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REVLIMID® (Lenalidomide) Approved by the European Commission for the Treatment of Adult Patients with Previously Untreated Multiple Myeloma who are Not Eligible for Transplant

Oral REVLIMID is approved for treatment until disease progression

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene International Sàrl, a wholly owned subsidiary of Celgene Corporation (NASDAQ: CELG), today announced that the European Commission (EC) has approved REVLIMID® (lenalidomide) for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

The REVLIMID Marketing Authorisation has been updated to include this new indication in multiple myeloma, building upon the already approved indication of REVLIMID in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

Multiple myeloma is a persistent and life-threatening blood cancer that is characterised by tumour proliferation and suppression of the immune system. It is a rare but deadly disease: around 38,900 people were newly diagnosed with multiple myeloma in Europe in 2012, and 24,300 people died from the disease in the same year. On average, multiple myeloma is diagnosed in people 65-74 years of age, and the majority of newly diagnosed patients may not be eligible for more aggressive treatment options such as high-dose chemotherapy with stem cell transplant.

Professor Thierry Facon, Services des Maladies du Sang, Hôpital Claude Huriez, and CHRU Lille, France, says: "Having a new treatment option now available for patients newly diagnosed with multiple myeloma is a real step forward. Treating patients continuously until disease progression is supported by several clinical studies, and will have an important impact on how we manage the disease over the long-term."

"We are very pleased that physicians can now offer their patients a new and different treatment option," said Tuomo Pätsi, President of Celgene in Europe, the Middle East and Africa (EMEA). "Multiple myeloma is rare, but it is devastating for those who have it, and it has a major impact on their friends and family too. We have seen significant progress in the treatment of the disease over the years, with an improvement of more than 50% in 5-year survival rates, but there continues to be a need for innovative new approaches to turn deadly diseases, like this one, into manageable, long-term, chronic conditions."

The EC decision in newly diagnosed multiple myeloma was based on the results of two pivotal studies: MM-020 (also known as the FIRST trial) and MM-015.

- The FIRST study, MM-020, was one of the largest phase III, multi-centre, open-label, randomised studies in patients newly diagnosed with multiple myeloma and not eligible for stem cell transplantation, including 1,623 patients. It compared lenalidomide plus dexamethasone administered in 28-day cycles until disease progression (Rd), with Rd for 72 weeks (18 cycles; Rd18) and melphalan-prednisone-thalidomide (MPT) for 72 weeks. Progression-free survival (PFS; study primary endpoint) was significantly improved in patients treated continuously with Rd, compared with those receiving MPT (primary comparison, p < 0.0001) or Rd18 (p < 0.0001). Median overall survival (OS) in patients receiving Rd continuous therapy was 58.9 months, vs. 48.5 months for patients treated with MPT (HR 0.75; 95% CI 0.62, 0.90), based on a March 3, 2014 interim OS analysis. The numbers of patients experiencing any grade 3 or 4 adverse event were similar in each group. The most frequent grade 3 or 4 adverse events were neutropenia, anaemia and infections.

- MM-015 was a multi-centre, randomised, double-blind, placebo-controlled phase III study of 459 patients that compared melphalan-prednisone-lenalidomide induction followed by lenalidomide maintenance (MPR-R) with melphalan-prednisone-lenalidomide (MPR) or melphalan-prednisone (MP) followed by placebo in patients ≥65 years or older with newly diagnosed multiple myeloma. Progression-free survival (PFS; study primary endpoint) was significantly improved in patients treated with MPR-R when compared with MPR and MP (p < 0.001 for comparisons of MPR-R over MPR and MP). In the MM-015 study, overall survival was not significantly improved when compared across any treatment arm. During induction, the most frequent adverse events were hematologic (including neutropenia, thrombocytopenia, and anaemia). During the maintenance phase, the incidence of new or worsened grade 3 or 4 adverse events was low (0 to 6%).
The EC decision for the use of REVLIMID in newly diagnosed multiple myeloma in adult patients ineligible for transplantation follows the positive opinion issued by the Committee for Medicinal Products for Human Use (CHMP) in December 2014. It is the second European Commission approval Celgene has received this year, following the approval of OTEZLA®️, the first phosphodiesterase-4 (PDE-4) inhibitor for use in psoriasis and psoriatic arthritis, in January 2015. A CHMP positive opinion was also issued in January for use of the company's oncology drug ABRAXANE®, in non-small cell lung cancer.

Celgene announced on 18 February 2015 that the U.S. Food and Drug Administration (FDA) has expanded the existing indication for REVLIMID (lenalidomide) in combination with dexamethasone to include patients newly diagnosed with multiple myeloma in the U.S.

About REVLIMID®️

In the United States, REVLIMID is approved in combination with dexamethasone for the treatment of patients with multiple myeloma. In the European Union, REVLIMID is approved for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant. REVLIMID is approved in combination with dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy in nearly 70 countries, encompassing Europe, the Americas, the Middle-East and Asia, and in combination with dexamethasone for the treatment of patients whose disease has progressed after one therapy in Australia and New Zealand.

REVLIMID is also approved in the United States, Canada, Switzerland, Australia, New Zealand and several Latin American countries, as well as Malaysia and Israel, for transfusion-dependent anaemia due to low- or intermediate-1-risk MDS associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities and in Europe 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.

In addition, REVLIMID is approved in the United States for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib. In Switzerland, REVLIMID is indicated for the treatment of patients with relapsed or refractory MCL after prior therapy that included bortezomib and chemotherapy/rituximab.

About Celgene

Celgene International Sàrl, located in Boudry, in the Canton of Neuchâtel, Switzerland, is a wholly-owned subsidiary and International Headquarters of Celgene Corporation. Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global pharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through gene and protein regulation. For more information, please visit www.celgene.com. Follow us on Twitter @Celgene, and on Pinterest and LinkedIn.

ADDITIONAL IMPORTANT SAFETY INFORMATION based on EU SmPC

Contraindications

REVLIMID®️️ (lenalidomide) is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients in the formulation.

REVLIMID®️️ (lenalidomide) is contraindicated during pregnancy, and also in women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met.

Warnings and precautions

Pregnancy: the conditions of the Pregnancy Prevention Programme must be fulfilled for all patients unless there is reliable evidence that the patient does not have childbearing potential.

Cardiovascular disorders: patients with known risk factors for myocardial infarction or thromboembolism should be closely monitored.

Neutropenia and thrombocytopenia: complete blood cell counts should be performed every week for the first 8 weeks of treatment and monthly thereafter to monitor for cytopenias. A dose reduction may be required.

Infection with or without neutopenia: all patients should be advised to seek medical attention promptly at the first sign of infection.
Renal impairment: monitoring of renal function is advised in patients with renal impairment.

Thyroid disorders: optimal control of co-morbid conditions influencing thyroid function is recommended before start of treatment. Baseline and ongoing monitoring of thyroid function is recommended.

Tumour lysis syndrome: patients with high tumour burden prior to treatment should be monitored closely and appropriate precautions taken.

Allergic reactions: patients who had previous allergic reactions while treated with thalidomide should be monitored closely.

Severe skin reactions: REVLIMID® (lenalidomide) must be discontinued for exfoliative or bullous rash, or if SJS or TEN is suspected, and should not be resumed following discontinuation for these reactions. Interruption or discontinuation of lenalidomide should be considered for other forms of skin reaction depending on severity. Patients with a history of severe rash associated with thalidomide treatment should not receive lenalidomide.

Lactose intolerance: patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Second primary malignancies (SPM): the risk of occurrence of hematologic SPM must be taken into account before initiating treatment with REVLIMID® (lenalidomide) either in combination with melphalan or immediately following high-dose melphalan and autologous stem cell transplant (ASCT). Physicians should carefully evaluate patients before and during treatment using standard cancer screening for occurrence of SPM and institute treatment as indicated.

Hepatic disorders: dose adjustments should be made in patients with renal impairment. Monitoring of liver function is recommended, particularly when there is a history of or concurrent viral liver infection or when REVLIMID® (lenalidomide) is combined with medicinal products known to be associated with liver dysfunction.

Newly diagnosed multiple myeloma patients: patients should be carefully assessed for their ability to tolerate REVLIMID® (lenalidomide) in combination, with consideration to age, ISS stage III, ECOG PS≤2 or CLcr < 60 mL/min.

Cataract: regular monitoring of visual ability is recommended.

Summary of the safety profile in multiple myeloma

Newly diagnosed multiple myeloma in patients treated with REVLIMID® (lenalidomide) in combination with low dose dexamethasone:

- The serious adverse reactions observed more frequently (≥5%) with REVLIMID® (lenalidomide) in combination with low dose dexamethasone (Rd and Rd18) than with melphalan, prednisone and thalidomide (MPT) were pneumonia (9.8%) and renal failure (including acute) (6.3%)
- The adverse reactions observed more frequently with Rd or Rd18 than MPT were: diarrhoea (45.5%), fatigue (32.8%), back pain (32.0%), asthenia (28.2%), insomnia (27.6%), rash (24.3%), decreased appetite (23.1%), cough (22.7%), pyrexia (21.4%), and muscle spasms (20.5%).

Newly diagnosed multiple myeloma patients treated with REVLIMID® (lenalidomide) in combination with melphalan and prednisone:

- The serious adverse reactions observed more frequently (≥5%) with melphalan prednisone, and REVLIMID® (lenalidomide) followed by REVLIMID® (lenalidomide) maintenance (MPR+R) or melphalan prednisone, and REVLIMID® (lenalidomide) followed by placebo (MPR+p) than melphalan, prednisone and placebo followed by placebo (MPp+p) were febrile neutropenia (6.0%) and anaemia (5.3%)
- The adverse reactions observed more frequently with MPR+R or MPR+p than MPp+p were: neutropenia (83.3%), anaemia (70.7%), thrombocytopenia (70.0%), leukopenia (38.8%), constipation (34.0%), diarrhoea (33.3%), rash (28.9%), pyrexia (27.0%), peripheral oedema (25.0%), cough (24.0%), decreased appetite (23.7%), and asthenia (22.0%).

Patients with multiple myeloma who have received at least one prior therapy:
The most serious adverse reactions observed more frequently with REVLIMID® (lenalidomide) and dexamethasone than with placebo and dexamethasone in combination were venous thromboembolism (deep vein thrombosis, pulmonary embolism) and grade 4 neutropenia.

The observed adverse reactions which occurred more frequently with REVLIMID® (lenalidomide) and dexamethasone than placebo and dexamethasone in pooled multiple myeloma clinical trials (MM-009 and MM-010) were fatigue (43.9%), neutropenia (42.2%), constipation (40.5%), diarrhoea (38.5%), muscle cramp (33.4%), anaemia (31.4%), thrombocytopenia (21.5%), and rash (21.2%).

Special populations

Paediatric population: REVLIMID® (lenalidomide) should not be used in children and adolescents from birth to less than 18 years.

Older people with newly diagnosed multiple myeloma: for patients older than 75 years of age treated with REVLIMID® (lenalidomide) in combination with dexamethasone, the starting dose of dexamethasone is 20 mg/day on Days 1, 8, 15 and 22 of each 28-day treatment cycle. No dose adjustment is proposed for patients older than 75 years who are treated with REVLIMID® (lenalidomide) in combination with melphalan and prednisone.

Older people with multiple myeloma who have received at least one prior therapy: care should be taken in dose selection and it would be prudent to monitor renal function.

Patients with renal impairment: care should be taken in dose selection and monitoring of renal function is advised. No dose adjustments are required for patients with mild renal impairment and multiple myeloma. Dose adjustments are recommended at the start of therapy and throughout treatment for patients with moderate or severe impaired renal function or end stage renal disease.

Patients with hepatic impairment: REVLIMID® (lenalidomide) has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations.

Please refer to the Summary of Product Characteristics for full European prescribing information.

Forward-Looking Statements

This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in Celgene Corporation's Annual Report on Form 10-K and other reports filed with the Securities and Exchange Commission.

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References


