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Ibrutinib (IMBRUVICA®) Granted Breakthrough Therapy Designation by U.S. Food and Drug Administration (FDA) for the Development of a Treatment for Chronic Graft-Versus-Host Disease (cGVHD)

- *In current clinical practice, there are no FDA-approved treatments for this life-threatening condition*
- *FDA designation suggests potential use of ibrutinib beyond hematologic malignancies*
- *The FDA also granted ibrutinib orphan drug designation for cGVHD*

RARITAN, NJ, June 29, 2016 – The U.S. Food and Drug Administration (FDA) has granted a fourth Breakthrough Therapy Designation (BTD) for ibrutinib (IMBRUVICA®): as monotherapy for the treatment of patients with chronic graft-versus-host-disease (cGVHD) after failure of one or more lines of systemic therapy, Janssen Research & Development, LLC announced today. The FDA also granted the therapy Orphan Drug Designation (ODD) for cGVHD. This marks the first time ibrutinib has been granted BTD or ODD for an indication beyond hematologic malignancies. In current clinical practice, there are no approved treatments or established standards of care specifically indicated for patients with active cGVHD who have failed first-line corticosteroid therapy and require additional therapy. GVHD is a life-threatening condition in which the body is attacked by donor immune cells after a patient undergoes an allogeneic stem cell or bone marrow transplant.[1,2] Currently, most GVHD patients are prescribed glucocorticoids, a type of steroid treatment, but many do not respond. IMBRUVICA is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company.

“We are excited to learn if the mechanism of action for ibrutinib may allow its use beyond its current indications in hematologic malignancies,” said Sen Zhuang, M.D., Ph.D., Vice President, Clinical Development, Hematology for Janssen Research & Development, LLC. “Two key kinase enzymes are believed to be involved

in the cell signaling associated with chronic graft-versus-host-disease: Bruton's tyrosine kinase and interleukin-2-inducible T-cell kinase, known as BTK and ITK respectively. Chronic GVHD is a debilitating condition with limited treatment options. We're hopeful ibrutinib can make a difference and look forward to working with the FDA and our strategic partner, Pharmacyclics, on this development program."

The FDA granted ibrutinib BTD for cGVHD based on data from a Phase 1b/2 study. Overall, ibrutinib showed early clinical activity in the reduction of cGVHD based on the National Institutes of Health (NIH) Consensus Response Criteria. Preliminary results from this trial were previously presented at the 42nd Annual Meeting of the European Society for Blood and Marrow Transplantation (ESBM) in April 2016 and the 51st American Society of Clinical Oncology (ASCO) Annual Meeting in May 2015.

According to the FDA, BTD is intended to expedite the development and review of treatments for serious or life-threatening diseases where "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development."[3] ODD provides special status to a therapy developed to treat a rare condition or disease.[4]

In February 2013, the FDA granted BTD to IMBRUVICA for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL) and for the treatment of patients with Waldenström's macroglobulinemia (WM). In April 2013, IMBRUVICA was awarded a third BTD for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) with a deletion of the short arm of chromosome 17 (del 17p).

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.[5] 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) 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, 19% to 29%), thrombocytopenia (range, 5% to 17%), and anemia (range, 0% to 9%) 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, 5% 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, 4% 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.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients with B-cell malignancies (MCL, CLL/SLL, and WM) were neutropenia* (64%), thrombocytopenia* (63%), diarrhea (43%), anemia*(41%), musculoskeletal pain (30%), rash (29%), nausea (29%), bruising (29%), fatigue (27%), hemorrhage (21%), 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%). Approximately 6% (CLL), 14% (MCL), and 11% (WM) of patients had a dose reduction due to adverse reactions.

Approximately 4%-10% (CLL), 9% (MCL), and 6% (WM) of patients discontinued due to adverse reactions. Most frequent adverse reactions leading to discontinuation were pneumonia, hemorrhage, atrial fibrillation, rash and neutropenia (1% each) in CLL patients and subdural hematoma (1.8%) in MCL 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/docs/librariesprovider7/default-document-library/prescribing_information.pdf.

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. 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 3, 2016, including in Exhibit 99 thereto, 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 June 2016.
[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 June 2016.
[3] U.S. Food and Drug Administration. Fact Sheet: Breakthrough Therapies. Available from: http://www.fda.gov/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAct/FDASIA/ucm329491.htm. Accessed June 2016.
[4] U.S. Food and Drug Administration. Developing Products for Rare Diseases & Conditions. Available from: http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm2005525.htm. Accessed June 2016.
[5] IMBRUVICA U.S. Prescribing Information, May 2016.
[6] Genetics Home Reference. Isolated growth hormone deficiency. Available from: http://ghr.nlm.nih.gov/condition/isolated-growth-hormone-deficiency. Accessed June 2016.