LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Cyklonova
Tranexamic acid

SE/H/644/01/MR

This module reflects the scientific discussion for the approval of Cyklonova 2 x 500 mg film-coated tablets. The procedure was finalised at 2007-04-26. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

Alternova A/S has applied for a marketing authorisation for Cyklonova 500 mg film-coated tablet claiming essential similarity to Cyklo-F 500 mg, marketed in Sweden by Meda AB. The original product Cyclokapron 500 mg tablets are marketed in Ireland by Pharmacia & Upjohn since 1983. The product contains tranexamic acid as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Cyklokapron 500 mg film-coated tablets, marketed in UK by Pharmacia & Upjohn, Pharmacia Laboratories Ltd.

II. QUALITY ASPECTS

II.1 Introduction

Cyklonova is presented in the form of tablets containing 500 mg of tranexamic acid. The excipients are microcrystalline cellulose, povidone K 90, croscarmellose sodium, colloidal anhydrous silica, talc, magnesium stearate and film coating. The tablets are packed in blister packs of PVC/aluminium.

II.2 Drug Substance

Tranexamic acid has a monograph in the Ph Eur. It is a white crystalline powder, freely soluble in water and in glacial acetic acid, practically insoluble in alcohol and in ether.

The structure of tranexamic acid has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on chirality is presented. 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

Cyklonova 500 mg tablet is formulated using excipients described in the current Ph Eur, except for **(**film coating) methacrylate polymers (Eudragit E 100) which is controlled according to internal specification. All raw materials used in the product are of vegetable origin.
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, at a temperature not higher than 30°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

One bioequivalence study was submitted evaluating bioequivalence of the test product Cyklonova 2 x 500 mg tablet, with the reference product on the UK market, Cyklokapron 2 x 500 mg tablet, Pharmacia Laboratories Ltd. Conventional statistical and pharmacokinetic analysis methods and a validated analytical method were used. The protocol stated that bioequivalence could be assumed if the 90 % confidence interval of the geometric mean ratio of the parameters $AUC_{0-\infty}$ and C_{max} for the test vs. the reference product would fall within 80-125 %. The results showed that the 90 % confidence intervals for $AUC_{0-\infty}$ and for C_{max} were within acceptable limits.

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 English.

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 risk/benefit ratio is considered positive and Cyklonova 2 x 500 mg film-coated tablet is recommended for approval.

VI. APPROVAL

The Mutual recognition procedure for Cyklonova 2 x 500 mg film-coated tablet was successfully finalised on 2007-04-26.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se