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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): panobinostat

Procedure No. EMEA/H/C/PSUSA/00010409/201608

Period covered by the PSUR: 23 February 2016 – 22 August 2016

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Scientific conclusions

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

From the available post-marketing data, the causal association between panobinostat and constipation is unclear. However the association between bortezomib and consitpation is well established. From the post-marketing data it is not possible to definitively assign causality between panobinostat and peripheral neuropathy at this time.

The reason for changing the panobinostat Summary of Product Characteristics (SmPC) section 4.8 (Undesirable effects) is to include a statement to clarify that the data presented are the most commonly reported adverse effects attributable to panobinostat alone.

The current panobinostat SmPC section 4.8 (Undesirable effects), the second paragraph states:

"The safety data reported below are based on the phase III clinical study (Panorama 1) in 381 patients with multiple myeloma treated with 20 mg panobinostat once a day three times per week, on a 2 weeks on and 1 week off dosing regimen in combination with bortezomib and dexamethasone."

This implies that the adverse effects shown in Table 7 of the SmPC are for panobinostat in combination with bortezomib and dexamethasone. However section 5.1 states that the Panorama 1 study compared two treatment arms 1) panobinostat + bortezomib + dexamethasone and 2) placebo + bortezomib + dexamethasone. The safety data analyses of the Panorama 1 study are likely to identify the most commonly reported adverse effects attributable to panobinostat rather than to the overall combination including bortezomib and dexamethasone and therefore, there is potential for misinterpretation by prescribers/healthcare professionals in the post-marketing settings.

The Marketing Authorisation Holder confirmed that Table 7 in section 4.8 of the Panobinostat SmPC shows adverse drug reactions (ADRs) for Panobiostat i.e. ADRs that occurred more frequently in the three treatment arm (panobinostat + bortezomib + dexamethasone) than in the treatment arm (bortezomib + dexamethasone + placebo) in the PANORAMA I study. Therefore the ADRs constipation and peripheral neuropathy for which causal association with panobinostat was not suspected but that are known to occur with bortezomib were not included in Table 7. In order to minimise the potential for confusion about the adverse effects data shown in section 4.8 (Undesirable effects) in particular, Table 7 of the panobinostat SmPC, a statement has now been added above Table 7 to clarify that the data presented are the most commonly reported adverse effect attributable to panobinostat alone.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of the medicinal product containing panobinostat were warranted.

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

Grounds for the variation to the terms of the marketing authorisation

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

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