LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Recikalc-D forte,
500 mg-800 IU, film-coated tablet
(calcium carbonate + vitamin D_3)

SE/H/805/03/DC

This module reflects the scientific discussion for the approval of Recikalc-D forte. The procedure was finalised on 2011-12-20. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Meda AB has applied for a marketing authorisation for Recikalc-D forte, film-coated tablet, 500 mg/800 IU. The combination of calcium carbonate and cholecalciferol products has been available on the market for more than 10 years, in the form of registered medicinal products and as food supplement products.

II. QUALITY ASPECTS

II.1 Introduction

Recikalc-D forte is presented in the form of film-coated tablets containing 1261 mg of calcium carbonate and 10.4 mg of cholecalciferol concentrate which corresponds to 500 mg calcium and 20 microgram cholecalciferol. The excipients are maltodextrin, croscarmellose sodium, anhydrous colloidal silica, magnesium stearate, hypromellose, macrogol, synthetic paraffin, DL-alfa-tocopherol, gelatine, sucrose, maize starch and partially hydrogenated soya-bean oil. The tablets are packed in plastic containers of HDPE with screw caps of HDPE.

II.2 Drug Substances

Calcium carbonate:
Calcium carbonate has a monograph in the Ph Eur. Relevant information on calcium carbonate is presented. The specification for calcium carbonate includes relevant tests and the limits have been justified.

Cholecalciferol (in the form of cholecalciferol concentrate, powder form):
Cholecalciferol and cholecalciferol concentrate (powder from) have both monographs in the Ph Eur. The concentrate can be considered the "drug substance" from a regulatory perspective (special case since it concerns a vitamin).

The specification for cholecalciferol concentrate (powder form) includes relevant tests and the limits have been justified.
Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Recikalc-D forte film-coated tablets are formulated using excipients described in the current Ph Eur, except for synthetic paraffin which is 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 substances.

The manufacturing process has been sufficiently described and critical steps identified.

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 in tightly closed original containers in order to protect from light and moisture.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Products containing calcium and vitamin D have been available in the EU for more than 20 years and their use is well-established with recognised efficacy and acceptable safety. The dose levels are within the dosage range commonly used in clinical practise. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate. No further studies are required or were provided.

III.2 Pharmacology

Pharmacodynamic properties of calcium and vitamin D are well-known and text-book knowledge.

III.3 Pharmacokinetics

There is no pharmacokinetic data specific for the currently applied product. This is acceptable in view of the well-established use of these products.

III.4 Toxicology

Pharmacodynamic, pharmacokinetic and toxicological properties of calcium and vitamin D are well-known and text-book knowledge. Literature references sufficiently addressed these aspects.

III.5 Ecotoxicity/environmental risk assessment

The product is intended to substitute for other products on the market and contains no components that result in additional hazard to the environment. The justification for absence of environmental risk assessment is considered adequate.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of calcium and vitamin D are well-known and text-book knowledge. Products containing calcium and vitamin D have been available in the EU for more than 20 years and their use is well-established with recognised efficacy and acceptable safety. The dose levels are within the dosage range commonly used in clinical practise.

IV. CLINICAL ASPECTS

IV.1 Introduction

Recikalc-D forte 500 mg/800 IU contains calcium carbonate and cholecalciferol (vitamin D_3) as the active ingredients. The indication is in accordance with that of the originator Recikalc-D forte chewable tablets (500 mg/800 IU) and with that of other combined calcium-vitamin D products on the market. The dosing schedule means administration of the full daily dose on the same occasion. The vitamin D dose is in accordance with present recommendations for daily

intake. As this product only contains 500 mg calcium per total daily dose, it is intended for use by patients who also have a certain dietary intake of calcium.

Clinical data for the combination of calcium and vitamin D was provided as literature references only.

IV.2 Pharmacokinetics

There is no pharmacokinetic data specific for the currently applied product, which is acceptable. Due to the nature of the active substances, it is not considered necessary to compare the bioavailability of calcium and vitamin D from the new product with that from existing products on the market.

IV.3 Pharmacodynamics

No new data were provided.

Clinical efficacy and safety

As vitamin D plus calcium supplement is widely used and both active substances are well-known, no further studies are required and the applicant provides none. An overview based on literature review is, thus, appropriate and the applicant has provided a satisfactory clinical review. The efficacy and safety can be expected to be similar to that of the previously approved products.

IV.4 Discussion on the clinical aspects

No new clinical data is considered necessary and none was submitted. The indication is in accordance with that of other combined calcium-vitamin D products on the market and is approvable.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User testing of the package leaflet has been performed and is acceptable.

The applicant has committed to undertake the following follow-up measures:

Area[1]	Description
Quality	The applicant has committed to develop a dissolution test that will be included in the drug product specification through a variation post approval.

1. Areas: Quality, Non-clinical, Clinical, Pharmacovigilance

The risk/benefit ratio is considered positive and Recikalc-D forte, 500 mg/800 IU, film-coated tablet is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Recikalc-D forte, 500 mg/800 IU, film-coated tablet was successfully finalised on 2011-12-20.

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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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