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**DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj)  
Becomes the First FDA-Approved Treatment for Patients with  
Newly Diagnosed Light Chain (AL) Amyloidosis**

*Accelerated approval of DARZALEX FASPRO-based combination regimen supported by the Phase 3 ANDROMEDA study demonstrating a significantly higher hematologic complete response rate in this rare and serious blood cell disorder*

**January 15, 2021 (HORSHAM, Pa.)** – 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), a subcutaneous formulation of daratumumab, in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd) for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis.<sup>1</sup> DARZALEX FASPRO® is the first and only FDA-approved treatment for patients with this blood cell disorder that is associated with the production of an abnormal protein, which leads to the deterioration of vital organs, most notably the heart, kidneys and liver.<sup>2,3</sup> This indication is approved under accelerated approval and is based on the hematologic complete response rate (hemCR) measure. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. 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.

“Today’s milestone is an important step for patients diagnosed with this rare disease,” said Isabelle Lousada, Founder and CEO, Amyloidosis Research Consortium. “Sadly, most patients with AL

amyloidosis are diagnosed more than one year after their initial symptoms present, at a time when they may already be experiencing organ deterioration or failure.<sup>4</sup> I believe this approval will increase awareness of and education around this life-threatening disease and offer new hope for people with AL amyloidosis and their caregivers.”

The FDA approval is based on positive results from the Phase 3 ANDROMEDA study, which were recently [presented](#) at the American Society of Hematology (ASH) 2020 Annual Meeting. The study evaluated DARZALEX *FASPRO*® in combination with VCd, compared with VCd alone, a common treatment regimen used in adult patients with newly diagnosed AL amyloidosis.<sup>5</sup> Patients receiving treatment with DARZALEX *FASPRO*® experienced a hemCR more than triple that of patients receiving VCd alone (42 percent for D-VCd and 13 percent for VCd;  $P < 0.0001$ ).<sup>1</sup>

“There is an urgent need for awareness and treatment options to help in the fight against this serious blood cell disorder,” said Raymond L. Comenzo, M.D., Director, John C. Davis Myeloma and Amyloid Program, Tufts Medical Center, and ANDROMEDA study investigator. “Achieving hematologic complete response is an important treatment goal, and today’s approval based on this clinical endpoint will provide doctors and the larger medical community with a new option to treat newly diagnosed patients.”

Approximately 4,500 people in the U.S. develop this rare disease each year.<sup>6</sup> AL amyloidosis is a life-threatening blood cell disorder that occurs when blood plasma cells in the bone marrow produce amyloid deposits, which build up in vital organs and eventually cause organ deterioration.<sup>3</sup> The disease can affect different organs in different people, but the most frequently affected organs are the heart, kidneys, liver, spleen, gastrointestinal tract and nervous system.<sup>2,3</sup> About one-third of patients visit five or more doctors before receiving a diagnosis, and 72 percent are diagnosed more than one year after they first experience symptoms.<sup>3,4</sup> Patients often have a poor prognosis due to the delay in diagnosis of AL amyloidosis, which frequently presents with non-specific symptoms that can mimic other, more common conditions.<sup>7</sup> As many as 30 percent of patients with AL amyloidosis die within the first year after diagnosis.<sup>8</sup>

“DARZALEX *FASPRO*, as the first and only FDA-approved treatment for newly diagnosed AL amyloidosis, marks a significant advance for a disease with high unmet medical need,” said Jessica Vermeulen, M.D., Ph.D., Global Medical Head/Clinical Leader, Hematology & Oncology, Janssen Research & Development, LLC. “Today’s approval underscores our commitment to deliver innovative therapies for patients with plasma cell diseases.”

The most common adverse reactions ( $\geq 20$  percent) were upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea and cough. Serious adverse reactions occurred in 43 percent of patients who received DARZALEX *FASPRO*<sup>®</sup> in combination with VCd. Serious adverse reactions that occurred in at least 5 percent of patients in the D-VCd arm were pneumonia (9 percent), cardiac failure (8 percent) and sepsis (5 percent). Fatal adverse reactions occurred in 11 percent of patients. Fatal adverse reactions that occurred in more than one patient included cardiac arrest (4 percent), sudden death (3 percent), cardiac failure (3 percent) and sepsis (1 percent).<sup>1</sup>

Among patients who received DARZALEX *FASPRO*<sup>®</sup> in combination with VCd, 72 percent of patients had baseline cardiac involvement with Mayo Cardiac Stage I (3 percent), Stage II (46 percent) and Stage III (51 percent). Serious cardiac disorders occurred in 16 percent of patients (8 percent of patients with Mayo Cardiac Stage I and II and 28 percent of patients with Stage III). Serious cardiac disorders in more than 2 percent of patients included cardiac failure (8 percent), cardiac arrest (4 percent) and arrhythmia (4 percent). Fatal cardiac disorders occurred in 10 percent of patients (5 percent of patients with Mayo Cardiac Stage I and II and 19 percent of patients with Stage III) who received DARZALEX *FASPRO*<sup>®</sup> in combination with VCd. Fatal cardiac disorders that occurred in more than one patient in the D-VCd arm included cardiac arrest (4 percent), sudden death (3 percent) and cardiac failure (3 percent).<sup>1</sup>

The FDA reviewed and approved this indication under the FDA Real-Time Oncology Review (RTOR) program, which allows data for certain applications to be reviewed before the applicant formally submits the complete application. The RTOR program aims to explore a more efficient and timely review process to help ensure treatments are available as soon as possible for patients. Selection into the RTOR program does not guarantee or influence approvability of the supplemental application. The submission was also reviewed under Project Orbis, an initiative of the FDA Oncology Center of Excellence, which provides a framework for concurrent submission and review of oncology medicine applications among international regulatory agencies.

### **About the ANDROMEDA Study<sup>1</sup>**

ANDROMEDA ([NCT03201965](https://clinicaltrials.gov/ct2/show/study/NCT03201965)) is an ongoing Phase 3, randomized, open-label study investigating the safety and efficacy of DARZALEX *FASPRO*<sup>®</sup> (daratumumab and hyaluronidase-fihj) in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd), compared to VCd

alone, for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis. The study includes 388 patients with newly diagnosed AL amyloidosis with measurable hematologic disease and one or more organs affected. The primary endpoint is overall complete hematologic response rate by intent-to-treat (ITT). Patients received DARZALEX FASPRO® 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity or a maximum of 2 years. Among patients who received D-VCd, 74 percent were exposed for 6 months or longer and 32 percent were exposed for greater than one year.

### **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
- 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

### **Access to DARZALEX FASPRO® (daratumumab hyaluronidase-fihj)**

Janssen offers comprehensive access and support information, resources and services to assist U.S. patients in gaining access to DARZALEX FASPRO® through the Janssen CarePath Savings Program. Through the program, patients with commercial insurance plans will pay \$5 per injection with a \$20,000 maximum program benefit per calendar year. This program is not valid for patients

using Medicare, Medicaid, or other government-funded programs to pay for their medications. Information on the enrollment process is available online at [www.CarePathSavingsProgram.com/DARZALEX](http://www.CarePathSavingsProgram.com/DARZALEX).

Full prescribing information will be available at [www.DARZALEX.com](http://www.DARZALEX.com).

## **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 Reactions<sup>1</sup>**

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX FASPRO™.

##### *Systemic Reactions*

In a pooled safety population of 683 patients with multiple myeloma (N=490) or light chain (AL) amyloidosis (N=193) who received DARZALEX FASPRO™ as monotherapy or in combination, 10% of patients experienced a systemic administration-related reaction (Grade 2: 3.5%, Grade 3: 1%). Systemic administration-related reactions occurred in 9% 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 117 systemic administration-related reactions that occurred in 66 patients, 100 (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*<sup>™</sup>. Consider administering corticosteroids and other medications after the administration of DARZALEX *FASPRO*<sup>™</sup> 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 9% of patients, including Grade 2 reactions in 0.7%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 5 minutes (range: 0 minutes to 4.7 days) after starting administration of DARZALEX *FASPRO*<sup>™</sup>. Monitor for local reactions and consider symptomatic management.

### **Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis<sup>1</sup>**

Serious or fatal cardiac adverse reactions occurred in patients with light chain (AL) amyloidosis who received DARZALEX *FASPRO*<sup>™</sup> 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.

### **Neutropenia<sup>1</sup>**

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*<sup>™</sup> until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO*<sup>™</sup>, higher rates of Grade 3-4 neutropenia were observed.

### **Thrombocytopenia<sup>1</sup>**

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*<sup>™</sup> until recovery of platelets.

### **Embryo-Fetal Toxicity<sup>1</sup>**

Based on the mechanism of action, DARZALEX *FASPRO*<sup>™</sup> can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*<sup>™</sup> 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*<sup>™</sup> and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*<sup>™</sup> 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 Testing<sup>1</sup>**

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*<sup>™</sup>. Type and screen patients prior to starting DARZALEX *FASPRO*<sup>™</sup>.

### **Interference with Determination of Complete Response<sup>1</sup>**

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*<sup>™</sup>-treated patients with IgG kappa myeloma protein.

### **ADVERSE REACTIONS<sup>1</sup>**

The most common adverse reaction ( $\geq 20\%$ ) with DARZALEX *FASPRO*<sup>™</sup> 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, and pneumonia.

The most common adverse reactions ( $\geq 20\%$ ) in patients with light chain (AL) amyloidosis who received DARZALEX *FASPRO*<sup>™</sup> 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 at [www.DARZALEX.com](http://www.DARZALEX.com).**

### **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](http://www.janssen.com). Follow us at [www.twitter.com/JanssenGlobal](https://www.twitter.com/JanssenGlobal) and [www.twitter.com/JanssenUS](https://www.twitter.com/JanssenUS). Janssen Biotech, Inc. and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

### **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 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 December 29, 2019, 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](http://www.sec.gov), [www.jnj.com](http://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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<sup>1</sup> DARZALEX FASPRO® Prescribing Information. Horsham, PA: Janssen Biotech, Inc.

<sup>2</sup> Mayo Clinic. Amyloidosis overview: symptoms and causes. <https://www.mayoclinic.org/diseases-conditions/amyloidosis/symptoms-causes/syc-20353178>. Accessed January 2021.

<sup>3</sup> Lousada I, Comenzo RL, Landau H, et al. Light chain amyloidosis: patient experience survey from the Amyloidosis Research Consortium. *Advances in Therapy*. 2015;32(10):920-928.

<sup>4</sup> McCausland KL, et al. *Patient*. 2018;11(2):207-216.

<sup>5</sup> Kastiris E, et al. Subcutaneous Daratumumab + Cyclophosphamide, Bortezomib, and Dexamethasone (CyBorD) in Patients with Newly Diagnosed Light Chain (AL) Amyloidosis: Primary Results from the Phase 3 ANDROMEDA Study. Available at:

[https://library.ehweb.org/eha/2020/eha25th/303396/efstathios.kastiris.subcutaneous.daratumumab.2B.cycl%20ophosphamide.bortezomib.html?f=listing%3D0%2Abrowseby%3D8%2Asortby%3D1%2Amedia%3D3%2Ace\\_i](https://library.ehweb.org/eha/2020/eha25th/303396/efstathios.kastiris.subcutaneous.daratumumab.2B.cycl%20ophosphamide.bortezomib.html?f=listing%3D0%2Abrowseby%3D8%2Asortby%3D1%2Amedia%3D3%2Ace_i). Accessed January 2021.

<sup>6</sup> Amyloidosis Foundation. AL amyloidosis facts. <http://www.amyloidosis.org/facts/al/>. Accessed January 2021.

<sup>7</sup> Mayo Clinic. Amyloidosis diagnosis and treatment. <https://mayocl.in/3jK50G4>. Accessed January 2021.

<sup>8</sup> Merlini G, et al. Light chain amyloidosis: the heart of the problem. *Haematologica*. 2013;98(10):1492-1495.