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): regorafenib

Procedure No. EMEA/H/C/PSUSA/00010133/202009

Period covered by the PSUR: 27 September 2017 – 26 September 2020

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Scientific conclusions

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

The adverse reactions (ADRs) pain (very common, i.e. ≥1/10) and headache (common) are listed ADRs for regorafenib in the Summary of Product Characteristics (SmPC). As requested, the Marketing Authorisation Holder (MAH) provided a review of the most frequently reported preferred terms (PTs) related to pain. From clinical trial (CT) data the most frequently reported PTs were abdominal pain and back pain (≥10%). It is justified to include "most frequently reported types of pain (≥10%) are abdominal pain and back pain" to the footnotes of the table of ADR.

The risk of severe liver injury (including fatal outcome) is a listed ADR (uncommon) in the SmPC. Acute liver failure refers to the development of severe acute liver injury with encephalopathy and impaired synthetic function (International Normalized Ratio (INR) of ≥1.5). The review of the MAH focuses on 16 cases, two of which next to severe liver injury also report encephalopathy (and in one case also INR≥1.5). Although both cases are reported in context of metastasis to liver, the TTO is suggestive in both cases (5 and 17 days respectively), and they both report a positive de-challenge, arguing against liver metastases as cause. The MAH is requested to update the table of ADRs of Section 4.8 to include Severe liver injury (including hepatic failure) under System Organ Class (SOC) Hepatobiliary disorders. Section 4.4 of the SmPC is also updated to add (hepatic failure) to the exiting hepatic effects.

The CT data show an imbalance for the risk of "constipation" in regorafenib arm vs. placebo (RR 1.3; 95%CI being 1.053-1.623 --> p= 0.007). The risk should be included in the table of ADRs with frequency very common based on CT data.

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