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## **Health Canada Approves DARZALEX® (daratumumab) for Newly Diagnosed Patients with Multiple Myeloma who are Transplant Ineligible**

*DARZALEX*® combination therapy significantly reduced the risk of disease progression or death compared to a preferred regimen alone.<sup>1,2</sup>

Toronto, ON, December 17, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that Health Canada has approved DARZALEX® (daratumumab), in combination with bortezomib, melphalan and prednisone (VMP), for the treatment of patients newly diagnosed with multiple myeloma who are ineligible for autologous stem cell transplantation.<sup>3</sup> DARZALEX® is the first monoclonal antibody to be approved for newly diagnosed patients in Canada.

Multiple myeloma is an incurable blood cancer that occurs when malignant plasma cells grow uncontrollably in the bone marrow.<sup>4,5</sup> The disease can be very complex to treat as most patients relapse or become resistant to standard therapies, but with increasing research and treatment advances, the outlook for patients is improving.<sup>6,7,8</sup> Eight Canadians are diagnosed each day, with an average age of diagnosis in the mid-sixties.<sup>9</sup> Work is ongoing with both public and private insurers to determine how DARZALEX® can be accessible for newly diagnosed, transplant ineligible patients.

"This daratumumab combination regimen for newly diagnosed patients who don't qualify for a transplant can result in lower risk of disease progression and higher rates of response," says Dr. Darrell White, Hematologist, Queen Elizabeth II Health Sciences Centre. "The data supports this regimen as an effective new option for this patient population."

This marks the third indication for DARZALEX®. In June 2016, Health Canada approved DARZALEX® for those with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), or who are refractory to both a PI and an IMiD (meaning they didn't respond to or relapsed while on those treatments).<sup>10</sup> In April 2017, the

medication was approved for use earlier in the disease - for patients who have received at least one prior therapy. For these patients, DARZALEX® is used in combination with either lenalidomide and dexamethasone, or with bortezomib and dexamethasone.<sup>11</sup> DARZALEX® is now publicly funded in the province of Québec for the treatment of patients with multiple myeloma who have received at least one prior therapy.

The Health Canada approval of DARZALEX® in combination with VMP is supported by data from the randomized, open-label, multicenter Phase 3 ALCYONE (MMY3007) study, published in the [New England Journal of Medicine](#). The combination of DARZALEX® with VMP reduced the risk of disease progression or death by 50 per cent, compared to treatment with VMP alone (Hazard Ratio [HR] = 0.50; 95 per cent confidence interval (CI) [0.38-0.65], p<0.0001).<sup>12</sup> The median progression-free survival (PFS) for DARZALEX® in combination with VMP had not yet been reached, compared to a median PFS of 18.1 months for patients who received VMP alone.<sup>13</sup>

Treatment with DARZALEX® in combination with VMP significantly improved overall response rates (90.9 vs. 73.9%) compared to VMP alone.<sup>14</sup> Additionally, measures of stringent complete response (18 vs. 7%), complete response (24.6 vs. 17.4%) and very good partial response (28.6 vs. 25.3%) all showed marked improvement.<sup>15</sup> Patients receiving DARZALEX® in combination with VMP achieved a more than three-fold increase in the minimal residual disease (MRD) negativity rate (21.1 vs. 6.2%) compared to those who received VMP alone.<sup>16</sup>

In the study, the most frequently reported Treatment Emergent Adverse Events (TEAEs) (≥20%) in the DARZALEX®-VMP (D-VMP) arm were: infusion-related reactions, neutropenia, thrombocytopenia, anemia, upper respiratory tract infection, pyrexia, diarrhea, nausea, and peripheral sensory neuropathy.<sup>17</sup> The overall incidence of serious TEAEs was 41.6% in the D-VMP arm and 32.5% in the VMP arm.<sup>18</sup> Serious TEAEs (≥2%) with at least a 2% higher incidence in the D-VMP arm compared to the VMP arm included infections (23.1% vs 11.9%), including pneumonia (D-VMP 10.1% vs VMP 3.1%).<sup>19</sup> Infusion-related reactions were reported in 27.7% of patients in the D-VMP group.<sup>20</sup> Treatment-emergent hematology laboratory abnormalities for D-VMP vs. VMP were lymphopenia (85% vs. 83%), neutropenia (86% vs. 87%), thrombocytopenia (88% vs. 88%) and anemia (47% vs. 50%).<sup>21</sup> The warnings and precautions for DARZALEX® include infusion reactions, infections, interference with indirect antiglobulin test, interference with determination of complete response, neutropenia, thrombocytopenia and infections.<sup>22</sup>

### **About Multiple Myeloma**

Multiple myeloma is the most common plasma cell cancer<sup>23</sup> and is characterized by an excess proliferation of plasma cells.<sup>24</sup> In Canada, there were an estimated 2,900 new cases in 2017 and an

estimated 1,450 deaths associated with the disease.<sup>25</sup> While some patients with multiple myeloma have no symptoms in the early stages, most patients are diagnosed due to symptoms that can include bone disease or pain, anemia, calcium elevation, and kidney problems.<sup>26</sup>

### **About DARZALEX® (daratumumab)**

DARZALEX® is the first CD38-directed monoclonal antibody (mAb) approved to treat multiple myeloma. It binds to CD38, a surface protein highly expressed across multiple myeloma cells.<sup>27</sup> DARZALEX® induces tumor cell death through cell lysis via multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).<sup>28</sup> DARZALEX® has also demonstrated immunomodulatory effects such as increasing CD4+ and CD8+ T-cells counts, which may contribute to clinical response.<sup>29</sup> Additional studies are ongoing to evaluate DARZALEX® in combination with standard of care regimens for newly diagnosed patients who are eligible and ineligible for autologous stem cell transplant (ASCT).

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize DARZALEX®. Janssen Inc. commercializes DARZALEX® in Canada. For full Prescribing Information and more information about DARZALEX®, please visit [www.janssen.com/canada](http://www.janssen.com/canada).

### **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/canada](http://www.janssen.com/canada). Follow us at @JanssenCanada. Janssen Inc. is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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*\*Dr. Darrell White was not compensated for any media work. He has been compensated as a consultant.*

### **References:**

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<sup>1</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>2</sup> NCBI. "Bortezomib, Melphalan, and Prednisone (VMP) Regimen for Multiple Myeloma," Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4321425/>. Accessed November 2018.

<sup>3</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

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<sup>4</sup> Kumar, SK et al. Leukemia. 2012 Jan; 26(1):149-57. ; American Cancer Society. "Multiple Myeloma Overview." Available at: <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma>. Accessed November 2018.

<sup>5</sup> American Cancer Society. "Multiple Myeloma Overview." Available at: <http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma>. Accessed November 2018.

<sup>6</sup> Kumar, SK et al. Improved survival in multiple myeloma and the impact of novel therapies. Blood 2008;111:2516–20.

<sup>7</sup> Turesson, I et al. Patterns of improved survival in patients with multiple myeloma in the twenty-first century: a population-based study. J Clin Oncol 2010;28: 830–34.

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<sup>9</sup> Myeloma Canada. "About Myeloma" <https://www.myelomacanada.ca/en/about-multiple-myeloma/what-is-myeloma>. Accessed November 2018.

<sup>10</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>11</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>12</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>13</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>14</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>15</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>16</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>17</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>18</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>19</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>20</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>21</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>22</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>23</sup> Canadian Cancer Society. "Types of Multiple Myeloma," Available at: <http://www.cancer.ca/en/cancer-information/cancer-type/multiple-myeloma/multiple-myeloma/types-of-multiple-myeloma/?region=on>. Accessed November 2018.

<sup>24</sup> American Cancer Society. "Multiple Myeloma Overview," Available at: <http://www.cancer.net/cancer-types/multiple-myeloma/overview>. Accessed November 2018.

<sup>25</sup> Canadian Cancer Society. "Canadian Cancer Statistics 2018." Available at: <http://www.cancer.ca/~media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2018-EN.pdf?la=en>. Accessed November 2018.

<sup>26</sup> Canadian Cancer Society. "Signs and Symptoms of Multiple Myeloma," Available at: <http://www.cancer.ca/en/cancer-information/cancer-type/multiple-myeloma/signs-and-symptoms/?region=on>. Accessed November 2018.

<sup>27</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>28</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]

<sup>29</sup> [DARZALEX™ Product Monograph, Janssen Inc., November 27, 2018]