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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: pomalidomide

Procedure No. EMEA/H/C/PSUSA/00010127/201408

Period covered by the PSUR: 08.02.2014 - 07.08.2014

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Scientific conclusions

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

There is sufficient evidence to conclude that pomalidomide can cause atrial fibrillation, ILD, angioedema, urticaria, cardiac failure, serious hepatic disorders and hyperuricaemia and increased blood uric acid.

Atrial fibrillation

There have been seven cases of atrial fibrillation reported where a causal relationship with pomalidomide is a reasonable possibility, based on plausible temporal relationship and the absence of a likely alternative cause. In addition, there was an increased incidence of treatment-emergent atrial fibrillation in the pomalidomide group compared to the high-dose dexamethasone group (3.1% vs 1.3%) in the pivotal Phase III study.

ILD

There have been 8 cases in which a causal association between pomalidomide and interstitial lung disease (ILD) is likely.

Angioedema and urticaria

There have been 5 cases reported under the MeDRA Preferred Term (PT) angioedema. There have also been 44 cases with PTs highly suggestive of angioedema (facial oedema/lip oedema/eyelid oedema/tongue or mouth swelling). In addition there have been 26 cases where the PT was urticaria (and for which features of angioedema were not documented in the case narratives).

In five cases, two cases of angioedema and three cases of urticaria, there was a plausible temporal relationship, recurrence of the allergic reaction on re-challenge and lack of an alternative explanation. In addition, for another four cases of angioedema, it was likely to be a causal association with pomalidomide.

Cardiac failure

Study CC-4047-MF-002 showed a notable increase in cardiac failure events in the pomalidomide group compared to placebo (8.4% vs 2.4%). A causal role for pomalidomide is further supported by cases of cardiac failure from the cumulative review.

Hepatic Disorders
There have been 5 cases in which elevated liver function tests were associated with (or progressed to) hepatitis, requiring hospitalization. In each of these 5 cases pomalidomide is likely to have caused the hepatitis.

There have also been cases (n=7) of hepatic failure (including some fatal outcomes). Of these seven cases, there is one which raises the possibility that pomalidomide-induced liver injury can progress to acute hepatic failure.

Hepatic events had a median time to onset of 70 days and approximately three-quarters (74%) of events occurred within 6 months. Also, in the 5 cases of pomalidomide-induced hepatitis, the time to onset was up to 74 days suggesting that the highest risk of serious hepatotoxicity is within the first few months of initiation of pomalidomide.

Hyperuricaemia and increased blood uric acid
A review of all cases of hyperuricaemia and increased blood uric acid levels has concluded on the need to include these adverse reactions with a frequency of common in the product information.

These risks can be addressed through changes to the product information. Additional risk minimisation

through an update to the Educational Health Care Professional's kit and a Direct Health Care Professionals Communication (DHPC) have been agreed.

Therefore, in view of available data regarding pomalidomide, the PRAC considered that changes to the product information and to the conditions of the marketing authorisation were warranted.

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 pomalidomide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pomalidomide is favourable subject to the proposed changes to the product information

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