Jaypirca®
pirtobrutinib 50, 100 mg tablets

# Electronic Health Record
# Treatment Plan Guide

**Disclaimer:** This guide is intended to provide information to develop a drug record for Jaypirca and/or to assist users with creating a standard treatment template for use of Jaypirca in the treatment of adult patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor, and adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor. Patients should be evaluated by a physician prior to the use of Jaypirca and deemed to meet both a confirmatory diagnosis of one of the above indications and be an appropriate candidate for the use of Jaypirca. Based on individual patient cases and unique scenarios, additional tests, assessments, and medications may be necessary for the proper care and treatment of patients receiving this regimen. This guide does not constitute a final order and may not meet the comprehensive needs of individual patients or institutions.

## Indications

Jaypirca is a kinase inhibitor indicated for the treatment of adult patients with:

- relapsed or refractory (R/R) mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor
- chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor

These indications are approved under accelerated approval based on response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial.

## Select Important Safety Information

**Infections:** Fatal and serious infections (bacterial, viral, fungal) and opportunistic infections (including *Pneumocystis jirovecii* pneumonia and fungal infection) have occurred in Jaypirca-treated patients. In a clinical trial of 593 patients with hematologic malignancies, Grade ≥3 infections occurred (24%), most commonly pneumonia (14%); fatal infections (4.4%), sepsis (6%), and febrile neutropenia (4%) occurred. In patients with CLL/SLL, Grade ≥3 infections occurred (32%), with fatal infections in 8%. Consider prophylaxis in patients at increased risk. Monitor patients for signs and symptoms of infection; based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

BCL-2=B-cell lymphoma 2; BTK=Bruton's tyrosine kinase.

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

Lilly

## Pharmacology[1]

| | |
|---|---|
| **Class** | BTK inhibitor |
| **Mechanism of action** | Small molecule noncovalent inhibitor of BTK |

## Treatment[1]

| Category | Details |
|---|---|
| **Regimen** | Jaypirca, days 1-30; until disease progression or unacceptable toxicity |
| **FDA-approved indications** | Jaypirca is a kinase inhibitor indicated for the treatment of adult patients with:<br>• R/R MCL after at least two lines of systemic therapy, including a BTK inhibitor<br>• CLL/SLL who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor<br>These indications are approved under accelerated approval based on response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial. |

## Treatment Medication[1]

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| **Dosing** | Recommended dosage is 200 mg orally once daily*<br>May be taken with or without food†; may be taken with gastric acid–reducing agents‡ |
| **Dosage form and strength** | Jaypirca is available as 50 mg and 100 mg tablets dispensed in 30-day supplies. |

## Treatment Schedule[1]

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|---|---|
| **Treatment days** | Daily |
| **Cycle length** | 30 days |
| **Treatment duration** | Continuously until disease progression or unacceptable toxicity |

*Jaypirca is also available in 50 mg tablets for use when dose reductions are needed.[1]

†Can be taken with a high-fat meal.[1]

‡No clinically significant differences in pirtobrutinib pharmacokinetics were observed when co-administered with omeprazole, a proton pump inhibitor.[1]

FDA=US Food and Drug Administration.

## Select Important Safety Information

**Hemorrhage:** Fatal and serious hemorrhage occurred in patients with hematologic malignancies treated with Jaypirca. Major hemorrhage occurred (3%), including gastrointestinal hemorrhage; fatal hemorrhage occurred (0.3%). Bleeding of any grade, excluding bruising and petechiae, occurred in 17%. Major hemorrhage occurred in patients taking Jaypirca with (0.7%) and without (2.3%) antithrombotic agents. Consider risks/benefits of co-administering antithrombotic agents with Jaypirca and of withholding Jaypirca for 3-7 days pre- and post-surgery. Monitor patients for signs of bleeding and reduce dose, temporarily withhold, or permanently discontinue Jaypirca, based on severity.

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

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| Monitoring[1] | |
|---|---|
| **Laboratory/clinical assessment(s)** | Laboratory and other clinical tests may be ordered more frequently at the discretion of the provider or according to institutional standards.<br>• **Infections:** Monitor patients for signs and symptoms of infection<br>• **Hemorrhage:** Monitor patients for signs of bleeding<br>• **Cytopenias:** Monitor CBCs regularly during treatment<br>• **Cardiac arrhythmias:** Monitor for signs and symptoms of arrhythmias<br>• **Second primary malignancies:** Monitor patients for the development of second primary malignancies, including skin cancers and other carcinomas<br>• **Embryo-fetal toxicity:** Verify pregnancy status in females of reproductive potential prior to initiating Jaypirca |
| **Treatment parameters** | Laboratory and clinical assessments should be monitored to evaluate treatment, toxicity, and for dose modifications at the discretion of the treating provider.<br>• **Infections:** Consider prophylaxis, including vaccinations, in patients who are at increased risk for infections, including opportunistic infections. Evaluate and treat promptly as medically appropriate. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca<br>• **Hemorrhage:** Consider the risks and benefits of antithrombotic agents when co-administered with Jaypirca. Consider the benefit-risk of withholding Jaypirca for 3-7 days pre-surgery and post-surgery depending upon the type of surgery and risk of bleeding. Based on severity of bleeding, reduce dose, temporarily withhold, or permanently discontinue Jaypirca<br>• **Cytopenias:** Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca<br>• **Cardiac arrhythmias:** Manage appropriately. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca<br>• **Second primary malignancies:** Advise patients to use sun protection<br>• **Embryo-fetal toxicity:** Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 1 week after the last dose<br>*See sections 2.2, 5, and 8 of the Jaypirca Prescribing Information (Dosage Modifications for Adverse Reactions, Warnings and Precautions, and Use in Specific Populations) for more complete information.* |

CBC=complete blood count.

## Select Important Safety Information

**Cytopenias:** Jaypirca can cause cytopenias, including neutropenia, thrombocytopenia, and anemia. In a clinical trial, Grade 3 or 4 cytopenias, including decreased neutrophils (26%), decreased platelets (12%), and decreased hemoglobin (12%), developed in Jaypirca-treated patients. Grade 4 decreased neutrophils (14%) and Grade 4 decreased platelets (6%) developed. Monitor complete blood counts regularly during treatment; based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

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## Administration Considerations[1]

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|---|---|
| **Administration** | • Swallow tablets whole with water. Do not cut, crush, or chew tablets<br>• Take at the same time each day<br>• May be taken with or without food<br>• If a dose is missed by more than 12 hours, do not make up the dose and take the next dose as scheduled |
| **Food interactions** | Jaypirca may be taken with or without food. |

## Dosage Modifications[1]

**Recommended Dosage Modifications of Jaypirca for Adverse Reactions**

| Adverse Reactions | Occurrences Requiring Dose Modification | Modification (Starting Dose 200 mg Once Daily) |
|---|---|---|
| • Grade 3 or greater nonhematologic toxicity*<br>• Absolute neutrophil count <1 to 0.5 x $10^9$/L with fever and/or infection<br>• Absolute neutrophil count <0.5 x $10^9$/L lasting ≥7 days<br>• Platelet count <50 to 25 x $10^9$/L with bleeding<br>• Platelet count <25 x $10^9$/L | **1st occurrence** | Interrupt until recovery to grade 1 or baseline<br>**RESTART** at original dose (200 mg once daily*) |
| | **2nd occurrence** | Interrupt until recovery to grade 1 or baseline<br>**RESTART** at 100 mg once daily |
| | **3rd occurrence** | Interrupt until recovery to grade 1 or baseline<br>**RESTART** at 50 mg once daily |
| | **4th occurrence** | **DISCONTINUE** |

Dose modification is not recommended for asymptomatic lymphocytosis. Asymptomatic lipase increase may not necessarily warrant dose modification.[1]

*Evaluate benefit-risk before resuming treatment at the same dose for a grade 4 nonhematologic toxicity.[1]

For patients with severe renal impairment (eGFR 15-29 mL/min), reduce the Jaypirca dose to 100 mg once daily if the current dose is 200 mg once daily; otherwise, reduce dose by 50 mg. If the current dose is 50 mg once daily, discontinue Jaypirca. No dose adjustment is recommended in patients with mild to moderate renal impairment (eGFR 30-89 mL/min).[1]

Avoid concomitant use of strong CYP3A inhibitors with Jaypirca. If concomitant use is unavoidable, reduce the Jaypirca dose by 50 mg. If the current dosage is 50 mg once daily, interrupt Jaypirca treatment for the duration of strong CYP3A inhibitor use. After discontinuation of a strong CYP3A inhibitor for 5 half-lives, resume the Jaypirca dose that was taken prior to initiating the strong CYP3A inhibitor.[1]

Avoid concomitant use of strong or moderate CYP3A inducers with Jaypirca. If concomitant use with moderate CYP3A inducers is unavoidable and the current dose of Jaypirca is 200 mg once daily, increase the dose to 300 mg. If the current dosage is 50 mg or 100 mg once daily, increase the dose by 50 mg.[1]

eGFR=estimated glomerular filtration rate.

## Select Important Safety Information

**Cardiac Arrhythmias:** Cardiac arrhythmias occurred in patients who received Jaypirca. In a clinical trial of 593 patients with hematologic malignancies, atrial fibrillation or flutter were reported in 3.2% of Jaypirca-treated patients, with Grade 3 or 4 atrial fibrillation or flutter in 1.5%. Other serious cardiac arrhythmias such as supraventricular tachycardia and cardiac arrest occurred (0.5%). Patients with cardiac risk factors may be at increased risk. Monitor for signs and symptoms of arrhythmias and reduce dose, temporarily withhold, or permanently discontinue Jaypirca, based on severity.

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## Patient Counseling[1]

| | |
|---|---|
| **Administration** | • Swallow tablets whole with water. Do not cut, crush, or chew tablets<br>• Take at the same time each day<br>• May be taken with or without food<br>• If a dose is missed by more than 12 hours, do not make up the dose and take the next dose as scheduled |
| **Drug interactions** | • Jaypirca is a P-gp inhibitor, a moderate CYP2C8 and BCRP inhibitor, and a weak CYP2C19 and CYP3A inhibitor. Concomitant use of Jaypirca with sensitive P-gp, CYP2C8, BCRP, CYP2C19, or CYP3A substrates increased their plasma concentrations, which may increase the risk of adverse reactions related to these substrates for drugs that are sensitive to minimal concentration changes. Follow recommendations for sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP substrates provided in their approved product labeling<br>• Avoid concomitant use of strong CYP3A inhibitors during treatment with Jaypirca. If concomitant use of strong CYP3A inhibitors is unavoidable, reduce the Jaypirca dosage. Concomitant use of Jaypirca with a strong CYP3A inhibitor increased pirtobrutinib systemic exposure, which may increase the risk of Jaypirca adverse reactions *(see section 2.4 of the Jaypirca Prescribing Information [Dosage Modifications for Concomitant Use with Strong CYP3A Inhibitors] for more complete information)*<br>• Concomitant use of Jaypirca with a strong or moderate CYP3A inducer decreased pirtobrutinib systemic exposure, which may reduce Jaypirca efficacy. Avoid concomitant use of Jaypirca with strong or moderate CYP3A inducers. If concomitant use of moderate CYP3A inducers is unavoidable, increase the Jaypirca dosage *(see section 2.5 of the Jaypirca Prescribing Information [Dosage Modifications for Concomitant Use with CYP3A Inducers] for more complete information)*<br>*See sections 7 and 12.3 of the Jaypirca Prescribing Information (Drug Interactions and Pharmacokinetics) for more complete information.* |

BCRP=breast cancer resistance protein; P-gp=P-glycoprotein.

## Select Important Safety Information

**Second Primary Malignancies:** Second primary malignancies, including non-skin carcinomas, developed in 9% of Jaypirca-treated patients. The most frequent malignancy was non-melanoma skin cancer (4.6%). Other second primary malignancies included solid tumors and melanoma. Advise patients to use sun protection and monitor for development of second primary malignancies.

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

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## Adverse Reactions[1]

| | |
|---|---|
| **CLL/SLL** | • The most common nonhematologic adverse reactions (≥20%) for patients with CLL/SLL (N=110) were fatigue, bruising, cough, musculoskeletal pain, COVID-19, diarrhea, pneumonia, abdominal pain, dyspnea, hemorrhage, edema, nausea, pyrexia, and headache<br>• The most common laboratory abnormalities (≥20%) for patients with CLL/SLL* were decreased neutrophil count, decreased hemoglobin, decreased calcium, decreased sodium, decreased platelet count, decreased lymphocyte count, increased ALT, increased AST, increased creatinine, increased lipase, and increased alkaline phosphatase<br>• Serious adverse reactions occurred in 56% of patients with CLL/SLL who received Jaypirca. Serious adverse reactions that occurred in ≥5% of patients were pneumonia (18%), COVID-19 (9%), sepsis (7%), and febrile neutropenia (7%). Fatal adverse reactions within 28 days of the last dose of Jaypirca occurred in 11% of patients, most commonly due to infections (10%), including sepsis (5%) and COVID-19 (2.7%).<br>• Adverse reactions led to dose reductions in 3.6%, treatment interruption in 42%, and permanent discontinuation of Jaypirca in 9%<br>• Adverse reactions that resulted in dose reductions in >1% of patients included neutropenia. Adverse reactions that resulted in treatment interruptions of Jaypirca in >5% of patients included pneumonia, neutropenia, febrile neutropenia, and COVID-19. Adverse reactions that resulted in permanent discontinuation of Jaypirca in >1% of patients included second primary malignancy, COVID-19, and sepsis<br>*See section 6.1 of the Jaypirca Prescribing Information (Clinical Trials Experience) for more complete information.* |
| **MCL** | • The most common nonhematologic adverse reactions (≥15%) for patients with MCL (N=128) were fatigue, musculoskeletal pain, diarrhea, edema, dyspnea, pneumonia, and bruising<br>• The most common laboratory abnormalities (≥10%) for patients with MCL† were decreased hemoglobin, decreased platelet count, decreased neutrophil count, decreased lymphocyte count, increased creatinine, decreased calcium, increased AST, decreased potassium, decreased sodium, increased lipase, increased alkaline phosphatase, increased ALT, and increased potassium<br>• Serious adverse reactions occurred in 38% of patients with MCL who received Jaypirca. Serious adverse reactions that occurred in ≥2% of patients were pneumonia (14%), COVID-19 (4.7%), musculoskeletal pain (3.9%), hemorrhage (2.3%), pleural effusion (2.3%), and sepsis (2.3%). Fatal adverse reactions within 28 days of the last dose of Jaypirca occurred in 7% of patients, most commonly due to infections (4.7%), including COVID-19 (3.1% of all patients)<br>• Adverse reactions led to dosage reductions in 4.7%, treatment interruption in 32%, and permanent discontinuation of Jaypirca in 9%. Adverse reactions that resulted in dose reductions in >5% of patients included pneumonia and neutropenia. Adverse reactions that resulted in permanent discontinuation of Jaypirca in >1% of patients included pneumonia<br>*See section 6.1 of the Jaypirca Prescribing Information (Clinical Trials Experience) for more complete information.* |

*The denominator used to calculate the rate varied from 83 to 108 based on the number of patients with a baseline value and at least 1 post-treatment value.

†The denominator used to calculate the rate varied from 90 to 127 based on the number of patients with a baseline value and at least 1 post-treatment value.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; COVID-19=coronavirus disease of 2019.

## Select Important Safety Information

**Embryo-Fetal Toxicity:** Jaypirca can cause fetal harm in a pregnant woman. Advise pregnant women of fetal risk and females of reproductive potential to use effective contraception during treatment and for one week after last dose.

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

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## How Supplied[1]

| Tablet Strength* | Quantity of Tablets per Bottle | NDC | Days' Supply |
|---|---|---|---|
| 100 mg | 60 | 0002-7026-60 | 30 days |
| 50 mg | 30 | 0002-6902-30 | |

*The standard dose for Jaypirca is two 100 mg tablets once daily, dispensed via a 100 mg 60-count bottle for a 30-day supply. Jaypirca is also available in 50 mg 30-count bottles for patients who require dose modifications.[1]

NDC=National Drug Code.

## Storage and Handling[1,2]

| | |
|---|---|
| **Strength[1]** | 50 mg and 100 mg tablets |
| **Hazardous classification[2]** | Physical hazards: Not classified<br>Health hazards: Reproductive toxicity; specific target organ toxicity, repeated exposure<br>OSHA defined hazards: Not classified |
| **Hazard statement[2]** | H360: May damage the unborn child<br>H373: May cause damage to organs (blood, eyes) through prolonged or repeated exposure |
| **Storage[1]** | Store Jaypirca tablets at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) ([see USP Controlled Room Temperature]) |
| **Precautions for safe handling[2]** | P201: Obtain special instructions before use<br>P202: Do not handle until all safety precautions have been read and understood<br>P260: Do not breathe dust<br>P273: Avoid release to the environment<br>P280: Wear protective gloves, protective clothing, eye protection, face protection |
| **Disposal[2]** | Dispose of contents/container in accordance with local, regional, national, or international regulations |
| **Stability and reactivity[2]** | • Reactivity: The product is stable and non-reactive under normal conditions of use, storage, and transport<br>• Chemical stability: Material is stable under normal conditions<br>• Possibility of hazardous reactions: No dangerous reaction known under conditions of normal use |

OSHA=Occupational Safety and Health Administration.

## Select Important Safety Information

**Serious Adverse Reactions (ARs) in patients who received Jaypirca occurred in**

- 38% of patients with MCL. Serious ARs occurring in ≥2% of patients were pneumonia, COVID-19, musculoskeletal pain, hemorrhage, pleural effusion, and sepsis
- 56% of patients with CLL/SLL. Serious ARs occurring in ≥5% of patients were pneumonia, COVID-19, sepsis, and febrile neutropenia

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

Jaypirca® pirtobrutinib 50,100 mg tablets

## Tablet Strength and Dosing Regimen: 30-Day Supply[1]

| Target Dose | Dose Modification | How Dispensed | Required Quantity of 100 mg 60-Count Bottles | | Required Quantity of 50 mg 30-Count Bottles |
|---|---|---|---|---|---|
| 200 mg orally once daily | Standard dose | Two (2) 100 mg tablets once daily | 1 | | 0 |
| 200 mg orally once daily | First AE occurrence requiring dose modification (dose interruption only) | Two (2) 100 mg tablets once daily | 1 | | 0 |
| 100 mg orally once daily | Second AE occurrence requiring dose modification (first dose reduction) | One (1) 100 mg tablet once daily* | 1 split bottle | OR | 2 |
| 50 mg orally once daily | Third AE occurrence requiring dose modification (second dose reduction) | One (1) 50 mg tablet once daily | 0 | | 1 |
| 300 mg orally once daily | Dose escalation for concomitant use with moderate CYP3A inducers† | Three (3) 100 mg tablets once daily | 1 full bottle<br>1 split bottle | | 0 |
| 150 mg orally once daily | Dose reduction for concomitant use with CYP3A inhibitors‡ | Three (3) 50 mg tablets once daily | 0 | | 3 |
| 100 mg orally once daily | Dose reduction for severe renal impairment§ | One (1) 100 mg tablet once daily* | 1 split bottle | OR | 2 |

AE=adverse event.

*For 100 mg once-daily dosing, dispensing a 100 mg 60-count bottle will provide a 60-day supply. For a 30-day supply, split the 100 mg 60-count bottle or dispense two 50 mg 30-count bottles.

†If concomitant use with moderate CYP3A inducers is unavoidable and the current dosage of Jaypirca is 200 mg once daily, increase the dose to 300 mg. If the current dosage is 50 mg or 100 mg once daily, increase the dose by 50 mg.

‡Patients receiving Jaypirca concomitantly with a strong CYP3A inhibitor should reduce their current dose by 50 mg. If the current dosage is 50 mg once daily, interrupt Jaypirca treatment for the duration of strong CYP3A inhibitor use. After discontinuation of a strong CYP3A inhibitor for 5 half-lives, resume the Jaypirca dose that was taken prior to initiating the strong CYP3A inhibitor.

§For patients with severe renal impairment, reduce the Jaypirca dose to 100 mg once daily if the current dose is 200 mg once daily, otherwise reduce the dose by 50 mg. If the current dosage is 50 mg once daily, discontinue Jaypirca. No dosage adjustment of Jaypirca is recommended in patients with mild to moderate renal impairment.

## Select Important Safety Information

**Fatal Adverse Reactions (ARs)** within 28 days of the last Jaypirca dose occurred in

- 7% of patients with MCL, most commonly due to infections (4.7%), including COVID-19 (3.1% of all patients)
- 11% of patients with CLL/SLL, most commonly due to infections (10%), including sepsis (5%) and COVID-19 (2.7%)

**Please see Important Safety Information on pages 10-12 and click for Prescribing Information and Patient Information for Jaypirca.**

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## Additional Resources

| | |
|---|---|
| **Lilly support services** | • LillyMedical.com • Lilly.com/resources/lilly-answers-center • LillyOncologySupportCenter.com |
| **Jaypirca savings and affordability** | • Savings Card: https://www.jaypirca.com/hcp/savings-support#savings |
| **Jaypirca patient initiation and support** | • Jaypirca Interim Access Program, Insurance and Coverage Assistance, Jaypirca Ongoing Support, Field Reimbursement Managers: https://www.jaypirca.com/hcp/savings-support |
| **Jaypirca reimbursement** | • Sample Letter of Medical Necessity, Sample Letter of Appeals, and Access, Distribution, and Reimbursement Guide: https://www.jaypirca.com/hcp/savings-support#access-resources |

## Select Important Safety Information

**Dose modifications and discontinuations due to ARs:**

- **Patients with MCL:** Dose reductions in 4.7%, treatment interruption in 32%, permanent discontinuation in 9%. ARs resulting in dosage modification in >5% of patients included pneumonia and neutropenia. ARs resulting in permanent discontinuation of Jaypirca in >1% of patients included pneumonia.
- **Patients with CLL/SLL:** Dose reductions in 3.6%, treatment interruption in 42%, permanent discontinuation in 9%. ARs resulting in dose reductions in >1% of patients included neutropenia; treatment interruptions in >5% of patients included pneumonia, neutropenia, febrile neutropenia, and COVID-19; and permanent discontinuation of Jaypirca in >1% of patients included second primary malignancy, COVID-19, and sepsis.

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## Important Safety Information for Jaypirca (pirtobrutinib)

**Infections:** Fatal and serious infections (including bacterial, viral, fungal) and opportunistic infections occurred in Jaypirca-treated patients. In a clinical trial, Grade ≥3 infections occurred in 24% of patients with hematologic malignancies, most commonly pneumonia (14%); fatal infections occurred in 4.4%. Sepsis (6%) and febrile neutropenia (4%) occurred. In patients with CLL/SLL, Grade ≥3 infections occurred (32%), with fatal infections occurring in 8%. Opportunistic infections included *Pneumocystis jirovecii* pneumonia and fungal infection. Consider prophylaxis, including vaccinations and antimicrobial prophylaxis, in patients at increased risk for infection, including opportunistic infections. Monitor patients for signs and symptoms, evaluate promptly, and treat appropriately. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

**Hemorrhage:** Fatal and serious hemorrhage has occurred with Jaypirca. Major hemorrhage (Grade ≥3 bleeding or any central nervous system bleeding) occurred in 3% of patients, including gastrointestinal hemorrhage; fatal hemorrhage occurred (0.3%). Bleeding of any grade, excluding bruising and petechiae, occurred in 17%. Major hemorrhage occurred in patients taking Jaypirca with (0.7%) and without (2.3%) antithrombotic agents. Consider risks/benefits of co-administering antithrombotic agents with Jaypirca. Monitor patients for signs of bleeding. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca. Consider benefit/risk of withholding Jaypirca 3-7 days pre- and post-surgery depending on type of surgery and bleeding risk.

**Cytopenias:** Jaypirca can cause cytopenias, including neutropenia, thrombocytopenia, and anemia. In a clinical trial, Grade 3 or 4 cytopenias, including decreased neutrophils (26%), decreased platelets (12%), and decreased hemoglobin (12%), developed in Jaypirca-treated patients. Grade 4 decreased neutrophils (14%) and Grade 4 decreased platelets (6%) developed. Monitor complete blood counts regularly during treatment. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

**Cardiac Arrhythmias:** Cardiac arrhythmias occurred in patients who received Jaypirca. In a clinical trial of patients with hematologic malignancies, atrial fibrillation or flutter were reported in 3.2% of Jaypirca-treated patients, with Grade 3 or 4 atrial fibrillation or flutter in 1.5%. Other serious cardiac arrhythmias such as supraventricular tachycardia and cardiac arrest occurred (0.5%). Patients with cardiac risk factors such as hypertension or previous arrhythmias may be at increased risk. Monitor for signs and symptoms of arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea) and manage appropriately. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

**Second Primary Malignancies:** Second primary malignancies, including non-skin carcinomas, developed in 9% of Jaypirca-treated patients. The most frequent malignancy was non-melanoma skin cancer (4.6%). Other second primary malignancies included solid tumors (including genitourinary and breast cancers) and melanoma. Advise patients to use sun protection and monitor for development of second primary malignancies.

**Embryo-Fetal Toxicity:** Jaypirca can cause fetal harm in pregnant women. Administration of pirtobrutinib to pregnant rats during organogenesis caused embryo-fetal toxicity, including embryo-fetal mortality and malformations at maternal exposures (AUC) approximately 3-times the recommended 200 mg/day dose. Advise pregnant women of potential fetal risk and females of reproductive potential to use effective contraception during treatment and for one week after last dose.

### Adverse Reactions (ARs) in Patients Who Received Jaypirca

The most common (≥20%) ARs in the BRUIN pooled safety population of patients with hematologic malignancies (n=593) were decreased neutrophil count (46%), decreased hemoglobin (39%), fatigue (32%), decreased lymphocyte count (31%), musculoskeletal pain (30%), decreased platelet count (29%), diarrhea (24%), COVID-19 (22%), bruising (21%), cough (20%).

**Please see Important Safety Information continued on pages 11 and 12 and click for Prescribing Information and Patient Information for Jaypirca.**



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# Important Safety Information for Jaypirca (pirtobrutinib) (continued)

## ARs in Patients Who Received Jaypirca (continued)

### Mantle Cell Lymphoma

**Serious ARs** occurred in 38% of patients. Serious ARs occurring in ≥2% of patients were pneumonia (14%), COVID-19 (4.7%), musculoskeletal pain (3.9%), hemorrhage (2.3%), pleural effusion (2.3%), and sepsis (2.3%). **Fatal ARs** within 28 days of last Jaypirca dose occurred in 7% of patients, most commonly due to infections (4.7%), including COVID-19 (3.1% of all patients).

**Dose Modifications and Discontinuations:** ARs led to dose reductions in 4.7%, treatment interruption in 32%, and permanent discontinuation of Jaypirca in 9% of patients. ARs resulting in dosage modification in >5% of patients included pneumonia and neutropenia. ARs resulting in permanent discontinuation in >1% of patients included pneumonia.

**ARs (all Grades %; Grade 3-4 %) in ≥10% of Patients:** fatigue (29; 1.6), musculoskeletal pain (27; 3.9), diarrhea (19; -), edema (18; 0.8), dyspnea (17; 2.3), pneumonia (16; 14), bruising (16; -), peripheral neuropathy (14; 0.8), cough (14; -), rash (14; -), fever (13; -), constipation (13; -), arthritis/arthralgia (12; 0.8), hemorrhage (11; 3.1), abdominal pain (11; 0.8), nausea (11; -), upper respiratory tract infections (10; 0.8), dizziness (10; -).

**Select Laboratory Abnormalities (all Grades %; Grade 3 or 4 %) that Worsened from Baseline in ≥10% of Patients:** hemoglobin decreased (42; 9), platelet count decreased (39; 14), neutrophil count decreased (36; 16), lymphocyte count decreased (32; 15), creatinine increased (30; 1.6), calcium decreased (19; 1.6), AST increased (17; 1.6), potassium decreased (13; 1.6), sodium decreased (13; -), lipase increased (12; 4.4), alkaline phosphatase increased (11; -), ALT increased (11; 1.6), potassium increased (11; 0.8). Grade 4 laboratory abnormalities in >5% of patients included neutrophils decreased (10), platelets decreased (7), lymphocytes decreased (6).

### Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

**Serious ARs** occurred in 56% of patients. Serious ARs occurring in ≥5% of patients were pneumonia (18%), COVID-19 (9%), sepsis (7%), and febrile neutropenia (7%). **Fatal ARs** within 28 days of last Jaypirca dose occurred in 11% of patients, most commonly due to infections (10%), including sepsis (5%) and COVID-19 (2.7%).

**Dose Modifications and Discontinuations:** ARs led to dose reductions in 3.6%, treatment interruption in 42%, and permanent discontinuation of Jaypirca in 9% of patients. ARs resulting in dose reductions in >1% included neutropenia; treatment interruptions in >5% of patients included pneumonia, neutropenia, febrile neutropenia, and COVID-19; permanent discontinuation in >1% of patients included second primary malignancy, COVID-19, and sepsis.

**ARs (all Grades %; Grade 3-4 %) in ≥10% of Patients:** fatigue (36; 2.7), bruising (36; -), cough (33; -), musculoskeletal pain (32; 0.9), COVID-19 (28; 7), pneumonia (27; 16), diarrhea (26; -), abdominal pain (25; 2.7), dyspnea (22; 2.7), hemorrhage (22; 2.7), edema (21; -), nausea (21; -), pyrexia (20; 2.7), headache (20; 0.9), arthritis/arthralgia (19; 1.8), rash (19; 0.9), peripheral neuropathy (16; 3.6), dizziness (15; -), fall (14; 0.9), constipation (14; -), insomnia (14; -), upper respiratory tract infections (13; 2.7), second primary malignancy (13; 2.7), renal insufficiency (12; 6), hypertension (12; 5), neurological changes (12; 2.7), mucositis (12; 0.9), decreased appetite (12; -), respiratory tract infection (11; 1.8), supraventricular tachycardia (10; 5).

**Please see Important Safety Information continued on page 12 and click for Prescribing Information and Patient Information for Jaypirca.**

Jaypirca® pirtobrutinib 50,100 mg tablets

# Important Safety Information for Jaypirca (pirtobrutinib) (continued)

## ARs in Patients Who Received Jaypirca (continued)

### Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (continued)

**Select Laboratory Abnormalities (all Grades %; Grade 3 or 4 %) that Worsened from Baseline in ≥20% of Patients:** neutrophil count decreased (63; 45), hemoglobin decreased (48; 19), calcium decreased (40; 2.8), platelet count decreased (30; 15), sodium decreased (30; -), lymphocyte count decreased (23; 8), ALT increased (23; 2.8), AST increased (23; 1.9), creatinine increased (23; -), lipase increased (21; 7), alkaline phosphatase increased (21; -). Grade 4 laboratory abnormalities in >5% of patients included neutrophils decreased (23).

## Drug Interactions

**Strong CYP3A Inhibitors:** Concomitant use with Jaypirca increased pirtobrutinib systemic exposure, which may increase risk of Jaypirca ARs. Avoid use of strong CYP3A inhibitors with Jaypirca. If concomitant use is unavoidable, reduce Jaypirca dosage according to approved labeling.

**Strong or Moderate CYP3A Inducers:** Concomitant use with Jaypirca decreased pirtobrutinib systemic exposure, which may reduce Jaypirca efficacy. Avoid concomitant use of Jaypirca with strong or moderate CYP3A inducers. If concomitant use with moderate CYP3A inducers is unavoidable, increase Jaypirca dosage according to approved labeling.

**Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP Substrates:** Concomitant use with Jaypirca increased their plasma concentrations, which may increase risk of adverse reactions related to these substrates for drugs that are sensitive to minimal concentration changes. Follow recommendations for these sensitive substrates in their approved labeling.

## Use in Special Populations

**Pregnancy and Lactation:** Due to potential for Jaypirca to cause fetal harm, verify pregnancy status in females of reproductive potential prior to starting Jaypirca and advise use of effective contraception during treatment and for one week after last dose. Presence of pirtobrutinib in human milk is unknown. Advise women not to breastfeed while taking Jaypirca and for one week after last dose.

**Geriatric Use:** In the pooled safety population of patients with hematologic malignancies, patients aged ≥65 years experienced higher rates of Grade ≥3 ARs and serious ARs compared to patients <65 years of age.

**Renal Impairment:** Severe renal impairment increases pirtobrutinib exposure. Reduce Jaypirca dosage in patients with severe renal impairment according to approved labeling.

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**Please click for Prescribing Information and Patient Information for Jaypirca.**

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**References: 1.** Jaypirca. Prescribing Information. Lilly USA, LLC.
**2.** Jaypirca. Safety Data Sheet. Lilly USA, LLC.





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