



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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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)

Teysuno

Active substance(s): tegafur/gimeracil/oteracil (as monopotassium)

Procedure no.: EMEA/H/C/PSUSA/00002875/201601

Period covered by the PSUR: 25 January 2015 – 24 January 2016



## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for gimeracil / oteracil monopotassium / tegafur, the scientific conclusions of CHMP are as follows:

The MAH was requested to provide a cumulative review of RCT and post-marketing cases of limbal stem cell deficiency (LSCD), including literature, and to discuss whether an update to the SmPC was necessary.

In total, 14 relevant cases, all from post-marketing sources, were identified. Three cases were consistent with LSCD, 6 had symptoms characteristic of LSCD and 5 may represent LSCD.

Of the 3 cases consistent with LSCD, one case reported a positive dechallenge and no other concomitant drugs or comorbidity. The other 2 cases, (dechallenge unknown) were confounded by comorbidity of glaucoma. Furthermore, 6 cases presented with symptoms indicative for LSCD, such as conjunctivalisation (invasion of conjunctival cells in the cornea) and corneal epithelial defects. Conjunctivalisation is one of the most important symptoms of LSCD. One case was confounded by cataract, but the corneal epithelium disorder exacerbated after surgery and subsided after reducing the dose of Teysuno. In another case, positive dechallenge was also seen after discontinuation of treatment after invasion of the cornea by atypical epithelium. Of the other 4 cases, detailed information was missing.

'Corneal epithelial defects' is already included in the SmPC as adverse reaction in section 4.8.

Corneal disorders are a known adverse reaction with Teysuno use. Only one case was reported with the PT LSCD, however, there were at least 8 other cases with symptoms consistent or indicative of LSCD after prolonged use of Teysuno, with 3 cases reporting a positive dechallenge. LSCD can be a very serious adverse reaction with permanent vision damage and limited treatment options, and discontinuation of treatment and/or early intervention may prevent permanent damage.

Based on the reported cases, it is deemed appropriate to include 'limbal stem cell deficiency' as a adverse drug reaction in the table regarding corneal disorders in the summary of product characteristics.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing tegafur, gimeracil and oteracil (as monopotassium) were warranted.

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

## **Grounds for the variation to the terms of the marketing authorisation**

On the basis of the scientific conclusions for gimeracil / oteracil monopotassium / tegafur the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing gimeracil / oteracil monopotassium / tegafur 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.