



Press Release

June 24, 2024

Nippon Shinyaku Co., Ltd.
Eli Lilly Japan K.K.

Japan's PMDA approves Antineoplastic Agent "Jaypirca[®] 50 mg and 100 mg tablets" for Patients with Relapsed or Refractory Mantle Cell Lymphoma Who are Resistant or Intolerant to Other BTK Inhibitors

Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters: Kyoto; President: Toru Nakai) and Eli Lilly Japan K.K. (Eli Lilly Japan; Headquarters: Kobe; President and Representative Director: Simone Thomsen) announced today, June 24, 2024, that Eli Lilly Japan has received marketing authorization in Japan for the antineoplastic agent "Jaypirca[®] 50 mg and 100 mg tablets" (generic name: pirtobrutinib; hereinafter referred to as "Jaypirca") for the treatment of "patients with relapsed or refractory mantle cell lymphoma who are resistant or intolerant to other BTK inhibitors."

Jaypirca is a Bruton tyrosine kinase (BTK) inhibitor that binds reversibly and noncovalently to BTK. BTK is recognized as a target for a variety of B-cell lymphomas, including mantle cell lymphoma (MCL), and leukemia, including chronic lymphocytic leukemia (CLL).^{1,2}

Approval of Jaypirca is based on the efficacy and safety results of Study BRUIN-18001, a global Phase 1/2 study. In this study, the efficacy and safety of Jaypirca were evaluated in patients with relapsed or refractory MCL who were resistant or intolerant to other covalent BTK inhibitors. The centrally assessed overall response rate, the primary endpoint, was 56.9% (95% confidence interval: 44.0, 69.2). The most common adverse drug reactions were fatigue, diarrhea, bruising, dyspnea, muscle pain, platelet count decreased, anemia, and cough.

Based on the alliance agreement concluded in March 2024, Eli Lilly Japan will be responsible for supply of Jaypirca in Japan, while Nippon Shinyaku will be responsible for distribution and sales, as well as information provision activities.

Summary of Product Information

Brand name:	Jaypirca [®] 50 mg tablet, Jaypirca [®] 100 mg tablet
Generic name:	Pirtobrutinib
Indications:	Patients with relapsed or refractory mantle cell lymphoma who are resistant or intolerant to other BTK inhibitors
Dosage and administration:	In adult patients, the recommended dosage is pirtobrutinib 200 mg orally once daily. Reduce the dose accordingly based on the patient's condition.
Date of marketing approval:	June 24, 2024

About the Global Phase 1/2 Study (BRUIN-18001)[※]

In the BRUIN-18001 trial, patients with relapsed or refractory mantle cell lymphoma who were resistant or intolerant to other covalent BTK inhibitors were randomized to receive Jaypirca 200 mg¹ orally once daily. Among 65 patients in the primary efficacy analysis population², the centrally assessed overall response rate, the primary endpoint, was 56.9% (95% confidence interval: 44.0, 69.2). The overall response rate in 8 Japanese patients³ was 50.0% (95% confidence interval: 15.7, 84.3). Among 15 patients with blastoid mantle cell lymphoma previously treated with other covalent BTK inhibitors, the overall response rate was 46.7% (95% confidence interval: 21.3, 73.4).*

Adverse drug reactions were reported in 104 (63.4%) of 164 subjects^{1, 4} in the safety analysis population. The most common adverse drug reactions were fatigue (22.0%), diarrhea (12.2%), bruising (9.8%), dyspnea (9.1%), muscle pain (8.5%), platelet count decreased (6.7%), anemia (6.1%), and cough (6.1%).

Note 1: Included patients whose starting dose of Jaypirca was not 200 mg.

Note 2: Among patients with non-blastoid mantle cell lymphoma previously treated with other covalent BTK inhibitors, up to 65 patients in the order of initiation of treatment were included in the primary efficacy analysis population.

Note 3: Among Japanese patients with non-blastoid mantle cell lymphoma previously treated with other covalent BTK inhibitors, up to 8 patients in the order of initiation of treatment were included in the primary efficacy analysis population.

Note 4: All patients with mantle cell lymphoma who received at least one dose of Jaypirca alone.

* The analysis was performed at the request of regulatory authorities after filing the application for marketing approval.

[※]Based on the package insert for Jaypirca.

About Mantle Cell Lymphoma

MCL is a rare blood cancer and a form of non-Hodgkin lymphoma. MCL arises in B lymphocytes, a type of white blood cell. MCL frequently begins in B cells located in the mantle zone of the outer edge of lymph nodes. As the cancer progresses, it can spread to bone marrow, the spleen, the liver, or the digestive tract.³ Annually, about one in 200,000 people worldwide develop MCL³.

About Nippon Shinyaku

Based on Nippon Shinyaku's business philosophy, "Helping people lead healthier, happier lives," we aim to be an organization trusted by the community through creating unique medicines that will bring hope to patients and families suffering from illness. Please visit our website (<https://www.nippon-shinyaku.co.jp/english/>) for products or detailed information.

About Eli Lilly Japan

Eli Lilly Japan is the Japanese subsidiary of Eli Lilly and Company based in the United States. We have been developing and supplying world-class, innovative medicines by uniting caring with discovery for 50 years to help patients in Japan achieve healthier and more fulfilling lives. We currently contribute to Japanese medicine in multiple areas, including cancer, diabetes, Alzheimer's disease and other central nervous system diseases, as well as autoimmune diseases, etc. For more details, please visit our website. <https://www.lilly.com/jp>

#

1. Hanel W, Epperla N. Emerging therapies in mantle cell lymphoma. *J Hematol Oncol.* 2020;13(1):79. Published 2020 Jun 17. doi:10.1186/s13045-020-00914-1
2. Gu D, Tang H, Wu J, Li J, Miao Y. Targeting Bruton tyrosine kinase using non-covalent inhibitors in B cell malignancies. *J Hematol Oncol.* 2021;14(1):40. Published 2021 Mar 6. doi:10.1186/s13045-021-01049-7
3. National Organization for Rare Disorders. Mantle cell lymphoma. Accessed 26 October 2022. <https://rarediseases.org/rare-diseases/mantle-cell-lymphoma>

Contact

Corporate Communications Dept., Nippon Shinyaku Co., Ltd.
FAX: +81-75-321-9128