

# NEW FORMULATION

## IMBRUVICA® (ibrutinib) is Now Approved in a New Formulation as One Pill, Once Daily



Pharmacyclics LLC and Janssen Biotech, Inc., are pleased to share that we received US FDA approval for a new formulation of IMBRUVICA® as one pill, once a day. The same active ingredient is now approved in one pill at multiple dosage strengths. No matter what dose a patient requires, they take just one pill a day.

In addition, we recently received FDA approval for a new dosage strength of 70 mg capsules recommended for patients with moderate hepatic impairment or patients with B-cell malignancies who are concomitantly taking specific posaconazole dosing regimens. Please refer to full IMBRUVICA® Prescribing Information for Dosing and Administration details.

Please ensure that your systems are updated to accommodate the transition to the new formulation of IMBRUVICA®.

### National Drug Codes (NDCs) for the new formulation of IMBRUVICA®<sup>1</sup>

					
<b>Strength</b>	560 mg Tablet	420 mg Tablet	280 mg Tablet	140 mg Tablet	70 mg* Capsule
<b>NDC</b>	57962-560-28	57962-420-28	57962-280-28	57962-014-28	57962-070-28
	57962-0560-28	57962-0420-28	57962-0280-28	57962-0014-28	57962-0070-28
<b>Date Available</b>	March 21, 2018				Now Available

\*The recommended dose is 70 mg daily for patients with moderate hepatic impairment (Child-Pugh class B) or patients with B-cell malignancies who are concomitantly taking specific posaconazole dosing regimens. Please refer to full IMBRUVICA® Prescribing Information for Dosing and Administration details.<sup>1</sup>

The 560 mg, 420 mg, 280 mg, and 140 mg pills come in a blister pack, and the 70 mg pills come in a bottle.

**Note:** The red zero converts the 10-digit NDC to the 11-digit NDC. The red is for emphasis and not for billing purposes.

**Please Note:** Some payers may require that each NDC number be listed on the claim. Payer requirements regarding the use of the 10- or 11-digit NDC may vary. Electronic data exchange generally requires use of the 11-digit NDC, as listed above.

**Same active ingredient.** The same active ingredient is now approved in one pill at multiple dosage strengths. No matter what dose the patient requires, everyone takes just one pill a day. The inactive ingredients have changed; please see full Prescribing Information. Patients shouldn't have different side effects. Advise your patients to alert you if they experience any side effects with this medication.

**New prescription needed.** The 140 mg capsules will no longer be available after May 15, 2018 so every patient will need to switch to the new formulation. This will require a new prescription at their specific dose.<sup>1</sup>

**New packaging.** The pill comes in a 4-week blister pack that was designed to help patients track their daily dose and transition to taking one pill a day.<sup>1</sup>

**Dose modification.** Dose modification guidelines for adverse reactions remain the same with the new formulation. If a patient requires a dose modification, they will need a new prescription for that specific dose.

### IMPORTANT SAFETY INFORMATION WARNINGS AND PRECAUTIONS

**Hemorrhage:** Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA®.

The mechanism for the bleeding events is not well understood.

IMBRUVICA® may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies and patients should be monitored for signs 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.

**Please see additional Important Safety Information on next page and accompanying full Prescribing Information.**

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

## IMPORTANT SAFETY INFORMATION (cont'd)

### WARNINGS AND PRECAUTIONS (cont'd)

**Infections:** Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA® (ibrutinib) therapy. Grade 3 or greater infections occurred in 14% to 29% of patients. 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.

**Cytopenias:** Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 13 to 29%), thrombocytopenia (range, 5 to 17%), and anemia (range, 0 to 13%) based on laboratory measurements occurred in patients with B-cell malignancies treated with single agent IMBRUVICA®.

Monitor complete blood counts monthly.

**Cardiac Arrhythmias:** Fatal and serious cardiac arrhythmias have occurred with IMBRUVICA® therapy. Grade 3 or greater ventricular tachyarrhythmias occurred in 0 to 1% of patients, and Grade 3 or greater atrial fibrillation and atrial flutter occurred in 0 to 6% of patients. These events have occurred particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of cardiac arrhythmias.

Periodically monitor patients clinically for cardiac arrhythmias. Obtain an ECG for patients who develop arrhythmic symptoms (e.g., palpitations, lightheadedness, syncope, chest pain) or new onset dyspnea. Manage cardiac arrhythmias appropriately, and if it persists, consider the risks and benefits of IMBRUVICA® treatment and follow dose modification guidelines.

**Hypertension:** Hypertension (range, 6 to 17%) has occurred in patients treated with IMBRUVICA® with a median time to onset of 4.6 months (range, 0.03 to 22 months). Monitor patients for new onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA®. Adjust existing anti-hypertensive medications and/or initiate anti-hypertensive treatment as appropriate.

**Second Primary Malignancies:** Other malignancies (range, 3 to 16%) including non-skin carcinomas (range, 1 to 4%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 2 to 13%).

**Tumor Lysis Syndrome:** Tumor lysis syndrome has been infrequently reported with IMBRUVICA® therapy. 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 women to avoid becoming pregnant while taking IMBRUVICA® and for 1 month after cessation of therapy. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. Advise men to avoid fathering a child during the same time period.

### ADVERSE REACTIONS

**B-cell malignancies:** The most common adverse reactions ( $\geq 20\%$ ) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were thrombocytopenia (62%)\*, neutropenia (61%)\*, diarrhea (43%), anemia (41%)\*, musculoskeletal pain (30%), bruising (30%), rash (30%), fatigue (29%), nausea (29%), hemorrhage (22%), and pyrexia (21%).

The most common Grade 3 or 4 adverse reactions ( $\geq 5\%$ ) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were neutropenia (39%)\*, thrombocytopenia (16%)\*, and pneumonia (10%).

Approximately 6% (CLL/SLL), 14% (MCL), 11% (WM) and 10% (MZL) of patients had a dose reduction due to adverse reactions. Approximately 4%-10% (CLL/SLL), 9% (MCL), and 9% (WM [6%] and MZL [13%]) of patients discontinued due to adverse reactions.

**cGVHD:** The most common adverse reactions ( $\geq 20\%$ ) in patients with cGVHD were fatigue (57%), bruising (40%), diarrhea (36%), thrombocytopenia (33%)\*, stomatitis (29%), muscle spasms (29%), nausea (26%), hemorrhage (26%), anemia (24%)\*, and pneumonia (21%).

The most common Grade 3 or 4 adverse reactions ( $\geq 5\%$ ) reported in patients with cGVHD were fatigue (12%), diarrhea (10%), neutropenia (10%)\*, pneumonia (10%), sepsis (10%), hypokalemia (7%), headache (5%), musculoskeletal pain (5%), and pyrexia (5%).

Twenty-four percent of patients receiving IMBRUVICA® in the cGVHD trial discontinued treatment due to adverse reactions. Adverse reactions leading to dose reduction occurred in 26% of patients.

\*Treatment-emergent decreases (all grades) were based on laboratory measurements and adverse reactions.

### DRUG INTERACTIONS

**CYP3A Inhibitors:** Dose adjustment may be recommended.

**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 baseline hepatic impairment. In patients with mild or moderate impairment, reduce IMBRUVICA® dose.

**Please see accompanying full Prescribing Information.**

**References:** 1. IMBRUVICA® (ibrutinib) Prescribing Information. Pharmacyclics LLC. 2018.