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Health Canada Approves IMBRUVICA® (ibrutinib) for the Treatment of Waldenström's Macroglobulinemia

IMBRUVICA® is an oral, once-daily, single-agent therapy associated with a durable response in patients with this rare B-cell lymphoma

Toronto, ON – May 12, 2016 – Janssen Inc. announced today that Health Canada has issued a Notice of Compliance (NOC) for IMBRUVICA® (ibrutinib), an oral, once-daily, single-agent therapy for the treatment of patients with Waldenström's macroglobulinemia (WM).[1] Waldenström's macroglobulinemia is a rare, incurable type of non-Hodgkin lymphoma, a cancer that begins in the body's immune system.[2,3]

IMBRUVICA® was first approved in Canada in November 2014 for the treatment of patients with chronic lymphocytic leukemia (CLL), including those with 17p deletion, who have received at least one prior therapy, or for the frontline treatment of patients with CLL with 17p deletion. In July 2015, IMBRUVICA® was approved with conditions for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL).

"Before now, treatment options for my patients with Waldenström's macroglobulinemia have been limited," said Dr. David Macdonald, MD, FRCPC, Assistant Professor, Dalhousie University, Hematologist, Capital Health. "The approval of IMBRUVICA® is a major advancement as this agent offers a targeted, chemotherapy-free treatment option for patients with WM, as it has done for those with other B-cell malignancies. It has shown clinically meaningful outcomes for these patients, as demonstrated by a high overall response rate."

This approval for WM is based on an investigator-led, multicenter, prospective, single-arm study in 63 patients who had received at least one prior therapy. The results of the study were published in the New England Journal of Medicine in 2015 by Treon SP, et al.[4]

The median age of patients was 63 (range of 44-86 years old) and the median number of prior therapies was two (range of 1-11).[5] Patients received IMBRUVICA® 420 mg once daily. After a median duration of follow-up of 14.8 months, IMBRUVICA® was associated with a 87.3 per cent overall response rate (ORR; the primary endpoint), and a 69.8 per cent major response rate as assessed by investigators using criteria adopted from the Third International Workshop on Waldenström's Macroglobulinemia. [6] The median time for patients to achieve at least a minor response to treatment was one month. [7] The median duration of response had not been reached. [8]

The most common adverse reactions in patients (≥20 per cent) were diarrhea, neutropenia, rash, nausea, muscle spasms, and fatigue.[9] Four (six per cent) of patients discontinued

treatment due to adverse events.[10] Overall, IMBRUVICA® was well-tolerated and the safety profile was consistent with that observed in CLL and MCL.

About Waldenström's macroglobulinemia

Waldenström's macroglobulinemia is a rare form of cancer and in Canada there will be an estimated 150 new cases in 2016.[11] WM is an indolent (slow-growing) subtype of non-Hodgkin lymphoma.[12] It begins with a malignant change to a B cell, a type of white blood cell (or lymphocyte), during its maturation, where the cell continues to reproduce more malignant B cells.[13] In WM, the malignant B cells create large amounts of a certain type of antibody protein called immunoglobulin M or IgM in the blood. Antibodies such as IgM normally help the body fight infection; however, the overproduction of IgM, a hallmark of WM, often leads to a thickening of the blood (hyperviscosity syndrome).Typically, patients with WM are diagnosed after developing symptoms associated with the disease such as anemia, fatigue and night sweats.[14]

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.[15] The recommended dose of IMBRUVICA® for WM is 420 mg (three 140-mg capsules) orally, once-daily.[16]

In Canada, IMBRUVICA® is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL), including those with 17p deletion, who have received at least one prior therapy, or for the frontline treatment of patients with CLL with 17p deletion. In addition, IMBRUVICA® was issued marketing authorization with conditions for the treatment of patients with relapsed or refractory mantle cell lymphoma (MCL), pending the results of trials to verify its clinical benefit.

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

About Janssen Inc.

Janssen Inc. and Cilag GmbH International are members of the Janssen Pharmaceutical Companies. At the Janssen Pharmaceutical Companies, 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 at @JanssenCanada

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

References:

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[4] Treon, SP., Tripsas, CK., et al. Ibrutinib in previously treated Waldenström's macroglobulimemia. *N Engl J Med*. April 9, 2015. http://www.nejm.org/doi/full/10.1056/NEJMoa1501548#t=articleResults
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[8] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated March 24, 2016.
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[10] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated March 24, 2016.
[11] Special Data Request to Statistics Canada: WM Incidence data from CANSIM Table 103-0550 'New Cases of Primary Cancer'; Canadian Cancer Registry – 3207.
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[15] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated March 24, 2016.
[16] IMBRUVICA® (Ibrutinib) Product Monograph, Janssen Inc. Updated March 24, 2016.