Package leaflet: Information for the patient

Imbruvica® 280 mg film-coated tablets

(ibrutinib)

xxxxxxxxxx-xxx-xx

The name of your medicine is Imbruvica 280 mg film-coated tablets but will be referred to as Imbruvica throughout this leaflet.
Please note that the leaflet also contains information about other strengths.

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

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.

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 problems, including if you ever had or now have a hepatitis B infection (a liver infection)
- 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 kidney problems.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before or while taking this medicine (see section **"Possible side effects"**).

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.

Tell your doctor immediately if you develop left upper belly (abdominal) pain, pain below the left rib cage or at the tip of your left shoulder (these may be symptoms of rupture of the spleen) after you stop taking Imbruvica.

<u>Effects on the heart</u>
Treatment with Imbruvica may affect the heart, especially if you already have heart diseases such as rhythm problems, heart failure, high blood pressure, have diabetes or are of advanced age. The effects may be severe and could cause death, including sometimes sudden death. Your heart function will be checked before and during treatment with Imbruvica. Tell your doctor immediately if you feel breathless, have difficulty breathing when lying down, swelling of the feet, ankles or legs and weakness/tiredness during treatment with Imbruvica – these may be signs of heart failure.

You may experience viral, bacterial, or fungal infections during treatment with Imbruvica.
Contact your doctor if you have fever, chills, weakness, confusion, body aches, cold or flu symptoms, feel tired or feel short of breath, yellowing of the skin or eyes (jaundice).
These could be signs of an infection.

<u>Haemophagocytic lymphohistiocytosis</u>
There have been rare reports of excessive activation of white blood cells associated
with inflammation (haemophagocytic lymphohistiocytosis), which can be fatal if not diagnosed and treated early. If you experience multiple symptoms such as fever, swollen glands, bruising, or skin rash, contact your doctor immediately.

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.

Events related to the liver: Your doctor will do some blood tests to check whether your liver is working properly or that you do not have a liver infection, known as viral hepatitis, or whether hepatitis B has become active again, which could be fatal.

Children and adolescents
Imbruvica should not be used in children and adolescents.

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 - nefazodone
- 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.
- 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 lactose
Imbruvica contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

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

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 560 mg once a day.

Chronic lymphocytic leukaemia (CLL)/Waldenström's macroglobulinaemia (WM)
The recommended dose of Imbruvica is 420 mg once a day.

Your doctor may adjust your dose.

Taking this medicine
- Take the tablets orally (by mouth) with a glass of water.
- Take the tablets about the same time each day.
- Swallow the tablets whole. Do not 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 tablets 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
- feeling dizzy
- headache
- constipation
- feeling or being sick (nausea or vomiting)
- indigestion
- 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
- an increase in the number or proportion of white blood cells shown in blood tests
- swollen hands, ankles or feet
- high blood pressure
- increased level of "creatinine" in the blood.

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
- heart failure
- missed heart beats, weak or uneven pulse, lightheadedness, shortness of breath, chest discomfort (symptoms of heart rhythm problems)
- low white blood cell counts with fever (febrile neutropenia)
- non-melanoma skin cancer, most frequently squamous cell and basal cell skin cancer
- blurred vision
- redness of the skin
- inflammation within the lungs that may lead to permanent damage
- high level of "uric acid" in the blood (shown in blood tests), which may cause gout
- breaking of the nails
- sudden kidney damage
- 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, including events with fatal outcome
- severe fungal infections
- confusion, headache with slurred speech or feeling faint – these could be signs of serious internal bleeding in your brain
- 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)
- 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 decreased brain or nerve function caused by loss of blood flow, stroke
- bleeding in the eye (in some cases associated with loss of vision)
- cardiac arrest (heart stops beating)
- abnormally fast heart beat
- painful skin ulceration (pyoderma gangrenosum) or red, raised painful patches on the skin, fever and an increase in white blood cells (these may be signs of acute febrile neutrophilic dermatosis or Sweet's syndrome)
- small, red bump on the skin that may bleed easily (pyogenic granuloma).

Rare (may affect up to 1 in 1,000 people)
- severely increased white blood cell count that may cause cells to clump together
- 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. You can also report side effects directly via the Yellow Card Scheme at: 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 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 after EXP.
The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

If this medicine becomes discoloured or shows any other signs of deterioration, please contact your pharmacist who will advise you on what to do.

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 Imbruvica contains
- The active substance is ibrutinib.
– Imbruvica 280 mg film-coated tablets: Each tablet contains 280 mg of ibrutinib.
- The other ingredients are:
- Tablet core: colloidal anhydrous silica, croscarmellose sodium, lactose monohydrate (see section 2 **"Imbruvica contains lactose"**), magnesium stearate, microcrystalline cellulose, povidone, sodium lauril sulfate (E487).
- Tablet film-coat: polyvinyl alcohol, macrogol, talc, titanium dioxide (E171).

Imbruvica 280 mg film-coated tablets also contain black iron oxide (E172) and red iron oxide (E172).

What Imbruvica looks like and contents of the pack
IMBRUVICA 280 mg film-coated tablets
Purple oblong (15 mm in length and 7 mm in width), written with "ibr" on one side and "280" on the other side. Each 28 day carton contains 28 film-coated tablets in 2 cardboard wallets of 14 film-coated tablets each.

Product Licence Holder and Manufacturer
Procured from within the EU by the Product Licence holder Orifarm UK Ltd., 236 Jubilee House, 3 The Drive, Great Warley, Brentwood, CM13 3FR, UK

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Imbruvica 280 mg film-coated tablets
PLGB 45985/0813

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Leaflet revision date: 13/02/2024

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