# Public Assessment Report
# Scientific discussion

# Kan Jang, oral solution

**(Soft extracts of**
***Justicia adhatoda* L., folium**
***Echinacea purpurea* (L.) Moench, radix**
***Eleutherococcus senticosus* (Rupr. et Maxim.) Maxim, radix)**

# Asp. No: 2008-0630

**This module reflects the scientific discussion for the approval of Kan Jang, oral solution. The procedure was finalised 24 June 2010. For information on changes after this date please refer to the module 'Update'.**

# LAY SUMMARY

The Medical Products Agency (Läkemedelsverket) has granted Bringwell AB, Stockholm, Sweden, a traditional-use registration for the herbal medicinal product Kan Jang, oral solution. This product is available without prescription and can be bought from pharmacies and other outlets.

Kan Jang is traditionally used for the relief of symptoms of common cold. The active ingredients are soft extracts from *Justicia adhatoda*, *Echinacea purpurea* and *Eleutherococcus senticosus*. This registration is based exclusively upon evidence of traditional use of the active substances contained in Kan Jang 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 Kan Jang could be registered as a traditional herbal medicinal product.

# I. INTRODUCTION

KG-Produkter AB, Göteborg, Sweden applied for a traditional-use registration for Kan Jang, oral solution. 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. During the procedure the Registration Holder (RH) was changed to Bringwell AB.

Kan Jang was authorised as a natural remedy (naturläkemedel) in 2006. The topic of the present application is re-classification to a traditional herbal medicinal product.

The active substances are soft extracts from:

- leaves of *Justicia adhatoda* (adhatoda, Swedish name: malabarnöt)
- roots of *Echinacea purpurea* (purple coneflower, Swedish name: röd solhatt) and
- roots of *Eleutherococcus senticosus* (eleutherococcus, Swedish name: rysk rot).

For approved indications, see the Summary of Product Characteristics (SmPC).

# II. QUALITY ASPECTS

## II.1 Introduction

Kan Jang is presented in the form of oral solution. 1 ml of the oral solution contains 14 mg *Justicia adhatoda* (adhatoda), leaf, soft extract (3.5-5.0:1) water; 9.3 mg *Echinacea purpurea* (purple coneflower), root, soft extract (2.5-7.0:1) ethanol 55 % and 2.14 mg *Eleutherococcus senticosus* (eleutherococcus), root, soft extract (17-30:1) 1) ethanol 70 % 2) water, which corresponds to approximately 60 mg dried leaves of *Justicia adhatoda* L., 44 mg dried root of *Echinacea purpurea* (L.) Moench and 50 mg dried root of *Eleutherococcus senticosus* (Rupr. et Maxim.) Maxim, respectively.

The excipients are:
Purified water, sorbitol, liquorice extract, hustenkräutaroma (propylene glycol, anethol, bitter-fennel fruit oil, eucalyptus oil, menthol, thyme oil), methyl parahydroxybenzoate, ginger extract, peppermint oil, polysorbate 80, eucalyptus oil, propyl parahydroxybenzoate, sodium benzoate and potassium sorbate.

Kan Jang oral solution is packed in glass bottles.

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

Specifications for the herbal substances *Echinacea purpurea* and *Eleutherococcus senticosus* comply with their respective monograph in the European Pharmacopoeia. *Justicia adhatoda* is controlled using an in-house specification.

The plants used are cultivated in Germany and China (*Echinacea purpurea*), collected from the wild in Pakistan (*Justicia adhatoda*) or collected from the wild in Russia and China (*Eleutherococcus senticosus*). Information on growing conditions and controls of the herbal substances (such as residues of heavy metals and pesticides as well as microbiological quality) has been provided.
The herbal drugs are cleaned and dried before further manufacturing to soft extracts.

For manufacturing reasons and preservation, the genuine extracts are mixed with sodium benzoate (*Justicia adhatoda*) or potassium sorbate and methyl parahydroxybenzoate (*Echinacea purpurea* and *Eleutherococcus* senticosus). The manufacturing process has been adequately described and satisfactory specifications have been provided for starting materials and solvents.

The specifications of the active substances (herbal preparations) include 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 for the eleutherococcus soft extract and the data provided are sufficient to confirm the retest period. The other extracts are tested according to specification prior to further manufacturing.

### II.3 Medicinal Product

Kan Jang oral solution is formulated using excipients described in the current European Pharmacopoeia, except for hustenkräuteraroma, liquorice extract and ginger extract which are controlled using internal specifications. 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 safety and efficacy of the combination of extracts contained in Kan Jang has not been evaluated by the Committee on Herbal Medicinal Products (HMPC). However, both *Echinacea purpurea* root and *Eleutherococcus senticosus* root have been evaluated, with regard to safety and efficacy, as single drug substances used for monotherapy. Also, the applicant has collected relevant information from the literature. This evaluation is based on information from the company as well as the HMPC evaluations.

### 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 the extracts in relation to their traditional medicinal use cannot be considered clarified.

A product specific study on mutagenic activity has been performed. The product 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 Kan Jang as a traditional herbal medicinal product.

## III.3 Ecotoxicity/environmental risk assessment

Kan Jang 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 the extracts contained in Kan Jang has a long tradition exceeding 30 years in the Community.

The applicant has provided a bibliographic review and expert evidence showing that Kan Jang has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the Community. The indication proposed for Kan Jang is consistent with the traditional use described in the literature.

## III.6 Clinical safety

The safety profile of Kan Jang is well known from its use for over 30 years as a marketed medicinal product in many countries world-wide with usage by many millions of patients.

Information about the large sales volumes of the extracts contained in Kan Jang, and a very long history of traditional use, indicate that Kan Jang, oral solution is generally safe under normal conditions of use. Reported adverse events are included in the SmPC.

Due to lack of adequate data in children, Kan Jang, oral solution cannot be recommended for use in children below the age of 12 years.

Due to lack of safety data, the use of Kan Jang, oral solution during pregnancy and lactation is not recommended.

Based on the clinical safety information available, no objections are raised to the approval of Kan Jang 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 Kan Jang, oral solution, the handling, manufacture and quality control of raw materials, active substances 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.

Two of the extracts in Kan Jang have been evaluated by the Committee on Herbal Medicinal Products (HMPC) but the combination of extracts has not. The applicant has provided evidence that the extracts in Kan Jang have 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.

Kan Jang, oral solution, can be recommended for registration as a traditional herbal medicinal product.

# VI. APPROVAL

Kan Jang, oral solution was approved in the national procedure on 24 June 2010.

# 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