Direct Healthcare Professional Communication

20 June 2016

Dear Healthcare professional

Thalidomide Celgene®: New important advice regarding viral reactivation and pulmonary hypertension

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:

Summary

Viral reactivation

- **Cases of viral reactivation, some serious, have been reported following treatment with thalidomide, particularly in patients previously infected with the varicella-zoster or hepatitis B viruses (HBV).**
- **Some of the cases of varicella-zoster reactivation resulted in disseminated herpes zoster, necessitating antiviral treatment and the temporary interruption of treatment with thalidomide.**
- **Some of the cases of HBV reactivation progressed to acute hepatic failure and resulted in discontinuation of thalidomide.**
- **Hepatitis B virus status should be established before initiating treatment with thalidomide.**
- **For patients who test positive for HBV infection, consultation with a physician with expertise in the treatment of hepatitis B is recommended.**
- **Previously infected patients should be closely monitored for signs and symptoms of viral reactivation, including active HBV infection, throughout therapy.**

Pulmonary hypertension

- **Cases of pulmonary hypertension, some fatal, have been reported following treatment with thalidomide.**
- **Patients should be evaluated for signs and symptoms of underlying cardiopulmonary disease prior to initiating and during thalidomide therapy.**

Background on the safety concern

Thalidomide Celgene in combination with melphalan and prednisone is indicated as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy.

Viral reactivation, including reactivation of varicella-zoster and hepatitis B viruses, has been reported during the post-marketing experience in patients receiving thalidomide. Some of the cases of hepatitis B reactivation progressed to hepatic failure. Reactivation of varicella- zoster virus resulted in some cases of disseminated herpes zoster, necessitating antiviral treatment and the temporary interruption of treatment

with thalidomide. Patients treated with thalidomide usually have pre-existing risk factors for viral reactivation, including old age and underlying progressive multiple myeloma. However, the immunosuppressive effect of thalidomide may further increase the risk of viral reactivation in these previously infected patients. Previously infected patients should be closely monitored for signs and symptoms of viral reactivation, including active HBV infection, throughout therapy.

Cases of pulmonary hypertension, some fatal, have also been reported during the post-marketing experience following treatment with thalidomide. Patients should be evaluated for signs and symptoms of underlying cardiopulmonary disease prior to initiating and during thalidomide therapy.

Call for reporting

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 thalidomide 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

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Medical Director, UK and Ireland
Celgene Limited