17 September 2020
EMA/630499/2020
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): lenvatinib

Procedure No. EMEA/H/C/PSUSA/00010380/202002

Period covered by the PSUR: From 11/02/2019 To: 11/02/2020

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Scientific conclusions

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

Osteonecrosis of jaw has been followed and assessed in previous PSURs. During the reporting period additional four cases of ONJ have been reported to the MAH. One case was from clinical trials and three spontaneous. Despite concomitant medications (such as bisphosphonate, everolimus) that can cause the ONJ, the causal relationship with lenvatinib was assessed as possible, probable and related by the reporter.

The MAH provided discussion on possible mechanism of the ONJ related to lenvatinib therapy and concluded that causal association between lenvatinib and ONJ is biologically plausible. Based on the assessment of the available data the update of the CCDS is ongoing.

In view of available data on osteonecrosis of the jaw from clinical trials, the literature, spontaneous reports, recognised class effect and in view of a plausible mechanism of action, the PRAC considers a causal relationship between lenvatinib and osteonecrosis of jaw is at least a reasonable possibility. The PRAC concluded that the product information of products containing lenvatinib should be amended accordingly.

Update of section 4.4 and 4.8 of the SmPC to add the adverse reaction osteonecrosis of the jaw with a frequency uncommon and a warning on the risk of osteonecrosis of the jaw. The Package leaflet is 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 lenvatinib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing lenvatinib 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.