NEWS RELEASE

European Commission approves additional indication for VELCADE® (bortezomib) in mantle cell lymphoma

2/6/2015

European Commission approves additional indication for VELCADE® (bortezomib) in mantle cell lymphoma BEERSE, BELGIUM, February 6, 2015 - Janssen-Cilag International NV (Janssen) announced today that the European Commission has approved a variation to the terms of the marketing authorisation of VELCADE® (bortezomib) in combination with rituximab, cyclophosphamide, doxorubicin and prednisone for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are unsuitable for blood stem-cell transplantation.

The decision from the European Commission follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) on 18 December 2014.[1] This approval allows for the marketing of VELCADE for the above indication in all 28 countries of the European Union (EU). The approval of VELCADE in MCL is based on data from the Phase 3 study, LYM-3002.[2]

In the European Union, VELCADE is currently indicated for the treatment of multiple myeloma (MM), another rare blood-based cancer, either as monotherapy or in combination with other treatment regimens.[3]

MCL is considered a rare and aggressive type of blood cancer which can be challenging to treat and is associated with a poor prognosis.[4,5]

"We are delighted that the European Commission has approved extending the indications for use of VELCADE to include first-line therapy for patients with mantle cell lymphoma. We already offer IMBRUVICA as a second-line treatment in MCL and are pleased to be able to provide additional treatment options for this disease to patients and physicians," said Thomas Stark, Vice President, Medical Affairs, Janssen Europe, Middle East and Africa (EMEA).

Study Efficacy Results

LYM-3002 was a randomised, open-label, active-controlled, multicentre, international, prospective Phase 3 study including 487 patients with newly diagnosed MCL who were ineligible, or not considered, for bone marrow

transplantation.

The results showed significant benefits when treating patients with MCL using a VELCADE-based combination (VR-CAP*), compared to a widely used standard of care combination (R-CHOP†) that did not include VELCADE.[2] The VR-CAP regimen significantly improved progression-free survival (PFS), the primary endpoint, and showed improvements across a range of secondary endpoints.[2] An independent review committee reported the increase in PFS to be 59 percent (median 24.7 vs. 14.4 months; HR 0.63; p<0.001), whereas the study investigators reported the increase in PFS to be 96 percent (median 30.7 vs. 16.1 months; HR 0.51; p<0.001).[2]

Study Safety Results

VR-CAP was associated with additional, but manageable, toxicity when compared to R-CHOP.[2] Overall, among patients receiving VR-CAP compared to R-CHOP, serious adverse events (AE) were reported in 38 percent vs. 30 percent of patients and grade ≥3 AEs were reported in 93 percent vs. 85 percent. Discontinuations of treatment due to AEs were nine percent (VR-CAP) vs. seven percent (R-CHOP) and on-treatment drug-related deaths were two percent vs. three percent.[2]

About VELCADE (bortezomib)

The European Commission approval of the variation to the terms of the marketing authorisation means that VELCADE is now licensed in the EU to treat mantle cell lymphoma (MCL), a blood-based cancer, in untreated adults who are unsuitable for blood stem-cell transplantation. For MCL, VELCADE is used in combination with rituximab, cyclophosphamide, doxorubicin and prednisone.[1]

VELCADE is also currently approved in the EU for the treatment of MM, another rare blood-based cancer, for the following groups of patients:[3]

- Previously untreated adults who are unsuitable for high-dose chemotherapy with a blood stem-cell transplant. In these patients, VELCADE is used in combination with melphalan and prednisone;
- Previously untreated patients who are going to receive high-dose chemotherapy followed by a blood stem-cell transplant. In this group of patients, VELCADE is used in combination with dexamethasone, or with dexamethasone plus thalidomide;
- Adults whose disease is getting worse after at least one other treatment and who have already had, or cannot undergo, a blood stem-cell transplant. VELCADE is either used on its own in these patients or in combination with pegylated liposomal doxorubicin or dexamethasone.

VELCADE contains an active substance called bortezomib and is the first in a specific class of medicines known as proteasome inhibitors. Proteasomes are present in all cells and play an important role in controlling cell function, growth and also how cells interact with other cells around them. Bortezomib reversibly interrupts the normal working of cell proteasomes, inducing the cancerous cells, to stop growing and die.[3]

VELCADE has a predictable safety profile and a favourable benefit-risk ratio, which can be used in elderly patients and people with mild to moderate renal impairment.[6] The most common side effects reported with VELCADE (bortezomib) include fatigue, gastrointestinal adverse events, transient thrombocytopenia and neuropathy.[3]

VELCADE is commonly used in the treatment of various stages of MM. The product is co-developed by Millennium, the Takeda Oncology Company, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, and Janssen Pharmaceutical Companies. Millennium is responsible for commercialisation of VELCADE in the U.S.; Janssen Pharmaceutical Companies are responsible for commercialisation in Europe and the rest of the world. Takeda Pharmaceutical Company Limited and Janssen Pharmaceutical K.K. co-promote VELCADE in Japan. VELCADE is approved in more than 90 countries and has been used to treat more than 550,000 patients worldwide.

VELCADE in MCL

In 2006, the US Food and Drug Administration (FDA) approved VELCADE for the treatment of patients with MCL who have received at least one prior therapy, with a subsequent frontline treatment approval in October 2014 for VELCADE in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP). VELCADE has also been approved for the treatment of relapsed MCL in 53 additional countries, including Canada and Switzerland.

About MCL

MCL is considered to be a rare and aggressive type of blood cancer which can be challenging to treat and is associated with a poor prognosis.[7] MCL is characterised by high unmet need and small patient populations, impacting fewer than 0.45 in 100,000 people in Europe and with a median age at diagnosis of 65.[8,9] MCL is much more predominant in men than women and accounts for six percent of all non-Hodgkin's lymphomas.[10,11] Median overall survival is typically four to five years, and only one to two years in patients following the first relapse.[7,12] MCL typically involves the lymph nodes, but can spread to other tissues, such as the bone marrow, liver, spleen and gastrointestinal tract.[9]

Janssen in Oncology

In oncology, our goal is to fundamentally alter the way cancer is understood, diagnosed, and managed, reinforcing our commitment to the patients who inspire us. In looking to find innovative ways to address the cancer challenge, our primary efforts focus on several treatment and prevention solutions. These include disease area strongholds that focus on haematologic malignancies and prostate cancer; cancer interception with the goal of developing products that interrupt the carcinogenic process; biomarkers that may help guide targeted, individualised use of our therapies; and safe and effective identification and treatment of early changes in the tumour microenvironment.

About Janssen

Janssen Pharmaceutical Companies of Johnson & Johnson are dedicated to addressing and solving the most important unmet medical needs of our time, including oncology (e.g., multiple myeloma and prostate cancer),

immunology (e.g., psoriasis), neuroscience (e.g., schizophrenia, dementia and pain), infectious disease (e.g., HIV/AIDS, hepatitis C and tuberculosis), and cardiovascular and metabolic diseases (e.g., diabetes). Driven by our commitment to patients, we develop sustainable, integrated healthcare solutions by working side-by-side with healthcare stakeholders, based on partnerships of trust and transparency. More information can be found on **www.janssen-emea.com**. Follow us on **www.twitter.com/janssenEMEA** for our latest news.

*VELCADE, rituximab, cyclophosphamide, doxorubicin and prednisone (VR-CAP)

† Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP)

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Media Inquiries:

Brigitte Byl

Mobile: +32 473 55 58 79

Email: **bbyl@its.jnj.com**

Investor Relations:

Lesley Fishman

Phone: +1 732 524 3922

Louise Mehrotra

Phone: +1 732 524 6491