19 September 2013
EMA/39018/2014
Committee for Medicinal Products for Human Use (CHMP)

Revlimid

International non-proprietary name: lenalidomide

Procedure No. EMEA/H/C/000717/PSUV/0069

Period covered by the PSUR: 27.12.2011 – 26.12.2012

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for Revlimid, the scientific conclusions of PRAC are as follows:

Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of the medicinal product containing the active substance lenalidomide remains favourable but recommends that the terms of the marketing authorisation should be varied as follows:

Update of section 4.5 and 4.8 of the SmPC to add the adverse reaction rhabdomyolysis, especially when statins are combined with lenalidomide.

During the assessment of rhabdomyolysis as a safety signal, 23 cases were evaluated, all of which were considered to be serious. A concomitant use of statin was reported in 4 cases. For these cases, patients recovered after lenalidomide and statins discontinuation. Statins were not re-introduced, lenalidomide was re-introduced for 3 cases: positive re-challenge was observed in 2 and negative re-challenge was observed in one. The temporal relationship between therapy and rhabdomyolysis suggests that a causal relationship is possible (5, 14 and 19 days after lenalidomide initiation and 8 days after lenalidomide dose increased for the remaining case).

For the remaining 19 cases, a fatal outcome was reported in 5 cases, 6 cases were insufficiently documented for a clinical assessment. Most of the cases were confounded by concurrent medical conditions or concomitant medications. However, due to the temporal association, the positive dechallenge observed in 5 cases, the positive re-challenge observed in one case, the increased risk of rhabdomyolysis when statins are combined to lenalidomide, the involvement of lenalidomide cannot be excluded.

The Package Leaflet should be updated accordingly.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds recommending the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for Revlimid the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance lenalidomide is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisation should be varied.