25 January 2018
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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): nivolumab

Procedure No. EMEA/H/C/PSUSA/00010379/201707

Period covered by the PSUR: 4 January 2017 - 3 July 2017

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Scientific conclusions

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

In the oncology, tumour lysis syndrome (TLS) is a well-known possible reaction in patients with high tumour burden treated with a potent anti-cancer compound. Overall, five SAE of TLS occurred in patients exposed to nivolumab as shown in the integrated cumulative summary tabulation of serious adverse events from clinical trials. In the post-marketing area, 13 serious events of tumour lysis syndrome (TLS) were cumulatively reported following nivolumab exposition including six TLS events in the present PSUR. No non-serious forms of TLS occurred. Additionally seven TLS were cumulatively reported from other spontaneous sources. Overall, there is sufficient biological plausibility that possible events of TLS occur following nivolumab exposition for the treatment of advanced or metastasising malignancies. Therefore, 'tumour lysis syndrome' should be added to the overview table (Table 2: Adverse reactions) under the SOC Metabolism and nutrition disorders in SmPC section 4.8 Undesirable effects and to section 4 (Possible side effects) of the Package leaflet for both nivolumab alone and nivolumab in combination with ipilimumab.

The frequency of TLS with nivolumab cannot be estimated as cases were retrieved from multiple sources, reporting multiple indications, and multiple treatment regimens.

No changes to the EU Risk Management Plan or Risk Minimization Measures risk are proposed. In this review, only 7 of the 36 TLS reports with documented elevated UA (uric acid) levels, mentioned diverse treatment, and there is therefore insufficient conclusive data to propose Risk Minimization Measures.

There is no change in the overall benefit-risk profile of nivolumab.

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 nivolumab the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing nivolumab 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.