LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2014-04-15

Public Assessment Report
Scientific discussion

Ginsana, soft capsule

(*Panax ginseng* C.A. Meyer, radix, standardised dry extract G115 Pharmaton (0.9-3.9:1, 40% ethanol))

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This module reflects the scientific discussion for the approval of Ginsana, soft capsule. The procedure was finalised in 2012-01-02. For information on changes after this date please refer to the module 'Update'.

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LAY SUMMARY

The Medical Products Agency (Läkemedelsverket) has granted Ginsana, soft capsule a registration as a traditional herbal medicinal product. This product is available without prescription and can be bought from pharmacies and other outlets.

Ginsana is traditionally used as a tonic in case of symptoms of asthenia, such as fatigue and weakness. The active ingredient is a dry ethanol extract from the root of ginseng (*Panax ginseng* C.A. Meyer). This registration is based exclusively upon evidence of traditional use of ginseng 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 Ginsana, soft capsule, could be registered as a traditional herbal medicinal product.

I. INTRODUCTION

Ginsana, soft capsule, was first authorised as a natural remedy in 1999. However, as a consequence of the new legislation regarding (traditional) herbal medicinal products, the product was reclassified to a traditional herbal medicinal product (pursuant to Article 16a of the Directive 2001/83 EC, as amended) in 2012.

The active substance is *Panax ginseng* C.A. Meyer, radix, standardised dry extract G115 Pharmaton.
For approved indications, see the SmPC (Summary of Product Characteristics).

II. QUALITY ASPECTS

II.1 Introduction

Ginsana is presented in the form of soft capsules and each capsule contains 100 mg of the active substance *Panax ginseng* C.A. Meyer, radix, standardised dry extract G115 Pharmaton (0.9-3.9:1). This amount corresponds to approximately 210 mg of dried roots of *Panax ginseng* C.A. Meyer. Extraction solvent is ethanol 40%.

The excipients are: gelatin, rapeseed oil (refined), lecithin, lactose monohydrate, glycerol 85%, soya-bean oil (partially hydrogenated), Anidrisorb 85/70, 85% (consists of starch (hydrogenated, partially hydrolysed), sorbitan, mannitol and sorbitol), soya-bean oil (hydrogenated), yellow beeswax, soya-bean lecithin, black and red iron oxide (E172), colloidal silica (anhydrous) and ethyl vanillin.

The soft capsules 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 herbal substance *Panax ginseng* C.A. Meyer complies with the requirements of the monograph "Ginseng (Ginseng radix)" in the European Pharmacopoeia, with additional controls for heavy metals, aflatoxins and pesticides.

The herbal substance Panax ginseng C.A. Meyer is cultivated in the Northern regions of China and in Canada, with climatic conditions of warm summers, cold winters and rainfall between 1000 and 2000 mm/year.
Harvesting is performed 5-6 years after sowing. The roots are washed, cut and dried and extracted with ethanol 40%. The obtained native extract is turned into a dry powder through heating and spray-drying.
For manufacturing reasons, the dry extract is mixed with colloidal silica (anhydrous). Furthermore, by addition of a suitable amount of lactose monohydrate, the extract is standardised on the total content (4.0% ± 0.4%) of eight major ginsenosides; Rb1, Rb2, Rc, Rd, Re, Rg1, Rg2 and Rf. The herbal preparation consists of 30-55% *Panax ginseng* native extract, 2% colloidal silica (anhydrous) and 43-68% lactose monohydrate.

The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials and solvents.

The control of the standardised extract includes relevant tests and the limits for impurities have been justified. The analytical methods applied are suitably described and validated.

Submitted stability data are sufficient to confirm the retest-period.

II.3 Medicinal Product

The excipients lecithin, soya lecithin, soya oil (partially hydrogenated), ethyl vanillin and Anidrisorb are controlled for compliance with acceptable in-house specifications. Representative certificates of analysis have been provided. The colouring agents fulfil the criteria of Commission Directive 95/45/EC (laying down specific purity criteria concerning colours for use in foodstuffs), whereas the other excipients are controlled in line with their corresponding monographs in the European Pharmacopoeia. As the gelatin is of animal origin, measures have been taken to minimise the risk of transmitting Animal Spongiform Encephalopathy Agents.

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.

Submitted stability data support the shelf-life claimed in the SmPC.

Based on the chemical/pharmaceutical information available, no objections are raised to the registration of Ginsana, soft capsule as a traditional herbal medicinal product.

III. NON-CLINICAL AND CLINICAL ASPECTS

III.1 Introduction

At the time of application for registration of Ginsana, soft capsules, the safety and efficacy of roots of *Panax ginseng* C.A. Meyer had not yet been evaluated by the European Committee on Herbal Medicinal Products, HMPC. Therefore, the applicant submitted relevant information from the literature for the Medical Products Agency to assess.

III.2 Non-clinical aspects

From the literature review, in the areas of non-clinical pharmacology and toxicology of *Panax Ginseng*, no serious concerns have been identified.

A product specific study on mutagenic activity (with and without metabolic activation) has been performed, using *Salmonella typhimurium* strains. The extract G115 has been shown not to be mutagenic in the Ames´ test, nor did it induce chromosomal aberrations in human lymphocytes *in vitro*.

III.3 Ecotoxicity/environmental risk assessment

Ginsana, soft capsule, 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 traditional medicinal use of *Panax ginseng* throughout a period of at least 30 years, including at least 15 years within the Community.
The recommended dosage of *Panax ginseng* 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 *Panax ginseng* give no reason for safety concern.

However, as data on use in children is insufficient, Ginsana cannot be recommended for use in children below the age of 12 years.
Furthermore, due to lack of safety data, the use of Ginsana during pregnancy and lactation is not recommended.

Based on the non-clinical and clinical safety information available, no objections are raised to the registration of Ginsana, soft capsule 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 Ginsana, soft capsule, 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 ensures both batch reproducibility and compliance with the product specification.

There is sufficient evidence for the traditional medicinal use of root of *Panax ginseng* throughout a period of 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.

Ginsana, soft capsule can therefore be recommended for registration as a traditional herbal medicinal product.

VI. APPROVAL

Ginsana, soft capsule was approved in the national procedure on 2012-01-02.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Läkemedelsverket 2014-04-15

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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