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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): cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide

Procedure No. EMEA/H/C/PSUSA/00010449/201811

Period covered by the PSUR: 04/11/2017 to: 04/11/2018

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide, the scientific conclusions of CHMP are as follows:

A cumulative review of all cases related to suicide-related events showed a total of 42 valid cases reporting 48 suicide-related events for Genvoya (13 from spontaneous, 29 from clinical trials). Since the previous review, 6 new cases were identified (5 valid and 1 invalid). The cases evaluated in this review mostly occurred in patients with history of psychiatric events or other external factors reported that may have contributed to the event. Disproportionality analysis did not highlight events that met the criteria for signal of disproportionate reporting. However, based on the information retrieved in literature and in the product information of integrase inhibitors containing medicinal products, it could be concluded that the following psychiatric disorders: depression, suicidal ideation and suicidal behaviour (particularly in patients with pre-existing history of psychiatric illness) are class-effect of integrase inhibitors and these are listed in the SmPC of other medicinal products containing integrase inhibitors in monotherapy and in fixed-dose combination (FDC).

Similar patterns of psychiatric disorders were observed in comparative studies of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) versus elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (E/C/F/TDF), which lists these events in its product information (studies GS-US-292-0104 or GS-US-292-0111). Based on this, section 4.8 of the SmPC of medicinal products containing elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide FDC has been updated to add suicidal ideation and suicide attempt (in patients with a pre-existing history of depression or psychiatric illness) as new adverse drug reactions. In clinical trials, the incidence of SAEs related to suicide for Genvoya was 0.6% (26/4137 subjects), therefore, the frequency proposed is "uncommon".

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 cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide 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.