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For Immediate Release

European Commission approves Johnson & Johnson's subcutaneous DARZALEX® (daratumumab)-based quadruplet regimen for the treatment of patients with newly diagnosed multiple myeloma, regardless of transplant eligibility

Approval cements daratumumab as a foundational therapy in newly diagnosed multiple myeloma and the only anti-CD38 antibody for all patient types in this setting

Phase 3 CEPHEUS study shows significant improvement in minimal residual disease (MRD)-negativity rate, progression-free survival and complete response or better versus standard of care[1]

BEERSE, BELGIUM (7 April 2025) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved an indication extension of DARZALEX® (daratumumab) subcutaneous (SC) formulation in the frontline setting. The approval is for daratumumab SC in combination with bortezomib, lenalidomide, and dexamethasone (daratumumab-VRd) for the treatment of adult patients with newly diagnosed multiple myeloma (NDMM).[1]

"Multiple myeloma is a complex and evolving disease. Starting with more effective regimens in the frontline setting offers patients the best chance of sustained long-term outcomes by preventing disease resistance and relapse," said Professor Katja Weisel, University Medical Centre Hamburg-Eppendorf. "The subcutaneous daratumumab-VRd regimen delivers an effective and convenient new standard of care for patients with newly diagnosed multiple myeloma, regardless of transplant eligibility, with responses that are deep and durable, and translate into significantly reduced risk of disease progression or death."

Daratumumab is now approved in nine indications for multiple myeloma, five of which are in the frontline setting, including as part of treatment regimens for newly diagnosed patients who are eligible or ineligible for autologous stem-cell transplant (ASCT).[1] Today's approval follows the indication extension approval for daratumumab-VRd in October 2024, for the treatment of newly diagnosed patients with multiple myeloma who are eligible for ASCT, based on the results from the Phase 3 PERSEUS study. The study evaluated this daratumumab SC-based quadruplet regimen for induction and consolidation therapy, followed by daratumumab SC and lenalidomide maintenance.[2,3]

"Daratumumab has become a cornerstone of multiple myeloma treatment over the past decade and is now the only anti-CD38 antibody approved to treat all patient types in the frontline setting, regardless of transplant eligibility," said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, Johnson & Johnson Innovative Medicine. "This latest approval confirms the enhanced benefit of daratumumab SC-based quadruplet regimens and its versatility and effectiveness in addressing the diverse needs of those affected by this complex disease."

The Phase 3 CEPHEUS (NCT03652064) study evaluated the efficacy and safety of daratumumab-VRd (n=197) compared to VRd (n=198) for patients with NDMM who are transplant ineligible or for whom ASCT was not planned as initial therapy (transplant ineligible or deferred).[1] Data from the study were previously presented at the 2024 International Myeloma Society (IMS) Annual Meeting.[4] At a median follow-up of 59 months, the primary endpoint was met, with an overall minimal residual disease (MRD)-negativity rate at a sensitivity of 10^{-5} (no cancer cells detected within 100,000 bone marrow cells) of 60.9

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percent for patients receiving daratumumab-VRd and 39.4 percent for VRd (Odds ratio [OR], 2.37; 95 percent confidence interval [CI], 1.58-3.55; *p*<0.0001).[1] Similarly, the proportion of patients achieving sustained MRD-negativity of ≥ 12 months almost doubled with daratumumab-VRd vs VRd (48.7 percent vs 26.3 percent; OR, 2.63; 95 percent CI, 1.73-4.00; *p*<0.0001).[1] The daratumumab SC-based quadruplet regimen, compared to VRd, also significantly increased the depth of response with higher rates of complete response (CR) or better.[1] The CR or better rate was 81.2 percent with daratumumab-VRd vs 61.6 percent with VRd (OR 2.73; 95 percent CI, 1.71-4.34; *p*<0.0001).[1] The study also demonstrated that daratumumab-VRd significantly reduced the risk of progression or death by 43 percent (Hazard ratio [HR], 0.57; 95 percent CI, 0.41-0.79; *p*<0.0005) vs VRd. The median progression-free survival was not reached for daratumumab-VRd vs 52.6 months for VRd.[1] Overall survival data were not yet mature.

The overall safety profile of daratumumab-VRd was consistent with the known safety profiles for daratumumab SC and VRd.[4] The most common (>10 percent) Grade 3/4 haematologic and non-haematologic adverse events with daratumumab-VRd vs VRd were neutropenia (44.2 percent vs 29.7 percent), thrombocytopenia (28.4 percent vs 20.0 percent), anaemia (13.2 percent vs 11.8 percent), peripheral neuropathies (8.1 percent vs 8.2 percent), diarrhoea (12.2 percent vs 9.2 percent), and COVID-19 (11.2 percent vs 4.6 percent).[4]

“At Johnson & Johnson, our dedication to advance multiple myeloma research spans more than 20 years and our commitment to transforming outcomes for patients has never been stronger than it is today,” said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, Johnson & Johnson Innovative Medicine. “This landmark approval enables us to offer all patient populations access regardless of age, fitness or risk to a daratumumab-based triplet or quadruplet regimen in the frontline setting – a critical step towards our ultimate goal of delivering a functional cure.”

Johnson & Johnson also submitted a supplemental Biologics License Application to the U.S. Food and Drug Administration seeking approval of a new indication for daratumumab SC in combination with VRd for the treatment of adult patients with NDMM for whom ASCT is deferred or who are ineligible for ASCT, on 30 September 2024.

About the CEPHEUS Study

CEPHEUS (NCT03652064) is an international, randomised, open-label, Phase 3 study comparing subcutaneous daratumumab, bortezomib, lenalidomide, and dexamethasone (daratumumab-VRd) with standard bortezomib, lenalidomide, and dexamethasone (VRd).[4,5] The trial enrolled 395 patients with newly diagnosed multiple myeloma who were either ineligible for stem cell transplantation (SCT) or for whom SCT is not planned.[4] The primary endpoint was overall minimal residual disease (MRD)-negativity rate.[4] The minimum age for participation was 18 years for patients in both the daratumumab-VRd arm and VRd arm, with a median patient age of 70 (range 31-80).[4] The study was conducted in 13 countries across North America, South America, and Europe.[4]

About daratumumab and daratumumab SC

Johnson & Johnson is committed to exploring the potential of daratumumab for patients with multiple myeloma across the spectrum of the disease.

In August 2012, Janssen Biotech, Inc., a Johnson & Johnson company, and Genmab A/S entered a worldwide agreement, which granted Johnson & Johnson an exclusive licence to develop, manufacture and commercialise daratumumab. Since launch, daratumumab has become a foundational therapy in the treatment of multiple myeloma, having been used in the treatment of more than 618,000 patients worldwide.[6] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma.[7] Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[7]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[7] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[7] Daratumumab may also have an effect on normal cells.[7] Data across ten Phase 3 clinical trials, in both the frontline and relapsed settings, have shown that daratumumab-based regimens resulted in significant improvement in progression-free survival and/or overall survival.[4,8,9,10,11,12,13,14,15]

For further information on daratumumab, please see the Summary of Product Characteristics at: https://ec.europa.eu/health/documents/community-register/html/h1101.htm.

About Multiple Myeloma

Multiple myeloma is currently an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[16,17] In multiple myeloma, these malignant plasma cells continue to proliferate, accumulating in the body and crowding out normal blood cells, as well as often causing bone destruction and other serious complications.[17] In the European Union, it is estimated that more than 35,000 people were diagnosed with multiple myeloma in 2022, and more than 22,700 patients died.[18] People living with multiple myeloma experience relapses which become more frequent with each line of therapy [19,20] while remissions become progressively shorter.[19,20,21] Whilst some patients with multiple myeloma initially have no symptoms, others

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can have common signs and symptoms of the disease, which can include bone fracture or pain, low red blood cell counts, fatigue, high calcium levels, infections, or kidney damage.[22]

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow. and profoundly impact health for humanity.

Learn more at www.innovativemedicine.jnj.com/emea. Follow us at www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen-Cilag International NV, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., and Janssen Research & Development, LLC are Johnson & Johnson companies.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of 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, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & Development, LLC 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behaviour 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 most recent Annual Report on Form 10-K, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson'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 http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen-Cilag International NV, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & Development, LLC nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

**Professor Katja Wesel, University Medical Centre Hamburg-Eppendorf, has provided consulting, advisory, and speaking services to Janssen; she has not been paid for any media work.*

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