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For Immediate Release

European Commission approves DARZALEX® (daratumumab) as the first licensed treatment for patients with high-risk smouldering multiple myeloma

Landmark approval is based on results from the Phase 3 AQUILA study, showing fixed-duration treatment with daratumumab significantly reduced the risk of progression to active multiple myeloma or death by 51 percent compared to active monitoring[1]

This milestone marks a critical advance in early intervention for multiple myeloma as the first authorised treatment, offering a new treatment paradigm for patients with high-risk smouldering disease[2]

BEERSE, BELGIUM (23 July 2025) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) has approved a new indication for DARZALEX® (daratumumab) subcutaneous (SC) formulation as monotherapy for the treatment of adult patients with smouldering multiple myeloma (SMM) at high-risk of developing multiple myeloma.[3] SMM is an asymptomatic intermediate disease state of multiple myeloma where abnormal cells can be detected in the bone marrow.[2,4,5]

“Until now, the absence of approved therapies for high-risk smouldering multiple myeloma has left clinicians with limited options beyond observation, despite evidence that 50 percent of this patient population progress to active multiple myeloma within two years,” said Professor Meletios A. Dimopoulos, M.D., National and Kapodistrian University of Athens School of Medicine.* “The approval of daratumumab offers the potential to change this trajectory. By intervening earlier in the disease course, we have a meaningful opportunity to delay or prevent progression to symptomatic disease, reduce irreversible end-organ damage and extend the window of improved patient outcomes.”

“This new indication for daratumumab SC is an exciting step forward in addressing a long-standing unmet clinical need for those diagnosed with high-risk smouldering multiple myeloma and is the first time a treatment has been approved for this patient population,” said Ester in ’t Groen, EMEA Therapeutic Area Head Haematology, Johnson & Johnson Innovative Medicine. “It means that eligible patients no longer have to live with the uncertainty or fear of waiting for progression to occur without active treatment, instead having the option to intercept the disease with therapeutic intervention.”

The Phase 3 AQUILA study (NCT03301220) is the largest randomised study of a well-defined high-risk SMM population, evaluating the efficacy and safety of fixed-duration, monotherapy daratumumab SC (n=194) compared with active monitoring (n=196).[1] At a median follow-up of 65.2 months (range, 0-76.6), patients who received daratumumab SC showed statistically significant improved progression-free survival (PFS; defined as progression to active multiple myeloma, as assessed according to the International Myeloma Working Group diagnostic criteria for multiple myeloma [SLiM-CRAB], or death) compared to patients who underwent active monitoring; 63.1 percent in the daratumumab arm versus 40.8 percent in the active monitoring arm remained alive and progression-free at 60 months (hazard ratio [HR], 0.49; 95 percent confidence interval [CI], 0.36-0.67; $p<0.001$).[1] Among patients who were retrospectively categorised as having high-risk SMM, per the current Mayo 2018 criteria (20/2/20), median PFS was not reached in the daratumumab arm and was 22.1 months in the active monitoring arm (HR, 0.36; 95 percent CI, 0.23-0.58).[1] Overall survival was also extended with daratumumab SC, with 5-year survival rates of 93.0 percent vs 86.9 percent for active monitoring (HR, 0.52; 95 percent CI, 0.27-0.98).[1]

Additionally, patients who received daratumumab SC saw a higher overall response rate of 63.4 percent compared to 2.0 percent with active monitoring ($p<0.001$).[1] Median time to first-line multiple myeloma treatment was not reached for patients receiving daratumumab SC compared to 50.2 months with active monitoring (HR, 0.46; 95 percent CI, 0.33-0.62; nominal $p<0.0001$).[1,6]

Daratumumab demonstrated a safety profile consistent with previous studies of daratumumab in other indications, with a low rate of treatment discontinuation due to treatment-emergent adverse events (TEAEs).[1] Grade 3/4 TEAEs occurred in 40.4 percent of patients treated with daratumumab SC and 30.1 percent of patients actively monitored.[1] The most common (≥5 percent in either group) Grade 3/4 TEAE was hypertension (5.7 percent vs 4.6 percent, respectively).[1] The frequency of TEAEs leading to discontinuation of daratumumab SC was low (5.7 percent), as was the incidence of fatal TEAEs in both groups (1.0 percent vs 2.0 percent, respectively).[1]

“Until now, there have been no approved treatment options for patients diagnosed with high-risk smouldering multiple myeloma,” said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, Johnson & Johnson Innovative Medicine. “With today’s approval, Johnson & Johnson has an innovative therapy for every stage of the disease. We can now offer physicians and patients the option to treat with daratumumab earlier, significantly delaying progression and the need for more intensive, continuous therapy, as well as extending overall survival. We remain steadfast in our mission to get in front of cancer.”

About the AQUILA Study

AQUILA (NCT03301220) is a randomised, multicentre Phase 3 study investigating daratumumab SC versus active monitoring in patients (n=390) with high-risk smouldering multiple myeloma (SMM).[7] The primary endpoint is progression-free survival and secondary endpoints include time to progression, overall response rate and overall survival.[7] Patients in the study were diagnosed with SMM in the last five years and were excluded if they had prior exposure to approved or investigational treatments for SMM or multiple myeloma.[7]

About Smouldering Multiple Myeloma

SMM is an asymptomatic intermediate disease state of multiple myeloma where abnormal cells can be detected in the bone marrow.[2,8] Patients living with SMM tend not to show signs or symptoms typically associated with active myeloma, such as bone pain, bone fractures, kidney problems, or anaemia, however as abnormal plasma cells are present, organ damage may begin and progress asymptomatically.[1,9] Approximately 15 percent of all cases of newly diagnosed multiple myeloma are classified as SMM, and half of those diagnosed with high-risk SMM are estimated to progress to active multiple myeloma within two years.[10]

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.[11,12] 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.[11,12] 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.[13] Patients living with multiple myeloma experience relapses which become more frequent with each line of therapy while remissions become progressively shorter.[14,15,16] Whilst some patients with multiple myeloma initially have no symptoms, others 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.[17]

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.[18] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma.[19] Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[19]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[19] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[19] Daratumumab may also have an effect on normal cells.[19] 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.[20,21,22,23,24,25,26,27,28]

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 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.

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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 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. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

**Professor Meletios A. Dimopoulos, M.D., National and Kapodistrian University of Athens School of Medicine, has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.*

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