30 January 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): sofosbuvir / velpatasvir

Procedure No. EMEA/H/C/PSUSA/00010524/201906

Period covered by the PSUR: 28 Dec 2018 to 27 Jun 2019

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Scientific conclusions

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

The MAH performed an updated cumulative review of bradyarrhythmia occurring when sofosbuvir-containing products are co-administered with amiodarone, cumulative to 27 June 2019. The review identified 40 valid cases, of which 31 occurred after 5 March 2015, when warnings regarding bradyarrhythmia were implemented. Of these, 5 cases involved discontinuation of amiodarone prior to initiation of the sofosbuvir-containing regimen. While this suggests that some physicians are aware of the risk of bradyarrhythmia and discontinue amiodarone prior to initiation of the sofosbuvir-containing products, not all physicians appear to take into account the long half-life of amiodarone, despite the existing labelling.

Of note, two cases reported discontinuation of amiodarone on the day of starting the sofosbuvir-containing regimen, which would result in significant levels of amiodarone still being present in the patient's plasma while on sofosbuvir. In the instances where amiodarone is coadministered, the reasons for coadministration were not reported in the majority of cases. However, when reported, prescribing error, patient error, medical need or the hepatologist not being aware of concomitant amiodarone treatment were cited as reasons for the concomitant use. In this context, it was considered that warnings regarding bradyarrhythmia and the recommendation of cardiac monitoring should be strengthened.

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