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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): empagliflozin, empagliflozin / metformin

Procedure No. EMEA/H/C/PSUSA/00010388/201704

Period covered by the PSUR: 18 October 2016 to 17 April 2017

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Scientific conclusions

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

The MAH has submitted an updated cumulative review of complicated urinary tract infections (UTIs) in the Periodic safety update report (PSUR) specific section “characterization of risk”. This review includes information on clinical trials and post-marketing sources. Current SmPC of empagliflozin and empagliflozin/metformin includes a warning in section 4.4 on UTI (including a recommendation of temporary interruption of empagliflozin in patients with complicated UTIs) and in section 4.8 UTI is included as an Adverse Drug Reaction (ADR) with frequency common. In relation to other Sodium-dependent glucose co-transporter type 2 (SLGT-2) inhibitors currently authorised in the EU (canagliflozin and dapagliflozin), information on pyelonephritis and urosepsis is reflected in both EU Product Informations.

In view of the fact that UTIs are an identified risk for empagliflozin but pyelonephritis and urosepsis are not specifically included in section 4.8 of EU-SmPC of empagliflozin and empagliflozin/metformin, that the cases of pyelonephritis and urosepsis with a positive dechallenge or no confounding factors have been seen in postmarketing data, data from Clinical Trials (CT) regarding UTIs leading to treatment discontinuation in addition to urosepsis data from clinical EMPA-REG study and known information of other SGLT2 on this issue, it is considered that there is enough evidence to include more information regarding these risks in the EU Product Information of empagliflozin (Jardiance) and empagliflozin/metformin (Synjardy).Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing empagliflozin and empaglifllozin/metformin 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 empagliflozin, empagliflozin / metformin the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing empagliflozin, empagliflozin / metformin 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.