# IMBRUVICA® (ibrutinib) PROVIDES THE MOST FLEXIBILITY IN FORMULATION CHOICES OF ANY BTKi


1L=first-line, BTKi=Bruton's tyrosine kinase inhibitor, CLL=chronic lymphocytic leukemia.

**IMBRUVICA® is the only BTKi with 3 different formulation options**
approved once a day in 1L CLL to meet your individual patient's administration needs.[1]


**420 mg**

**Tablet (blister pack)**


**140 mg** **140 mg** **140 mg**

**Capsule (bottle)**

**The only BTKi with an oral suspension***

*A formulation option for patients who may have trouble swallowing tablets or capsules.

Swallow tablets or capsules whole. Do not open, break, or chew the capsules. Do not cut, crush, or chew the tablets. If a dose of IMBRUVICA® is not taken at the scheduled time, 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 extra doses of IMBRUVICA® to make up for the missed dose.

**Dose modifications can help optimize patient management to enable continued IMBRUVICA® treatment where appropriate[1]**

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## INDICATIONS

IMBRUVICA® is a kinase inhibitor indicated for the treatment of:
- Adult patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL).
- Adult patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

**Hemorrhage:** Fatal bleeding events have occurred in patients who received IMBRUVICA®. Major hemorrhage (≥ Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) occurred in 4.2% of patients, with fatalities occurring in 0.4% of 2,838 patients who received IMBRUVICA® in 27 clinical trials. Bleeding events of any grade including bruising and petechiae occurred in 39%, and excluding bruising and petechiae occurred in 23% of patients who received IMBRUVICA®, respectively.

The mechanism for the bleeding events is not well understood.

Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA® increases the risk of major hemorrhage. Across clinical trials, 3.1% of 2,838 patients who received IMBRUVICA® without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA®. Monitor for signs and symptoms of bleeding.

Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

**Infections:** Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 21% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and *Pneumocystis jirovecii* pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Consider prophylaxis according to standard of care in patients who are at increased risk for opportunistic infections. Monitor and evaluate patients for fever and infections and treat appropriately.

**Cardiac Arrhythmias, Cardiac Failure, and Sudden Death:** Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These adverse reactions occurred in patients with and without preexisting hypertension or cardiac comorbidities. Patients with cardiac comorbidities may be at greater risk of these events.

Grade 3 or greater ventricular tachyarrhythmias were reported in 0.2%, Grade 3 or greater atrial fibrillation and atrial flutter were reported in 3.7%, and Grade 3 or greater cardiac failure was reported in 1.3% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These events have occurred particularly in patients with cardiac risk factors including hypertension and diabetes mellitus, a previous history of cardiac arrhythmias, and in patients with acute infections.

Evaluate cardiac history and function at baseline, and monitor patients for cardiac arrhythmias and cardiac function. Obtain further evaluation (e.g., ECG, echocardiogram) as indicated for patients who develop symptoms of arrhythmia (e.g., palpitations, lightheadedness, syncope, chest pain), new onset dyspnea, or other cardiovascular concerns. Manage cardiac arrhythmias and cardiac failure appropriately, follow dose modification guidelines, and consider the risks and benefits of continued IMBRUVICA® treatment.

**Hypertension:** Hypertension occurred in 19% of 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from a subset of these patients (N=1,124), the median time to onset was 5.9 months (range, 0 to 24 months). In a long-term safety analysis over 5 years of 1,284 patients with B-cell malignancies treated for a median of 36 months (range, 0 to 98 months), the cumulative rate of hypertension increased over time. The prevalence for Grade 3 or greater hypertension was 4% (year 0-1), 7% (year 1-2), 9% (year 2-3), 9% (year 3-4), and 9% (year 4-5); the overall incidence for the 5-year period was 11%. Monitor blood pressure in patients treated with IMBRUVICA®, initiate or adjust anti-hypertensive medication throughout treatment with IMBRUVICA® as appropriate, and follow dosage modification guidelines for Grade 3 or higher hypertension.

**Please see additional Important Safety Information on the next page and click here for full Prescribing Information.**

imbruvica®
(ibrutinib)
420, 280, 140 mg tablets | 140, 70 mg capsules
70 mg/mL oral suspension

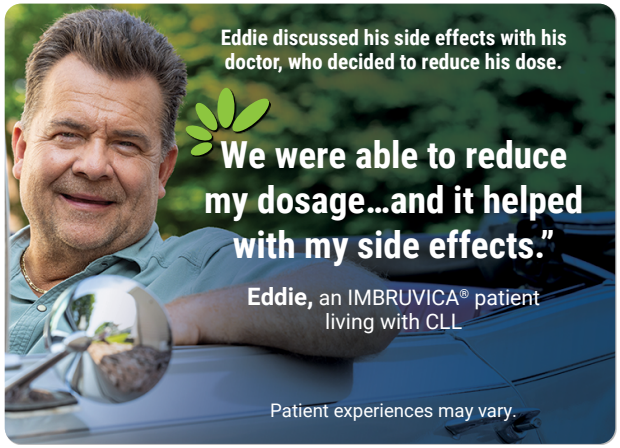
# DOSE MODIFICATIONS FOR ADVERSE REACTIONS[1]*

**If an adverse reaction (AR) listed below occurs, interrupt IMBRUVICA® therapy at each occurrence of the same AR. Once the AR has improved to Grade 1 or baseline, follow the recommended dosage modifications below.[1]**

**Why consider dose modifications for ARs?**

**START AT APPROVED DOSE 420 mg (6 mL)**
Once daily until disease progression or unacceptable toxicity

| ADVERSE REACTION†‡ | 1ST OCCURRENCE | 2ND OCCURRENCE | 3RD OCCURRENCE |
|---|---|---|---|
| **NON-CARDIAC** | | | |
| GRADE 3 or 4: other non-hematological toxicities§<br>GRADE 3 or 4: neutropenia with infection or fever<br>GRADE 4: hematological toxicities | RESTART AT 280 (4 mL) mg DAILY | RESTART AT 140 mg (2 mL) DAILY | DISCONTINUE |
| **CARDIAC** | | | |
| GRADE 2: cardiac failure | RESTART AT 280 (4 mL) mg‖ DAILY | RESTART AT 140 mg (2 mL)‖ DAILY | DISCONTINUE |
| GRADE 3: cardiac arrhythmias | | DISCONTINUE | |
| GRADE 3 or 4: cardiac failure<br>GRADE 4: cardiac arrhythmias | DISCONTINUE | | |




*Certain types and severity of cardiac ARs require discontinuation after first occurrence for only IMBRUVICA®.
†See full Prescribing Information for Warnings and Precautions.
‡Grading based on National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) criteria, or International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria for hematological toxicities in CLL/SLL.
§For Grade 4 non-hematological toxicities, evaluate the benefit-risk before resuming treatment.
‖Evaluate the benefit-risk before resuming treatment.

**For further information on use with CYP3A inhibitors and inducers, and in patients with hepatic impairment, please see the full Prescribing Information. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA®. Monitor for signs and symptoms of bleeding. Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.**

## IMPORTANT SAFETY INFORMATION (CONT'D)

### WARNINGS AND PRECAUTIONS (CONT'D)

**Cytopenias:** In 645 patients with B-cell malignancies who received IMBRUVICA® as a single agent, grade 3 or 4 neutropenia occurred in 23% of patients, grade 3 or 4 thrombocytopenia in 8% and grade 3 or 4 anemia in 2.8%, based on laboratory measurements. Monitor complete blood counts monthly.

**Second Primary Malignancies:** Other malignancies (10%), including non-skin carcinomas (3.9%), occurred among the 1,476 patients with B-cell malignancies who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

**Hepatotoxicity, Including Drug-Induced Liver Injury:** Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury (DILI), has occurred in patients treated with Bruton tyrosine kinase inhibitors, including IMBRUVICA®. Evaluate bilirubin and transaminases at baseline and throughout treatment with IMBRUVICA®. For patients who develop abnormal liver tests after IMBRUVICA®, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold IMBRUVICA®. Upon confirmation of DILI, discontinue IMBRUVICA®.

**Tumor Lysis Syndrome:** Tumor lysis syndrome has been infrequently reported with IMBRUVICA®. Assess the baseline risk (e.g., high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

**Embryo-Fetal Toxicity:** Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMBRUVICA® and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during the same time period.

### ADVERSE REACTIONS

The most common adverse reactions (≥30%) in adult patients with B-cell malignancies were thrombocytopenia (55%)*, diarrhea (44%), fatigue (39%), musculoskeletal pain (39%), neutropenia (39%)*, rash (36%), anemia (35%)*, bruising (32%), and nausea (30%).

The most common Grade ≥ 3 adverse reactions (≥5%) in adult patients with B-cell malignancies were neutropenia (21%)*, thrombocytopenia (14%)*, pneumonia (8%), and hypertension (8%).
Approximately 9% (CLL/SLL) and 14% (WM) of adult patients had a dose reduction due to adverse reactions.
Approximately 4-10% (CLL/SLL) and 5% (WM) of adult patients discontinued due to adverse reactions.
*Treatment-emergent decreases (all grades) were based on laboratory measurements.

### DRUG INTERACTIONS

**CYP3A Inhibitors:** Coadministration of IMBRUVICA® with strong or moderate CYP3A inhibitors may increase ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of drug-related toxicity. Dose modifications of IMBRUVICA® are recommended when used concomitantly with posaconazole, voriconazole, and moderate CYP3A inhibitors. Avoid concomitant use of other strong CYP3A inhibitors. Interrupt IMBRUVICA® if strong inhibitors are used short-term (e.g., for ≤ 7 days). Avoid grapefruit and Seville oranges during IMBRUVICA® treatment, as these contain strong or moderate inhibitors of CYP3A. See dose modification guidelines in USPI sections 2.3 and 7.1.

**CYP3A Inducers:** Avoid coadministration with strong CYP3A inducers.

### SPECIFIC POPULATIONS

**Hepatic Impairment** (based on Child-Pugh criteria)**:** Avoid use of IMBRUVICA® in patients with severe hepatic impairment. In patients with mild or moderate impairment, reduce recommended IMBRUVICA® dose and monitor more frequently for adverse reactions of IMBRUVICA®.

**Please click here for full Prescribing Information.**

**Reference: 1.** IMBRUVICA® (ibrutinib) Prescribing Information.

1L=first-line, AR=adverse reaction, CLL=chronic lymphocytic leukemia, CYP3A=cytochrome P450, family 3, subfamily A, SLL=small lymphocytic lymphoma.

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70 mg/mL oral suspension

pharmacyclics® An AbbVie Company

Johnson&Johnson



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