

Health Canada Approves IMBRUVICA® (ibrutinib) for First-line Treatment of Chronic Lymphocytic Leukemia

IMBRUVICA® significantly improved progression-free, overall survival, and overall response rate versus an established chemotherapy

Toronto, ON – July 20, 2016 – Janssen Inc. announced that Health Canada has approved IMBRUVICA® (ibrutinib) an oral, once-daily, single-agent targeted therapy for previously untreated patients with active chronic lymphocytic leukemia (CLL).¹ This is the 4th approval for IMBRUVICA®, which now is approved for use in all lines of CLL therapy for patients needing treatment, considerably expanding the number of Canadian patients who may benefit from this chemotherapy-free treatment. Chronic lymphocytic leukemia is one of the most common types of leukemia in adults.²

The latest approval is based on data from the Phase 3 [RESONATE-2](#) (PCYC-1115-CA) study, a head-to-head clinical trial comparing IMBRUVICA® to chlorambucil (a chemotherapy agent). Results showed using IMBRUVICA® first-line was associated with statistically significant improvements in progression-free survival (PFS), overall survival (OS) and overall response rate (ORR) compared with chlorambucil treatment.³

"The clinical data showed that IMBRUVICA® (ibrutinib) is much more effective than the comparator traditional chemotherapy," says Dr. Carolyn Owen, Associate Professor, Division of Hematology and Hematological Malignancies, Foothills Medical Centre*. "Hopefully, this approval will provide an increase in treatment options for patients with CLL that will ensure their disease is well controlled, allowing them to enjoy their life to the fullest."

The expanded IMBRUVICA® indication is based on data from the randomized, international, multi-center, open-label Phase 3 RESONATE-2 trial, involving 269 previously untreated patients with CLL aged 65 years or older. It showed IMBRUVICA® significantly improved PFS, OS and ORR versus chlorambucil. At a median follow up of 18.4 months, the PFS, as assessed by an Independent Review Committee (IRC), indicated an 84 per cent statistically significant reduction in the risk of death or progression in the IMBRUVICA® arm versus the chlorambucil arm (HR=0.16 [95 per cent CI, 0.091-0.28]).⁴ Median PFS was not reached for IMBRUVICA® versus 18.9 months for chlorambucil (95 per cent CI: 14.1, 22.0).⁵ Analysis of OS demonstrated an 84 per cent statistically significant reduction in risk of death for patients in the IMBRUVICA® arm (HR=0.16 [95 per cent CI, 0.048-0.56]). Results also showed a statistically significant improvement in ORR in the IMBRUVICA® arm versus the chlorambucil arm (82 per cent versus 35 per cent, respectively; p<0.0001).⁶ Data from [RESONATE-2](#) were presented in an oral session at the American Society of Hematology (ASH) Annual Meeting on December 7, 2015, in addition to being featured in the official ASH press program and simultaneously published online in [The New England Journal of Medicine](#).

"We are pleased with the recent approval of IMBRUVICA[®] by Health Canada," says Shelagh Tippet-Fagyas, president of the Leukemia and Lymphoma Society of Canada. "This approval means broader drug access and options for CLL patients, such as the benefit of earlier chemotherapy-free treatments."

The adverse reactions (AR) reported in the Phase 3 RESONATE-2 trial reflect exposure to IMBRUVICA[®] with a median duration of 17.4 months.⁷ The most common ARs (≥ 20 per cent) of any Grade were diarrhea (42 per cent), musculoskeletal pain** (36 per cent), cough (22 per cent) and rash** (21 per cent). The most common Grade 3/4 AR (\geq five per cent) was pneumonia** (eight per cent).⁸ Approximately five per cent of patients receiving IMBRUVICA[®] in the studies supporting the CLL indications (PCYC-1102, RESONATE [PCYC-1112] and RESONATE-2) discontinued treatment due to ARs.⁹ These reactions included pneumonia, subdural hematoma and atrial fibrillation. ARs leading to dose reduction occurred in approximately four per cent of patients.¹⁰ Serious warnings and precautions include major bleeding events (some fatal), not to use in patients with moderate or severe hepatic impairment, and not to use concomitantly with a strong CYP3A inhibitor. Other warnings and precautions include effects on ability to drive and use machines, second primary malignancies, atrial fibrillation and atrial flutter, hypertension, decrease in QTcF interval, drug interactions, tumor lysis syndrome, diarrhea, cytopenias, lymphocytosis, leukostasis, minor bleeding events, infections, perioperative considerations, embryo-fetal toxicity, other reproductive risks, risk of exposure to infants through breast milk, and occurrence of certain adverse events more frequently in the elderly.¹¹

About Chronic Lymphocytic Leukemia (CLL)

Chronic lymphocytic leukemia is a slow-growing blood cancer of cells that become white blood cells called lymphocytes, most commonly B cells.¹² Chronic lymphocytic leukemia is one of the most common types of leukemia in adults.¹³ In Canada, there were approximately 2,195 adults diagnosed with CLL in 2010.¹⁴ Historically, CLL treatment has been challenging since the more effective treatment regimens were usually associated with high toxicity.¹⁵ There has been a real need to develop therapies for CLL that can offer better efficacy and tolerability, especially in older patients.¹⁶

About IMBRUVICA[®] (ibrutinib)

IMBRUVICA[®] contains the medicinal ingredient ibrutinib which is a targeted inhibitor of Bruton's tyrosine kinase (BTK). Ibrutinib blocks BTK activity, inhibiting cancer cell survival and spread.¹⁷ The recommended dose of IMBRUVICA[®] for CLL is 420 mg (three 140-mg capsules) orally, once-daily.¹⁸

IMBRUVICA[®] is approved in Canada for the treatment of patients with previously untreated active chronic lymphocytic leukemia (CLL), including those with 17p deletion. It is also approved for the treatment of patients with CLL who have received at least one prior therapy, including those with 17p deletion. IMBRUVICA[®] is approved for the treatment of patients with Waldenström's macroglobulinemia (WM), and approved (with conditions) for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL).

IMBRUVICA[®] is co-developed by Cilag GmbH International (a member of the Janssen Pharmaceutical Companies) and Pharmacylics LLC, an AbbVie company. Janssen Inc. markets IMBRUVICA[®] in Canada.



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/canada. Follow us on Twitter [@JanssenCanada](https://twitter.com/JanssenCanada).

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* Dr. Owen was not compensated for any media work. She has been a paid consultant to Janssen.

** Includes multiple AR terms

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¹ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

²The Leukemia and Lymphoma Society of Canada "What is Chronic Lymphocytic Leukemia?" Available online at: <http://www.cancer.ca/en/cancer-information/cancer-type/leukemia-chronic-lymphocytic-cll/chronic-lymphocytic-leukemia/?region=on>. Accessed June 2016.

³ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

⁴ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

⁵ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

⁶ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

⁷ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

⁸ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

⁹ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

¹⁰ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

¹¹ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

¹² American Cancer Society. "Leukemia--Chronic Lymphocytic". Available online at: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003111-pdf.pdf>. Accessed June 2016.

¹³The Leukemia and Lymphoma Society of Canada "What is Chronic Lymphocytic Leukemia?" Available online at: <http://www.cancer.ca/en/cancer-information/cancer-type/leukemia-chronic-lymphocytic-cll/chronic-lymphocytic-leukemia/?region=on>. Accessed June 2016.

¹⁴ Canadian Cancer Society "Chronic lymphocytic leukemia statistics," Available online at: <http://www.cancer.ca/en/cancer-information/cancer-type/leukemia-chronic-lymphocytic-cll/statistics/?region=on>. Accessed June 2016.

¹⁵ Shanafelt, T. American Hematology Association, "Treatment of older patients with chronic lymphocytic leukemia: key questions and current answers," 2013. Available online at: <http://asheducationbook.hematologylibrary.org/content/2013/1/158.full>. Accessed June 2016.

¹⁶ Shanafelt, T. American Hematology Association, "Treatment of older patients with chronic lymphocytic leukemia: key questions and current answers," 2013. Available online at: <http://asheducationbook.hematologylibrary.org/content/2013/1/158.full>. Accessed June 2016.

¹⁷ IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated July 19, 2016.

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Cautions Regarding Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding expectations for 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 Inc. 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 continued clinical success and 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 to applicable laws and regulations, including 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 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.