

## Important Safety Information on DARZALEX (daratumumab) and Hepatitis B Virus Reactivation



2019/03/25

### **Audience**

Healthcare professionals including haematologists, oncologists, oncology nurses, oncology pharmacists, and other healthcare professionals providing care to cancer patients, including those who work in hospitals, cancer centres, oncology clinics and hospital pharmacies

### **Key messages**

- **Cases of hepatitis B virus (HBV) reactivation, some with a fatal outcome, have been reported in patients treated with DARZALEX.**
- **Healthcare professionals are advised to:**
  - **Perform HBV screening in all patients before starting DARZALEX treatment.**
  - **Monitor patients with evidence of positive HBV serology for clinical and laboratory signs of HBV reactivation during, and for at least six months following the end of, DARZALEX treatment. Manage patients according to clinical guidelines.**
  - **Suspend DARZALEX, any concomitant steroids and chemotherapy treatment in patients who develop reactivation of HBV and start appropriate treatment.**
  - **Discuss with physicians who have expertise in managing HBV before resuming DARZALEX treatment in patients with adequately controlled HBV reactivation.**
- **Health Canada is currently working with the manufacturer to include the risk of HBV reactivation in the DARZALEX Canadian Product Monograph.**

### **What is the issue?**

Cases of HBV reactivation, some with a fatal outcome, have been reported in patients treated with DARZALEX. As of December 14, 2018, there were 15 cases of HBV reactivation in patients treated with DARZALEX. No Canadian cases of HBV reactivation related to DARZALEX treatment have been reported.

### **Products affected**

DARZALEX (daratumumab), concentrate for infusion solution, 20 mg / mL, in 5mL and 20mL single use vials

### **Background information**

DARZALEX has received market authorization in Canada for use in the following clinical settings:

- In combination with bortezomib, melphalan and prednisone, for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.
- In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.
- For the treatment of patients 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.

A recent cumulative review of clinical trial and post-marketing data identified 15 cases of HBV reactivation in patients treated with DARZALEX. Ten of the 15 cases were reported as serious. Of the 10 serious cases, 2 cases had a fatal outcome. No Canadian cases of HBV reactivation related to DARZALEX treatment have been reported at the time of the cumulative analysis. As of November 15, 2018, DARZALEX has been received by approximately 4,407 patients in clinical trial settings, and an estimated world-wide post-marketing exposure of 34,316 person-years. The estimated patient exposure in Canada is 390 person-years. The overall frequency of HBV reactivation in DARZALEX clinical trials, including serious and non-serious reports, is uncommon (0.2%). The majority of clinical trial cases were considered non-serious, although fatal HBV reactivation cases have been reported in clinical trials and in the post-market setting.

### **Information for consumers**

DARZALEX is used in adults 18 years or older to treat a type of cancer called multiple myeloma. This is a cancer of plasma cells which are found in bone marrow.

DARZALEX could cause the hepatitis B virus to become active again (hepatitis B virus reactivation) in patients with previously stable or undetectable levels. Patients should tell their doctor if they have ever had or might now have a hepatitis B infection.

Patients should contact their healthcare professional for more details on this new safety information.

Patients should immediately tell their healthcare professional if they get worsening tiredness or yellowing of the skin or white part of the eyes, as these may be symptoms of hepatitis B virus reactivation.

Patients receiving DARZALEX should also inform their healthcare professional if they experience any other side effects.

### **Information for healthcare professionals**

- HBV screening should be performed in all patients before starting treatment with DARZALEX.
- For patients with evidence of positive HBV serology, the clinical and laboratory signs of HBV reactivation should be monitored during, and for at least six months following the end of, DARZALEX treatment. Patients should be managed according to clinical guidelines.
- In patients who develop reactivation of HBV, treatment with DARZALEX, any concomitant steroids and chemotherapy should be suspended, and appropriate treatment should be instituted.
- Resumption of DARZALEX treatment in patients whose HBV reactivation is adequately controlled should be discussed with physicians with expertise in managing HBV.

### **Action taken by Health Canada**

Health Canada, in collaboration with Janssen Inc., will update the DARZALEX Product Monograph to include information related to the risk of HBV reactivation. Health Canada is communicating this important safety information to healthcare professionals and Canadians via the [Recalls and Safety Alerts Database on the Healthy Canadians Web Site \(www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php\)](http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php). This communication will be further distributed through the MedEffect™ e-Notice email notification system.

### **Report health or safety concerns**

Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any case of HBV reactivation or other serious or unexpected side effects in patients receiving DARZALEX should be reported to Janssen Inc. or Health Canada.

**Janssen Inc.**

19 Green Belt Drive  
Toronto, ON, M3C 1L9  
Tel: 1-800-567-3331  
www.janssen.com/canada

**To correct your mailing address or fax number, contact Janssen Inc.**

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on [Adverse Reaction Reporting](https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate  
E-mail: [mhpd\\_dpssc\\_public@hc-sc.gc.ca](mailto:mhpd_dpssc_public@hc-sc.gc.ca)  
Telephone: 613-954-6522  
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