



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 July 2017
EMA/627404/2017
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): lenalidomide

Procedure No. EMEA/H/C/PSUSA/00001838/201612

Period covered by the PSUR: 27 Dec 2015 – 26 Dec 2016



Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for lenalidomide, the scientific conclusions of CHMP are as follows:

The signal of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) was raised by the PRAC in the previous PSUR. Cumulatively, the review performed by the MAH retrieved 56 cases of DRESS, all serious, none fatal, mainly in multiple myeloma (MM) indication (76.8%), from post marketing reporting (50.0%). The event resolved/was resolving in 73.2% of cases and impacted lenalidomide treatment in 89.2 % of cases. Using the RegiSCAR criteria, 23 of the 56 cases (41.1%) were probable (score 4-5) or definite DRESS syndrome (score >5) and 16 cases (28.6%) were considered possible DRESS (score 2-3). 31 cases reported organ involvement (55.3%). Two (2) of the 56 cases reported a positive rechallenge, despite confounding factors. Among the 54 remaining cases, a total of 36 cases reported positive dechallenge. Despite confounding prior/concomitant treatment reported in 33 of the total 56 cases (including sulfamethoxazole/trimethoprim (39.3%) and allopurinol (18.0%)), 4 of the 36 cases with positive dechallenge were highly suggestive for causal relationship with lenalidomide, considering diagnosis criteria, suggestive time to occurrence, absence of alternative root cause reported, and concurrent HHV-6 reactivation. Regarding both cases from clinical studies, one was highly confounded by co-suspect strontium renalate treatment. In the second case, with concurrent co-suspect allopurinol, the causal relationship between lenalidomide and DRESS cannot be excluded in this well documented case. No further significant information was raised from the remaining 16 cases providing insufficient information.

Based on the high number of cases, all serious, 40% of cases with diagnosis according to the RegiSCAR criteria and the causal relationship with lenalidomide being highly probable, including cases with positive rechallenge / dechallenge this signal is considered confirmed and the Product Information should be updated accordingly.

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

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for lenalidomide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing lenalidomide is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.