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Janssen Receives CHMP Positive Opinion for Expanded Use of IMBRUVICA® (ibrutinib) in Combination with Rituximab for Previously Untreated Patients with Chronic Lymphocytic Leukaemia (CLL)

Positive Opinion is supported by Phase 3 E1912 study evaluating ibrutinib-rituximab combination versus chemo-immunotherapy in first-line treatment of CLL

BEERSE, BELGIUM, 24 July 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued a Positive Opinion recommending marketing authorisation for IMBRUVICA® (ibrutinib) to include the combination with rituximab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).

The Positive Opinion is based on data from the Phase 3 E1912 study, designed and conducted in the United States (U.S.) by the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN) and sponsored by the National Cancer Institute (NCI), which is part of the U.S. National Institutes of Health. The study evaluated 529 patients with previously untreated CLL aged 70 years or younger (median age 58) who were randomly assigned in a 2:1 ratio to receive ibrutinib plus rituximab (n=354) or the standard of care chemo-immunotherapy fludarabine, cyclophosphamide and rituximab (FCR) (n=175). The primary study results were published in *The New England Journal of Medicine*, and the extended four-year median follow-up

results were presented at the 2019 American Society of Hematology (ASH) Annual Meeting.[1,2]

"Ibrutinib in combination with rituximab represents an important new targeted and non-chemotherapy option for patients with CLL," said John Gribben, MD DSc, Professor of Medical Oncology at St Bartholomew's Hospital, Barts Cancer Institute, Queen Mary, University of London. "For people living with CLL, relapse is often inevitable. Using this combination in the frontline setting has the potential to not only extend life, but also offer a tolerability profile with less of the known chemotherapy-related events."

The CHMP Positive Opinion comes after the U.S. Food and Drug Administration's (FDA) approval of this expanded indication for ibrutinib in April 2020. The application will now be reviewed by the European Commission (EC).

"Ibrutinib has been used to treat more than 200,000 people globally, and this latest milestone further highlights its potential for patients diagnosed with CLL," said Dr Patrick Laroche, Haematology Therapy Area Lead, Europe, Middle East and Africa (EMEA), Janssen-Cilag. "We look forward to working with the European Commission to bring this new, ibrutinib-based, non-chemotherapy frontline treatment option to adult patients with CLL."

"This landmark head-to-head study, conducted by the ECOG-ACRIN Cancer Research Group and the National Cancer Institute has generated important, practice changing results which challenge FCR, the gold standard of chemotherapy-based treatment regimens for younger, fit patients with previously untreated CLL for over a decade," said Craig Tendler, M.D., Vice President, Clinical Development and Global Medical Affairs, Oncology, Janssen Research & Development. "We are pleased to build upon the robust body of data supporting the most widely studied BTK inhibitor as we continue to study further ibrutinib-based regimens in our mission to improve the lives of patients with complex blood cancers, like CLL."

#ENDS#

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About ibrutinib

Ibrutinib is a once-a-day, first-in-class Bruton's tyrosine kinase (BTK) inhibitor that is administered orally.[3] Ibrutinib blocks the BTK protein; the BTK protein sends important signals that tell B cells to mature and produce antibodies. BTK signaling is needed by specific cancer cells to multiply and spread.[4] By blocking BTK, ibrutinib may help move abnormal B cells out of their nourishing environments in the lymph nodes, bone marrow, and other organs.[5]

Ibrutinib is currently approved in Europe for:[3]

- Chronic lymphocytic leukaemia (CLL): As a single agent or in combination with obinutuzumab for the treatment of adult patients with previously untreated CLL, and 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
- Mantle cell lymphoma (MCL): As a single agent for the treatment of adult patients with relapsed or refractory MCL
- Waldenström's macroglobulinemia (WM): As a single agent for the treatment of adult patients who have received at least one prior therapy or in first-line treatment for patients unsuitable for chemo-immunotherapy, and in combination with rituximab for the treatment of adult patients

Ibrutinib is approved in more than 99 countries for at least one indication, and to date, has been used to treat more than 200,000 patients worldwide across its approved indications.[6]

The most common adverse reactions seen with ibrutinib include diarrhoea, neutropenia, haemorrhage (e.g., bruising), musculoskeletal pain, nausea, rash, and pyrexia.[3]

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

About chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is typically a slow-growing blood cancer of the white blood cells.[7] The overall incidence of CLL in Europe is approximately 4.92 cases per 100,000 persons per year and is about 1.5 times more common in men than in women.[8] CLL is predominantly a disease of the elderly, with a median age of 72 years at diagnosis.[9]

The disease eventually progresses in the majority of patients, and they are faced with fewer treatment options with each relapse. Patients are often prescribed multiple lines of therapy as they relapse or become resistant to treatments.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension. Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen-Cilag and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding ibrutinib. 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 Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or 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; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained

by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; 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 Annual Report on Form 10-K for the fiscal year ended December 29, 2019, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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