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): sofosbuvir / ledipasvir

Procedure No. EMEA/H/C/PSUSA/00010306/201510

Period covered by the PSUR: 10 April 2015 – 09 October 2015

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Scientific conclusions

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

There were 32 serious cases of hypersensitivity or events related to severe cutaneous adverse reactions. Of these, 8 may be attributed to concomitant medications, including ribavirin, which list rash and/or severe cutaneous reactions as a known adverse reaction. Causality assessment was confounded or limited in 16 of the cases by factors such as prior medical history, lack of clinical outcome, negative re-challenge or resolution of events while sofosbuvir / ledipasvir was continued. In the remaining 8 cases, a causal relationship to sofosbuvir / ledipasvir could not be excluded, but no signature type of rash was identified and none of these cases resulted in known long term sequelae or death.

There were 161 non serious cases of hypersensitivity or events related to cutaneous adverse reactions. 15 of the cases may be attributed to concomitant medications, including ribavirin. Causality assessment was confounded or limited in 135 of the cases by the same factor as described above. In the remaining 11 cases, a causal relationship to sofosbuvir / ledipasvir could not be excluded, but similarly to the serious cases, no signature type of rash was identified and none of the cases resulted in known long term sequelae or death.

Upon review of the available safety data, there was insufficient evidence to establish a causal association between severe cutaneous events and sofosbuvir / ledipasvir. However, the data were considered supportive of a possible idiosyncratic relationship between sofosbuvir / ledipasvir and rash.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing sofosbuvir / ledipasvir 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 sofosbuvir / ledipasvir the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing sofosbuvir / ledipasvir 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.