CMDh/223/2005
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Public Assessment Report

Scientific discussion

Dexketoprofen Farmak 25 mg granules for oral solution
(dexketoprofen trometamol)

Date: 13 January 2025

This module reflects the scientific discussion for the approval of Dexketoprofen Farmak 25 mg granules for oral solution. The procedure was finalised at 10/09/2024. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Dexketoprofen Farmak 25 mg granules for oral solution, from Farmak International Sp. z o.o.

The product is indicated for the short term symptomatic treatment of acute pain of mild to moderate intensity.
A comprehensive description of the indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10.1 of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

The finished product is presented as granules for oral solution containing 25 mg of Dexketoprofen (as trometamol) as active substance. The maximum daily dose is 75 mg.

The product is available in single dose sachets made of aluminium foil laminated with paper and polyethylene, as described in section 6.4 of the SmPC.

II.2 Drug Substance

Dexketoprofen trometamol is a known active substance not described in the Ph.Eur. The Active Substance Master File (ASMF) procedure is used to support the quality of the drug substance Dexketoprofen trometamol.

General Information

Nomenclature:

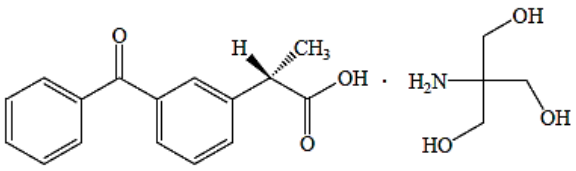
INN: Dexketoprofen Tromethamine

Chemical name: (+)-(S)-2-(3-benzoyl phenyl) propionic acid trometamol salt

CAS-No: 156604-79-4

Structure:

Structure:



MW: 375.41 g/mol

Chemical formula: C16H14O3·C4H11NO3

General Properties:

Dexketoprofen trometamol is a white or almost white crystalline powder that exhibits polymorphism. is slightly hygroscopic and soluble in water and absolute ethanol.

Manufacture, process controls and characterisation

The description of the manufacturing processes are properly detailed. The specifications of the materials used in the synthesis are sufficient and adequate. The profile of impurities, including residual solvents, of these materials which can influence the quality of the active substance are well defined and controlled. The acceptance criteria for the critical stages and the information on the quality and control of intermediates are adequate.

Specification, analytical procedures, batch analysis

Active substance specifications are considered appropriate and limits justified. Analytical methods are correctly described and validation carried out according to ICH. Batch results support consistent production.

Container closure system

The choice of the container closure systems is properly justified. Compliance with the relevant requirements and/or regulations is confirmed.

Stability

Stability studies have been performed in accordance with current guidelines. Protocol, controlled parameters and test methods are considered adequate. The packaging materials are similar to those proposed for storage. Proposed re-test period and storage conditions are justified.

II.3 Medicinal Product

Description of the product

Dexketoprofen Farmak is presented as white or almost white loose granular powder with lemon odour. The formulation includes sucrose, ammonium glycyrrhizate, neohesperidin dihydrochalcone, silica coloidal anhidrous and lemon flavour (that contains flavouring preparations, natural flavouring substances, flavouring substances, maltodextrin and gum arabic).

The granules are packaged in sachets made of an aluminium foil laminated with paper and polyethylene.

Pharmaceutical Development

The development of the product has been described, the choice of excipients is justified and their functions explained.
The physicochemical characteristics of the active substance that may affect the pharmaceutical form are identified and their control strategy is justified.

Manufacture of the product

The manufacturing process is fully described and in-process controls are appropriate considering the nature of the product and the manufacturing process. The industrial batch size is well-defined.

Sufficient validation data are provided.

Excipients

Excipients used are well known and of appropriate quality.

None of the excipients is of animal origin.

Product specification, analytical procedures, batch analysis

The finished product specifications are adequate to control the finished product. Provided description and validation data for the analytical methods are adequate. Batch analysis data have been submitted and the results show that the finished product meets the proposed release specification.

Container closure system

The finished product is packaged in sachets made of an aluminium foil laminated with paper and polyethylene. The choice of the container closure system is justified considering the nature of the finished product. Compliance with the relevant requirements and/or regulations is confirmed.

Stability

Stability studies have been performed in accordance with current guidelines. The proposed protocol is considered adequate. The packaging material is the same as that intended for marketing. Proposed shelf-life and storage conditions are properly established.

Shelf-life: 3 years.

Storage conditions: This medicinal product does not require any special storage conditions.

In-use shelf life: Not applicable

III. NON-CLINICAL ASPECTS

III.1 Critical evaluation of the Non-Clinical Overview

Pharmacodynamic, pharmacokinetic and toxicological properties of dexketoprofen trometamol are well known. As dexketoprofen trometamol is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Overview based on literature review is, thus, appropriate.

III.2 Environmental Risk Assessment (ERA)

Since Krofan 25 mg granules for oral solution is a generic product, it will not lead to an increased exposure to the environment. Therefore, additional ERA studies are not deemed necessary.

IV. CLINICAL ASPECTS

IV.1 Introduction

Dexketoprofen trometamol is a well-known active substance with established efficacy and safety. A clinical overview has been provided, which is based on scientific literature. The clinical overview justifies that there no need to generate additional clinical data.

For this generic application of an immediate/prolonged release formulation, the MAH, the Applicant did not conduct any clinical study to support this application.

IV.2 Pharmacokinetics

Biowaiver

According to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**), if the test is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved oral solution, bioequivalence studies may be waived considering that they do not contain excipients that may affect gastrointestinal transit, absorption, *in vivo* solubility or *in vivo* stability of the active substance.

Krofan 25 mg granules for oral solution has the same active substance as Enantyum® 25 mg granules for oral solution or as Delaxin 25 mg granules for oral solution, and there is a qualitative difference in excipients between both regarding silica colloidal anhydrous. However, the differences in composition in terms of excipients (in this case the presence or not of anhydrous colloidal silica) is not relevant since the applied product is an aqueous solution at the time of administration, the mentioned excipient does not affect bioavailability and dexketoprofen is considered a BCS class I molecule.

The justification for the biowaiver can be accepted.

IV.3 Pharmacodynamics

No new studies on pharmacodynamics have been submitted.

IV.4 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Dexketoprofen Farmak 25 mg granules for oral solution (dexketoprofen).

There are neither proposed additional pharmacovigilance activities nor proposed additional risk minimisation measures planned for Dexketoprofen Farmak 25 mg granules for oral solution (dexketoprofen).

IV.5 Discussion on the clinical aspects

The efficacy and safety of the active substance dexketoprofen are established and documented for the reference product.

The test and reference products are considered similar as they are aqueous solutions at the time of administration with the same concentration and with no excipients that could affect the bioavailability.

V. USER CONSULTATION

1) The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was Lithuanian.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product Dexketoprofen Farmak 25 mg granules for oral solution is found adequate. There are no objections to the approval of Dexketoprofen Farmak 25 mg granules for oral solution from a non-clinical and clinical point of view. Bioequivalence between the test and reference product can be assumed provided that they are aqueous solutions with the same concentration and without critical excipientes. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.