Ibrutinib Fact Sheet

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Generic Name: Ibrutinib
Trade Name(s): Imbruvica

Drug Type:
Ibrutinib is a targeted therapy that inhibits the function of Bruton's tyrosine kinase (BTK).

What Conditions Are Treated by Ibrutinib:
Ibrutinib is currently approved for the treatment of Waldenstrom's macroglobulinemia by the US Food and Drug Administration (FDA), the European Commission, Health Canada, and England (Cancer Drugs Fund). The approval was based on results of a Phase II study in previously treated WM patients that showed overall response rate (ORR) of 91% and median time to response of 4 weeks.

How Ibrutinib Is Given:
Ibrutinib is either in capsule or tablet form, taken by mouth once daily. Typically, capsules or tablets are taken at approximately the same time each day. The capsules or tablets should be swallowed whole with at least 8 ounces of water. The dosage for WM is typically three 140-mg capsules or one 420-mg tablet daily. Swallow capsules and tablets whole. Do not open, break, or chew the capsules and do not cut, crush, or chew the tablets. Ibrutinib may be taken with food or on an empty stomach. A multicenter study suggests that ibrutinib therapy should be continued indefinitely (until disease progression or unacceptable toxicity), and dosage compliance is strongly emphasized to optimize outcomes.

Ibrutinib may also be combined with other drugs. The combination of ibrutinib with the monoclonal antibody rituximab (Rituxan) was approved by the US FDA in 2018. Ibrutinib alone and the combination of ibrutinib and rituximab are included in the National Comprehensive Cancer Network (NCCN®) Clinical Practice Guidelines list of preferred regimens for the treatment of relapsed/refractory WM; they are not considered preferred regimens for first-line therapy but can be used as alternate options

Ibrutinib Side Effects:
Most people will not experience all the side effects listed. Side effects are often predictable in terms of their onset, duration, and severity. They are almost always reversible and will go away after therapy is completed.

The following ibrutinib side effects are common (occurring in greater than 30% of patients): decreased platelets or altered platelet function resulting in bleeding complications, diarrhea, decreased neutrophils, decreased hemoglobin, fatigue, musculoskeletal pain, swelling, upper respiratory tract infection, nausea, and bruising.

The following are less common side effects (occurring in about 10-30% of patients): hypertension (high blood pressure), shortness of breath, constipation, rash, abdominal pain, vomiting, decreased appetite, cough, fever, inflammation of the mouth and lips, dizziness, urinary tract infection, pneumonia, skin infections, weakness or loss of body strength, muscle spasms, sinusitis, headache, dehydration, indigestion, petechiae (red or purple spots caused by capillary bleeding), joint pain, and nosebleeds.

Abnormal heartbeats, such as atrial fibrillation, occur in 5-10% of patients taking this drug. Call your doctor right away if you have a fast (>100 beats per minute at total rest) or abnormal heartbeat, chest pain, dizziness, low blood pressure, or if you feel like passing out. Atrial fibrillation caused by ibrutinib is generally treated with medications; sometimes dose modifications or interventional procedures are required. Atrial fibrillation can be intermittent, and you can have atrial fibrillation without knowing it.

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Very serious bleeding problems have rarely happened with ibrutinib. The use of ibrutinib in patients requiring anticoagulants or other medications that inhibit platelet function may increase the risk of bleeding, and care should be taken if anticoagulant therapy is used. Acquired von Willebrand disease is a bleeding disorder and may occur with a high IgM level. It is recommended that testing for von Willebrand activity in WM patients with a history of bleeding be considered before starting ibrutinib. You should discuss the bleeding risk with your doctor.

This drug may add to the chance of getting some types of cancer, especially skin cancer.

Biotin is being used to manage nail/skin/hair changes related to ibrutinib without clear scientific evidence to support its safety or efficacy. The FDA advises patients to tell their health care providers about any supplements they may be taking that contain biotin.

Patients with cancer who take this drug may rarely develop a serious health problem called tumor lysis syndrome (TLS). Call your doctor right away if you have a fast heartbeat or a heartbeat that does not feel normal, any passing out, trouble passing urine, muscle weakness or cramps, upset stomach, throwing up, loose stools, not able to eat, or feel sluggish.

Very serious kidney problems have happened with this drug. Call your doctor right away if you are unable to pass urine or if you have blood in the urine or a change in the amount of urine passed.

Approximately 11% of patients with WM have had unacceptable side effects develop while on ibrutinib, requiring a dose reduction or drug discontinuation, as determined by their oncologist.

If you are 65 or older, use this drug with care. You could have more side effects.

When to Contact Your Doctor or Health Care Provider:
Contact your doctor or health care provider immediately, day or night, if you should experience any of the following symptoms: fever of 100.5° F (38° C) or higher or chills (both are possible signs of infection), shortness of breath or other breathing problems, cough, and bleeding that won't stop.

The following symptoms also require medical attention. Contact your doctor or health care provider if you notice any of the following: frequent diarrhea, black or tarry stools or blood in your stools, long-lasting headache, confusion, change in speech, nausea, vomiting, inability to eat or drink for 24 hours, signs of dehydration, yellowing of the skin or whites of the eyes, dark or brown urine, pain on the right side of the stomach, easy bleeding or bruising, rash, itching, blisters, cough with or without mucus, mouth sores, pain or burning with urination, and extreme fatigue.

Always inform your health care provider if you experience any unusual symptoms.

Self-Care Tips While Taking Ibrutinib:
Do not drink grapefruit juice, eat grapefruit, Seville oranges, or starfruit while taking ibrutinib.

Other medications can affect the removal of ibrutinib from your body, which may affect how well ibrutinib works. Examples include azole antifungals (such as itraconazole, ketoconazole), boceprevir, nefazodone, St. John's wort, telaprevir, HIV protease inhibitors, macrolide antibiotics (such as erythromycin, clarithromycin), rifamycin antibiotics (such as rifampin, rifabutin), certain drugs used to treat seizures (such as carbamazepine, phenytoin), among others. This document does not contain all possible drug interactions.

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Stay well hydrated and drink at least 2-3 quarts of fluid every 24 hours, unless you are instructed otherwise.

Wash your hands often and after taking each dose of ibrutinib.

You may be at risk of infection so try to avoid crowds or people with colds and report fever or any other signs of infection immediately to your doctor.

Make sure you tell your doctor and pharmacist about any other medications you are taking (including prescription, over-the-counter, vitamins, herbal remedies, etc.), with emphasis on anticoagulants and other medications that affect platelet aggregation.

Use an electric razor and a soft toothbrush to minimize bleeding.

Avoid contact sports or activities that could cause injury.

To help treat/prevent mouth sores while taking ibrutinib, rinse mouth three times a day with 1 teaspoon of baking soda mixed with 8 ounces of water.

To reduce nausea, take anti-nausea medications as prescribed by your doctor and eat small, frequent meals. In general, drinking alcoholic beverages should be kept to a minimum or avoided while taking ibrutinib. Maintain good nutrition and get plenty of rest.

Do not receive any kind of immunization or vaccination without your doctor's approval.

Avoid sun exposure. Wear SPF 15 (or higher) sun block and protective clothing.

Tell all of your health care providers that you take ibrutinib. This includes your doctors, nurses, pharmacists, and dentists. This drug may need to be stopped temporarily before certain types of surgery. If it is stopped, your doctor will tell you when to start taking this drug again after your surgery or procedure.

Temporary interruption of ibrutinib is sometimes needed to manage toxicities or before an operation to minimize bleeding. One in five patients with WM develop withdrawal symptoms (fever, body aches, night sweats, muscle aches, chills, headache, fatigue) while being off ibrutinib (usually within 2 days of stopping the drug), which then resolve promptly after starting ibrutinib again. The rate of withdrawal symptoms was lower in patients who start ibrutinib at serum IgM levels ≥4,000 mg/dL and CXCR4 mutated patients, and higher in patients who had achieved a very good partial response (VGPR) on ibrutinib. In two thirds of the patients who experience withdrawal, there is no evidence of disease progression while stopping the ibrutinib. In the patients who progress during the period they are off the drug, response is regained within 3 months of restarting ibrutinib. The current recommendation for discontinuing ibrutinib prior to surgical procedures is one week for major surgery, three days for minor surgery, and no interruption for procedures like cataract surgery, minor dental work, and colonoscopy without biopsy.

Monitoring and Testing While Taking Ibrutinib:
You will be checked regularly by your doctor while you are taking ibrutinib to monitor side effects and check your response to therapy. Periodic blood work will be obtained to monitor your complete blood count (CBC) as well as the function of other organs (such as your kidneys and liver). The development of resistance to ibrutinib has been

described in patients, leading to disease progression and symptom recurrence. The mechanisms of this resistance are associated with BTK mutations.

How Ibrutinib Works:
Ibrutinib is termed a "targeted therapy." Targeted therapy is the result of years of research dedicated to understanding the differences between cancer cells and normal cells. This information is used to create a therapy to attack the cancer cells while causing minimal damage to the normal cells, leading to fewer side effects. Each type of targeted therapy works a little differently, but all interfere with the ability of the cancer cell to grow, divide, repair and/or communicate with other cells.

Ibrutinib inhibits the function of Bruton's tyrosine kinase (BTK). BTK is a key signaling molecule of the B-cell receptor signaling complex that plays an important role in the survival of malignant B-cells. Ibrutinib blocks signals that stimulate malignant B-cells to grow and divide uncontrollably.

NOTE: The information in this fact sheet is intended to be helpful and educational, but it does not constitute an endorsement by the IWMF and is not meant to be a substitute for professional medical advice.

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