Echinacin Juice MADAUS

THR 25843/0009

UKPAR

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ECHINACIN JUICE MADAUS

THR 25843/0009

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted MADAUS GmbH a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Echinacin Juice MADAUS (Traditional Herbal Registration number: THR 25843/0009) on 8 August 2012. Echinacin Juice MADAUS is available without prescription and can be bought from pharmacies and other outlets.

Echinacin Juice MADAUS is a traditional herbal medicinal product used to relieve the symptoms of the common cold and influenza type infections based on traditional use only. The active ingredient in Echinacin Juice MADAUS comes from the herb of the *Echinacea purpurea* plant, which is also known as *Echinacea purpurea* (L.) Moench.

This registration is based exclusively upon evidence of the use of *Echinacea purpurea* herb as a traditional herbal medicine and not upon data generated from clinical trials. There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product works.

No new or unexpected safety concerns arose from this application and it was, therefore, decided that a Traditional Herbal Registration Certificate could be granted.
ECHINACIN JUICE MADAUS

THR 25843/0009

SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Echinacin Juice MADAUS (THR 25843/0009) to MADAUS GmbH on 8 August 2012. This product is on the general sales list (GSL).

A Marketing Authorisation for this product was granted to MADAUS AG (under product licence number PL 04638/0007) on 15 June 1998. Following a Change of Ownership on 27 January 2008 the Marketing Authorisation was transferred to MADAUS GmbH (under product licence number PL 25843/0007). PL 25843/0007 was cancelled on 8 August 2012 when THR 25843/0009 was granted.

This THR application was made under Article 16.c of Directive 2001/83 EC in accordance with arrangements to transfer certain herbal products with a Marketing Authorisation to a THR (according to MHRA Guidance dated January 2009). The application falls within the simplified THR application Category A, as no significant changes have been made to the formulation of the product. No new data were submitted, nor was it necessary for this application, as the data are essentially identical to those of the existing product.
**PHARMACEUTICAL ASSESSMENT**

**HERBAL SUBSTANCE:**  
**ECHINACEA PURPUREA FRESH HERB**

**Scientific name of the plant:**  
Echinacea purpurea (L.) Moench

**Plant family:**  
Asteraceae

The herbal substance is controlled by a suitable specification and is, therefore, acceptable.

**HERBAL PREPARATION:**  
**ECHINACEA PURPUREA FRESH HERB DRIED PRESSED JUICE**

**Drug extract ratio (DER):**  
31.5 - 53.6: 1

The herbal preparation specification is in line with that applied to the herbal preparation used in the already licensed product. It is, therefore, acceptable.

**HERBAL PRODUCT:**  
**ECHINACIN JUICE MADAUS**

**Description and Composition of the Herbal Product**

Echinacin Juice MADAUS is a yellow to brown, viscous, oral solution. 5 ml of the solution contains 0.117 g of dried pressed juice from Echinacea purpurea fresh herb and the excipients xylitol, xanthan gum, potassium sorbate, citric acid, orange aroma and purified water. The formulation is identical to that of the already licensed product and is, therefore, acceptable.

**Manufacture**

The manufacturing process is in line with that of the already licensed product and is satisfactory.

**Finished Product Specification**

The finished product specification is in line with that of the already licensed product and is satisfactory.

**Container Closure System**

Echinacin Juice MADAUS is sold in 100 ml glass bottles. This type of packaging has been used to store the already licensed product and is satisfactory.

**Stability**

A product shelf-life of 3 years is applied to the product when stored in unopened bottles and a product shelf-life of 6 months is applied once the bottle is first opened. These shelf-lives were applied to the already licensed product and are appropriate. The storage precautions are ‘Do not store above 25°C’ and ‘Store in the original container’.
Summary of Product Characteristics, labels and Patient Information Leaflet
The text proposed for use in the Summary of Product Characteristics, labels and Patient Information Leaflet is in line with other products registered under the THR scheme and is acceptable.

No mock-ups or user test report are provided with this application, this is acceptable as this product is not currently marketed and the applicant has confirmed that prior to marketing an Article 61(3) application will be made for approval of the user tested leaflet and label mock-ups with Braille.

ASSESSOR’S OVERALL CONCLUSIONS
It is recommended that a Traditional Herbal Registration can be granted.
PRECLINICAL ASSESSMENT

INTRODUCTION
No new preclinical data have been supplied with this application and none is required for an application of this type.

Assurance has been given that the results of genotoxicity testing will be provided by the renewal date of the Traditional Herbal Registration.

PRODUCT LITERATURE
All product literature is satisfactory from a preclinical point of view.

ASSESSOR'S OVERALL CONCLUSIONS
It is recommended that a Traditional Herbal Registration can be granted.
CLINICAL ASSESSMENT

INTRODUCTION
The clinical particulars for Echinacin Juice MADAUS are identical to those for the already licensed product. This is satisfactory.

PRODUCT LITERATURE
All product literature is medically satisfactory.

ASSESSOR’S OVERALL CONCLUSIONS
It is recommended that a Traditional Herbal Registration can be granted.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
Echinacin Juice MADAUS is identical to an already licensed product. It is, therefore, pharmaceutically satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type. The results of genotoxicity testing will be provided before the THR is renewed.

EFFICACY
No clinical efficacy data are required for registration of Traditional Herbal Medicinal Products.

SAFETY
No new or unexpected safety concerns arose from this application.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The benefit: risk balance is acceptable and a THR should be granted.
ECHINACIN JUICE MADAUS

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STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Traditional Herbal Registration application on 21 February 2012
2 Following standard checks and communication with the applicant the MHRA considered the application valid on 14 March 2012
3 Following assessment of the application the MHRA requested further information relating to the dossier on 23 March 2012
4 The applicant responded to the MHRA’s requests, providing further information on the dossier on 23 June 2012
5 A THR was granted on 8 August 2012
1 NAME OF THE MEDICINAL PRODUCT
Echinacin Juice MADAUS

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
5 ml of oral liquid contains 0.117 g of dried pressed juice from Echinacea purpurea (fresh herb) [31.5 - 53.6 : 1] equivalent to 3.7 – 6.3 g Echinacea purpurea (L.) Moench).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Oral solution (yellow to brown, viscous liquid)

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used to relieve the symptoms of the common cold and influenza type infections, based on traditional use only.

4.2 Posology and method of administration
For oral use only.
Start at first signs of a common cold.
Adults, the elderly and children over 12 years:
one 5 ml teaspoonful to be taken 3 times a day.
Duration of use:
Do not take this product for more than ten days.
If symptoms worsen or persist for more than ten days or high fever occurs, a doctor or qualified healthcare practitioner should be consulted.
Not recommended for use in children under 12 years (see section 4.4 special warnings and precautions for use)

4.3 Contraindications
Hypersensitivity to the active substance or to plants of the Asteraceae (Compositae) family, e.g. daisies, marigolds, artichokes.
Because of its immunostimulating activity, Echinacea must not be used in cases of progressive systemic disorders (tuberculosis, sarcoidosis), autoimmune diseases (e.g.: collagenoses, multiple sclerosis), immunodeficiencies (e.g.: HIV infection; AIDS), immunosuppression (e.g.: oncological cytostatic therapy; history of organ or bone marrow transplant), diseases of the white blood cell system (e.g.: agranulocytosis, leukemias) and allergic diathesis (e.g.: urticaria, atopic dermatitis, asthma).

4.4 Special warnings and precautions for use
Do not exceed the stated dose.
If symptoms worsen or persist for more than ten days or high fever occurs, a doctor or qualified healthcare practitioner should be consulted.
There is a possible risk of anaphylactic reactions in atopic patients. Atopic patients should consult their doctor or qualified healthcare practitioner before using Echinacea.
This product is not recommended for children under 12 years of age because data are not sufficient and medical advice should be sought.

4.5 Interaction with other medicinal products and other forms of interaction
Not to be used concomitantly with immunosuppressant medications such as ciclosporin and methotrexate.

4.6 Pregnancy and lactation
Safety during pregnancy and lactation has not been established. In the absence of sufficient data the use in pregnancy and lactation is not recommended.
Limited data (several hundreds of exposed pregnancies) indicate no adverse effects of Echinacea on pregnancy or on the health of the foetus/newborn child. Data concerning the immune system of the newborn child are not available. To date, no other relevant epidemiological data are available. The potential risk for humans is unknown.
No studies have been performed on fertility.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Hypersensitivity reactions (skin rash, urticaria, Stevens-Johnson Syndrome, angioedema of the skin, Quincke edema, bronchospasm with obstruction, asthma and anaphylactic shock) have been reported.
Echinacea can trigger allergic reactions in atopic patients.
Association with autoimmune diseases (encephalitis disseminata, erythema nodosum, immunothrombocytopenia, Evans Syndrome, Sjögren syndrome with renal tubular dysfunction) has been reported.
Leucopenia may occur in long-term use (more than 8 weeks). The frequency is not known.
If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

4.9 Overdose
No cases of overdose have been reported

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Not required as per Article 16 c (1) (a) (iii) of Directive 2001/83/EC as amended
5.2 Pharmacokinetic properties
Not required as per Article 16 c (1) (a) (iii) of Directive 2001/83/EC as amended

5.3 Preclinical safety data
Echinacea purpurea showed no toxicity in single-dose toxicity (rodents), repeated dose toxicity (rodents) and genotoxicity studies. Tests on reproductive toxicity and on carcinogenicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Xylitol
Xanthan gum
Potassium sorbate
Citric acid
Orange aroma
Purified water

6.2 Incompatibilities
None known

6.3 Shelf life
3 years.
Shelf life after first opening: 6 months

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Glass bottles containing 100 ml.

6.6 Special precautions for disposal
No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER
MADAUS GmbH
51101 Cologne
Germany

8 MARKETING AUTHORISATION NUMBER(S)
THR 25843/0009
9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
08/08/2012

10 DATE OF REVISION OF THE TEXT
08/08/2012
PATIENT INFORMATION LEAFLET

The following text is the approved Patient Information Leaflet (PIL) text. No PIL mock-ups have been provided. In accordance with medicines legislation, the product shall not be marketed until approval of the PIL mock-ups has been obtained.
PATIENT INFORMATION LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

ECHINACIN JUICE MADAUS

Oral solution
Active substance: Dried pressed juice from Echinacea purpurea herb

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to take Echinacin Juice MADAUS carefully to get the best results from it.

Keep this leaflet. You may need to read it again. Ask your pharmacist if you need more information or advice. You must contact a doctor if your symptoms worsen or do not improve after ten days. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet please tell your doctor or pharmacist.

In this leaflet:
1. What this product is and what it is used for
2. Before you take Echinacin Juice MADAUS
3. How to take Echinacin Juice MADAUS
4. Possible side effects
5. How to store Echinacin Juice MADAUS
6. Further information

1. WHAT THIS PRODUCT IS AND WHAT IT IS USED FOR

Echinacin Juice MADAUS is a traditional herbal medicinal product used to relieve the symptoms of:

- Colds
- Flu.

This is based on traditional use only.

2. BEFORE YOU TAKE ECHINACIN JUICE MADAUS

Do not take Echinacin Juice MADAUS

- If you are allergic (hypersensitive) to the active substance or to plants of the daisy family, or any of the other ingredients of Echinacin Juice MADAUS (Please see section 6, Further information)
- if you have a tendency to allergies such as hives, allergic eczema or asthma
- suffer from the infection tuberculosis
- suffer from connective tissue disease with formation of clumps of cells (sarcoidosis), mainly occurring in the lymph nodes, lung and liver
- suffer from autoimmune diseases such as inflammation of the connective tissue (collagenoses) or multiple sclerosis
- suffer from conditions which decrease your resistance to infections (e.g. HIV infections or AIDS) or are on therapy to reduce your natural response to infection (immunosuppression e.g. chemo therapy for cancer, history oof organ or bone marrow transplant)
• suffer from blood disorders involving the white blood cell system such as low white blood cell count due to bone marrow disorders (granulocytosis) or blood cell cancer (leukemias).

Do not give Echinacin Juice MADAUS to children below 12 years of age.

Take special care with Echinacin Juice MADAUS
- if the symptoms worsen or high fever occurs while using this product, consult your doctor or pharmacist.
There is a possible risk of anaphylactic reactions in people who are prone to allergies. If you have suffered from hypersensitivity reactions in the past, consult your doctor before using Echinacin Juice MADAUS.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
Do not take Echinacin Juice MADAUS with:
• medicines that suppress your immune system (such as ciclosporin and methotrexate).

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
There are only limited data on the use of this medicine during pregnancy and breast-feeding. Therefore, the use in pregnancy and breast-feeding is not recommended.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed.

3. HOW TO TAKE ECHINACIN JUICE MADAUS
Always take Echinacin Juice MADAUS as described in this leaflet. You should check with your doctor or pharmacist if you are not sure.
The usual dose is:
Adults, the elderly and children over 12 years: one 5 ml teaspoonful to be taken 3 times a day with sufficient liquid.
Start taking it at the first signs of a common cold. Echinacin Juice MADAUS should not be used for longer than 10 days.

If you take more Echinacin Juice MADAUS than you should
No cases of overdose with preparations containing Echinacea purpurea herba (purple coneflower) are known to date.
Eventually the side effects described in section 4 may increasingly occur. In this case, please inform a doctor, who will decide on any measures to be taken.

If you forget to take Echinacin Juice MADAUS
If you have not taken enough Echinacin Juice MADAUS or if you have forgotten to take it, do not take a double dose to make up for a missed dose but continue taking the medicine as described in this leaflet.
If you have any further questions on the use of this product, ask your doctor or pharmacist.
4. POSSIBLE SIDE EFFECTS
Like all medicines, Echinacin Juice MADAUS can cause side effects, although not everybody gets them.

Stop taking Echinacin Juice MADAUS and consult your doctor at once if one of the following side effects occur:

- allergic reactions such as itching (hives), rash
- difficulty in breathing (bronchospasm with obstruction)
- asthma or allergic shock (a life-threatening allergic reaction)
- inflammatory disorder of the skin (Steven-Johnson-Syndrome)
- swelling of the skin due to fluid (angioedema) or swelling of the facial area (Quincke’s oedema).

Echinacea can trigger allergic reactions people who are prone to allergies.

Other side effects
There have been isolated reports suggesting an association between Echinacea products and autoimmune diseases which can cause:

- confusion, delirium, loss of consciousness (disseminated encephalitis)
- reddish, painful, tender lumps on the skin usually below the knees (erythema nodosum)
- blood disorders with bruising, bleeding, purple rashes (immunothermocytopenia, and Evans Syndrome)
- general dryness including reduced tears and saliva, with kidney problems (Sjögren syndrome with renal tubular dysfunction)

A low white blood cell count (leucopenia) may occur in long-term use (more than 8 weeks). This may mean you are more likely to have infections.

The frequency of these side effects is not known.

If any of the side effects gets serious, or if symptoms persist for more than 10 days, or if you notice any side effects not listed in this leaflet, consult your doctor or pharmacist.

You can help to make medicines safer by reporting any side-effects to the Yellow Card Scheme at www.mhra.gov.uk/yellowcard. Alternatively you can get a paper Yellow Card form from your GP’s surgery or pharmacy, or call freephone 0808 100 3352 (available 10am-2pm Monday – Friday).

5. HOW TO STORE ECHINACIN JUICE MADAUS
Keep out of the sight and reach of children.

Do not store above 25 °C. Keep in the original container.

After opening the container, Echinacin Juice MADAUS should be used within 6 months.

Do not use Echinacin Juice MADAUS after the expiry date which is stated on the label and on the carton after “EXP”. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines which are no longer required. These measures will help to protect the environment.
6. FURTHER INFORMATION

What Echinacin Juice MADAUS contains

The active substance is:
dried pressed Juice from fresh flowering Echinacea purpurea herb (31.5-53.6:1).
100 g contain 2.34 g dried pressed juice from fresh flowering Echinacea purpurea herb.

The other ingredients are:
Potassium sorbate, Citric acid anhydrous, Xanthan gum, Xylitol, Orange flavour, Water.

5 ml Echinacin Juice MADAUS correspond to 2.5 ml pressed juice from fresh flowering purple coneflower herb.

What Echinacin Juice MADAUS looks like and contents of the pack

Viscous yellow to brown solution in amber glass bottles of 100 ml.

Traditional Registration Holder and Manufacturer

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51101 Cologne, Germany
Telephone: 0221/8998-0
Fax: 0221/8998-711
e-mail: info@rottapharm-madaus.de

Distributed by

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Solihull, West Midlands, B91 1 NF

This leaflet was last revised in July 2012.
Echinacin is a trade mark.
LABELLING

The following text is the approved label text. No label mock-ups have been provided. In accordance with medicines legislation, the product shall not be marketed until approval of the label mock-ups has been obtained.

### PARTICULARS TO APPEAR ON THE OUTER AND IMMEDIATE PACKAGING

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT</th>
</tr>
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<tbody>
<tr>
<td>Echinacin Juice MADAUS</td>
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</table>

<table>
<thead>
<tr>
<th>2. STATEMENT OF ACTIVE SUBSTANCE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active ingredient: Dried pressed juice from fresh flowering Echinacea purpurea [31.5 : 53.6 : 1] 100 ml contains dried pressed juice from fresh flowering Echinacea purpurea herb 2.34 g 5 ml contains the juice from 3.7 – 6.3 g fresh plant</td>
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</tbody>
</table>

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<tr>
<th>3. LIST OF EXCIPIENTS</th>
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<tbody>
<tr>
<td>Potassium sorbate, Citric acid anhydrous, Xanthan gum, Xylitol, Orange flavour, Water.</td>
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</table>

<table>
<thead>
<tr>
<th>4. PHARMACEUTICAL FORM AND CONTENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral solution</td>
</tr>
<tr>
<td>Contents</td>
</tr>
<tr>
<td>100 ml</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. METHOD AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>For oral use only</td>
</tr>
<tr>
<td>Read the package leaflet before use.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN</th>
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</thead>
<tbody>
<tr>
<td>Keep out of the sight and reach of children</td>
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<tr>
<th>7. OTHER SPECIAL WARNING(S), IF NECESSARY</th>
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<tbody>
<tr>
<td>Do not use if the bottle seal is broken when purchased. Like other natural plant preparations cloudiness or settling may occur. This is a natural process and does not affect the quality and efficacy of the product.</td>
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<table>
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<tr>
<th>8. EXPIRY DATE</th>
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</thead>
<tbody>
<tr>
<td>EXP: MM/YYYY</td>
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<tr>
<td>Shelf-life after first opening: 6 months.</td>
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<tr>
<th>9. SPECIAL STORAGE CONDITIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not store above 25°C.</td>
</tr>
</tbody>
</table>
Keep in the original container.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPLICABLE**
    N/A

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**
    MADAUS GmbH
    51101 Cologne
    Germany

12. **MARKETING AUTHORISATION NUMBER(S)**
    THR 25843/0009

13. **BATCH NUMBER**
    Batch no: [combination of a letter followed by 7 numbers]

14. **GENERAL CLASSIFICATION FOR SUPPLY**
    GSL

15. **INSTRUCTIONS ON USE**

   Echinacin Juice MADAUS is a traditional herbal medicinal product to relieve the symptoms of the common cold and influenza type infections based on traditional use only.

   **Dosage**
   Start at first signs of a common cold.

   Adults, the elderly and children over 12 years: one 5 ml teaspoonful to be taken 3 times a day.
   Do not take this product for more than ten days.
   If symptoms worsen or persist for more than ten days or high fever occurs, see your doctor or pharmacist.
   Not recommended for use in children under 12 years.
   This product does not contain any alcohol.

   ![Certification Mark]

MHRA PAR; ECHINACIN JUICE MADAUS, THR 25843/0009 21