LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

# Public Assessment Report

# Scientific discussion

# Vinelle
# (desogestrel)

# SE/H/1356/01/DC

**This module reflects the scientific discussion for the approval of Vinelle. The procedure was finalised on 2014-10-09. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

The application for Vinelle, 75 micrograms, tablet, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, CampusPharma AB, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, FI and NO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Cerazette®, 75 micrograms, tablet authorised in France since 1998, with Schering Plough as marketing authorisation holder.
The reference product used in the bioequivalence study is Cerazette®, 75 micrograms, film-coated tablet from France with Schering Plough as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

# II. QUALITY ASPECTS

## II.1 Introduction

Vinelle is presented in the form of tablets containing 75 mg of desogestrel. The excipients are anhydrous lactose, potato starch, povidone, all-rac-α-tocopherol, anhydrous colloidal silica and stearic acid. The tablets are packed in blisters.

## II.2 Drug Substance

Desogestrel has a monograph in the Ph Eur.

Desogestrel is a white or almost white, crystalline powder which is practically insoluble in water, very soluble in methanol, freely soluble in anhydrous ethanol and in methylene chloride. The structure of desogestrel has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism, chirality etc. 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

Vinelle, 75 micrograms, tablet is formulated using excipients described in the current Ph Eur. 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, with no special storage precautions.

# 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

Bioequivalence was evaluated in one single-dose, two-treatment, two-period, two-sequence crossover study conducted in 30 healthy female volunteers, comparing Desogestrel, 2 tablets of 75 µg, with Cerazette, 2 tablets of 75 µg, under fasting conditions. The study was conducted at Lambda Therapeutic Research Ltd., India between 26$^{th}$ February 2011 and 2$^{nd}$ April 2011. Blood samples were collected pre-dose and up to 96 hours post-dose. The study design is considered acceptable. Plasma concentrations of 3-ketodesogestrel (etonogestrel) were determined with an adequately validated LC-MS/MS method. For $AUC_{0-t}$ and $C_{max}$ the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Based on the submitted bioequivalence study, Desogestrel, 75 µg, tablet is considered bioequivalent with Cerazette, 75 µg, tablet.

## 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.

## IV.3 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 Vinelle.

Summary table of safety concerns

| **Summary of safety concerns** | |
|---|---|
| Important identified risks | • Disturbances of the vaginal bleeding pattern |
| Important potential risks | • Venous thrombolic events<br>• Cerebrovascular accidents<br>• Breast cancer<br>• Effects on liver/liver cancer |
| Important missing information | None |

The following table summarizes important potential risks and proposed actions:

| **Safety concern** | **Planned action** | **Additional risk minimisation measures** |
|---|---|---|
| Venous thromboembolic events | Routine pharmacovigilance, including ICR, screening of literature, PBRER and ongoing signal detection | Information is given in section 4.4 of the SPC. |
| Cerebrovascular accidents | Routine pharmacovigilance, including ICR, screening of literature, PBRER and ongoing signal detection | Information is given in section 4.4 of the SPC. |
| Breast cancer | Routine pharmacovigilance, including ICR, screening of literature, PBRER and ongoing signal detection | Information is given in section 4.4 of the SPC. |
| Effects on liver / liver cancer | Routine pharmacovigilance, including ICR, screening of literature, PBRER and ongoing signal detection | Information is given in section 4.4 of the SPC. |

These safety concerns are endorsed, and it is agreed that routine pharmacovigilance activities are appropriate.

# 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 Vinelle, 75 micrograms, tablet, is recommended for approval.

# VI. APPROVAL

The Decentralised procedure for Vinelle, 75 micrograms, tablet, was successfully finalised on 2014-10-09.

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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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