Medicines Evaluation Board

Public Assessment Report
Scientific discussion

Lidocaine/Chloorhexidine C-Four gel (lidocaine hydrochloride monohydrate and chlorhexidine digluconate solution)

NL/H/5728/001/DC

Date: 21 April 2026

This module reflects the scientific discussion for the non-approval of Lidocaine/Chloorhexidine C-Four gel. The procedure was finalised on 7 August 2024.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have refused a marketing authorisation for Lidocaine/Chloorhexidine C-Four gel, from C4 Health GmbH.

The indications applied for included:
Topical anaesthesia gel with lubricant and infection reducing properties for:
- Urethral procedures in man and female, e.g. during cystoscopy, catheterisation, probing.

This application has been assessed with The Netherlands as Reference Member State (RMS) and Estonia, Croatia, Italy, Lithuania, Poland, Slovenia and Spain as concerned Member States (CMS).

The marketing authorisation was applied pursuant to Article 10a Well established use application (literature only) of Directive 2001/83/EC. This concerns a bibliographic application based on well-established medicinal use (WEU) of lidocaine and chlorhexidine. For this type of application, the applicant needs to demonstrate that the active substances of the medicinal product has been in well-established medicinal use within the Community for at least 10 years in the specific therapeutic use. The results of non-clinical and clinical trials are replaced by detailed references to published scientific literature.

The application was discussed in the Board meeting of 1 August 2024 (nr. 1058). A breakout session (BOS) was offered but declined by the applicant.

II. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The marketing authorisation could not be granted due to major objections qualifying as potential serious risk to public health as defined in the Guideline on the definition of a potential serious risk to public health in the context of Article 29(1) and (2) of Directive 2001/83/EC — March 2006 (2006/C 133/05):

Quality
The proposed production and quality control methods cannot guarantee that a major deficiency in the quality of the product will not occur. In the Board meeting, the following was discussed:

a. In order to sustain the comparability of the new proposed version of the product (without preservatives) to the product used in literature (Instillagel), IVRT comparison between these two products should be provided. The results should be assessed in line with the requirements for extended pharmaceutical equivalence testing listed under point 5 of Annex I to the Draft Guideline on quality and equivalence of topical products.
b. A description of the Quality Control IVRT procedure should be provided. The validation data of the IVRT should be provided. The discriminative power of the selected IVRT should be demonstrated by providing the results of IVRT testing conducted on one or more batches of the newly proposed product (without preservative) having out of specification values for viscosity or other relevant quality attributes. Reference is made to points 3 and 4 of Annex I to the Draft Guideline on quality and equivalence of topical products. The specification of the drug product should be amended to include a test for IVRT (not a dissolution test) with suitable limits for rate and extend of release (based on the batch results of the test product at issue a above). The footnote regarding ‘dissolution’ testing should be removed

The provided justification for the fact that IVRT results of the product with preservative should be representative of the product without preservatives is not acceptable. Without supportive data it cannot be accepted that the omission of preservatives from the formulation has no impact on the release of the active substances from the drug product.

As no *in vitro* release tests (IVRT) data of the new proposed formulation has been submitted and the IVRT test conditions including limits are not acceptable, the comparison between the proposed product and the product used in literature is not considered acceptable. The benefit/risk of the product is considered negative.

Therefore, the Board concluded that the marketing authorisation for Lidocaine/Chloorhexidine C-Four gel cannot be granted. Agreement on this conclusion was reached with the concerned member states. The decentralised procedure was finalised with a negative outcome on 7 August 2024.