



News Release

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Janssen Announces U.S. FDA Approval of DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) in Combination with Pomalidomide and Dexamethasone for Patients with Multiple Myeloma After First or Subsequent Relapse

DARZALEX FASPRO® is now the first and only subcutaneous anti-CD38 monoclonal antibody approved in combination with pomalidomide and dexamethasone

July 12, 2021 (HORSHAM, P.A.) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today the U.S. Food and Drug Administration (FDA) approval of DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) in combination with pomalidomide and dexamethasone (Pd) for the treatment of adult patients with multiple myeloma who have received at least one prior line of therapy, including lenalidomide and a proteasome inhibitor. The approval follows the regulatory [submission](#) to the FDA in November 2020 and marks the sixth indication for DARZALEX FASPRO® in the treatment of multiple myeloma. Findings from the Phase 3 APOLLO study were [presented](#) at the 2020 American Society of Hematology (ASH) Annual Meeting and were recently published in [The Lancet Oncology](#).

“Clinical studies including APOLLO have continued to show the ability of daratumumab-based combination treatment regimens to significantly reduce the risk of progression in patients with multiple myeloma,” said Meletios A. Dimopoulos, M.D.*, Professor and Chairman of the

Department of Clinical Therapeutics at the National and Kapodistrian University of Athens School of Medicine, Athens, Greece, and principal investigator. "With this approval, we are now able to combine pomalidomide and dexamethasone with a daratumumab subcutaneous option that can be administered in minutes rather than the hours needed for intravenous administration."

The APOLLO study met its primary endpoint of improved progression-free survival (PFS), demonstrating that DARZALEX *FASPRO*[®]-Pd significantly reduced the risk of progression or death by 37 percent, compared to Pd alone (hazard ratio, 0.63; 95 percent confidence interval [CI], 0.47-0.85; *P*=0.0018).¹ The median PFS for the DARZALEX *FASPRO*[®]-Pd arm vs. Pd arm was 12.4 vs. 6.9 months, respectively.¹ Study findings additionally showed the rate of overall response to be significantly higher in DARZALEX *FASPRO*[®]-Pd compared to Pd alone (69 percent vs. 46 percent), as well as rates of complete response or better (25 percent vs. 4 percent) and very good partial response or better (51 percent vs. 20 percent).¹ Additionally, more patients treated with DARZALEX *FASPRO*[®]-Pd showed a negative status for minimal residual disease than patients receiving Pd alone (9 percent vs. 2 percent).¹

Permanent treatment discontinuation due to an adverse reaction occurred in 2 percent of patients who received DARZALEX *FASPRO*[®]-Pd. No adverse reactions resulting in permanent discontinuation occurred in more than 1 patient. The most common adverse reactions (≥ 20 percent) were fatigue, pneumonia, upper respiratory tract infection, and diarrhea. Serious adverse reactions occurred in 50 percent of patients who received DARZALEX *FASPRO*[®]-Pd. The most frequent serious adverse reactions in >5 percent of patients who received DARZALEX *FASPRO*[®]-Pd were pneumonia (15 percent) and lower respiratory tract infection (12 percent). Fatal adverse reactions occurred in 7 percent of patients who received DARZALEX *FASPRO*[®]-Pd.

"We are focused on the continued development of DARZALEX *FASPRO* and advancing this innovative therapy for patients who are in need of additional treatment options," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Janssen Research & Development, LLC. "Today's approval further distinguishes DARZALEX *FASPRO* in the treatment of multiple myeloma as the first and only subcutaneously administered anti-CD38 monoclonal antibody approved in combination with the widely used pomalidomide and dexamethasone regimen."

About the APOLLO Study²

APOLLO ([NCT03180736](#)) is an ongoing multicenter, Phase 3, randomized, open-label study comparing DARZALEX *FASPRO*[®]/ daratumumab SC in combination with pomalidomide and low-dose dexamethasone with pomalidomide and low-dose dexamethasone alone in patients with relapsed or refractory multiple myeloma who have received at least one prior treatment regimen, have received both lenalidomide and a proteasome inhibitor, and have demonstrated disease progression. The study enrolled 304 participants. The primary endpoint is PFS. Secondary endpoints include rates of overall response (ORR), very good partial response (VGPR) or better, complete response (CR) or better, and duration of response.

About DARZALEX *FASPRO*[®]

In [August 2012](#), Janssen Biotech, Inc. and Genmab A/S entered into a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize daratumumab. DARZALEX *FASPRO*[®] is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma and now AL amyloidosis. DARZALEX *FASPRO*[®] is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE[®] drug delivery technology.

DARZALEX *FASPRO*[®] is indicated for the treatment of adult patients with multiple myeloma:

- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
- as monotherapy, in patients 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

DARZALEX *FASPRO*[®] in combination with bortezomib, cyclophosphamide, and dexamethasone is indicated for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Limitations of Use

DARZALEX *FASPRO*[®] is not indicated and is not recommended for the treatment of patients with light chain (AL) amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials.

Full prescribing information for DARZALEX *FASPRO*[®] is available [here](#).

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.^{2,3} When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow. In 2021, it is estimated that more than 34,000 people will be diagnosed and close to 12,500 will die from the disease in the U.S.^{2,4} While some patients with multiple myeloma have no symptoms, most patients are diagnosed due to symptoms, which can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.⁴

DARZALEX *FASPRO*[®] IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX *FASPRO*[®] is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions²

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*[®]. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX *FASPRO*[®].

Systemic Reactions

In a pooled safety population of 832 patients with multiple myeloma (N=639) or light chain (AL) amyloidosis (N=193) who received DARZALEX *FASPRO*[®] as monotherapy or in combination, 9% of

patients experienced a systemic administration-related reaction (Grade 2: 3.5%, Grade 3: 0.8%). Systemic administration-related reactions occurred in 8% of patients with the first injection, 0.4% with the second injection, and cumulatively 1% with subsequent injections. The median time to onset was 3.2 hours (range: 9 minutes to 3.5 days). Of the 129 systemic administration-related reactions that occurred in 74 patients, 110 (85%) occurred on the day of DARZALEX FASPRO® administration. Delayed systemic administration-related reactions have occurred in 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritis, chills, vomiting, nausea, and hypotension.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX FASPRO®. Consider administering corticosteroids and other medications after the administration of DARZALEX FASPRO® depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 5.5 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX FASPRO®. Monitor for local reactions and consider symptomatic management.

Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis²

Serious or fatal cardiac adverse reactions occurred in patients with light chain (AL) amyloidosis who received DARZALEX FASPRO® in combination with bortezomib, cyclophosphamide and dexamethasone. Serious cardiac disorders occurred in 16% and fatal cardiac disorders occurred in 10% of patients. Patients with NYHA Class IIIA or Mayo Stage IIIA disease may be at greater risk. Patients with NYHA Class IIIB or IV disease were not studied. Monitor patients with cardiac involvement of light chain (AL) amyloidosis more frequently for cardiac adverse reactions and administer supportive care as appropriate.

Neutropenia²

Daratumumab 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. Consider withholding DARZALEX *FASPRO*[®] until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO*[®], higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia²

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX *FASPRO*[®] until recovery of platelets.

Embryo-Fetal Toxicity²

Based on the mechanism of action, DARZALEX *FASPRO*[®] can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*[®] may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX *FASPRO*[®] and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*[®] with lenalidomide is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

Interference with Serological Testing²

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 administration. 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 *FASPRO*[®]. Type and screen patients prior to starting DARZALEX *FASPRO*[®].

Interference with Determination of Complete Response²

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 DARZALEX *FASPRO*[®]-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS²

The most common adverse reaction ($\geq 20\%$) with DARZALEX *FASPRO*[®] monotherapy is: upper respiratory tract infection. The most common adverse reactions with combination therapy ($\geq 20\%$ for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, pyrexia, cough, muscle spasms, back pain, vomiting, upper respiratory tract infection, peripheral sensory neuropathy, constipation, pneumonia, and peripheral edema.

The most common adverse reactions ($\geq 20\%$) in patients with light chain (AL) amyloidosis who received DARZALEX *FASPRO*[®] are upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea, and cough.

The most common hematology laboratory abnormalities ($\geq 40\%$) with DARZALEX *FASPRO*[®] are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please see full [Prescribing Information](#) for DARZALEX *FASPRO*[®].

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at [@JanssenUS](#) and [@JanssenGlobal](#). Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

*Dr. Dimopoulos has served as a consultant to Janssen; he has not been paid for any media work.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding DARZALEX FASPRO®. 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., or 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 January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, 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 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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¹ Dimopoulos, MA et al. APOLLO: Phase 3 Randomized Study of Subcutaneous Daratumumab Plus Pomalidomide and Dexamethasone (D-Pd) Versus Pomalidomide and Dexamethasone (Pd) Alone in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM).

² Kumar, SK et al. Risk of progression and survival in multiple myeloma relapsing after therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. *Leukemia*. 2012 Jan; 26(1):149-57.

³ American Cancer Society. "What Is Multiple Myeloma?" Available at: <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma>. Accessed May 2021.

⁴ American Cancer Society. "Key Statistics About Multiple Myeloma." Available at: <https://www.cancer.org/cancer/multiple-myeloma/about/key-statistics.html>. Accessed May 2021.