LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Paracut Brus, 500 mg, effervescent tablets (Paracetamol)

This module reflects the scientific discussion for the approval of Paracut Brus. The procedure was finalised at 2012-03-29. 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 Paracut Brus 500 mg effervescent tablets claiming essential similarity to Alvedon 500 mg effervescent tablets marketed Sweden since 1974 by GlaxoSmithKline. Paracut Brus is a line extension (new pharmaceutical form) to Paracut 500 mg tablets. The product contains paracetamol as active substance. For approved indications see the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

Paracut Brus is presented in the form of effervescent containing 500 mg of paracetamol. The excipients are citric acid anhydrous, magnesium stearate, povidone, saccharin sodium, sodium carbonate anhydrous, sodium chloride, sodium citrate, sodium hydrogen carbonate, sodium laurilsulfate, lemon flavour, and citrus flavour The effervescent tablets are packed in polypropylene tubes.

II.2 Drug Substance

Paracetamol has a monograph in the Ph Eur.

Paracetamol is a white, or almost white, crystalline powder which is sparingly soluble in water and freely soluble in alcohol. The structure of paracetamol has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism 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

Paracut Brus effervescent tablets are formulated using excipients described in the current Ph Eur, except for the flavouring agents which are controlled according to acceptable in house specifications. All raw materials used in the product have 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.

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

Paracetamol is well absorbed following oral administration. Maximum plasma concentration is reached within 30-60 minutes. The half-life of paracetamol in plasma is approximately 2 hours. The metabolism occurs mainly in liver by glucuronide and sulphate conjugation. Also some oxidation mediated by cytochrome P450 (CYP) enzymes takes place. In overdose, this metabolic route involves an intermediate production of a reactive, potentially toxic N-acetylp-benzoquinonimine (NAPQI). Paracetamol and its metabolites are excreted via kidneys.

Generally, for a product claiming essential similarity bioequivalence with the reference product must be shown. For the applied product, the applicant has not submitted any bioequivalence study but claims that the applied product has been shown to fulfil the criteria for exemption of in vivo bioequivalence studies.

According to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1), bioequivalence studies may be waived if the test product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved oral solution. However, if there are differences regarding excipients that may affect the bioavailability, a study should be conducted unless the differences in the amounts of these excipients can be adequately justified. According to the Quality documentation the active substance may not be completely in solution at time of administration, but since all excipients are qualitatively the same as for the reference product (including the taste modifiers which contain sorbitol and mannitol), waiving bioequivalence studies is considered acceptable.

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
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Paracut Forte 111:2008/67715, approval date 2010-12-10. The bridging report submitted by the applicant has been found acceptable.

The layout has been discussed and is also considered as acceptable.

The risk/benefit ratio is considered positive and Paracut Brus is recommended for approval.

VI. APPROVAL

Paracut Brus 500 mg effervescent tablets were approved in the national procedure on 2012-03-29.

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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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