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Janssen Submits U.S. & EU Regulatory Applications Seeking Approval of DARZALEX® (daratumumab) Split Dosing Regimen

RARITAN, NJ and BEERSE, BELGIUM, August 8, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the submission of a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) and a Type II Variation to the European Medicines Agency (EMA) seeking approval of a split dosing regimen for DARZALEX® (daratumumab). The applications seek to update the Prescribing Information and Summary of Product Characteristics to provide health care professionals with the option to split the first infusion of DARZALEX® over two consecutive days. The submissions are supported by data from the Phase 1b MMY1001 clinical trial, which demonstrated DARZALEX® pharmacokinetics (PK) concentrations were comparable regardless of whether the first dose was administered as a split infusion or single first infusion in patients with multiple myeloma.[1] The safety profile of DARZALEX® was comparable when administered initially as a split or single dose.[1]

"We are committed to exploring options that may improve the administration profile of DARZALEX® and the overall treatment experience for patients and physicians," said Craig Tendler, MD, Vice President, Clinical Development and Global Medical Affairs, Janssen Research & Development, LLC. "We look forward to reviewing the data in support of these applications with regulators and hope to make a DARZALEX® split-dose option available to patients and health care professionals to provide additional flexibility in administration of the initial infusion."

The regulatory submission is based on data from the global, multi-arm Phase 1b MMY1001 study in multiple myeloma, which evaluated DARZALEX® in combination with various treatment regimens.[1] Splitting the first dose of DARZALEX® effectively reduced the duration of the first infusion and resulted in a similar rate and pattern of infusion reactions.[1] Data from MMY1001 demonstrated that DARZALEX® concentrations were comparable after administration of the first 16 mg/kg dose regardless of whether it was administered as a split infusion or single first infusion in all approved indications.[1] No new safety events were observed with split dosing.[1]

In the U.S., DARZALEX® first received FDA approval in November 2015 as a monotherapy for patients with multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent, or who are double refractory to a PI and an immunomodulatory agent.[2] DARZALEX® received additional approvals in November 2016 in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.[3] In June 2017, DARZALEX® received approval in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies, including lenalidomide and a PI.[4] Most recently, in May 2018, DARZALEX® received approval in combination with bortezomib, melphalan and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT), making it the first monoclonal antibody approved for newly diagnosed patients with this disease.[5]

In the European Union (EU), DARZALEX® first received European Commission approval in May 2016 as a monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a PI and an immunomodulatory agent, and who have demonstrated disease progression on the last therapy.[6] DARZALEX® received an additional approval in April 2017 for use in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.[6] Finally, in July 2018, DARZALEX® received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) recommending broadening the existing marketing authorization for use in combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT).

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered into a global license and development agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize DARZALEX®.[7] For the full U.S. Prescribing Information, please visit www.DARZALEX.com. For the full EU Summary of Product Characteristics, please click here.

About DARZALEX® (daratumumab) Injection, for Intravenous Infusion

DARZALEX® (daratumumab) injection for intravenous use is the first CD38-directed antibody approved anywhere in the world.[5] CD38 is a surface protein that is highly expressed across multiple myeloma cells, regardless of

disease stage.[8] DARZALEX® is believed to induce tumor cell death through multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), as well as through apoptosis, in which a series of molecular steps in a cell lead to its death.[5] Subsets of myeloid derived suppressor cells (MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by DARZALEX®.[5] DARZALEX® is being evaluated in a comprehensive clinical development program across a range of treatment settings in multiple myeloma, such as in frontline and relapsed settings.[9,10,11,12,13,14,15,16] Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant hematologic diseases in which CD38 is expressed, such as smoldering myeloma, as well as in solid tumors.[17,18,19] DARZALEX® is the first and only CD38-directed antibody to receive regulatory approval to treat multiple myeloma.[5]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.[20,21] Refractory cancer occurs when a patient's disease is resistant to treatment or in the case of multiple myeloma, patients progress within 60 days of their last therapy.[22,23] Relapsed cancer means the disease has returned after a period of initial, partial or complete remission.[24] In 2018, it is estimated that 30,700 people will be diagnosed, and 12,770 will die from the disease in the United States.[25] Additionally, there were 40,570 new cases of multiple myeloma in Europe in 2015.[26] 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.[27] While some patients with multiple myeloma have no symptoms at all, most patients are diagnosed due to symptoms, which can include bone fracture or pain, low red blood counts, fatigue, calcium elevation, kidney problems or infections.[28]

IMPORTANT SAFETY INFORMATION[5]

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion Reactions – DARZALEX® can cause severe and/or serious infusion reactions, including anaphylactic reactions. In clinical trials, approximately half of all patients experienced an infusion reaction. Most infusion reactions occurred during the first infusion and were grade 1-2. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing an infusion. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema and pulmonary edema. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting and nausea. Less

common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt infusion for reactions of any severity and institute medical management as needed. Permanently discontinue therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Interference with Serological Testing – Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Neutropenia – DARZALEX® may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. DARZALEX® dose delay may be required to allow recovery of neutrophils. No dose reduction of DARZALEX® is recommended. Consider supportive care with growth factors.

Thrombocytopenia – DARZALEX® may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. DARZALEX® dose delay may be required to allow recovery of platelets. No dose reduction of DARZALEX® is recommended. Consider supportive care with transfusions.

Interference with Determination of Complete Response – Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa

myeloma protein.

Adverse Reactions – The most frequently reported adverse reactions (incidence ≥20%) in clinical trials were: infusion reactions, neutropenia, thrombocytopenia, fatigue, nausea, diarrhea, constipation, vomiting, muscle spasms, arthralgia, back pain, pyrexia, chills, dizziness, insomnia, cough, dyspnea, peripheral edema, peripheral sensory neuropathy and upper respiratory tract infection.

In patients who received DARZALEX® in combination with bortezomib, melphalan, and prednisone (DVMP), the most frequently reported adverse reactions (incidence ≥20%) were: upper respiratory tract infection (48%), infusion reactions (28%), and peripheral edema (21%). Serious adverse reactions (≥2% compared to the VMP arm) were pneumonia (11%), upper respiratory tract infection (5%), and pulmonary edema (2%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were lymphopenia (58%), neutropenia (44%), and thrombocytopenia (38%).

In patients who received DARZALEX® in combination with lenalidomide and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were: upper respiratory tract infection (65%), infusion reactions (48%), diarrhea (43%), fatigue (35%), cough (30%), muscle spasms (26%), nausea (24%), dyspnea (21%) and pyrexia (20%). The overall incidence of serious adverse reactions was 49%. Serious adverse reactions (≥2% compared to Rd) were pneumonia (12%), upper respiratory tract infection (7%), influenza (3%), and pyrexia (3%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were neutropenia (53%) and lymphopenia (52%).

In patients who received DARZALEX® in combination with bortezomib and dexamethasone, the most frequently reported adverse reactions (incidence ≥20%) were: peripheral sensory neuropathy (47%), infusion reactions (45%), upper respiratory tract infection (44%), diarrhea (32%), cough (27%), peripheral edema (22%), and dyspnea (21%). The overall incidence of serious adverse reactions was 42%. Serious adverse reactions (≥2% compared to Vd) were upper respiratory tract infection (5%), diarrhea (2%) and atrial fibrillation (2%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were lymphopenia (48%) and thrombocytopenia (47%).

In patients who received DARZALEX® in combination with pomalidomide and dexamethasone, the most frequent adverse reactions (>20%) were fatigue (50%), infusion reactions (50%), upper respiratory tract infection (50%), cough (43%), diarrhea (38%), constipation (33%), dyspnea (33%), nausea (30%), muscle spasms (26%), back pain (25%), pyrexia (25%), insomnia (23%), arthralgia (22%), dizziness (21%), and vomiting (21%). The overall incidence of serious adverse reactions was 49%. Serious adverse reactions reported in ≥5% patients included pneumonia (7%). Treatment-emergent hematology Grade 3-4 laboratory abnormalities ≥20% were anemia (30%), neutropenia (82%), and lymphopenia (71%).

In patients who received DARZALEX® as monotherapy, the most frequently reported adverse reactions (incidence ≥20%) were: infusion reactions (48%), fatigue (39%), nausea (27%), back pain (23%), pyrexia (21%), cough (21%), and upper respiratory tract infection (20%). The overall incidence of serious adverse reactions was 33%. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities ≥20% were lymphopenia (40%) and neutropenia (20%).

DRUG INTERACTIONS

Effect of Other Drugs on Daratumumab: The coadministration of lenalidomide, pomalidomide or bortezomib with DARZALEX® did not affect the pharmacokinetics of daratumumab.

Effect of Daratumumab on Other Drugs: The coadministration of DARZALEX® with bortezomib or pomalidomide did not affect the pharmacokinetics of bortezomib or pomalidomide.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

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 @JanssenGlobal, @JanssenUS and @JanssenEMEA. Janssen Research & Development, LLC, Janssen Biotech, Inc. and Janssen-Cilag International NV are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding the benefits of DARZALEX® (daratumumab) for the treatment of patients with multiple myeloma. 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 Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag International NV and any of the other Janssen Pharmaceutical Companies 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 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 behavior and spending patterns 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 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 December 31, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's subsequent Quarterly Reports on Form 10-Q and other 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. Neither the Janssen Pharmaceutical Companies of Johnson & Johnson nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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