Direct Healthcare Professional Communication

07 November 2016

Dear Healthcare professional

Lenalidomide (Revlimid®▼): New important advice regarding viral reactivation

Celgene Europe Limited in agreement with the European Medicines Agency and the Medicines & Healthcare Products Regulatory Agency would like to inform you of the following concern about the immunomodulator, lenalidomide:

Summary

- **Cases of viral reactivation have been reported following treatment with lenalidomide, particularly in patients previously infected with the varicella zoster or hepatitis B viruses (HBV).**
- **Some cases of HBV reactivation progressed to acute hepatic failure and resulted in death.**
- **Hepatitis B virus status should be established before initiating treatment with lenalidomide.**
- **A physician with expertise in the treatment of hepatitis B should be consulted for patients who test positive for HBV infection.**
- **Previously infected patients should be closely monitored for signs and symptoms of viral reactivation, including active HBV infection, throughout therapy.**

Background on the safety concern

Viral reactivation, including reactivation of varicella-zoster and hepatitis B viruses, has been reported during the postmarketing period for lenalidomide. Cases of hepatitis B reactivation have been reported very rarely (<1/10,000), but in 4 cases they progressed to hepatic failure. In these 4 cases, lenalidomide was discontinued and the patients required antiviral treatment. Previously infected patients should be closely monitored throughout therapy for signs and symptoms of viral reactivation, including active HBV infection.

Reactivation of varicella-zoster led in some cases to disseminated herpes zoster, meningitis herpes zoster or ophthalmic herpes zoster necessitating antiviral treatment and the permanent discontinuation or temporary interruption of treatment with lenalidomide.

Patients treated with lenalidomide usually have pre-existing risk factors for viral reactivation, including old age, underlying progressive disease and prior or concomitant treatment with immunosuppressive treatments including stem cell transplant. The immunosuppressive effect of lenalidomide may further increase the risk of viral reactivation in these previously infected patients.

Revlimid is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant and in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least one prior therapy. Further, Revlimid is indicated for the treatment of patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate and for the treatment of adult patients with relapsed or refractory mantle cell lymphoma.

Call for reporting

▼This medicinal product is subject to additional monitoring. This is intended to facilitate early identification of new safety information.

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme. Please report:

- All suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- All suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

It is easiest and quickest to report ADRs online via the Yellow Cards website – https://yellowcard.mhra.gov.uk/

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.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, treatment dates, and product brand name.

Adverse reactions associated with the use of Revlimid (lenalidomide) may also be reported to Celgene:
Celgene Drug Safety, Celgene Ltd, 1 Longwalk Road, Stockley Park, Uxbridge, UB11 1DB
Telephone: 0808 238 9908
Fax: 0844 801 0468
email: drugsafetyuk@celgene.com

Communication information

If you have any further questions or require further information, please contact your local Celgene representative at:
Celgene Medical Information, Celgene Ltd, 1 Longwalk Road, Stockley Park, Uxbridge, UB11 1DB
Telephone: 0844 801 0045
Fax: 0844 801 0046
email: medinfo.uk.ire@celgene.com

Yours faithfully

Dr Adrian Kilcoyne
Medical Director, UK and Ireland
Celgene Limited