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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): tacrolimus (systemic formulations)

Procedure No. EMEA/H/C/PSUSA/00002839/202103

Period covered by the PSUR: 01/04/2018 - 31/03/2021

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## Scientific conclusions

Taking into account the PRAC Assessment Report on the PSURs for tacrolimus (systemic formulations), the scientific conclusions of CHMP are as follows:

In view of available data on cytomegalovirus infection from spontaneous reports (including some cases with a close temporal relationship) and in view of the plausible mechanism of action, the PRAC considers that a causal relationship between systemic tacrolimus and cytomegalovirus infection is at least a reasonable possibility. The PRAC concluded that the product information of products containing systemic tacrolimus should be amended accordingly.

In view of available data on infections from spontaneous reports and in view of the plausible mechanism of action, the PRAC considers that the product information of products containing systemic tacrolimus should be amended accordingly.

In view of available data on interactions with flucloxacillin from the literature and in view of the plausible mechanism of action, the PRAC considers that pharmacokinetic interactions with flucloxacillin are at least a reasonable possibility. The PRAC concluded that the product information of products containing systemic tacrolimus should be amended accordingly.

In view of available data on the pharmacodynamics interaction with trimethoprim and sulfamethoxazole/trimethoprim from spontaneous reports and the literature, the PRAC considers that the pharmacodynamic interaction with trimethoprim and sulfamethoxazole/trimethoprim is at least a reasonable possibility. The PRAC concluded that the product information of products containing systemic tacrolimus should be amended accordingly.

In view of available data on nephrotoxicity and the risk of progression to chronic renal impairment from the literature, the PRAC considers that the product information should be updated to strengthen the warning relating to nephrotoxicity.

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

## Grounds for the variation to the terms of the marketing authorisations

On the basis of the scientific conclusions for tacrolimus (systemic formulations) the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing tacrolimus (systemic formulations) is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisations should be varied.