EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EMA/CHMP/14619/2014
Committee for Medicinal Products for Human Use (CHMP)

INCIVO

International non-proprietary name: telaprevir

Procedure No. EMEA/H/C/002313/PSUV/0021

Period covered by the PSUR: 20.09.2012 – 19.03.2013

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for INCIVO, the scientific conclusions of PRAC are as follows:

This is the 3rd PSUR for telaprevir covering the reporting period 20 September 2012 to 19 March 2013.

Review of the cumulative summary of SAEs from clinical trials and the cumulative/interval summary of serious and non-serious events from postmarketing sources reveals, in general, a similar pattern of events to what is described in the SmPC or are currently being discussed as signals in this PSUR.

As requested by the PRAC as part of the review of PSUR 02, the MAH performed a comprehensive review of renal failure. The MedDRA SMQ Acute renal failure (broad) was selected to identify cases for review. A total of 713 cases (343 from current period and 370 from previous reviews through 19 September 2012) reporting at least 1 event in the Acute renal failure (broad) SMQ were identified.

From the assessment of these data, a concern remained regarding the occurrence of renal failure by a pre-renal mechanism which may be related to receipt of telaprevir. The clinical picture of concern is that exhibited by 14 cases in which there is an onset of acute renal failure within a fairly short time from initiation of therapy (range 2-22 days) which is improved with intravenous hydration. There was a similar pattern of cases observed and discussed in the last PSUR. Within the previous reporting period, all cases were reported from Japan. Within this reporting period, 3 of the 14 subjects are reported from other countries: France, the United States and Australia.

In addition, the US has recently requested a labelling change to warn of the occurrence of “pre-renal azotemia with or without acute renal failure and uric acid nephropathy”.

The MAH has also proposed the addition of acute renal failure to the RMP as important potential risks.

From the review of these data, the PRAC concluded that the identified risk of blood creatinine increase has been further characterised to pre-renal azotemia with or without acute renal failure. Hence, the section 4.8 of the SmPC should be updated to add the adverse reaction prerenal azotemia with or without acute renal failure. The frequency should be uncommon. The Package leaflet should be updated accordingly.

The following changes to the product information of medicinal products containing the active substance telaprevir are recommended (text underlined/strikethrough):

Summary of product characteristics

- Section 4.8

Pre-renal azotemia with or without acute renal failure (frequency uncommon)

Package leaflet

- Section 4

- Dehydration. Signs and symptoms of dehydration include increased thirst, dry mouth, decreased urine frequency or volume, and dark colored urine. It is important to stay hydrated with fluids during INCIVO combination treatment.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds recommending the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for INCIVO, the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance telaprevir is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisation should be varied.