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DARZALEX®▼ (daratumumab) Receives Positive CHMP Opinion for the Treatment of Multiple Myeloma in Patients who have Received At Least One Prior Therapy

Janssen's first-in-class CD38-directed monoclonal antibody now recommended for approval earlier in the treatment pathway in combination with two standard of care regimens

BEERSE, BELGIUM, 24 February, 2017 – Janssen-Cilag International NV announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended broadening the existing marketing authorisation for DARZALEX®▼ (daratumumab).[1] If approved by the European Commission, daratumumab can be used in combination with lenalidomide and dexamethasone; or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma (MM) who have received at least one prior therapy.[1]

Despite the incredible work of the oncology community over the past decade, MM remains an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.[2]

The Positive Opinion of the CHMP was based on a review of data from the Phase 3 MMY3003 (POLLUX) study, published in *The New England Journal of Medicine in October 2016*,[3] and the Phase 3 MMY3004 (CASTOR) study, also published in *The New England Journal of Medicine in August 2016*.[4]

The safety profile of daratumumab in combination with standard-of-care regimens was consistent with monotherapy studies. In combination with lenalidomide, and dexamethasone (POLLUX) the most common adverse events of grade 3 or 4 during treatment were neutropenia (51.9%), thrombocytopenia (12.7%), and anaemia (12.4%).[3] Daratumumab-associated infusion-related reactions occurred in 47.7% of the patients and were mostly of grade 1 or 2.[3] In combination with bortezomib and dexamethasone (CASTOR) three of the most common grade 3 or 4 adverse events reported were thrombocytopenia (45.3%), anaemia (14.4%), and neutropenia (12.8%).[4] Infusion-related reactions that were associated with daratumumab treatment were reported in 45.3% of the patients; these reactions were mostly grade 1 or 2 (grade 3 in 8.6% of patients), and in 98.2% of these patients, they occurred during the first infusion.[4]

"This Positive Opinion recognises progress in the treatment of multiple myeloma and has the potential to offer new treatment options to eligible patients." said Torben Plesner, M.D., Vejle Hospital, Vejle, Denmark, a daratumumab clinical trial investigator. "Daratumumab has already demonstrated single-agent efficacy in highly refractory patients. Now, consistent with these data, the results when used in combination with standard-of-care regimens after one prior line of therapy are also encouraging."

Daratumumab first received conditional approval from the European Commission (EC) in May 2016, indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor (PI) and an immunomodulatory agent, and who have demonstrated disease progression on the last therapy.[5,6] Daratumumab was the first CD38-directed monoclonal antibody approved for use worldwide.

"Almost all patients with multiple myeloma have to endure relapses which typically become more aggressive," said Dr Catherine Taylor, Haematology Therapeutic Area Lead, Janssen Europe, the Middle East and Africa (EMEA). "I am heartened by this important and rapid recommendation which recognises the progress in multiple myeloma treatment."

The CHMP's Positive Opinion will now be reviewed by the European Commission, which has the authority to grant approval of the new indication.

This milestone follows last year's decision by the U.S. Food and Drug Administration (FDA) on 21 November 2016, to approve the expanded use of daratumumab in combination with

bortezomib/dexamethasone or lenalidomide/dexamethasone in patients with multiple myeloma who have received at least 1 prior therapy.[7]

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About Multiple Myeloma

Multiple myeloma (MM) is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.[2] MM is the second most common form of blood cancer, with around 39,000 new cases worldwide in 2012.[8] MM most commonly affects people over the age of 65 and is more common in men than in women.[9] The most recent five-year survival data for 2000-2007 show that across Europe, up to half of newly diagnosed patients do not reach five-year survival.[10] Almost 29% of patients with MM will die within one year of diagnosis.[11] Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure. While some patients with MM have no symptoms at all, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[9] Patients who relapse after treatment with standard therapies, including PIs and immunomodulatory agents, have poor prognoses and few treatment options available.[12]

About Daratumumab

Daratumumab is a first-in-class biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[13-15] Daratumumab induces rapid tumour cell death through apoptosis (programmed cell death)[6,16] and multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).[6,17,18] Daratumumab has also demonstrated immunomodulatory effects that contribute to tumour cell death via a decrease in immune suppressive cells including T-regs, B-regs and myeloid-derived suppressor cells.[6,19] Daratumumab is being evaluated in a comprehensive clinical development programme that includes five Phase 3 studies across a range of treatment settings in multiple myeloma. Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant diseases in which CD38 is expressed. For more information, please see www.clinicaltrials.gov.

For further information on daratumumab, please see the Summary of Product Characteristics at http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004077/human_med_001979.jsp&mid=WC0b01ac058001d124.

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialise daratumumab.

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/emea. Follow us at www.twitter.com/janssenEMEA.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the potential benefits of, and expanded indication for, DARZALEX® (daratumumab). 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 materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: the uncertainties inherent in product development, including the uncertainty of clinical success and of obtaining 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 in behaviour and spending patterns or financial distress of purchasers of health care products and services; 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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