



Lilly's Jaypirca (pirtobrutinib) recommended by CHMP for approval in the European Union for adults with chronic lymphocytic leukemia (CLL) across all lines of therapy

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The positive opinion is based on results from the Phase 3 BRUIN CLL-313 and BRUIN CLL-314 trials, previously presented at the 2025 American Society of Hematology Annual Meeting and published in The Journal of Clinical Oncology

BRUIN CLL-313 is the first Phase 3 study to evaluate a non-covalent BTK inhibitor exclusively in patients with treatment-naïve CLL and BRUIN CLL-314 is the first Phase 3 CLL trial to compare non-covalent and covalent BTK inhibitors, as well as the first to compare any BTK inhibitors in the treatment-naïve setting

If granted marketing authorization, this would expand pirtobrutinib's indication as a treatment option for patients with CLL in the European Union across all lines of therapy

INDIANAPOLIS, June 26, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion for Jaypirca (pirtobrutinib), a non-covalent Bruton tyrosine kinase (BTK) inhibitor, for the treatment of adults with chronic lymphocytic leukemia (CLL) across all lines of therapy and regardless of prior BTK inhibitor treatment. Following this positive opinion, the application is now referred to the European Commission for final action. The European Commission's decision is expected in the next one to two months.

"Results from BRUIN CLL-313 and BRUIN CLL-314 provide compelling evidence that pirtobrutinib can make a meaningful difference for people living with CLL across multiple lines of therapy," said Paolo Ghia, M.D., professor, medical oncology, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy. "The strong efficacy and tolerability demonstrated in these trials underscores the clinical value pirtobrutinib may offer patients. This positive opinion from the CHMP is an exciting and significant milestone, bringing us closer to a future where pirtobrutinib is an option for more people with CLL across the European Union."

Results from [BRUIN CLL-313](#) and [BRUIN CLL-314](#) were presented at the American Society of Hematology (ASH) Annual Meeting and Exposition in December 2025 and published in *The Journal of Clinical Oncology*.

"Based on the strong results from the BRUIN CLL-313 and CLL-314 studies, we believe Jaypirca has the potential to serve as a meaningful new option for newly diagnosed patients and those who have not yet received a BTK inhibitor," said Jacob Van Naarden, executive vice president and president of Lilly Oncology. "Thanks to the impact of contemporary CLL treatments, many patients may receive fewer lines of therapy over their lifetime, making treatment choices in earlier lines profoundly important. This CHMP opinion represents a step toward an important global approval for Jaypirca in this indication and reflects our ambition to make Jaypirca available to every CLL patient who may benefit, at any line of therapy. Today, we are on the brink of making that a reality across the European Union as we await the European Commission's final decision."

Lilly has also submitted these results to the U.S. Food and Drug Administration (FDA) for approval for adult patients with CLL, with a decision expected in the second half of 2026.

About BRUIN CLL-313

BRUIN CLL-313 is a Phase 3, global, randomized, open-label study of pirtobrutinib versus chemoimmunotherapy (BR) in people with CLL/SLL without 17p deletions who have not been previously treated. The trial enrolled 282 patients who were randomized 1:1 to receive pirtobrutinib (200 mg orally, once daily) or BR per labeled doses. BR is a chemoimmunotherapy regimen used in the treatment of CLL. The primary endpoint is PFS as assessed by blinded IRC. Secondary endpoints include investigator and IRC assessed ORR, duration of response (DoR), and PFS, OS, time to next treatment (TTNT), safety and tolerability and patient-reported outcomes (PRO).

About BRUIN CLL-314

BRUIN CLL-314 is a Phase 3, randomized, open-label study of Jaypirca (pirtobrutinib) versus Imbruvica (ibrutinib) in patients with CLL/SLL who were either treatment-naïve, or who were previously treated and were BTK inhibitor-naïve. The trial enrolled 662 patients who were randomized 1:1 to receive pirtobrutinib (200 mg orally, once daily) or ibrutinib (420 mg orally, once daily). The primary endpoint is ORR as assessed by blinded IRC. Secondary endpoints include investigator and IRC-assessed PFS, duration of response (DoR) and event-free survival (EFS), and time to next treatment (TTNT), OS, safety and tolerability, and patient-reported outcomes (PRO).

About Jaypirca (pirtobrutinib)

Jaypirca (pirtobrutinib, formerly known as LOXO-305) (pronounced jay-pihr-kaa) is a highly selective (300 times more selective for BTK versus 98% of other kinases tested in preclinical studies), non-covalent inhibitor of the enzyme BTK.¹ BTK is a validated molecular target found across numerous B-cell leukemias and lymphomas including mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL).^{2,3} Jaypirca is a U.S. FDA-approved oral prescription medicine, 100 mg or 50 mg tablets taken as a once-daily 200 mg dose with or without food until disease progression or unacceptable toxicity.

About Chronic Lymphocytic Leukemia (CLL)

CLL is a form of slow-growing non-Hodgkin lymphoma that develops from white blood cells known as lymphocytes.^{4,5} CLL is one of the most common types of leukemia in adults.⁶ There are roughly 100,000 new cases of CLL globally each year, and the overall incidence of CLL in Europe is approximately 4.92 cases per 100,000 persons per year.^{6,7} In CLL, the cancer cells are present in the blood.⁶

INDICATIONS FOR JAYPIRCA (pirtobrutinib) (in the United States)

- Adult patients with relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have previously been treated with a covalent BTK inhibitor.
- 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 trial benefit in a confirmatory trial.

IMPORTANT SAFETY INFORMATION FOR JAYPIRCA (pirtobrutinib)

Infections: Fatal and serious infections (including bacterial, viral, fungal) and opportunistic infections occurred in Jaypirca-treated patients. Across clinical trials, Grade ≥ 3 infections occurred (25%), most commonly pneumonia (20%); fatal infections (5%), sepsis (6%), and febrile neutropenia (3.8%) 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 for signs and symptoms, evaluate, and treat. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Hemorrhage: Fatal and serious hemorrhage has occurred with Jaypirca. Across clinical trials, major hemorrhage (Grade ≥ 3 bleeding or any central nervous system bleeding) occurred (2.6%), including gastrointestinal hemorrhage; fatal hemorrhage occurred (0.3%). Bleeding of any grade, excluding bruising and petechiae, occurred (16%). Major hemorrhage occurred when taking Jaypirca with (2.0%) and without (0.6%) antithrombotic agents. Consider risks/benefits of co-administering antithrombotic agents with Jaypirca. Monitor for signs of bleeding. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca. Consider withholding Jaypirca 3-7 days pre- and post-surgery based on surgery type and bleeding risk.

Cytopenias: Jaypirca can cause cytopenias, including neutropenia, thrombocytopenia, and anemia. Across clinical trials, Grade 3 or 4 cytopenias, including decreased neutrophils (27%), decreased platelets (13%), and decreased hemoglobin (11%), developed. Grade 4 decreased neutrophils (15%) and Grade 4 decreased platelets (6%) developed. Monitor complete blood counts regularly. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Cardiac Arrhythmias: Cardiac arrhythmias occurred in patients taking Jaypirca. Across clinical trials, atrial fibrillation or flutter were reported in 3.4% of Jaypirca treated patients, with Grade 3 or 4 atrial fibrillation or flutter in 1.6%. Other serious cardiac arrhythmias such as supraventricular tachycardia and cardiac arrest occurred (0.4%). Cardiac risk factors such as hypertension or previous arrhythmias may increase risk. Monitor and manage signs and symptoms of arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea). Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Second Primary Malignancies: Across clinical trials, second primary malignancies, including non-skin carcinomas, developed in 9% of Jaypirca-treated patients, most frequently non-melanoma skin cancer (4.4%). 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.

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

Embryo-Fetal Toxicity: Jaypirca can cause fetal harm. Administration of pirtobrutinib to pregnant rats 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 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 ($\geq 30\%$) ARs in the pooled safety population of patients with hematologic malignancies (n=704) were decreased neutrophil count (54%), decreased hemoglobin (43%), decreased leukocytes (32%), fatigue (31%), decreased platelets (31%), decreased lymphocyte count (31%), calcium decreased (30%).

Mantle Cell Lymphoma

Serious ARs occurred in 38% of patients, with pneumonia (14%), COVID-19 (4.7%), musculoskeletal pain (3.9%), hemorrhage (2.3%), pleural effusion (2.3%), and sepsis (2.3%) occurring in $\geq 2\%$ of patients. **Fatal ARs** within 28 days of last 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 Due to ARs: Dose reductions in 4.7%, treatment interruption in 32%, and permanent discontinuation of Jaypirca in 9% of patients. Permanent discontinuation in $>1\%$ of patients included pneumonia.

Most common ARs ($\geq 15\%$) and Select Laboratory Abnormalities ($\geq 10\%$) (all Grades %; Grade 3-4 %): hemoglobin decreased (42; 9), platelet count decreased (39; 14), neutrophil count decreased (36; 16), lymphocyte count decreased (32; 15), creatinine increased (30; 1.6), fatigue (29; 1.6), musculoskeletal pain (27; 3.9), calcium decreased (19; 1.6), diarrhea (19; -), edema (18; 0.8), dyspnea (17; 2.3), AST increased (17; 1.6), pneumonia (16; 14), bruising (16; -), potassium decreased (13; 1.6), sodium decreased (13; -), lipase increased (12; 4.4), ALT increased (11; 1.6), potassium increased (11; 0.8), alkaline phosphatase increased (11; -). Grade 4 laboratory abnormalities in $>5\%$ of patients included neutrophils decreased (10), platelets decreased (7), lymphocytes decreased (6).

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma from Single-Arm and Randomized Controlled Clinical Trials

Serious ARs occurred in 47-56% of patients across clinical trials. Serious ARs in $\geq 5\%$ of patients in the single-arm trial were pneumonia (18%), COVID-19 (9%), sepsis (7%), febrile neutropenia (7%). Serious ARs in $\geq 3\%$ of patients in the randomized controlled trial were pneumonia (21%), COVID-19 (5%), sepsis (3.4%). **Fatal ARs** within 28-30 days of last Jaypirca dose occurred in 8-11% of patients, most commonly due to infections

(7-10%), including sepsis (5%), COVID-19 (2.7-5%), and pneumonia (3.4%).

Dose Modifications and Discontinuations Due to ARs: Dose reductions in 3.6-10%, treatment interruption in 42-51%, and permanent discontinuation of Jaypirca in 9-17% of patients. Permanent discontinuation in >1% of patients included second primary malignancy, pneumonia, COVID-19, neutropenia, sepsis, anemia, and cardiac arrhythmias.

Most common ARs and Select Laboratory Abnormalities (≥20%) (all Grades %, Grade 3-4 %)—in a randomized controlled trial: neutrophil count decreased (54; 26), hemoglobin decreased (45; 10), platelet count decreased (37; 17), pneumonia (28; 16), ALT increased (25; 1.8), creatinine increased (25; -), calcium decreased (23; 0.9), sodium decreased (22; 0.9), bilirubin increased (21; 0.9), upper respiratory tract infections (21; 0.9); **in a single-arm trial:** neutrophil count decreased (63; 45), hemoglobin decreased (48; 19), calcium decreased (40; 2.8), fatigue (36; 2.7), bruising (36; -), cough (33; -), musculoskeletal pain (32; 0.9), platelet count decreased (30; 15), sodium decreased (30; -), COVID-19 (28; 7), pneumonia (27; 16), diarrhea (26; -), abdominal pain (25; 2.7), lymphocyte count decreased (23; 8), ALT increased (23; 2.8), AST increased (23; 1.9), creatinine increased (23; -), dyspnea (22; 2.7), hemorrhage (22; 2.7), lipase increased (21; 7), alkaline phosphatase increased (21; -), edema (21; -), nausea (21; -), pyrexia (20; 2.7), headache (20; 0.9). Grade 4 laboratory abnormalities in >5% of patients included neutrophils decreased (23).

Drug Interactions

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

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

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

Use in Specific 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. Presence of pirtobrutinib in human milk is unknown. Advise women to use effective contraception and to not 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: Because severe renal impairment increases pirtobrutinib exposure, reduce Jaypirca dose in these patients according to approved labeling.

PT HCP ISI MCL_CLL Q42025

Please see [Prescribing Information](#) and [Patient Information](#) for Jaypirca.

About Lilly

Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for 150 years, and today our medicines help tens of millions of people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit [Lilly.com](#) and [Lilly.com/news](#), or follow us on [Facebook](#), [Instagram](#), and [LinkedIn](#). P-LLY

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Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Jaypirca (pirtobrutinib), as a potential treatment for adults with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL), and the timeline for future readouts, presentations, and other milestones relating to Jaypirca and its clinical trials, and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that Jaypirca will receive additional regulatory approvals, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

Endnotes & References

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