



## Direct Healthcare Professional Communication

June 2019

### Darzalex▼ (daratumumab): risk of reactivation of hepatitis B virus

Dear Healthcare Professional,

Janssen-Cilag International N.V. in agreement with the European Medicines Agency (EMA) and the Malta Medicines Authority would like to inform you about the risk of hepatitis B virus reactivation in patients treated with Darzalex:

#### **Summary**

- **Hepatitis B virus (HBV) reactivation, including some fatal cases, has been reported in patients treated with Darzalex (daratumumab).**
- **All patients should be screened for HBV before initiation of treatment with daratumumab. Patients already under treatment with daratumumab and for which HBV serology is unknown should also be tested for HBV.**
- **Patients with positive HBV serology should be monitored for clinical and laboratory signs of HBV reactivation during treatment, and for at least 6 months following the end of daratumumab treatment. Experts in the treatment of HBV infection should be consulted, as necessary.**
- **In patients with HBV reactivation, treatment with daratumumab should be stopped and experts in the treatment of HBV infection should be consulted.**
- **Resumption of daratumumab treatment in patients whose HBV reactivation is adequately controlled should be discussed with physicians with expertise in managing HBV.**

#### **Background**

Daratumumab is indicated:

- in combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant;
- as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy;

- in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

A recent cumulative review of data from clinical trials and post-marketing cases has identified reports of HBV reactivation in patients treated with daratumumab. 6 cases of HBV reactivation were observed in clinical trials. Most of these cases were considered non-serious, although fatal HBV reactivation cases have been reported in clinical trials and in the post-marketing setting. In some cases, daratumumab has been continued once HBV reactivation has been controlled with antiviral medication. Nearly all cases have been observed in the first six months of daratumumab treatment. In daratumumab patients with HBV reactivation, observed risk factors include the following: previous ASCT, concurrent and/or prior lines of immunosuppressive therapy, and patients who live in or who have immigrated from regions of high HBV prevalence.

The role of daratumumab therapy in the reported cases of HBV reactivation is confounded by the underlying medical condition, given that patients with multiple myeloma are immunosuppressed. In several cases patients were also receiving concomitant medications associated with viral reactivation. However, as a causal relationship cannot be ruled out, the product information for daratumumab will be updated to reflect the new safety information.

### **Call for reporting**

Darzalex▼ (daratumumab) is subject to additional monitoring. This will allow quick identification of new safety information.

Healthcare professionals should report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system.

### **Call for reporting**

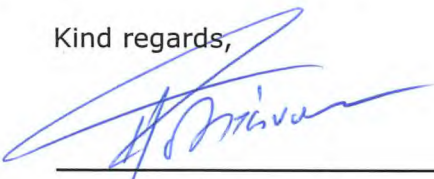
Healthcare professionals are reminded to continue to report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system. Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the ADR Reporting Website: [www.medicinesauthority.gov.mt/adrportal](http://www.medicinesauthority.gov.mt/adrportal)

Alternatively, kindly contact directly Mr Nigel Cauchi at A.M. Mangion Ltd, Mangion Building, New Street Off Valletta Road, Luqa LQA 6000, Malta or on phone number 00356 23976333 or email at [pv@ammangion.com](mailto:pv@ammangion.com)

### **Company contact points**

If you have further questions or require additional information, please contact Ms Gaby Ganado on +356 23976888 or [gganado@ammangion.com](mailto:gganado@ammangion.com)

Kind regards,



---

Angeliki Politsinou, MD  
Medical Affairs Director for Greece, Cyprus and Malta  
Janssen-Cilag, Pharmaceutical S.A.C.I.