



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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): pembrolizumab

Procedure No. EMEA/H/C/PSUSA/00010403/201909

Period covered by the PSUR: 3 September 2018 to 3 September 2019



Scientific conclusions

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

Seven cases of glomerulonephritis were identified by the MAH, of which 4 had biopsy confirmation together with improvement of the event following steroid treatment, suggesting that the mechanism of action was an immune-related event. As a result, the term 'glomerulonephritis' is included to the footnotes of the table of ADRs in SmPC section 4.8 under the description of the term nephritis.

A review on the risk of gastric ulceration showed a relatively high number of reported cases. Of the 15 cases of gastric ulcer and duodenal ulcer that were reviewed, in several cases a recovery following steroid therapy was observed or the event was reported as related to the therapy, indicating pembrolizumab having a role in causing ulceration. Ulceration is a known listed risk in the SmPC of other class products. The SmPC of pembrolizumab already lists small intestinal perforation (in section 4.8) and potential risk of gastrointestinal perforation (section 4.4), and it is considered plausible that perforation follows ulceration. Taken together, a causal association between pembrolizumab and gastrointestinal ulceration is considered plausible. The term 'gastrointestinal ulceration' is included to the SmPC section 4.8 with frequency 'uncommon'.

Of the 24 cases of myelitis retrieved from the MAH's safety database, 4 cases (three reporting PT "myelitis transverse" and one "myelitis") present positive de-challenge from pembrolizumab and/or improvement with steroid treatment, supporting a causal association between myelitis and pembrolizumab use. The term 'myelitis' is included to the table of ADRs in the SmPC section 4.8 with frequency 'rare', based on CT data for pembrolizumab monotherapy (2 cases (1 case of myelitis and 1 case of myelitis transverse) in 5,884 treated patients (0.03%)). The term 'myelitis transverse' is also added to the footnotes of the table linked to the risk of myelitis. In addition, the term 'myelitis' is included in the Warnings and Precautions of section 4.4 of the SmPC under the "Other immune-related adverse reactions" subheading.

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.