

Jaypirca[®] (pirtobrutinib) EHR Order Set Manual Instructions for the Epic[®] EHR System

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; EHR=electronic health record.

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.



Jaypirca[®]
pirtobrutinib 50, 100 mg
tablets

Lilly



Disclaimer:

- **This document is solely intended to provide health systems with instructions to manually add Jaypirca as an additional treatment option for CLL/SLL or MCL within the approved indication and consistent with Prescribing Information. This document is not intended to be a sole treatment option in any line of therapy for CLL/SLL and MCL or to establish Jaypirca as a preferred treatment option. Provider shall ensure other treatment options for CLL/SLL and MCL remain available for all lines of therapy after implementation of instructions. If a Jaypirca order set is present within the EHR system, please disregard these manual instructions**
- The Customers (ie, physician, medical group, integrated delivery network) shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each Customer's EHR system
- Capabilities, functionality, and setup (customization) for each EHR system may vary. Lilly shall not be responsible for revising the implementation instructions it provides to any Customer if the Customer modifies or changes its software, or the configuration of its EHR system, after such time as the implementation instructions have been initially provided by Lilly
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- While EHRs may assist providers in identifying appropriate patients for consideration of assessment, treatment, and referral, the decision and action should ultimately be decided by a provider in consultation with the patient, after a review of the patient's records to determine eligibility, and Lilly shall have no liability thereto
- The instructions have not been designed to, and are not tools and/or solutions for, meeting Advancing Care Information and/or any other quality/accreditation requirement
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Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Background and Considerations

These EHR instructions serve as guidance for the Epic® EHR system, are specific to CLL/SLL and MCL, and are not appropriate for other conditions, treatments, therapeutic areas, or for other EHR systems. Separate instructions are provided for each indication and can be easily reached through the top navigation.

The process outlined hereafter is variable, and not all steps will apply to every health system. Any steps or settings hereafter that are not part of a health system's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The practice is solely responsible for implementing, testing, monitoring, and the ongoing operation of any EHR tools.

EHR vendor updates may result in 2 separate product entries, at which time the manually added entry can be deleted.

Please check your policies to ensure manual addition of a medication into the EHR system is permitted.

This guide is not endorsed, certified, or sponsored by Epic. Epic is not affiliated with Lilly's products and services.

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Epic Manual Instructions: CLL/SLL

Existing protocols may be used as a foundation for CLL/SLL. Consider modifying a Beacon protocol as a starting template, while saving the original protocol.

There are 3 steps to update a Beacon protocol in the Epic EHR system.

1. Create order groups to hold Jaypirca 200 mg and the Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions. Note: Additional order groups may be available. Review the health system's current governance regarding order sets and adjust the instructions appropriately
2. Add the Jaypirca Prescribing Information and resource links to the medication record
3. Add the order groups to the Beacon protocol

STEP 1 General Instructions for Creating the Order Groups

1. Review the Regimen Category Order Group to confirm Medications are values in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new Order Group named "Medications"
4. Set the default category to Medications
5. Create the following Order Groups:

Order Group 1: Jaypirca

1. Right click in the empty field located on the bottom of the window
2. Select Add > Orders
3. Select Jaypirca
4. Complete the Jaypirca medication details. *The recommended dosage of Jaypirca is 200 mg orally once daily, taken as two 100 mg tablets, until disease progression or unacceptable toxicity. For the administration instructions, dose reductions, dose modifications, and other information, refer to the full Prescribing Information*

Advise patients of the following:

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

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: CLL/SLL (continued)

Additional Order Group(s): Jaypirca Treatment Conditions (alternatively, consider Monitoring and Hold Parameters) **and Warnings and Precautions**

1. Review the Regimen Category Order Group to confirm Treatment Conditions (or Monitoring and Hold Parameters, and Warnings and Precautions) are values in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new Order Group named *Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions*
4. Set the default category to Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions
5. Complete the following Order Group(s):
 - Right click in the empty field located at the bottom of the window
 - Select Add > Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions
 - Enter:
 - For all of the latest dosage and administration, warnings and precautions, and adverse reactions information:
See Jaypirca Prescribing Information for most recent version: <https://uspl.lilly.com/jaypirca/jaypirca.html?s=pi>
 - Recommended dosage: *The recommended dosage of Jaypirca is 200 mg orally once daily, taken as two 100 mg tablets, until disease progression or unacceptable toxicity*
 - › Advise patients of the following:
 - › Swallow tablets whole with water. Do not cut, crush, or chew tablets
 - › Take Jaypirca at the same time each day. Jaypirca may be taken with or without food
 - › If a dose of Jaypirca is missed by more than 12 hours, do not make up the dose and take the next dose as scheduled

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: CLL/SLL (continued)

– Recommended Dosage Modifications of Jaypirca for Adverse Reactions

Adverse Reactions	Occurrences Requiring Dose Modification	Modification (Starting Dose 200 mg Once Daily)
<ul style="list-style-type: none"> • Grade 3 or greater nonhematologic toxicity* • Absolute neutrophil count <1 to $0.5 \times 10^9/L$ with fever and/or infection • Absolute neutrophil count $<0.5 \times 10^9/L$ lasting ≥ 7 days • Platelet count <50 to $25 \times 10^9/L$ with bleeding • Platelet count $<25 \times 10^9/L$ 	1st occurrence	Interrupt until recovery to grade 1 or baseline RESTART at original dose (200 mg once daily*)
	2nd occurrence	Interrupt until recovery to grade 1 or baseline RESTART at 100 mg once daily
	3rd occurrence	Interrupt until recovery to grade 1 or baseline 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.

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

For patients with severe renal impairment (eGFR 15-29 mL/min), reduce Jaypirca dose to 100 mg 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 recommended in patients with mild to moderate renal impairment (eGFR 30-89 mL/min).

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.

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.

eGFR=estimated glomerular filtration rate.

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: CLL/SLL (continued)

- *Warnings and Precautions (See Jaypirca Prescribing Information for more detailed information)*
 - › Infections
 - › Hemorrhage
 - › Cytopenias
 - › Cardiac Arrhythmias
 - › Second Primary Malignancies
 - › Embryo-Fetal Toxicity
- *Adverse Reactions*

The following clinically significant adverse reactions are described elsewhere in the labeling:

 - › Infections [see Warnings and Precautions (5.1)]
 - › Hemorrhage [see Warnings and Precautions (5.2)]
 - › Cytopenias [see Warnings and Precautions (5.3)]
 - › Cardiac Arrhythmias [see Warnings and Precautions (5.4)]
 - › Second Primary Malignancies [see Warnings and Precautions (5.5)]

STEP 2 Add the Jaypirca Prescribing Information links to the medication record

1. Log in the Medication Master File (ERX) with authorized user credentials
2. Use the search feature in the Medication Master File to search and select the desired Jaypirca record
3. Select the Patient Medication References Screen and create 2 new rows
 - **Row 1:** For Display Name, enter “Jaypirca Prescribing Information.”
In the Text field, enter: *See URL for additional Jaypirca dosing and administration information*
In the URL field, enter this hyperlink: <https://uspl.lilly.com/jaypirca/jaypirca.html?s=pi>
 - **Row 2:** For Display Name, enter “Jaypirca Resources for Healthcare Providers (HCPs) and Patients”
In the Text field, enter: *See URL for additional Jaypirca resources for HCPs and Patients such as a Treatment Guide, Patient Brochure, and Patient Savings Offers*
In the URL field, enter this hyperlink: <https://www.jaypirca.com/hcp/savings-support#access-resources>
4. Save the record
5. Release the record to production after satisfactory testing has been completed

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: CLL/SLL (continued)

STEP 3

Add the Order Groups to the Beacon protocol for Jaypirca for adult patients with CLL/SLL who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor

The steps detail how to add the Order Groups created in Step 1 to an existing Beacon protocol to create a new Jaypirca order set for adult patients with CLL/SLL who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor:

1. Click the Epic logo > Admin > Beacon Admin > Protocol Builder
Search for order sets using the search query “Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma” or “CLL/SLL.”
Note: The existing order set will serve as a template for the new Jaypirca order set only.
2. Select the treatment regimen and add the newly created order group(s) from the previous **Step 1** to the treatment regimen: 200 mg orally once daily until disease progression or unacceptable toxicity
3. Add in the additional Jaypirca Order Group(s) created in **Step 1** with the Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Jaypirca Warnings and Precautions
4. Update the Beacon protocol description to: “Jaypirca is a kinase inhibitor indicated for the treatment of 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. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.”
5. Click Save
6. Release to production environment after satisfactory testing has been completed

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: MCL

Existing protocols may be used as a foundation for MCL. Consider modifying a Beacon protocol as a starting template, while saving the original protocol.

There are 3 steps to update a Beacon protocol in the Epic EHR system.

1. Create order groups to hold Jaypirca 200 mg and the Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions. Note: Additional order groups may be available. Review the health system's current governance regarding order sets and adjust the instructions appropriately
2. Add the Jaypirca Prescribing Information and resource links to the medication record
3. Add the order groups to the Beacon protocol

STEP 1 General Instructions for Creating the Order Groups

1. Review the Regimen Category Order Group to confirm Medications are values in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new Order Group named "Medications"
4. Set the default category to Medications
5. Create the following Order Groups:

Order Group 1: Jaypirca

1. Right click in the empty field located on the bottom of the window
2. Select Add > Orders
3. Select Jaypirca
4. Complete the Jaypirca medication details. *The recommended dosage of Jaypirca is 200 mg orally once daily, taken as two 100 mg tablets, until disease progression or unacceptable toxicity. For the administration instructions, dose reductions, dose modifications, and other information, refer to the full Prescribing Information*

Advise patients of the following:

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

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: MCL (continued)

Additional Order Group(s): Jaypirca Treatment Conditions (alternatively, consider Monitoring and Hold Parameters) **and Warnings and Precautions**

1. Review the Regimen Category Order Group to confirm Treatment Conditions (or Monitoring and Hold Parameters, and Warnings and Precautions) are values in the category list
2. Select the Order Group Builder (Admin > Beacon Admin > Order Group Builder)
3. Create a new Order Group named *Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions*
4. Set the default category to Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions
5. Complete the following Order Group(s):
 - Right click in the empty field located at the bottom of the window
 - Select Add > Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Warnings and Precautions
 - Enter:
 - For all of the latest dosage and administration, warnings and precautions, and adverse reactions information:
See Jaypirca Prescribing Information for most recent version: <https://uspl.lilly.com/jaypirca/jaypirca.html?s=pi>
 - Recommended dosage: *The recommended dosage of Jaypirca is 200 mg orally once daily, taken as two 100 mg tablets, until disease progression or unacceptable toxicity*
 - › Advise patients of the following:
 - › Swallow tablets whole with water. Do not cut, crush, or chew tablets
 - › Take Jaypirca at the same time each day. Jaypirca may be taken with or without food
 - › If a dose of Jaypirca is missed by more than 12 hours, do not make up the dose and take the next dose as scheduled

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: MCL (continued)

– Recommended Dosage Modifications of Jaypirca for Adverse Reactions

Adverse Reactions	Occurrences Requiring Dose Modification	Modification (Starting Dose 200 mg Once Daily)
<ul style="list-style-type: none"> Grade 3 or greater nonhematologic toxicity* Absolute neutrophil count <1 to $0.5 \times 10^9/L$ with fever and/or infection Absolute neutrophil count $<0.5 \times 10^9/L$ lasting ≥ 7 days Platelet count <50 to $25 \times 10^9/L$ with bleeding Platelet count $<25 \times 10^9/L$ 	1st occurrence	Interrupt until recovery to grade 1 or baseline RESTART at original dose (200 mg once daily*)
	2nd occurrence	Interrupt until recovery to grade 1 or baseline RESTART at 100 mg once daily
	3rd occurrence	Interrupt until recovery to grade 1 or baseline 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.

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

For patients with severe renal impairment (eGFR 15-29 mL/min), reduce Jaypirca dose to 100 mg 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 recommended in patients with mild to moderate renal impairment (eGFR 30-89 mL/min).

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.

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.

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: MCL (continued)

- *Warnings and Precautions (See Jaypirca Prescribing Information for more detailed information)*
 - › Infections
 - › Hemorrhage
 - › Cytopenias
 - › Cardiac Arrhythmias
 - › Second Primary Malignancies
 - › Embryo-Fetal Toxicity
- *Adverse Reactions*

The following clinically significant adverse reactions are described elsewhere in the labeling:

 - › Infections [see Warnings and Precautions (5.1)]
 - › Hemorrhage [see Warnings and Precautions (5.2)]
 - › Cytopenias [see Warnings and Precautions (5.3)]
 - › Cardiac Arrhythmias [see Warnings and Precautions (5.4)]
 - › Second Primary Malignancies [see Warnings and Precautions (5.5)]

STEP 2 Add the Jaypirca Prescribing Information links to the medication record

1. Log in the Medication Master File (ERX) with authorized user credentials
2. Use the search feature in the Medication Master File to search and select the desired Jaypirca record
3. Select the Patient Medication References Screen and create 2 new rows
 - **Row 1:** For Display Name, enter “Jaypirca Prescribing Information.”
In the Text field, enter: *See URL for additional Jaypirca dosing and administration information*
In the URL field, enter this hyperlink: <https://uspl.lilly.com/jaypirca/jaypirca.html?s=pi>
 - **Row 2:** For Display Name, enter “Jaypirca Resources for Healthcare Providers (HCPs) and Patients”
In the Text field, enter: *See URL for additional Jaypirca resources for HCPs and Patients such as a Treatment Guide, Patient Brochure, and Patient Savings Offers*
In the URL field, enter this hyperlink: <https://www.jaypirca.com/hcp/savings-support#access-resources>
4. Save the record
5. Release the record to production after satisfactory testing has been completed

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Epic Manual Instructions: MCL (continued)

STEP 3

Add the Order Groups to the Beacon protocol for Jaypirca for adult patients with R/R MCL after at least two lines of systemic therapy, including a BTK inhibitor

The steps detail how to add the Order Groups created in Step 1 to an existing Beacon protocol to create a new Jaypirca order set for adult patients with R/R MCL after at least two lines of systemic therapy, including a BTK inhibitor:

1. Click the Epic logo > Admin > Beacon Admin > Protocol Builder
Search for order sets using the search query “Mantle Cell Lymphoma” or “MCL.”
Note: The existing order set will serve as a template for the new Jaypirca order set only.
2. Select the treatment regimen and add the newly created order group(s) from the previous **Step 1** to the treatment regimen: 200 mg orally once daily until disease progression or unacceptable toxicity
3. Add in the additional Jaypirca Order Group(s) created in **Step 1** with the Jaypirca Treatment Conditions (or Monitoring and Hold Parameters) and Jaypirca Warnings and Precautions
4. Update the Beacon protocol description to: *“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. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.”*
5. Click Save
6. Release to production environment after satisfactory testing has been completed

Please see Important Safety Information on pages 15-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





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.

Please see Important Safety Information continued on pages 16-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Important Safety Information for Jaypirca (pirtobrutinib) (continued)

Adverse Reactions (ARs) in Patients Who Received Jaypirca

The most common ($\geq 20\%$) 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%).

Mantle Cell Lymphoma

Serious ARs occurred in 38% of patients. Serious ARs occurring in $\geq 2\%$ 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 $\geq 10\%$ 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 $\geq 10\%$ 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 $\geq 5\%$ 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.

Please see Important Safety Information continued on pages 17-18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Important Safety Information for Jaypirca (pirtobrutinib) (continued)

ARs in Patients Who Received Jaypirca (continued)

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (continued)

ARs (all Grades %; Grade 3-4 %) in $\geq 10\%$ 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/arthritis (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).

Select Laboratory Abnormalities (all Grades %; Grade 3 or 4 %) that Worsened from Baseline in $\geq 20\%$ 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.

Please see Important Safety Information continued on page 18 and click for [Prescribing Information](#) and [Patient Information](#) for Jaypirca.





Important Safety Information for Jaypirca (pirtobrutinib) (continued)

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.

Reference: Jaypirca. Prescribing Information. Lilly USA, LLC.

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