LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2014-01-28

Public Assessment Report
Scientific discussion

Arctic Root, coated tablet
(*Rhodiola rosea* L., root, dry extract)

Asp.no.: 2006-2005

This module reflects the scientific discussion for the approval of Arctic Root. The procedure was finalised at 19 November 2008. 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 Bringwell AB, Sweden, a traditional-use registration for the herbal medicinal product Arctic Root, coated tablets. This product is available without prescription and can be bought from pharmacies and other outlets.

Arctic Root is traditionally used as an adaptogen in stress-related reduced performance ability with symptoms such as tiredness, fatigue, irritability and mild anxiety. The active ingredient is a dry ethanol/water extract from the root and rhizome of golden root (rosenrot, *Rhodiola rosea* L.). This registration is based exclusively upon evidence of traditional use of golden root 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 Arctic Root could be registered as a traditional herbal medicinal product.

I. INTRODUCTION

The application for a traditional-use registration for Arctic Root, coated tablet, was submitted under Article 16a traditional use registration for herbal medicinal product of the Directive 2001/83 EC, as amended. The application was a national application for Sweden only.

The active substance is *Rhodiola rosea* L. root and rhizome, dry extract (2.5-5.0:1).
For approved indications, see the SmPC (Summary of Product Characteristics).

II. QUALITY ASPECTS

II.1 Introduction

Arctic Root is presented in the form of coated tablets and each tablet contains 144 mg of the active substance *Rhodiola rosea* L., radix et rhizoma, dry extract (2.5-5:1). This amount corresponds to approximately 540 mg of dried roots/rhizome of *Rhodiola rosea* L. Extraction solvents are ethanol 70% and water.
The excipients are: microcrystalline cellulose, maltodextrin, potato starch, calcium hydrogen phosphate dihydrate, colloidal silica (anhydrous), magnesium stearate, shellac, potassium sorbate, methyl parahydroxybenzoate (E218), macrogol and olive oil.
The coated tablets are packed in blisters.

All manufacturers involved in the production operate in accordance with EU-GMP (Good Manufacturing Practice) or, where relevant, GACP (Good Agricultural and Collection Practice).

II.2 Drug Substance

The plants used are wild growing and collected manually in the Mountain Altai region, Russia. The roots are immediately cut and dried. Relevant information on harvesting and control of the herbal substance (such as residues of heavy metals and pesticides as well as microbiological quality) has been provided. Analysis of radioactivity is performed.

Before extraction the herbal drug is ground. The extraction is a two cycle process; the first extraction is performed with ethanol 70% and the second with water. Ethanol and water evaporate during drying, resulting in the final dry extract.
The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials and solvents.

The control of the active substance (herbal preparation) *Rhodiola rosea* L. radix and rhizome, dry extract (2.5-5.0:1) 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

Arctic Root coated tablets are formulated using excipients described in the current European Pharmacopoeia (Ph. Eur.) and they are all controlled for compliance with their corresponding Ph. Eur. monograph. 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 SmPC.

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 *Rhodiola rosea* L., radix and rhizome in 2012. However, at the time of application for registration of Arctic Root coated tablets, the safety and efficacy of *Rhodiola rosea* L. had not been evaluated by the HMPC, and therefore the applicant submitted relevant information from the literature for the MPA to assess.

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 *Rhodiola rosea* 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 ethanol/water extract of *Rhodiola rosea* as active ingredient in a traditional herbal medicinal product.

III.3 Ecotoxicity/environmental risk assessment

Arctic Root, coated tablet, 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 applicant has provided a bibliographic review, which shows sufficient evidence for the medicinal use of *Rhodiola rosea* throughout a period of at least 30 years, including at least 15 years within the Community.
The recommended dosage of Arctic Root is in the same range as the doses recorded in the bibliographic review.

III.6 Clinical safety

The submitted bibliographic review, including published clinical studies, and the extensive post marketing experience with preparations of *Rhodiola rosea* give no reason for safety concern.

As no data on use in children are available, Arctic Root cannot be recommended for use in children below the age of 12 years.

Due to lack of safety data, the use of Arctic Root during pregnancy and lactation is not recommended.

Based on the clinical safety information available, no objections are raised to the registration of Arctic Root 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.

V. OVERALL CONCLUSION, RISK ASSESSMENT AND RECOMMENDATION

For Arctic Root, 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.

There is sufficient evidence for the medicinal use of *Rhodiola rosea* root and rhizome, throughout a period of at least 30 years, including at least 15 years within the Community. The extract in Arctic Root is covered by the Community monograph on *Rhodiola rosea* L., radix and rhizome.

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

Arctic Root, coated tablets, can therefore be recommended for registration as a traditional herbal medicinal product.

VI. APPROVAL

Arctic Root coated tablet was approved in the national procedure on 2008-11-19.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2014-01-28

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
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