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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): certolizumab

Procedure No. EMEA/H/C/PSUSA/00000624/201703

Period covered by the PSUR: 7 March 2014 to 6 March 2017

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Scientific conclusions

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

Dermatomyositis

"*Worsening of symptoms of dermatomyositis*" is a known side effect for other TNFα inhibitors (infliximab, adalimumab and etanercept). In this PSUR, the MAH presented two cases of dermatomyositis with a temporal relationship to treatment with certolizumab pegol.

The risk for worsening of symptoms of dermatomyositis is believed to be a class effect for the TNFα inhibitors, and the MAH was therefore requested to add this information into section 4.8 of the SmPC for CZP.

Serious skin reactions

In a cumulative review, the MAH presented 5 cases of *Stevens-Johnson syndrome* (SJS) and 16 cases of *erythema multiforme* (EM). Although all cases were not biopsy-proven and there were concomitant infections or medications in some cases, a causal relationship seems reasonable in a few of the cases. Further, there are already descriptions of some serious skin events in section 4.8 of the SmPC for Cimzia, and SJS and EM are also included in SmPCs for other anti-TNF agents. Thus, these events should be reflected in section 4.8 of the SmPC also for Cimzia.

The following frequency categories can be established based on a pooling of RA studies dated 29 Jun 2015 (data lock point 31 Dec 2014):

- Erythema multiforme : 1 case in 5445 subjects exposed to Cimzia, which leads to a frequency category rare (≥ 1/10,000 to < 1/1000);
- Stevens-Johnson syndrome and dermatomyositis: no cases in 5445 subjects exposed to Cimzia, so the upper limit of the 95% CI is 3/5445 which also leads to a frequency category rare (≥ 1/10,000 to < 1/1000).

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