



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 October 2018
DOC_REF_ID
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): pembrolizumab

Procedure No. EMEA/H/C/PSUSA/00010403/201803

Period covered by the PSUR: 04/09/2017 - 03/03/2018



Scientific conclusions

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

Vogt-Koyanagi-Harada syndrome: In several cases, the role of pembrolizumab in triggering VKH cannot be excluded given the autoimmune pathogenesis of PD-1 inhibitor. The fact that the latest event is reported by the physician as related to pembrolizumab, with statements such as “with no other causative factor” further strengthens the signal. Further, the risk of VKH is listed for other products in the same class. Therefore, VKH should be added to SmPC section 4.8 as a new ADR with the frequency ‘rare’.

Myasthenia gravis (including exacerbation): The ADR Myasthenia gravis is already included in the product information. With regard to the risk of exacerbation, the review of the cases led to the conclusion that also this risk should be reflected in the SmPC. In almost all cases the time to onset of the exacerbation was reported within the first 2 cycles of treatment, including a spontaneous fatal case of MG where the physician concludes “the severe exacerbation of myasthenia gravis, which was possibly related to the treatment with pembrolizumab, ultimately led to the patient's death.” Therefore, the wording ‘including exacerbation’ should be added to the existing ADR Myasthenia gravis in section 4.8 of the SmPC.

Pure red cell aplasia (PRCA): The role of pembrolizumab triggering PRCA cannot be excluded in several cases. Furthermore, several case reports are published in literature regarding PRCA in patients treated with checkpoint inhibitors. Although the exact mechanism through which pembrolizumab may cause PRCA is not known, it is presumed to be related to widespread activation of cytotoxic T cells. Therefore, the ADR PRCA should be included in section 4.8 of the SmPC with frequency rare and the Package Leaflet 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 pembrolizumab the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pembrolizumab 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.