How IMBRUVICA® (ibrutinib) may affect your white blood cell counts

What is lymphocytosis?

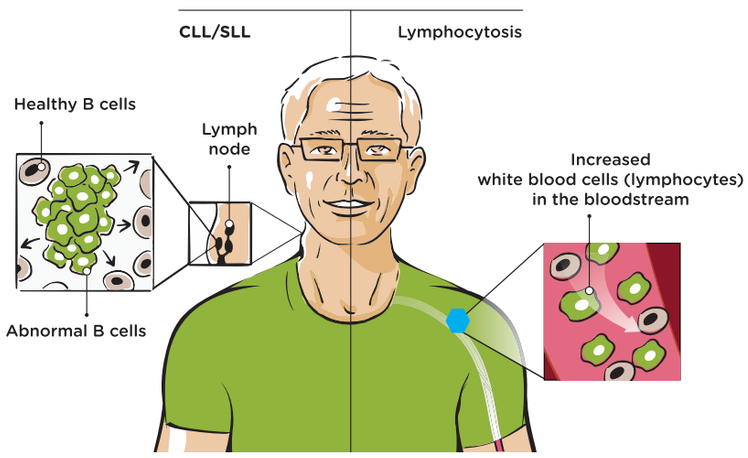
After starting IMBRUVICA®, your doctor will monitor your blood cell counts. Your lab results may show an increase in lymphocytes, a type of white blood cell.[1] This is called lymphocytosis and can occur with IMBRUVICA® treatment. In the absence of other signs and symptoms, this increase may not necessarily mean your condition is worsening.[2]

How does IMBRUVICA® work?

IMBRUVICA® works differently than chemotherapy. It blocks a protein called Bruton's tyrosine kinase, or BTK—an action that may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.

In 3 clinical trials, 66% of people with chronic lymphocytic leukemia (CLL) on IMBRUVICA® developed lymphocytosis. This typically occurred during their first month of IMBRUVICA® therapy and resolved by a median* of 14 weeks ranging from 0.1 to 104 weeks.[1] In 2 other clinical trials, 7% of patients developed lymphocytosis when treated with IMBRUVICA® + BR (bendamustine plus rituximab).[1] BR is a commonly used chemoimmunotherapy regimen for people with CLL/SLL.[3] 7% of patients also developed lymphocytosis when treated with IMBRUVICA® + obinutuzumab.

The exact process by which lymphocytosis occurs in IMBRUVICA®-treated patients is not entirely known, so it's important to speak with your doctor if you have questions about your blood cell counts. Your doctor will monitor you for lymphocytosis and manage the symptoms if needed.



CLL/SLL

In CLL and SLL, abnormal B cells grow out of control and may crowd out healthy cells in the lymph nodes (small glands containing immune cells that fight infection), bone marrow (soft inner part of bones responsible for making blood cells), and other organs.

B cells

B cells are a type of white blood cell. They are an important part of your immune system—your body's defense against infection.

BTK

BTK is a protein necessary for B cells to multiply and survive.

How to take IMBRUVICA®

IMBRUVICA® 420 mg **ONCE DAILY** — Continue to take IMBRUVICA® daily as directed by your doctor

For CLL/SLL, IMBRUVICA® is dosed once a day as either a single 420-mg tablet or three 140-mg capsules. Talk to your doctor about which dosing option is right for you.

Swallow the tablet or capsules whole with a glass of water at about the same time each day. Do not open, break, or chew the capsules. Do not cut, crush, or chew the tablets.

Take IMBRUVICA® as prescribed by your doctor. Do not change or skip your dose without talking to your healthcare provider first.

IMPORTANT SIDE EFFECT INFORMATION

IMBRUVICA® may cause serious side effects, including bleeding problems (hemorrhage), infections, decrease in blood cell counts, heart rhythm problems (ventricular arrhythmias, atrial fibrillation and atrial flutter), high blood pressure (hypertension), second primary cancers, and tumor lysis syndrome (TLS).

The information in this handout is not intended to replace the advice of your doctor. If you have any questions about your IMBRUVICA® treatment, be sure to contact your healthcare provider.

imbruvica®
(ibrutinib)
560, 420, 280, 140 mg tablets | 140, 70 mg capsules

*Median is the middle number in a group of numbers that are arranged from lowest to highest. For example, in the group of numbers 1-11, 6 is the median.

Please review the reverse side for additional Important Side Effect Information and review the accompanying full Important Product Information.

Talk with your doctor about any side effects that you experience while taking IMBRUVICA® (ibrutinib).

What is IMBRUVICA® (ibrutinib)?

IMBRUVICA® (ibrutinib) is a prescription medicine used to treat adults with:

- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion

It is not known if IMBRUVICA® is safe and effective in children.

Before taking IMBRUVICA®, tell your healthcare provider about all of your medical conditions, including if you:

- have had recent surgery or plan to have surgery. Your healthcare provider may stop IMBRUVICA® for any planned medical, surgical, or dental procedure.
- have bleeding problems.
- have or had heart rhythm problems, smoke, or have a medical condition that increases your risk of heart disease, such as high blood pressure, high cholesterol, or diabetes.
- have an infection.
- have liver problems.
- are pregnant or plan to become pregnant. IMBRUVICA® can harm your unborn baby. If you are able to become pregnant, your healthcare provider will do a pregnancy test before starting treatment with IMBRUVICA®.
  - **Females** should not become pregnant during treatment and for 1 month after the last dose of IMBRUVICA®.
  - **Males** should avoid getting female partners pregnant during treatment and for 1 month after the last dose of IMBRUVICA®.
- are breastfeeding or plan to breastfeed. You and your healthcare provider should decide if you will take IMBRUVICA® or breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking IMBRUVICA® with certain other medicines may affect how IMBRUVICA® works and can cause side effects.

How should I take IMBRUVICA®?

- Take IMBRUVICA® exactly as your healthcare provider tells you to take it.
- Take IMBRUVICA® 1 time a day.
- Swallow IMBRUVICA® capsules and tablets whole with a glass of water.
- Do not open, break or chew IMBRUVICA® capsules.
- Do not cut, crush or chew IMBRUVICA® tablets.
- Take IMBRUVICA® at about the same time each day.
- 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 doses of IMBRUVICA® to make up for a missed dose.
- If you take too much IMBRUVICA® call your healthcare provider or go to the nearest hospital emergency room right away.

What should I avoid while taking IMBRUVICA®?

- You should not drink grapefruit juice, eat grapefruit, or eat Seville oranges (often used in marmalades) during treatment with IMBRUVICA®. These products may increase the amount of IMBRUVICA® in your blood.

What are the possible side effects of IMBRUVICA®?

IMBRUVICA® may cause serious side effects, including:

- **Bleeding problems (hemorrhage) are common** during treatment with IMBRUVICA®, and can also be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs of bleeding, including: blood in your stools or black stools (looks like tar), pink or brown urine, unexpected bleeding, or bleeding that is severe or that you cannot control, vomit blood or vomit looks like coffee grounds, cough up blood or blood clots, increased bruising, dizziness, weakness, confusion, change in your speech, or a headache that lasts a long time.
- **Infections** can happen during treatment with IMBRUVICA®. These infections can be serious and may lead to death. Tell your healthcare provider right away if you have fever, chills, weakness, confusion, or other signs or symptoms of an infection during treatment with IMBRUVICA®.
- **Decrease in blood cell counts.** Decreased blood counts (white blood cells, platelets, and red blood cells) are common with IMBRUVICA®, but can also be severe. Your healthcare provider should do monthly blood tests to check your blood counts.
- **Heart rhythm problems (ventricular arrhythmias, atrial fibrillation and atrial flutter).** Serious heart rhythm problems and death have happened in people treated with IMBRUVICA®, especially in people who have an increased risk for heart disease, have an infection, or who have had heart rhythm problems in the past. Tell your healthcare provider if you get any symptoms of heart rhythm problems, such as feeling as if your heart is beating fast and irregular, lightheadedness, dizziness, shortness of breath, chest discomfort, or you faint. If you develop any of these symptoms, your healthcare provider may do a test to check your heart (ECG) and may change your IMBRUVICA® dose.
- **High blood pressure (hypertension).** New or worsening high blood pressure has happened in people treated with IMBRUVICA®. Your healthcare provider may start you on blood pressure medicine or change current medicines to treat your blood pressure.
- **Second primary cancers.** New cancers have happened during treatment with IMBRUVICA®, including cancers of the skin or other organs.
- **Tumor lysis syndrome (TLS).** TLS is caused by the fast breakdown of cancer cells. TLS can cause kidney failure and the need for dialysis treatment, abnormal heart rhythm, seizure, and sometimes death. Your healthcare provider may do blood tests to check you for TLS.

The most common side effects of IMBRUVICA® in adults with B-cell malignancies (MCL, CLL/SLL, WM and MZL) include:

- diarrhea
- muscle and bone pain
- rash
- bruising
- nausea
- tiredness
- fever

The most common side effects of IMBRUVICA® in adults with cGVHD include:

- tiredness
- bruising
- diarrhea
- mouth sores (stomatitis)
- muscle spasms
- nausea
- pneumonia

Diarrhea is a common side effect in people who take IMBRUVICA®. Drink plenty of fluids during treatment with IMBRUVICA® to help reduce your risk of losing too much fluid (dehydration) due to diarrhea. Tell your healthcare provider if you have diarrhea that does not go away.

These are not all the possible side effects of IMBRUVICA®. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of IMBRUVICA®

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use IMBRUVICA® for a condition for which it was not prescribed. Do not give IMBRUVICA® to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about IMBRUVICA® that is written for health professionals.

Please see the accompanying full Important Product Information.

References: 1. IMBRUVICA® (ibrutinib) Prescribing Information. Pharmacyclics LLC 2019. **2.** Cheson BD, Byrd JC, Rai KR, et al. Novel targeted agents and the need to refine clinical end points in chronic lymphocytic leukemia. *J Clin Oncol.* 2012;30(23):2820-2822. **3.** Lymphoma Research Foundation. Getting the facts: chronic lymphocytic leukemia/small lymphocytic lymphoma. https://www.lymphoma.org/wp-content/uploads/2018/04/LRF_FACTSHEET_CLL_SLL.pdf. Accessed January 30, 2019.

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