LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2013-04-29

# Public Assessment Report
# Scientific discussion

# Pascoflair, coated tablet
**(*Passiflora incarnata* L., *herba*, dry extract (5-7:1), ethanol 50%)**

# Asp. No: 2010-0733

**This module reflects the scientific discussion for the approval of Pascoflair. The procedure was finalised at 24 May 2011. 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

# LAY SUMMARY

The Medical Products Agency (Läkemedelsverket) has granted Pascoe Pharmazeutische Präparate GmbH, Germany, a traditional-use registration for the herbal medicinal product Pascoflair, coated tablets. This product is available without prescription and can be bought from pharmacies and other outlets.

Pascoflair is traditionally used for the relief of mild anxiety and temporary difficulties in falling asleep. The active ingredient is a dry ethanolic extract from aerial parts of passion flower (passionsblomma, *Passiflora incarnata* L.). This registration is based exclusively upon evidence of traditional use of passion flower as a herbal medicinal product and not upon data generated from clinical trials. For traditional herbal medicinal products there is no requirement to scientifically prove the effect; adequate evidence of traditional use is sufficient.

The chemical/pharmaceutical quality of the product is acceptable and no new or unexpected safety concerns have been identified during the assessment. It was therefore decided that Pascoflair could be registered as a traditional herbal medicinal product.

# I. INTRODUCTION

Pascoe Pharmazeutische Präparate GmbH has applied for a traditional-use registration for Pascoflair, coated tablet. The application was submitted under Article 16a traditional use registration for herbal medicinal product of the Directive 2001/83 EC, as amended.
The application is a national application for Sweden but the product already has traditional-use registrations in Austria and the United Kingdom.

The active substance is *Passiflora incarnata* L., herba, dry extract (5-7:1), ethanol 50 %.
For approved indications, see the Summary of Product Characteristics.

# II. QUALITY ASPECTS

## II.1 Introduction

Pascoflair is presented in the form of coated tablets containing 425 mg of the active substance "*Passiflora incarnata* L. herba, dry extract (5-7:1), ethanol 50 %" which corresponds to approximately 2.5 g of dried aerial parts of *Passiflora incarnata* L.
The excipients are: sucrose, maltodextrin, talc, calcium carbonate, croscarmellose sodium, colloidal anhydrous silica, powdered cellulose, stearic acid, hypromellose, acacia, magnesium stearate, titanium dioxide, spraydried liquid glucose, tragacanth, shellac, white beeswax, carnauba wax, yellow iron oxide.
The coated tablets are packed in blisters.
All manufacturers involved in the production operate in accordance with EU-GMP, or where relevant, GACP (Good Manufacturing Practise, respectively Good Agricultural and Collection Practice).

## II.2 Drug Substance

The herbal substance *Passiflora incarnata* L. complies with the monograph "passion flower" in the European Pharmacopoeia.

The plants used are cultivated in Europe. Relevant information on growing conditions and controls of the herbal substance (such as residues of heavy metals and pesticides as well as microbiological quality) has been provided. Aerial parts of the plants are cut and extracted with 50 % ethanol at 40-50 ° C.

For manufacturing reasons, the genuine extract is mixed with maltodextrin and anhydrous colloidal silica to obtain the manufacturing extract which is a slightly hygroscopic brown powder. The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials and solvents.

Control of the active substance (herbal preparation) *Passiflora incarnata* L. herba, dry extract (5-7:1), ethanol 50 % is based on the monograph "passion flower dry extract" in the European Pharmacopoeia.

The active substance specification includes relevant tests and the limits for impurities 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

Pascoflair coated tablets are formulated using excipients described in the current European Pharmacopoeia (Ph. Eur.), except for yellow iron oxide which is controlled according to acceptable in house specifications/USP. All raw materials used in the product are safe with view to possible TSE/BSE risk.

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 AND CLINICAL ASPECTS

### III.1 Introduction

The Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA) has issued a Community monograph on *Passiflora incarnata* in 2007.
The reader is referred to the Community monograph and the pertinent assessment report for details.

### III.2 Non-clinical aspects

The applicant has collected available information from the literature in the areas of non-clinical pharmacology and toxicology. This information has been assessed by the MPA and no signals of non-clinical safety concern have been identified. The exact mechanism of action of *Passiflora incarnata* dry extract in relation to its traditional medicinal use cannot be considered clarified.

A product/extract specific study on mutagenic activity has been performed. The extract has been shown not to be mutagenic in Ames test.

Based on the non-clinical information, both from the literature and the product specific study, no objections are raised to the approval of an ethanolic extract of *Passiflora incarnata* as active ingredient in a traditional herbal medicinal product.

### III.3 Ecotoxicity/environmental risk assessment

Pascoflair is a traditional herbal medicinal product. According to “Guideline on the environmental risk assessment of medicinal products for human use” (EMEA/CHMP/SWP/4447/00), (traditional) herbal medicinal products are exempted from the obligation to present an environmental risk assessment due to the nature of their constituents.

### III.4 Clinical aspects

Results of clinical trials concerning clinical efficacy and safety are not required for the registration of a traditional herbal medicinal product.

### III.5 Traditional use

The medicinal use of *Passiflora incarnata* has a long traditional use exceeding 30 years in the Community. It is mainly used in form of tincture or liquid extracts for relief of mild symptoms of mental stress and to aid sleep (HMPC monograph). The recommended dosage of Pascoflair is in the same range as the ones listed in the HMPC monograph and in the literature.
The product itself has been registered as a traditional herbal medicinal product, under the Article 16a of the Directive 2001/83 EC as amended, in Austria and the UK.

The applicant has provided a bibliographic review which shows sufficient evidence for the medicinal use of *P. incarnata* throughout a period of at least 30 years, including at least 15 years within the Community.

### III.6 Clinical safety

Conventional clinical safety data are virtually absent. However, longstanding medicinal use and experience of *Passiflora incarnata,* herb has been documented within the Community. During this time, no clinical signals that *Passiflora incarnata,* herb is harmful under normal conditions of use have been identified.

As no data on use in children are available, products containing *Passiflora incarnata* herb *cannot* be recommended for use in children below the age of 12 years.

Due to lack of safety data, the use of products containing *Passiflora incarnata,* herb during pregnancy and lactation is not recommended.

Based on the clinical safety information available, no objections are raised to the approval of Pascoflair as a traditional herbal medicinal product.

## IV. PRODUCT INFORMATION

The product information (Summary of Product Characteristics, Package Leaflet and labelling) has been assessed and accepted by the Medical Products Agency.

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 German.*
*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.*

# V. OVERALL CONCLUSION, RISK ASSESSMENT AND RECOMMENDATION

For Pascoflair, coated tablet, the handling, manufacture and quality control of raw materials, active substance and finished product are in line with GMP and pharmacopoeial requirements. The applicant has shown that the chemical/pharmaceutical quality is acceptable and can confirm that the process is under control and ensure both batch reproducibility and compliance with the product specification.

The extract in Pascoflair is covered by the Community monograph on *Passiflora incarnata* L., herba. It has thus been adequately documented that the extract in Pascoflair had a medicinal use for at least 30 years, including at least 15 years within the Community.

No signals of preclinical or clinical safety concern have been identified under normal conditions of use.

Pascoflair, coated tablets, can be recommended for registration as a traditional herbal medicinal product.

# VI. APPROVAL

Pascoflair, coated tablets was approved in the national procedure on 2011-05-24.

# 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