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20 June 16

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

Dear Healthcare professional,

Celgene Europe Limited in agreement with the European Medicines Agency and the Medicines Authority 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 herpes zoster or hepatitis B viruses (HBV).**
- **Some of the cases of herpes 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 of the herpes 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. Viral reactivation of herpes zoster resulted in some cases in 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 be reminded that adverse reactions associated with the use of Thalidomide Celgene should be reported in accordance with the national spontaneous reporting system -
Medicines Authority Post-licensing Department, 203, Level 3,Rue D'Argens, Gzira GZR1368, Malta or at www.medicinesauthority/adrportal

Company contact point

If you have further questions or require further information, please contact your local Celgene representative at
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