Care Dry Cough Oral Solution for Children

PL 00240/0362

UKPAR

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LAY SUMMARY

The Medicine and Healthcare Regulatory Agency (MHRA) granted Thornton & Ross Limited a Marketing Authorisation (licence) for the medicinal product Care Dry Cough Oral Solution for Children on 26 August 2010. This is a general sales list (GSL) medicine, available to the general public without prescription and used for the relief of dry, irritating coughs.

Care Dry Cough Oral Solution for Children contains the active ingredient citric acid monohydrate, which is a demulcent. It coats the throat and relieves dry irritating coughs.

This application is an abridged simple (duplicate) application, referring to the previously granted application for Simple Linctus Paediatric BP (PL 00240/6427R), which was granted a product licence of right to Thornton & Ross Limited in 1972.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Care Dry Cough Oral Solution for Children outweigh the risks, hence a Marketing Authorisation has been granted.
CARE DRY COUGH ORAL SOLUTION FOR CHILDREN
PL 00240/0362

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a Marketing Authorisation for the medicinal product Care Dry Cough Oral Solution for Children (PL 00240/0362) to Thornton & Ross Limited on 26 August 2010. The product is available as a general sales list (GSL) medicine and is used for the relief of non-productive (dry) coughs.

The application was submitted as a simple abridged application, according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Simple LinctusPaediatric BP (PL 00240/6427R), which was granted a product licence of right to Thornton & Ross Limited in 1972.

No new data was submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product.

The product contains the active ingredient citric acid monohydrate BP, which is an acid preparation used for relief of non-productive (dry) coughs.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 00240/0362
PROPRIETARY NAME: Care Dry Cough Oral Solution for Children
ACTIVE(S): Citric acid monohydrate
COMPANY NAME: Thornton & Ross Limited
LEGAL STATUS: GSL

1. INTRODUCTION
This is an abridged simple, piggyback application for Care Dry Cough Oral Solution for Children submitted under Article 10c of Directive 2001/83/EC. The proposed Marketing Authorisation Holder is Thornton & Ross Limited, Linthwaite, Huddersfield, West Yorkshire, HD7 5QH, United Kingdom.

The application cross-refers to Simple Linctus Paediatric BP (PL 00240/6427R), which was granted a product licence of right to Thornton & Ross Limited in 1972.

The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed name of the product is Care Dry Cough Oral Solution for Children. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product contains citric acid monohydrate BP, equivalent to 31.25mg/5ml. It is to be stored in either a:
- amber glass bottle, sealed with a plastic cap and liner in pack sizes of 100, 200, 500 and 2000ml
- amber glass bottle, sealed with white child-resistant cap, tamper evident band and expanded polyethylene/Saranex liner in pack sizes of 100, 200 and 500ml.

It has been stated that not all pack sizes may be marketed, however, the marketing authorisation holder has committed to submitting the mock-ups for any pack size to the relevant regulatory authorities for approval before marketing.

The proposed shelf-life (36 months unopened and 3 months after first opening) and storage conditions (“Do not store above 25°C”, additionally the 2000ml pack has, “Do not store part full bottles. Pre-pack in tightly closed dispensing containers once opened”) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a general sales list (GSL) medicine.

2.4 Marketing Authorisation Holder/Contact Persons/Company
Thornton and Ross Limited, Linthwaite, Huddersfield, West Yorkshire, HD7 5QH, United Kingdom.
The qualified person responsible for pharmacovigilance is stated and their CV is included.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
No materials of animal or human origin are included in the product. This is consistent with the cross-reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula utilising the same process as the cross-reference product Simple Linctus Paediatric BP (PL 00240/6427R).

3. EXPERT REPORTS
The applicant cross-refers to the data for Simple Linctus Paediatric BP (PL 00240/6427R), to which it claims identicality. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The proposed Summary of Product Characteristics is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL)/LABEL (combined)
The patient information leaflet/label has been prepared in-line with the details registered for the cross-reference product.
The applicant has previously submitted results of PIL user testing for the reference product Simple Linctus Paediatric BP (PL 00240/6427R). The results indicate that the leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains. As the leaflet for the reference product and this product is considered the same, no further user testing of the leaflet for this product is necessary.

The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In-line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging.

7. CONCLUSIONS
The data submitted with the application are acceptable. The grant of a marketing authorisation is recommended.
PRECLINICAL ASSESSMENT

No new preclinical data have been submitted with this application and none are required for an application of this type.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As the application is for an identical version of an already authorised reference product, it is not expected that the environmental exposure to citric acid monohydrate will increase following the marketing approval of the product.
CLINICAL ASSESSMENT

No new clinical data have been submitted with this application and none are required for an application of this type.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the Marketing Authorisation Holder has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Marketing Authorisation Holder has provided an adequate justification for not submitting a Risk Management Plan (RMP). As the application is for an identical version of an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for this application is consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
This application is identical to a previously granted application for Simple Linctus Paediatric BP (PL 00240/6427R).

No new or unexpected safety concerns arise from this application.

The SPC and combined leaflet/label are satisfactory and consistent with that for the cross-reference product.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with citric acid monohydrate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
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<thead>
<tr>
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<th>The MHRA received the marketing authorisation application on 10 March 2009.</th>
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<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 20 March 2009.</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 02 October 2009, 29 April 2010 and 30 June 2010.</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on 29 April 2010, 02 June 2010 and 24 July 2010.</td>
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<td>5</td>
<td>The application was determined on 26 August 2010.</td>
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### STEPS TAKEN AFTER ASSESSMENT

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<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Care Dry Cough Oral Solution for Children

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Citric Acid Monohydrate BP 31.25mg/5ml dose.
Excipients: Sucrose (syrup) 4.3g per 5ml. Ethanol (Alcohol) 1.5 vol %.
For full list of excipients see section 6.1

3 PHARMACEUTICAL FORM
Oral Solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
For relief of non productive (dry) coughs

4.2 Posology and method of administration
Oral.
Children’s Dosage
1 to 5 years: Give one 5ml spoonful.
6 to 12 years: Give two 5ml spoonfuls.
Repeat up to four times a day if necessary.

4.3 Contraindications
Hypersensitivity to any of the ingredients.

4.4 Special warnings and precautions for use
Keep out of the reach and sight of children
Consult a doctor if symptoms persist for more than 5 days
Contains 1.5% vol ethanol (alcohol) i.e. up to 118mg per 10ml dose, equivalent to 3ml beer and of
1ml wine per dose. Harmful if suffering from alcoholism. To be taken into account in pregnant or
breast feeding women, children and high-risk groups such as patients with liver disease or epilepsy.
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or
sucrase-isomaltase insufficiency should not take this medicine.
Also contains 8.6g of sucrose per 10ml. This should be taken into account in patients with diabetes.

4.5 Interaction with other medicinal products and other forms of interaction
None known.

4.6 Pregnancy and lactation
There are no or limited amount of data from the use of citric acid monohydrate in pregnant women.
Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).
There is insufficient information on the excretion of citric acid monohydrate metabolites in human
milk.

4.7 Effects on ability to drive and use machines
There are no known side effects from using this medicine when used as directed, however, if you
notice and side effects, stop use and consult a doctor or pharmacist.

4.8 Undesirable effects
There are no known side effects from using this medicine when used as directed, however, if you
notice any side effects, stop use and consult a doctor or pharmacist.
4.9  Overdose
Overdose with this preparation is unlikely to occur due to the low concentrations of the ingredients. However, in the event treatment should be symptomatic.

5  PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic Group: Acid Preparations
ATC Code: A09 AB

5.2 Pharmacokinetic properties
Citric acid is absorbed after oral administration. It is found naturally in the body and is widely distributed. It is metabolised to carbon dioxide and water in Kreb’s citric acid cycle. Citric acid is normally excreted in the urine in amounts ranging from 0.4 to 1.5g daily and this amount is not increased unless very large doses are administered.

5.3 Preclinical safety data
No data of relevance, which is additional to that included on other sections of the SPC.

6  PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Chloroform
Anise oil
Ethanol (96%)
Glycerol (E422)
Purified water
Syrup.

6.2 Incompatibilities
None.

6.3 Shelf life
100ml: 36 months unopened, 3 months after first opening.
200ml: 36 months unopened, 3 months after first opening.
500ml: 36 months unopened, 3 months after first opening.
2000ml: 36 months unopened, 3 months after first opening.

6.4 Special precautions for storage
Do not store above 25°C
The following additional phrases appear on the 2 litre pack:
Do not store part full bottles.
Pre-pack in tightly closed dispensing containers once opened.

6.5 Nature and contents of container

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<tr>
<th>Volume</th>
<th>Description</th>
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<tr>
<td>100ml</td>
<td>Amber glass bottle with plastic cap and liner or white 28mm Child-resistant cap with Tamper Evident band and EPE/Saranex liner</td>
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<tr>
<td>200ml</td>
<td>Amber glass bottle with plastic cap and liner or white 28mm Child-resistant cap with Tamper Evident band and EPE/Saranex liner</td>
</tr>
<tr>
<td>500ml</td>
<td>Amber glass bottle with plastic cap and liner or white 28mm Child-resistant cap with Tamper Evident band and EPE/Saranex liner</td>
</tr>
<tr>
<td>2000ml</td>
<td>Amber glass bottle with plastic cap and liner.</td>
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6.6 Special precautions for disposal
Any unused product or waste material should be dispersed of in accordance with local requirements.
MARKETING AUTHORISATION HOLDER
Thornton & Ross Ltd.
Linthwaite Laboratories
Huddersfield
HD7 5QH.

MARKETING AUTHORISATION NUMBER(S)
PL: 00240/0362

DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
26/08/2010

DATE OF REVISION OF THE TEXT
26/08/2010
IMPORTANT: Peel this label at corner and read BEFORE use. Do not tear off, re-fix for future use.

For relief of dry, irritating coughs.
Take the solution by mouth.
Children 1-5 years: Give 1 x 5ml spoonful.
Children 6-12 years: Give 2 x 5ml spoonfuls.
Repeat the dose up to four times a day if necessary.
If symptoms persist for more than 5 days consult a doctor.

Peel where shown for further precautions.
Active ingredient per 5ml: citric acid monohydrate (E330) 31.25 mg.

Also contains amongst other ingredients: ethanol, glycerol (E422) and sucrose.
Sucrose 4.2g per 5ml, alcohol 1.5 vol%.

Peel where shown for full list of ingredients.
Do not store above 25°C.
Once opened, use within three months.
Keep out of the reach and sight of children.
Manufactured by the licence holder: Thornton and Ross Ltd., Huddersfield, HD7 5QH, UK.
PL 00240/0362
M546
200ml
This medicine is a demulcent. It coats the throat and relieves dry irritating coughs.

**1. Before you use this medicine**

Avoid using this medicine if your child has...

- An allergy to any of the ingredients listed in section 3.

**Pregnant or breastfeeding**

Ask your doctor or pharmacist for advice before using this medicine if you are pregnant, might be pregnant or are breastfeeding. Care Dry Cough Oral Solution for Children should not be used in pregnancy unless the doctor has told you to do so.

**Important ingredient information**

- This product contains 8.6g of sucrose per 10ml dose. To be taken into account in people with diabetes. If you have been told by your doctor that your child has an intolerance to some sugars, contact your doctor before giving this medicine.
- It also contains 1.5 vol% ethanol (alcohol), i.e. up to 118mg per 10ml dose, equivalent to 3ml of beer or 1ml of wine per dose. Harmful to those suffering from alcoholism. To be taken into account in pregnant or breastfeeding women, children and high risk groups such as patients with liver disease or epilepsy.

**2. Possible side effects**

There are no known side effects from using this medicine when used as directed.
- If taken excessively above the stated dose, glycerrhizal present in the medicine may cause headache, stomach upset and diarrhoea.
- If you notice any side effects, stop use and tell your doctor or pharmacist. They will tell you what to do.

M546
3. Further information

⚠️ If you accidentally give too much see a doctor straight away. Take the pack with you to show which medicine your child has swallowed.
- Do not use after the expiry date. The expiry date refers to the last day of that month.
- Return any unused medicine to the pharmacy for disposal.

The active ingredient per 5ml is: citric acid monohydrate (E330) 31.25mg.
The other ingredients are: chloroform, anise oil, ethanol, glycerol (E422), sucrose and purified water.

What the medicine looks like:
Care Dry Cough Oral Solution for Children is a colourless syrupy liquid.
It is supplied in 200ml bottles.
This label was revised in July 2010.
M54S