Celgene Limited
1 Longwalk Rd
Stockley Park
Uxbridge
UB11 1DB
United Kingdom
Tel: +44(0)208 831 8300
Fax: +44(0)208 831 8301
www.celgene.com

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Direct Healthcare Professional Communication on the association between Thalidomide Celgene™ (thalidomide) and thromboembolism

Dear Healthcare Professional,

Celgene would like to inform you about important new safety information on Thalidomide Celgene™ (thalidomide).

Summary:

- Patients treated with thalidomide have an increased risk of arterial thromboembolism, including myocardial infarction and cerebrovascular events, in addition to the established risk of venous thromboembolism.
- Most patients presenting with venous or arterial thromboembolic events in association with thalidomide treatment have had identifiable risk factors for thromboembolism.
- Action should be taken to minimise all modifiable risk factors for thromboembolic events (e.g. smoking, hypertension and hyperlipidaemia).
- Healthcare professionals are advised to consider venous and arterial thrombotic risk and the need for thromboprophylaxis in the evaluation of patients suitable for treatment with thalidomide.

Healthcare professionals should also note the following regarding thromboembolism:

- The risk appears to be greatest during the first 5 months of therapy
- Thromboprophylaxis should be administered for at least the first 5 months of treatment, especially in patients with thrombotic risk factors in addition to multiple myeloma. Antithrombotic prophylactic measures should be prescribed after a careful assessment of the individual patient's underlying risk factors.
- Previous history of thromboembolic events and concomitant administration of erythropoietic agents or other agents such as hormone replacement therapy may increase the risk of thromboembolic events. These agents should be used with caution in multiple myeloma patients receiving thalidomide. A haemoglobin concentration above 12g/dL (7.5 mmol/L) in particular should lead to discontinuation of erythropoietic agents.

The content of this letter and the updates to the Thalidomide Celgene™ Product Information have been endorsed by the Committee for Medicinal products for Human Use (CHMP) and the Irish Medicines Board (IMB).

Additional information about arterial thromboembolic events

Thalidomide Celgene™ 50 mg hard capsules have been granted a European Marketing Authorisation for use in combination with melphalan and prednisone as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years, or those ineligible for high dose chemotherapy.

A recent review of the post marketing data showed that approximately one third of all thromboembolic reactions reported in association with thalidomide were arterial, most of which were myocardial infarction and cerebrovascular events (54.2% and 19.8%, respectively). The mechanisms involved in the physiopathology of arterial thromboses in patients treated with thalidomide are unknown.

Sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) of the Thalidomide Celgene™ Summary of Product Characteristics have been updated to reflect the newly identified risk of arterial thromboembolic reactions, including myocardial infarction and cerebral vascular events, and to advise on minimisation of modifiable risk factors for thrombosis.

It should be reminded that, due to the powerful human teratogenic effects of thalidomide and its important clinical risks, a Risk Management Plan has been implemented for thalidomide in agreement with the European Medicines Agency (EMA) and IMB. This plan includes a **Pregnancy Prevention Programme** to avoid any thalidomide exposure during pregnancy, the monitoring of other clinically important risks associated with thalidomide such as peripheral neuropathy and thromboembolism and the provision of educational materials.

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

Adverse events (and cases of suspected or confirmed pregnancy and foetal exposure) should be reported. Adverse event report forms and pregnancy reporting forms are included in the Healthcare Professionals Information Pack and can also be found on www.celgene.ie. Completed forms should be forwarded to Celgene Drug Safety using the contact details below:

Celgene Limited
1 Longwalk Road
Stockley Park
Uxbridge
Middlesex
UB11 1DB
United Kingdom

Tel: 1800 936 217
Fax: 1800 936 477
Email: drugsafetyuk@celgene.com

Any suspected adverse reaction may also be reported direct to the IMB using the online form at www.imb.ie or using the freepost Yellow Card reporting system.

For further information please contact:

Celgene Limited
1 Longwalk Road
Stockley Park
Uxbridge
Middlesex
UB11 1DB
United Kingdom

Tel: 1800 333 111
Fax: 1800 333 112
Email: medinfo.uk.ire@celgene.com
Website: www.celgene.ie

Yours sincerely,

Dr Michael Thompson
Medical Director
Celgene Limited

Annex: Summary of Product Characteristics of Thalidomide Celgene™ (thalidomide) with changes highlighted