Thalidomide (Thalidomide Celgene): The starting dose of thalidomide when combined with melphalan should be reduced in patients over 75 years.

10 November 2015

Dear Healthcare Professional

Celgene, in agreement with the European Medicines Agency (EMA) and Health Products Regulatory Authority (HPRA), wishes to inform you about a new important recommendation of a reduced initial dose of thalidomide when combined with melphalan and prednisone (MPT) in patients >75 years of age with untreated multiple myeloma.

Summary

- ***A 100 mg/day starting dose of thalidomide is now recommended in patients > 75 years of age.***
- ***When combined with thalidomide a reduced starting dose of melphalan should be used in patients > 75 years of age.***
- ***The overall adverse reaction profile reported in patients > 75 years of age treated with thalidomide 100 mg once daily was similar to the adverse reaction profile observed in patients ≤ 75 years of age treated with thalidomide 200 mg once daily. However, patients aged > 75 years are potentially at risk for a higher frequency of serious adverse reactions.***

Further information on the new dosing recommendation and safety concern

Thalidomide Celgene 50 mg hard capsules are licensed in the European Union for use in combination with melphalan and prednisone as first-line treatment of patients with untreated multiple myeloma who are aged ≥ 65 years or ineligible for high-dose chemotherapy.

The new age-adjusted dosing recommendations are based on the results of a Celgene-sponsored Phase 3 Study (CC-5013-MM-020[i]) and are supported by a study conducted by the Intergroupe Francophone du Myélome (Study IFM 01/01[ii]).

A review of safety results from Study CC-5013-MM-020 as part of the regular safety monitoring indicated that the overall frequency of serious adverse reactions and Grade 5 adverse reactions was higher in older patients (> 75 years) compared with younger patients (56.5% versus 46.5% and 10.3% versus 5.3%, respectively). However, no clinically relevant differences or unexpected trends were observed between age groups (≤ 75 years and > 75 years) with respect to specific serious adverse reactions and there were no notable differences for primary causes of death between the age groups. The age-adjusted MPT dosing regimen was generally well tolerated in the > 75 age group.

In summary, the adverse reaction profile reported in patients > 75 years of age treated with thalidomide 100 mg once daily was similar to the adverse reaction profile observed in patients ≤ 75 years of age treated with thalidomide 200 mg once daily. However, patients with age > 75 years are potentially at risk for a higher frequency of serious adverse reactions.

It should be noted that in the study CC-5013-MM-020 the melphalan starting dose was 0.1 to 0.2 mg/kg daily according to bone marrow reserve along with a further 50% dose reduction for moderate (creatinine clearance: < 50 mL/minute) or severe (CrCl: < 30 mL/minute) renal insufficiency which should be taken into account in treatment of patients (> 75 years of age).

Call for reporting

Suspected adverse reactions should be reported to the HPRA using a Yellow Card obtained either from the HPRA, or electronically via the website at www.hpra.ie. Adverse reactions can also be reported to the HPRA by calling (01) 676 4971.

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

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. UK
Telephone: 1808 936 217
Fax: 1800 936 477
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. UK
Telephone: 1800 333 111
Fax: 1800 333 112
email: medinfo.uk.ire@celgene.com

Yours faithfully

Dr Adrian Kilcoyne
Medical Director, UK and Ireland
Celgene Limited

[i] Study MM-020 – Phase 3, multicenter, randomized, open-label, 3-arm study to determine the efficacy and safety of lenalidomide plus low-dose dexamethasone when given until progressive disease or for 18 four-week cycles versus the combination of melphalan, prednisone, and thalidomide given for 12 six-week cycles in newly diagnosed MM subjects either ≥ 65 years or not candidates for stem cell transplant

[ii] Study IFM 01/01 – Comparison of Melphalan-Prednisone (MP) to MP Plus Thalidomide in the Treatment of Newly Diagnosed Very Elderly Patients (> 75 Years) With Multiple Myeloma