LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Dicuno
(diclofenac potassium)

SE/H/791/01-02/DC

This module reflects the scientific discussion for the approval of Dicuno. The procedure was finalised at 2011-03-03. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Vitabalans Oy has applied for a marketing authorisation for Dicuno, 25 and 50 mg, film-coated tablets claiming essential similarity to Voltaren T, 25 and 50 mg film-coated tablets, marketed in Sweden by Novartis Sverige AB. The product contains diclofenac potassium as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Voltaren Rapid 50 mg tablets marketed by Novartis in Finland.

II. QUALITY ASPECTS

II.1 Introduction

Dicuno is presented in the form of film-coated tablets containing 25 mg or 50 mg of diclofenac potassium. The excipients are calcium hydrogen phosphate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, pregelatinised starch (maize), colloidal anhydrous silica, polyvinyl alcohol, macrogol, talc, titanium dioxide, iron oxide (red), iron oxide (yellow) and iron oxide, black (25 mg) or Ponceau 4R aluminium lake (50 mg). The film-coated tablets are packed in blisters.

II.2 Drug Substance

Diclofenac potassium has a monograph in the Ph. Eur.

Diclofenac potassium is a white or slightly yellowish hygroscopic crystalline powder which is freely soluble in methanol and sparingly soluble in water. The structure of diclofenac potassium has been adequately proven and its physico-chemical properties sufficiently described. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active substance specification includes relevant tests and the limits for impurities/degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Dicuno film-coated tablets are formulated using excipients described in the current Ph Eur, except for the coating pre-mixes, which are described by in house specifications. All raw materials used in the product are of vegetable origin or has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored below 25 °C.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

The submitted dossier includes two bioequivalence studies and publicly available literature on diclofenac. No efficacy or safety studies for the applied product have been performed by the applicant.

The clinical overview has been written by Hannu Raunio, MD, PhD, Professor of Pharmacology, and is dated 27th August 2010. The report refers to 80 publications, published between years 1978 to 2010.

The original study was likely under dimensioned to be able to show bioequivalence. In the applicant´s response to this, the applicant submitted a new bioequivalence study, study code V-1003. The study compared the relative bioavailability between the test product, Diclofenac Vitabalans 50 mg tablets and the reference product, Voltaren Rapid 50 mg tablets from Novartis.

Bioequivalence is shown, with 90 % confidence intervals of AUC_t, AUC_∞ and C_{max} within 0.80-1.25. Approval can be recommended from a pharmacokinetic point of view.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation
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 the Czech language.
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.

The results of the conducted bioequivalence study can be extrapolated to other strengths since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Dicuno, 25 & 50 mg film-coated tablets is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Dicuno, 25 and 50 mg, film-coated tablet was successfully finalised on 2011-03-03.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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