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U.S. FDA Accepts for Review the Application of Ibrutinib (IMBRUVICA®) for Chronic Graft-Versus-Host-Disease (cGVHD) After Failure of One or More Lines of Systemic Therapy

GVHD is a life-threatening condition with limited treatment options

Milestone highlights the potential benefit of ibrutinib beyond blood cancers

RARITAN, NJ, April 4, 2017 – Janssen Research & Development, LLC announced today the U.S. Food and Drug Administration (FDA) has accepted for review a supplemental New Drug Application (sNDA) for ibrutinib (IMBRUVICA®) for the treatment of patients with chronic graft-versus-host-disease (cGVHD) after failure of one or more lines of systemic therapy. GVHD is a potential life-threatening consequence of stem cell or bone marrow transplant, with no approved treatments or established standards of care specifically indicated for the condition in patients who have failed initial steroid therapy.[1,2] IMBRUVICA is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.

“Patients with chronic graft-versus-host-disease face an unpredictable, debilitating and sometimes life-threatening disease journey, which is further complicated by lack of FDA-approved medicines. We hope this filing acceptance and the robust body of evidence supporting ibrutinib in this condition will translate into a future indication in cGVHD and a new, much-needed treatment option,” said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Development, Hematology for Janssen Research & Development, LLC. “We continue to study the mechanism of action of IMBRUVICA, and are committed to exploring its potential to transform treatment paradigms and patient outcomes beyond its current indications in blood cancers. Our investigation into cGVHD is one of a range of disease areas we are looking at outside of the hematologic malignancy category.”

The sNDA is supported by data from a single-arm Phase 1b/2 trial (PCYC-1129) examining the safety and efficacy of ibrutinib in patients with cGVHD who have failed first-line corticosteroid therapy and require additional therapy. The data was accepted as a late-breaker and presented at the American Society of

Hematology Annual Meeting in December 2016 and the Blood and Marrow Transplantation Tandem Meeting in February 2017. Based on this data, a Phase 3 study was initiated to evaluate ibrutinib with corticosteroid versus placebo with corticosteroid as a first-line therapy for patients with new onset moderate or severe cGVHD; the trial is currently ongoing. The FDA granted Breakthrough Therapy Designation and Orphan Drug Designation in June 2016 for ibrutinib as a potential treatment for cGVHD after failure of one or more lines of systemic therapy.

GVHD is a medical complication of allogeneic stem cell or bone marrow transplant and can be a serious and debilitating condition. The condition occurs when donor immune cells attack the patients' tissues and it can affect almost any organ in the body.[1] The incidence of cGVHD has continued to increase over time.[3] In fact, approximately 30-70 percent of post-allogeneic transplant patients develop cGVHD.[4]

About IMBRUVICA

IMBRUVICA was one of the first therapies to receive U.S. approval after having received the FDA's Breakthrough Therapy Designation. IMBRUVICA works by blocking a specific protein called Bruton's tyrosine kinase (BTK).[5] The BTK protein transmits important signals that tell B cells to mature and produce antibodies and is needed by specific cancer cells to multiply and spread.[5,6] IMBRUVICA targets and blocks BTK, inhibiting cancer cell survival and spread.[6] For more information, visit www.IMBRUVICA.com.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage - Fatal bleeding events have occurred in patients treated with IMBRUVICA®. Grade 3 or higher bleeding events (intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post-procedural hemorrhage) have occurred in up to 6% of patients. Bleeding events of any grade, including bruising and petechiae, occurred in approximately half of patients treated with IMBRUVICA®.

The mechanism for the bleeding events is not well understood. IMBRUVICA® may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies and patients should be monitored for signs of bleeding. Consider the benefit-risk of withholding IMBRUVICA® for at least 3 to 7 days pre- and postsurgery depending upon the type of surgery and the risk of bleeding.

Infections - Fatal and nonfatal infections have occurred with IMBRUVICA® therapy. Grade 3 or greater infections occurred in 14% to 29% of patients. Cases of progressive multifocal leukoencephalopathy (PML) and *Pneumocystis jirovecii* pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Evaluate patients for fever and infections and treat appropriately.

Cytopenias - Treatment-emergent Grade 3 or 4 cytopenias including neutropenia (range, 13% to 29%), thrombocytopenia (range, 5% to 17%), and anemia (range, 0% to 13%) based on laboratory measurements occurred in patients treated with single agent IMBRUVICA®. Monitor complete blood counts monthly.

Atrial Fibrillation - Atrial fibrillation and atrial flutter (range, 6% to 9%) have occurred in patients treated with IMBRUVICA®, particularly in patients with cardiac risk factors, hypertension, acute infections, and a previous history of atrial fibrillation. Periodically monitor patients clinically for atrial fibrillation. Patients who develop arrhythmic symptoms (eg, palpitations, lightheadedness) or new-onset dyspnea should have an ECG performed. Atrial fibrillation should be managed appropriately and if it persists, consider the risks and benefits of IMBRUVICA® treatment and follow dose modification guidelines.

Hypertension - Hypertension (range, 6% to 17%) has occurred in patients treated with IMBRUVICA® with a median time to onset of 4.6 months (range, 0.03 to 22 months). Monitor patients for new-onset hypertension or hypertension that is not adequately controlled after starting IMBRUVICA®. Adjust existing antihypertensive medications and/or initiate antihypertensive treatment as appropriate.

Second Primary Malignancies - Other malignancies (range, 3% to 16%) including non-skin carcinomas (range, 1% to 4%) have occurred in patients treated with IMBRUVICA®. The most frequent second primary malignancy was non-melanoma skin cancer (range, 2% to 13%).

Tumor Lysis Syndrome - Tumor lysis syndrome has been infrequently reported with IMBRUVICA® therapy. Assess the baseline risk (eg, high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity - Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise women to avoid becoming pregnant while taking IMBRUVICA® and for 1 month after cessation of therapy. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. Advise men to avoid fathering a child during the same time period.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were neutropenia* (61%), thrombocytopenia* (62%), diarrhea (43%), anemia* (41%), musculoskeletal pain (30%), rash (30%), nausea (29%), bruising (30%), fatigue (29%), hemorrhage (22%), and pyrexia (21%).

* Based on adverse reactions and/or laboratory measurements (noted as platelets, neutrophils, or hemoglobin decreased).

The most common Grade 3 or 4 non-hematologic adverse reactions (≥5%) in MCL patients were pneumonia (7%), abdominal pain (5%), atrial fibrillation (5%), diarrhea (5%), fatigue (5%), and skin infections (5%). The most common Grade 3 or 4 non-hematologic adverse reactions (≥5%) in MZL patients were pneumonia (10%), fatigue (6%), diarrhea (5%), rash (5%), and hypertension (5%).

Approximately 6% (CLL/SLL), 14% (MCL), 11% (WM) and 10% (MZL) of patients had a dose reduction due to adverse reactions. Approximately 4%-10% (CLL/SLL), 9% (MCL), and 9% (WM [6%] and MZL [13%]) of patients discontinued due to adverse reactions. Most common adverse reactions leading to discontinuation were pneumonia, hemorrhage, atrial fibrillation, rash, and neutropenia (1% each) in CLL/SLL patients and subdural hematoma (1.8%) in MCL patients. The most common adverse reactions leading to discontinuation were interstitial lung disease, diarrhea, and rash (1.6% each) in WM and MZL patients.

DRUG INTERACTIONS

CYP3A Inhibitors - Avoid coadministration with strong and moderate CYP3A inhibitors. If a moderate CYP3A inhibitor must be used, reduce the IMBRUVICA® dose.

CYP3A Inducers - Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment - Avoid use in patients with moderate or severe baseline hepatic impairment. In patients with mild impairment, reduce IMBRUVICA® dose.

Please see Full Prescribing Information: https://www.imbruvica.com/prescribing-information.

About the Janssen Pharmaceutical Companies

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal.

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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, including potential benefits of ibrutinib (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 materialize, actual results could vary materially from the expectations and projections of Janssen Biotech, Inc, Janssen Research & Development, LLC and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges inherent in product research and development,

including the uncertainty of clinical success and obtaining regulatory approvals; uncertainty of commercial success for new products or new indications; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and description 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 January 1, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," 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 or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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[1] Leukemia and Lymphoma Society. Graft Versus Host Disease. Available from: https://www.lls.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease. Accessed March 2017.
[2] MedlinePlus, U.S. National Library of Medicine. Graft-versus-host-disease. Available from: http://www.nlm.nih.gov/medlineplus/ency/article/001309.htm. Accessed March 2017.
[3] Arai, et al. Increasing Incidence of Chronic Graft-versus-Host Disease in Allogeneic Transplantation: A Report from the Center for International Blood and Marrow Transplant Research. *Biol Blood Marrow Transplant*: 21 (2015) 266-274.
[4] Grube, et al. Risk Factors and Outcome of Chronic Graft-versus-Host Disease after Allogeneic Stem Cell Transplantation—Results from a Single-Center Observational Study. *Biol Blood Marrow Transplant*: 2016; 22 (11): 1781-1791.
[5] IMBRUVICA U.S. Prescribing Information, January 2017.
[6] Genetics Home Reference. Isolated growth hormone deficiency. Available from: http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed March 2017.