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For Immediate Release

European Commission approves IMBRUVICA® (ibrutinib) as the first targeted therapy for patients with previously untreated mantle cell lymphoma who would be eligible for autologous stem cell transplant

Ibrutinib is the first approved Bruton's tyrosine kinase (BTK) inhibitor to demonstrate statistically meaningful outcomes versus autologous stem cell transplant (ASCT) for the frontline treatment of transplant eligible patients with mantle cell lymphoma[1]

Data from the Phase 3 TRIANGLE study defines the fixed-duration ibrutinib-based regimen as a new standard of care (SOC) with significantly improved overall survival and failure-free survival versus ASCT[1]

BEERSE, BELGIUM (July 23, 2025) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved an indication extension of IMBRUVICA® (ibrutinib) in frontline mantle cell lymphoma (MCL).[1] The approval is for ibrutinib in combination with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (ibrutinib + R-CHOP) alternating with R-DHAP (or R-DHAOx)* without ibrutinib, followed by ibrutinib monotherapy, for the treatment of adult patients with previously untreated MCL who would be eligible for autologous stem cell transplant (ASCT).[1]

"MCL is still an aggressive, incurable disease and patients suffer under the burden associated with transplant," said Martin Dreyling, M.D., Ph.D., Ludwig Maximilian University of Munich.** "As a targeted therapy, ibrutinib represents an opportunity to improve long term outcomes earlier in the treatment pathway. Patients now have a new standard of care in first line treatment that not only offers prolonged survival but also avoids short and long-term toxicities associated with high-dose chemotherapy and autologous stem cell transplant."

"For more than a decade, ibrutinib has been the standard of care in relapsed or refractory MCL, transforming patient outcomes in later lines. Today's approval for frontline use offers patients facing this aggressive blood cancer improved survival outcomes from the outset of treatment," said Ester in 't Groen, EMEA Therapeutic Area Head Haematology, Johnson & Johnson Innovative Medicine. "This milestone reinforces our commitment to evolving treatment paradigms in haematological malignancies through targeted, science-driven innovation."

The approval for ibrutinib is supported by data from the open-label, randomised, Phase 3 TRIANGLE study conducted by the European MCL Network (NCT02858258).[2] It evaluated 870 patients across three treatment arms to assess whether the addition of ibrutinib to chemoimmunotherapy (CIT) with or without ASCT could improve outcomes, when compared to ASCT + CIT alone, and potentially remove the need for transplant in patients with previously untreated MCL who were eligible for ASCT.[2] At a median follow-up of 55 months, the findings demonstrated that treatment with ibrutinib plus CIT delivered significantly superior failure-free survival (FFS) while omitting the burden of ASCT (77 percent vs 68 percent at 54-months respectively; hazard ratio [HR], 0.639; 98 percent confidence interval [CI], 0.428–0.953; two-sided p=0.0068) and that ibrutinib + CIT provided significantly longer overall survival versus ASCT plus CIT (88 percent vs 78 percent at 54-months respectively; HR, 0.522; 95 percent CI, 0.341–0.799; two-sided p=0.0023).[1]

The overall safety profile of the ibrutinib + CIT regimen was consistent with the previously known safety profile of ibrutinib.[3] The most common (>5 percent) Grade 3-5 adverse events observed in the ibrutinib + CIT arm (N=265) compared with the ASCT + CIT arm (N=268) were blood and lymphatic system disorders (64.9 percent vs 75.0 percent),

neutrophil count decrease (24.2 percent vs 23.1 percent), platelet count decrease (29.4 percent vs 33.2 percent) and infections and infestations (28.7 percent vs 23.1 percent).[3]

“Until now, fit patients with mantle cell lymphoma have only had the option of frontline treatment with ASCT and chemotherapy. We’re incredibly proud that with this approval, ibrutinib has become the first alternative therapy for this patient population after demonstrating superior outcomes compared to the current standard of care,” said Jessica Vermeulen, Vice President, Lymphoma & Leukemia Disease Area Stronghold Leader, Johnson & Johnson Innovative Medicine. “This approval reinforces our ongoing commitment to haematological malignancies, and the power of our collaborations with academics and researchers to bring cutting edge science to areas of high unmet need.”

About the TRIANGLE Study

TRIANGLE (NCT02858258) is an ongoing, European, randomised, open-label, Phase 3 investigator initiated study (IIS) led by the European MCL Network.[2] It compared three treatment arms: ibrutinib combined with standard induction immunochemotherapy with or without autologous stem cell transplantation (ASCT) followed by 2-year fixed-duration ibrutinib therapy versus induction immunochemotherapy followed by ASCT.[2] The trial enrolled 870 patients with previously untreated mantle cell lymphoma (MCL).[2] The primary endpoint was failure-free survival (FFS).[2] Overall survival (OS) and safety and tolerability were also assessed as secondary endpoints.[2] The age for participation was ≥18 years and ≤65 years for patients who were suitable for high-dose treatment.[2] The study was conducted by the European MCL Network across 14 countries.[2]

About Ibrutinib

Ibrutinib is a once-daily oral medication that is jointly developed and commercialised by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.[1] Ibrutinib blocks the BTK protein, which is needed by normal and abnormal B-cells, including specific cancer cells, to multiply and spread.[4] By blocking BTK, ibrutinib may help move abnormal B-cells out of their nourishing environments and inhibits their proliferation.[5]

Ibrutinib is approved in more than 100 countries and has been used to treat more than 325,000 patients worldwide.[6] There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of ibrutinib.[1,7] In October 2021, ibrutinib was added to the World Health Organization’s Model Lists of Essential Medicines (EML), which refers to medicines that address global health priorities and which should be available and affordable for all.[8]

Ibrutinib was first approved by the European Commission (EC) in 2014, and approved indications to date include:[1]

- As a single agent or in combination with rituximab or obinutuzumab or venetoclax for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL)
- As a single agent or in combination with bendamustine and rituximab (BR) for the treatment of adult patients with CLL who have received at least one prior therapy
- As a single agent for the treatment of adult patients with relapsed or refractory MCL
- As a single agent for the treatment of adult patients with Waldenström’s macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. In combination with rituximab for the treatment of adult patients with WM
- In combination with R-CHOP alternating with R-DHAP (or R-DHAOx)* without ibrutinib, followed by ibrutinib monotherapy, for the treatment of adult patients with previously untreated MCL who would be eligible for autologous stem cell transplant

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using ibrutinib please refer to the Summary of Product Characteristics.

About Mantle Cell Lymphoma (MCL)

MCL is an aggressive, incurable type of blood cancer that spreads quickly and originates from the B lymphocytes, a functional component of the human immune system.[9] The overall incidence of MCL globally is approximately 1-2 cases per 100,000 persons per year and it has a higher prevalence in men than women.[10] MCL is diagnosed at a median age of 65 years and while patient outcomes have dramatically improved over the latest few decades, MCL remains a difficult disease to treat with patients relapsing or becoming resistant to therapy.[10]

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity.

Learn more at www.innovativemedicine.jnj.com/emea. Follow us at www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen-Cilag International NV, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc. and Janssen Research & Development, LLC are Johnson & Johnson companies.

Cautions Concerning Forward-Looking Statements

This press release contains “forward-looking statements” as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of IMBRUVICA. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or

uncertainties materialise, actual results could vary materially from the expectations and projections of Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's most recent Annual Report on Form 10-K, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

**R-DHAP refers to rituximab, dexamethasone, high-dose cytarabine (Ara-C) and cisplatin; R-DHAOx refers to rituximab, dexamethasone, high-dose cytarabine (Ara-C) and oxaliplatin.[1]*

***Professor Martin Dreyling, M.D., Ph.D., Ludwig Maximilian University of Munich, has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.*

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[1] European Medicines Agency. IMBRUVICA Summary of Product Characteristics. July 2025. Available at: https://www.ema.europa.eu/en/documents/product-information/imbruvica-epar-product-information_en.pdf. Last accessed: July 2025.
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