibrutinib capsules

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

What is in this leaflet

- What IMBRUVICA is and what it is used for
- What you need to know before you take IMBRUVICA
- How to take IMBRUVICA
- Possible side effects
- How to store IMBRUVICA
- Contents of the pack and other information

1. What IMBRUVICA is and what it is used for

What IMBRUVICA is

IMBRUVICA is an anticancer medicine that contains the active substance ibrutinib. It belongs to a class of medicines called protein kinase inhibitors.

What IMBRUVICA is used for

It is used to treat the following blood cancers in adults:

- Mantle cell lymphoma (MCL), a type of cancer affecting the lymph nodes, when the disease has come back or has not responded to treatment.
- Chronic lymphocytic leukaemia (CLL) a type of cancer affecting white blood cells called lymphocytes that also involves the lymph nodes. IMBRUVICA is used in patients who have not previously been treated for CLL or when the disease has come back or has not responded to treatment.
- Waldenström’s macroglobulinaemia (WM), a type of cancer affecting white blood cells called lymphocytes. It is used in patients who have not previously been treated for WM or when the disease has come back or has not responded to treatment or in patients for whom chemotherapy given together with an antibody is not a suitable therapy.

How IMBRUVICA works

In MCL, CLL and WM, IMBRUVICA works by blocking Bruton's tyrosine kinase, a protein in the body that helps these cancer cells grow and survive. By blocking this protein, IMBRUVICA helps kill and reduce the number of cancer cells. It also slows down the worsening of the cancer.

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2. What you need to know before you take IMBRUVICA

Do not take IMBRUVICA

- if you are allergic to ibrutinib or any of the other ingredients of this medicine (listed in section 6)
- if you are taking a herbal medicine called St. John’s Wort, used for depression. If you are not sure about this, talk to your doctor, pharmacist or nurse before taking this medicine.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking IMBRUVICA:

- if you have ever had unusual bruising or bleeding or are on any medicines or supplements that increase your risk of bleeding (see section “**Other medicines and IMBRUVICA**”)
- if you have irregular heart beat or have a history of irregular heart beat or severe heart failure, or if you feel any of the following: shortness of breath, weakness, dizziness, light-headedness, fainting or near fainting, chest pain or swollen legs
- if you have liver or kidney problems
- if you have high blood pressure
- if you have recently had any surgery, especially if this might affect how you absorb food or medicines from your stomach or gut
- if you are planning to have any surgery– your doctor may ask you to stop taking IMBRUVICA for a short time (3 to 7 days) before and after your surgery.
- if you have ever had or might now have a hepatitis B infection. This is because IMBRUVICA could cause hepatitis B to become active again. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before taking this medicine.

When taking IMBRUVICA, tell your doctor immediately if you notice or someone notices in you: memory loss, trouble thinking, difficulty walking or sight loss – these may be due to a very rare but serious brain infection which can be fatal (Progressive Multifocal Leukoencephalopathy or PML).

Tell your doctor immediately if you notice or someone notices in you: sudden numbness or weakness in the limbs (especially on one side of the body), sudden confusion, trouble speaking or understanding speech, sight loss, difficulty walking, loss of balance or lack of coordination, sudden severe headache with no known cause. These may be signs and symptoms of stroke.

Tests and check-ups before and during treatment

Tumour lysis syndrome (TLS): Unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells have happened during treatment of cancer and sometimes even without treatment. This may lead to changes in kidney function, abnormal heartbeat, or seizures. Your doctor or another healthcare provider may do blood tests to check for TLS.

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

Children and adolescents

IMBRUVICA should not be used in children and adolescents. This is because it has not been studied in these age groups.

Other medicines and IMBRUVICA

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, herbal medicines and supplements. This is because IMBRUVICA may affect the way some other medicines work. Also some other medicines can affect the way IMBRUVICA works.

IMBRUVICA may make you bleed more easily. This means you should tell your doctor if you take other medicines that increase your risk of bleeding. This includes:

- acetyl salicylic acid and non-steroidal anti-inflammatories (NSAIDs) such as ibuprofen or naproxen
- blood thinners such as warfarin, heparin or other medicines for blood clots
- supplements that may increase your risk of bleeding such as fish oil, vitamin E or flaxseed.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before taking IMBRUVICA.

Also tell your doctor if you take any of the following medicines – The effects of IMBRUVICA or other medicines may be influenced if you take IMBRUVICA together with any of the following medicines:

- medicines called antibiotics to treat bacterial infections – clarithromycin, telithromycin, ciprofloxacin, erythromycin or rifampicin
- medicines for fungal infections – posaconazole, ketoconazole, itraconazole, fluconazole or voriconazole
- medicines for HIV infection – ritonavir, cobicistat, indinavir, nelfinavir, saquinavir, amprenavir, atazanavir, or fosamprenavir
- medicines to prevent nausea and vomiting associated with chemotherapy - aprepitant
- medicines for depression - nefazodon
- medicines called kinase inhibitors for treatment of other cancers – crizotinib or imatinib
- medicines called calcium channel blockers for high blood pressure or chest pain – diltiazem or verapamil
- medicines called statins to treat high cholesterol - rosuvastatin
- heart medicines/anti-arrhythmics – amiodarone or dronedarone
- medicines to prevent seizures or to treat epilepsy, or medicines to treat a painful condition of the face called trigeminal neuralgia – carbamazepine or phenytoin.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before taking IMBRUVICA.

If you are taking digoxin, a medicine used for heart problems, or methotrexate, a medicine used to treat other cancers and 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.

IMBRUVICA with food

Do not take IMBRUVICA with grapefruit or Seville oranges (bitter oranges) – this includes eating them, drinking the juice or taking a supplement that might contain them. This is because it can increase the amount of IMBRUVICA in your blood.

Pregnancy and breast-feeding

Do not get pregnant while you are taking this medicine. IMBRUVICA should not be used during pregnancy. There is no information about the safety of IMBRUVICA in pregnant women.

Women of childbearing age must use a highly effective method of birth control during and up to three months after receiving IMBRUVICA, to avoid becoming pregnant while being treated with IMBRUVICA. If using hormonal contraceptives such as birth control pills or devices, a barrier method of contraception (e.g. condoms) must also be used.

- Tell your doctor immediately if you become pregnant.
- Do not breast-feed while you are taking this medicine.

Driving and using machines

You may feel tired or dizzy after taking IMBRUVICA, which may affect your ability to drive or use any tools or machines.

IMBRUVICA contains sodium

IMBRUVICA contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

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3. How to take IMBRUVICA

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

How much to take

Mantle cell lymphoma (MCL)

The recommended dose of IMBRUVICA is four capsules (560 mg) once a day.

Chronic lymphocytic leukaemia (CLL)/Waldenström’s macroglobulinaemia (WM)
The recommended dose of IMBRUVICA is three capsules (420 mg) once a day.

Your doctor may adjust your dose.

Taking this medicine

- Take the capsules orally (by mouth) with a glass of water.
- Take the capsules about the same time each day.
- Swallow the capsules whole. Do not open, break or chew them.

If you take more IMBRUVICA than you should

If you take more IMBRUVICA than you should, talk to a doctor or go to a hospital straight away. Take the capsules and this leaflet with you.

If you forget to take IMBRUVICA

- If you miss a dose, it can be taken as soon as possible on the same day with a return to the normal schedule the following day.
- Do not take a double dose to make up for a forgotten dose.
- If you are not sure, talk to your doctor, pharmacist or nurse about when to take your next dose.

If you stop taking IMBRUVICA

Do not stop taking this medicine unless your doctor tells you.

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. The following side effects may happen with this medicine:

Stop taking IMBRUVICA and tell a doctor straight away if you notice any of the following side effects:

itchy bumpy rash, difficulty breathing, swelling of your face, lips, tongue or throat – you may be having an allergic reaction to the medicine.

Tell a doctor straight away if you notice any of the following side effects:

Very common (may affect more than 1 in 10 people)

- fever, chills, body aches, feeling tired, cold or flu symptoms, being short of breath – these could be signs of an infection (viral, bacterial or fungal). These could include infections of the nose, sinus or throat (upper respiratory tract infection), or lung, or skin.
- bruising or increased tendency of bruising.

- mouth sores
- headache
- constipation
- feeling or being sick (nausea or vomiting)
- diarrhoea, your doctor may need to give you a fluid and salt replacement or another medicine
- skin rash
- painful arms or legs
- back pain or joint pain
- muscle cramps, aches or spasms
- low number of cells that help blood clot (platelets), very low number of white blood cells – shown in blood tests
- swollen hands, ankles or feet
- high blood pressure.

Common (may affect up to 1 in 10 people)

- severe infections throughout the body (sepsis)
- infections of the urinary tract
- nose bleeds, small red or purple spots caused by bleeding under the skin
- blood in your stomach, gut, stools or urine, heavier periods, or bleeding that you cannot stop from an injury
- fast heart rate, missed heart beats, weak or uneven pulse, lightheadedness, shortness of breath, chest discomfort (symptoms of heart rhythm problems)
- an increase in the number or proportion of white blood cells shown in blood tests
- low white blood cell counts with fever (febrile neutropenia)
- unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells have happened during treatment of cancer and sometimes even without treatment (tumour lysis syndrome)
- non-melanoma skin cancer, most frequently squamous cell and basal cell skin cancer
- feeling dizzy
- blurred vision
- redness of the skin
- high level of “uric acid” in the blood (shown in blood tests), which may cause gout
- inflammation within the lungs that may lead to permanent damage
- breaking of the nails
- weakness, numbness, tingling or pain in your hands or feet or other parts of the body (peripheral neuropathy).

Uncommon (may affect up to 1 in 100 people)

- liver failure
- severe fungal infections
- confusion, headache with slurred speech or feeling faint – these could be signs of serious internal bleeding in your brain
- allergic reaction, sometimes severe, that may include a swollen face, lip, mouth, tongue or throat, difficulty swallowing or breathing, itchy rash (hives)
- inflammation of the fatty tissue underneath the skin.
- temporary episode of neurologic dysfunction caused by loss of blood flow, stroke.

Rare (may affect up to 1 in 1,000 people)

- severely increased white blood cell count that may cause cells to clump together.

Not known (frequency cannot be estimated from available data)

- severe rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

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5. How to store IMBRUVICA

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

Do not store above 30°C.

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.

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6. Contents of the pack and other information

What IMBRUVICA contains

- The active substance is ibrutinib. Each hard capsule contains 140 mg of ibrutinib.
- The other ingredients are:
 - capsule content: croscarmellose sodium, magnesium stearate, microcrystalline cellulose and sodium lauril sulfate (E487)
 - capsule shell: gelatin and titanium dioxide (E171)
 - printing ink: shellac, black iron oxide (E172), and propylene glycol (E1520).

What IMBRUVICA looks like and contents of the pack

IMBRUVICA are white opaque, hard capsules marked with “ibr 140 mg” in black ink on one side. The capsules are provided in a plastic bottle with a child resistant polypropylene closure. Each bottle contains either 90 or 120 capsules. Each pack contains one bottle.

Marketing Authorization Holder:

Janssen Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium

Manufacturer:

Cilag AG, Hochstrasse 201, CH-8205 Schaffhausen Switzerland

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To contact us, go to www.janssen.com/contact-us

<p>THIS IS A MEDICAMENT</p> <ul style="list-style-type: none">- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you. - Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament. The doctor and the pharmacist are the experts in medicines, their benefits and risks. - Do not by yourself interrupt the period of treatment prescribed. - Do not repeat the same prescription without consulting your doctor. - Keep all medicaments out of the reach of children
<p>Council of Arab Health Ministers, Union of Arab Pharmacists</p>