

Direct Healthcare Professional Communication

26th June 2019

DARZALEX® ▼ (daratumumab) and risk of reactivation of hepatitis B virus

Dear Healthcare Professional,

Janssen in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA), 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. Six cases of HBV reactivation were observed in clinical trials. Most of these 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, risk factors included the following: previous autologous stem cell transplant (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.

Please continue to report suspected adverse reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme. All suspected ADRs associated with new drugs and vaccines identified by the black triangle▼ should be reported.

It is easiest and quickest to report adverse drug reactions online via the Yellow Card website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing yellowcard@mhra.gov.uk, at the back of the British National Formulary (BNF), by telephoning the Commission on Human Medicines (CHM) free phone line: 0800 731 6789, or by downloading and printing a form from the Yellow Card section of the MHRA website.

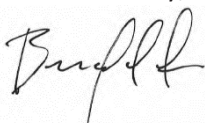
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset dates, treatment dates, product brand name and batch numbers.

Suspected adverse reactions should also be reported to Janssen-Cilag Limited, on tel.: 01494 567447, or by e-mail at dsafety@its.jnj.com.

Company contact points

If you have further questions or require additional information, please contact: Janssen Medical Information Department: email: medinfo@its.jnj.com, telephone: 0800 731 8450 or 01494 567 444.

Yours faithfully,



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Medical Director UK