COVERAGE AUTHORIZATION REQUESTS AND APPEALS GUIDE

Composing a Letter of Medical Necessity

Jaypirca® pirtobrutinib 50,100 mg tablets

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Many health plans require that a Letter of Medical Necessity accompanies a Coverage Authorization Appeals Letter.* The purpose of a Letter of Medical Necessity is to explain the prescribing healthcare professional's (HCP's) rationale and clinical decision-making when choosing a treatment.

This resource, **Composing a Letter of Medical Necessity**, provides information on the process of drafting a Letter of Medical Necessity. Included on the following page is a list of considerations that can be followed when creating a Letter of Medical Necessity. In addition, 2 sample letters are attached to this document and include information that plans often require. Note that some plans have specific Coverage Authorization Forms that must be used to document a Letter of Medical Necessity. Also see **Preparing a Coverage Authorization Appeals Letter** for more information.

Follow the patient's plan requirements when requesting Jaypirca; otherwise, treatment may be delayed.

*For Medicare beneficiaries, specific requirements must be met for the HCP to be considered a legal representative of the patient in an appeal. For additional information, please visit https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/downloads/cms1696.pdf.

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.

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

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.

Please see Important Safety Information on pages 5-7 and click for Prescribing Information and Patient Information for Jaypirca.

Composing a Letter of Medical Necessity

Letter of Medical Necessity Considerations

1. If required and following the patient's consent, include the patient's full name, date of birth, plan identification number, and case identification number if a decision has already been rendered.
2. Add the prescribing HCP's National Provider Identifier (NPI) number and specialty.
3. Provide a copy of the patient's records with the following details: patient's history (including relevant clinical and progress notes), diagnosis with specific International Classification of Diseases (ICD) code, and condition.
4. Note the severity of the patient's condition.
5. Document prior treatments, the duration of each, and the rationale for discontinuation. It may be beneficial to include Common Procedural Terminology, 4th edition (CPT-4) codes and/or J-codes to define prior services/treatments, so that the health plan can conduct research and make a timely determination.
6. Attach clinical documentation that supports your recommendation; this information may be found in the Jaypirca Prescribing Information and/or clinical, peer-reviewed literature. Disclaimer: may not be all-encompassing.

Sample Letter of Medical Necessity

HCPs can follow this format for patients who are **NOT** currently receiving treatment with Jaypirca® (pirtobrutinib).

[Date]
[Medical director]
[Name of health plan]
[Mailing address]

Re: **[Patient's name]**
[Plan identification number]
[Date of birth]
[Case identification number]

To whom it may concern:

I am writing to provide additional information to support my claim for **[patient's name]**'s treatment of **[relapsed or refractory (R/R) mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor,** or **chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) after at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor]** with Jaypirca® (pirtobrutinib). In brief, treatment with Jaypirca **200 mg orally once daily** is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Jaypirca.

[Please select the indication that applies for your patient.]

Patient's history, diagnosis, condition, and symptoms*:
Patient must have a diagnosis for an indication of Jaypirca.
Jaypirca is a kinase inhibitor indicated for the treatment of adult patients with:

- R/R MCL after at least two lines of systemic therapy, including a BTK inhibitor
- CLL/SLL who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor

Past Treatments†	Start/Stop Dates	Reason(s) for Discontinuation

[Please detail all that apply and add additional lines as needed.]

[Provide clinical rationale for this treatment; this information may be found in the Jaypirca Prescribing Information and/or clinical, peer-reviewed literature.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Jaypirca.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI #]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]

Encl: Medical records
Clinical trial information

*Include patient's medical records and supporting documentation.
†Identify drug name, strength, dosage form, and therapeutic outcome.

Sample Letter of Medical Necessity

HCPs can follow this format for patients who **HAVE** been treated with Jaypirca® (pirtobrutinib) and have had treatment interruption.

[Date]
[Medical director]
[Name of health plan]
[Mailing address]

Re: **[Patient's name]**
[Plan identification number]
[Date of birth]
[Case identification number]

To whom it may concern:

I am writing to provide additional information to support my claim for **[patient's name]**'s treatment of **[relapsed or refractory (R/R) mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor,** or **chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) after at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor]** with Jaypirca® (pirtobrutinib). In brief, treatment with Jaypirca **200 mg orally once daily** is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Jaypirca.

[Please select the indication that applies for your patient.]

[In this section, describe the severity of the cancer at the time when the patient was first prescribed Jaypirca. In addition, include a summary of the patient's clinical response to Jaypirca and list improvements (if any) in clinical presentation since treatment began.]

Patient's history, diagnosis, condition, and symptoms*:
Patient must have a diagnosis for an indication of Jaypirca.
Jaypirca is a kinase inhibitor indicated for the treatment of adult patients with:
- R/R MCL after at least two lines of systemic therapy, including a BTK inhibitor
- CLL/SLL who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor

Past Treatments†	Start/Stop Dates	Reason(s) for Discontinuation

[Please detail all that apply and add additional lines as needed.]

[Provide clinical rationale for this treatment; this information may be found in the Jaypirca Prescribing Information and/or clinical, peer-reviewed literature.]

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Jaypirca.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI #]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]

Encl: Medical records
Clinical trial information

*Include patient's medical records and supporting documentation.
†Identify drug name, strength, dosage form, and therapeutic outcome.

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 6 and 7 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).

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).

Please see Important Safety Information continued on page 7 and click for Prescribing Information and Patient Information for Jaypirca.

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Important Safety Information for Jaypirca (pirtobrutinib) (continued)

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.

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

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