28 June 2018
EMA/714062/2018
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

Procedure No. EMEA/H/C/PSUSA/00010134/201712

Period covered by the PSUR: 06 June 2017 to 05 December 2017

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

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

1. Cases of arrhythmias with sofosbuvir and amiodarone have been reported without another direct-acting antiviral (DAA) co-administered. These included reports of close temporal association with initiation of sofosbuvir + ribavirin and reports of positive de-challenge. On this basis, the existing warnings about severe bradycardia and heart block and the corresponding information about cardiac arrhythmias are updated to cover reactions reported without another DAA present.

2. With regards to Stevens-Johnson Syndrome (SJS), the MAH's review of severe cutaneous adverse reactions identified 37 relevant cases. There were alternative explanations for most of the events reported and causality with sofosbuvir treatment could thus not be established in these instances. However, there were several cases of severe cutaneous adverse reactions where a causal role of sofosbuvir remained a possibility, including one case of SJS, two cases of drug reaction with eosinophilia and systemic symptoms (DRESS) and one case of erythema multiforme. Furthermore, there was a case in the published literature (Verma 2017) that provided very strong evidence of a causal role of sofosbuvir in the SJS reaction, including positive re-challenge to sofosbuvir. Considering this strong case in the context of the totality of available data, the PRAC considered that SJS should be added as an adverse drug reaction to the Product Information.

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