26 March 2026
EMADOC-1700519818-2995672
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): difelikefalin

Procedure No. PSUSA/00010995/202508

Period covered by the PSUR: 1 year to 22 August 2025

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Scientific conclusions

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

A detailed analysis of the cases of elderly patients with deteriorating mental states assessed as related to treatment with difelikefalin (i.e., those with a temporal causality and positive de-challenge was performed during this PSUR assessment. In this analysis 24 cases with positive de-challenge and 1 case with positive rechallenge (hallucination) were found. "Mental status changes (including confusional state)" is already described in SmPC section 4.8 but the PRAC considers that the warning in 4.4 should be amended as the present warning in section 4.4 only describes dizziness and somnolence. Therefore, it is proposed to add "**mental status changes"** to the already present warning, with a reference to section 4.8. The PRAC concluded that the product information of products containing difelikefalin should be amended accordingly.

Having reviewed the PRAC recommendation, the CHMP agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for difelikefalin the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing difelikefalin 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.