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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: aflibercept (oncological indication(s))

Procedure No.: EMEA/H/C/PSUSA/00010019/201508

Period covered by the PSUR: 04 February 2015 - 03 August 2015

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Scientific conclusions

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

The PRAC agrees with the MAH's proposal to maintain the cut-off value for UPCR (urinary protein creatinine ratio) and to add the units for PCR (protein creatinine ratio) expressed as mg protein/mmol creatinine. Therefore, the summary of product information (SmPC) of aflibercept should be revised to include the protein/creatinine ration (PCR) >100 mg/mmol.

With regard to osteonecrosis of the jaw (ONJ), the PRAC considered that based on review of the MAH's global pharmacovigilance database, clinical data, labelling of other drugs of the same class, worldwide scientific literature and biological plausibility, the weighted cumulative evidence is sufficient to support a causal association between aflibercept and ONJ. Associated contributing factors may include bisphosphonates and dental infection/procedure. Therefore, the PRAC concluded that the product information of aflibercept should be updated to include a warning on osteonecrosis of the jaw and add it as an adverse reaction with a frequency uncommon. In addition, osteonecrosis of the jaw should be recategorised as an important identified risk. The PRAC also considered that a direct healthcare professional communication should be distributed to the relevant healthcare professionals.

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

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 aflibercept (oncological indication(s)) the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing aflibercept (oncological indication(s)) is unchanged subject to the proposed changes to the product information

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