# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lay Summary</td>
<td>2</td>
</tr>
<tr>
<td>Scientific discussion</td>
<td>3</td>
</tr>
<tr>
<td>Steps taken for assessment</td>
<td>11</td>
</tr>
<tr>
<td>Steps taken after authorisation – summary</td>
<td></td>
</tr>
<tr>
<td>Summary of Product Characteristics</td>
<td>12</td>
</tr>
<tr>
<td>Product Information Leaflet/Labelling</td>
<td>15</td>
</tr>
</tbody>
</table>
THORNTON & ROSS BRONCHIAL BALSAM SYRUP  
(dextromethorphan hydrobromide and menthol)  
PL 00240/0365

LAY SUMMARY

The MHRA granted Thornton & Ross Limited a Marketing Authorisation (licence) for the medicinal product Thornton & Ross Bronchial Balsam Syrup on 25 August 2010. This is a pharmacy (P) medicine for the relief of the symptoms of dry coughs from colds and bronchitis.

Thornton & Ross Bronchial Balsam Syrup contains the active ingredients dextromethorphan hydrobromide and menthol. Dextromethorphan hydrobromide reduces the desire to cough and menthol relieves irritation, reduces congestion, and helps you breathe more easily.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Thornton & Ross Bronchial Balsam Syrup outweigh the risks; hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction Page 4
Pharmaceutical assessment Page 5
Non-clinical assessment Page 8
Clinical assessment Page 9
Overall conclusions and risk assessment Page 10
INTRODUCTION

The UK granted a Marketing Authorisation for the medicinal product Thornton & Ross Bronchial Balsam Syrup PL 00240/0365 to Thornton & Ross Limited on 25 August 2010. The product is available as a pharmacy (P) medicine and is indicated for the symptomatic relief of non-productive coughs, such as those associated with the common cold and bronchitis.

The application was submitted as an abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. This application cross-refers to Covonia Original Balsam (PL 00240/5033R), which was granted a product licence of right to the same Marketing Authorisation Holder in May 1972.

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

The product contains the active ingredients dextromethorphan hydrobromide and menthol. Dextromethorphan hydrobromide acts as a non-narcotic cough suppressant. Menthol relieves irritation, diminishes congestion and checks excessive secretion of mucous membranes in the upper respiratory tract.
1. INTRODUCTION
This is a simple, piggyback application for Thornton & Ross Bronchial Balsam Syrup submitted under Article 10c of Directive 2001/83/EC. The proposed Marketing Authorisation Holder is Thornton & Ross Limited, Linthwaite, Huddersfield, HD7 5QH.

The application cross-refers to Covonia Original Bronchial Balsam (PL 00240/5033R) which was granted (a product licence of right) to Thornton & Ross Limited in May 1972. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)
The proposed name of the product is Thornton & Ross Bronchial Balsam Syrup. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each 5ml of syrup contains 7.5mg dextromethorphan hydrobromide and 2.5 mg menthol. The product is packaged in 150ml flat sloping shoulder amber glass bottles, with tamper-evident child-resistant closures and expanded polyethylene/Saranex liner.

The proposed shelf-life (36 months unopened) and storage conditions (Do not store above 25°C) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a pharmacy-only (P) medicine.

2.4 Marketing Authorisation Holder/Contact Persons/Company
Thornton & Ross Limited, Linthwaite, Huddersfield, HD7 5QH.

The qualified person responsible for pharmacovigilance is stated and his CV is included.

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

All aspects of the manufacture and control of the active substances dextromethorphan hydrobromide and menthol are covered by European Directorate for the Quality of Medicines (EDQM) Certificates of Suitability.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin.

2.11 Bioequivalence
No bioequivalence data are required to support this application, as the proposed product is manufactured to the same formula and utilising the same process as the reference product Covonia Original Bronchial Balsam (PL 00240/5033R)

3. EXPERT REPORTS
The applicant cross-refers to the data for Covonia Original Bronchial Balsam (PL 00240/5033R), 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
The proposed Summary of Product Characteristics is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING
PIL-Label
The patient information leaflet (label-leaflet) has been prepared in-line with the details registered for the cross-reference product and is attached to the product information provided for the bottle label

The applicant has previously submitted results of consultations with target patient groups (“user testing”), in accordance with Article 59 of Council Directive 2001/83/EC for the reference product Covonia Original Bronchial Balsam (PL 00240/5033R). The results indicate that the label-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 label-leaflet for Covonia Original Bronchial Balsam (PL 00240/5033R) and this product are considered the same, no further user testing of the label-leaflet for this product is necessary.

**Bottle label**
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. **CONCLUSION**
The data submitted with the application are acceptable. A Marketing Authorisation should be granted.
NON-CLINICAL ASSESSMENT
As this is an abridged simple application, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided an adequate justification for not submitting an Environment Risk Assessment (ERA), given that this is an application for a duplicate licence for a product that will lead to a very limited increase in environmental exposure to its drug substances and excipients.
**CLINICAL ASSESSMENT**

As this is an abridged simple application, no new clinical data have been supplied and none are required.

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

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

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type.

EFFICACY
This application is identical to a previously granted application for Covonia Original Bronchial Balsam (PL 00240/5033R). No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling 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 dextromethorphan hydrobromide and menthol is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
THORNTON & ROSS BRONCHIAL BALSAM SYRUP
(dextromethorphan hydrobromide and menthol)
PL 00240/0365

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the marketing authorisation application on 19 November 2009.
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 07 December 2009.
3. Following assessment of the application the MHRA requested further information relating to the dossier on 07 May 2008 and 21 July 2010.
4. The applicant responded to the MHRA’s requests, providing further information on 21 July 2010 and 05 August 2010.
5. The application was determined on 25 August 2010.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Thornton & Ross Bronchial Balsam Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Dextromethorphan Hydrobromide BP 7.5mg/5ml
Menthol BP 2.5mg/5ml

This medicinal product contains small amounts of ethanol (alcohol), less than 100mg per 10ml dose. Contains 3.07g sucrose per 5ml dose, to be taken into account in people with diabetes.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Syrup

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
For the symptomatic relief of non-productive coughs such as those associated with the common cold and bronchitis.

4.2 Posology and method of administration
Oral

Recommended doses
Adults and children over 12 years: 10ml
Elderly: as adults dose with caution

Dosage schedule
The dose may be repeated after 4 hours if required.

4.3 Contraindications
Contraindicated in patients with liver disease and/or known hypersensitivity to dextromethorphan hydrobromide, and menthol. Patients being treated with monoamine oxidase inhibitors should avoid using the product. Persistent or productive cough. Dextromethorphan should not be administered to patients in or at risk of developing respiratory failure or during an acute asthma attack. Do not use within 2 weeks of discontinuation of MAOI use.

Children under 12 years of age.

4.4 Special warnings and precautions for use
Do not exceed the stated dose.
Keep out of the reach and sight of children.
If symptoms persist consult your doctor.
Thornton & Ross Bronchial Balsam Syrup normally works without causing drowsiness, but care should be taken initially as rare exceptions can occur.
Use with caution in a history of asthma.
Label states: Consult a doctor or pharmacist before use if you have a history of asthma.
Do not give to children under 12 years.
This medicinal product contains small amounts of ethanol (alcohol), less than 100mg per 10ml dose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-Isomaltase insufficiency should not take this medicine.
Contains 3.07g sucrose, to be taken into account in people with diabetes.
4.5 Interaction with other medicinal products and other forms of interaction
Cimetidine may delay the elimination of dextromethorphan. It is therefore imperative that the dose of Thornton & Ross Bronchial Balsam Syrup is not exceeded when it is taken with other medicines. Dextromethorphan interacts with MAOI’s.

4.6 Pregnancy and lactation
There is no evidence of safety in human pregnancy. However, the drugs in the formulation have been widely used for many years without apparent ill consequence. No information is available on the excretion of dextromethorphan or its metabolites in breast milk. It is therefore best avoided during breastfeeding.

4.7 Effects on ability to drive and use machines
At the stated dose, no evidence has been found that the formulation has any effect on the ability to drive or use machinery however dextromethorphan hydrobromide may cause dizziness and drowsiness rarely.

4.8 Undesirable effects
At the stated dose constipation, gastrointestinal discomfort, nausea, vomiting, dizziness and drowsiness may occur rarely.

4.9 Overdose
Serious overdoses have been reported with other dextromethorphan containing products. Taken in large doses, may cause drowsiness, dizziness, excitation, nausea, vomiting, gastrointestinal disturbance, blurred vision, nystagmus, ataxia, urinary retention, stupor, coma, facial oedema and urticaria. Very large doses may produce respiratory depression and some patients may be particularly sensitive to this. This may be combated with trial small doses (1.5 - 3UG/KG to be repeated only if there is a response) of morphine antagonists such as naloxone. Symptoms arising from oral poisoning with menthol are severe abdominal pain, nausea, vomiting, vertigo, ataxia, drowsiness and coma.

Treatment of overdose: acutely, gastric lavage: otherwise, general supportive measures should be used.

Dependence has been reported occasionally with dextromethorphan.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Cough suppressants and expectorants, combinations.
ATC Code: RO5F

Dextromethorphan acts as a non-narcotic cough suppressant. The drug acts centrally to elevate the threshold for coughing.

Menthol relieves irritation, diminishes congestion and checks excessive secretion of mucous membranes in the upper respiratory tract and is used for the treatment of the symptoms of bronchitis.

5.2 Pharmacokinetic properties
Dextromethorphan is fully absorbed from the gastro-intestinal tract and passes via the portal vein to the liver before entering the general circulation. Dextromethorphan has three metabolites, principally dextrorphan which has approximately the same antitussive potency as dextromethorphan itself. Dextromethorphan is not metabolised to either morphine or codeine. In general, approximately 50% of dextromethorphan plus metabolites is excreted in the urine within 24 hours. Plasma levels of therapeutic doses are very low, due to metabolism in the liver. Plasma levels of the principal metabolite, dextrorphan, are higher than dextromethorphan, plasma levels reaching a peak 2 hours after administration. The plasma half life of dextrorphan has been determined as approximately 0.5 – 1.0 hour in the dog.

After absorption menthol is excreted in the urine and bile as a glucuronide.
5.3 Preclinical safety data
None

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Water purified
Citric acid monohydrate (E330)
Peppermint oil
Anise oil
Capsicum tincture
Macrogol cetostearyl ether
Caramel (E150)
Glycerol (E422)
Diethyl ether
Cineole
Chloroform
Syrup

6.2 Incompatibilities
No major incompatibilities are known

6.3 Shelf life
150ml: 36 months unopened

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

6.5 Nature and contents of container
150ml flat sloping shoulder amber glass bottle, with 28mm tamper evident child resistant closure with EPE/ Saranex liner.

6.6 Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER
Thornton & Ross Ltd
Huddersfield
HD7 5QH
England

8 MARKETING AUTHORISATION NUMBER(S)
PL 00240/0365

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
25/08/2010

10 DATE OF REVISION OF THE TEXT
25/08/2010
LEAFLET/LABELLING

TOP PLY FACE

50 mm

90 mm

IMPORTANT: Peel top leaf and peel read all text inside BEFORE use. Do not peel off, re-fix for future use. Here

Thornton & Ross Bronchial Balsam Syrup is for relief of the symptoms of dry coughs from colds and bronchitis. SHAKE THE BOTTLE VIGOROUSLY.

Take the solution by mouth.

Adults, the elderly and children over 12 years; Take 2 x 5ml spoonfuls every 4 hours if required.

Do not give to children under 12 years old unless your doctor tells you to.

DO NOT EXCEED THE STATED DOSE.

Talk to your doctor before use if you have a history of asthma.

Peel where shown for further precautions

If symptoms persist consult your doctor.

Do not store above 25°C.

Keep out of the reach and sight of children.

Active ingredients per 5ml: dextromethorphan hydrobromide 7.5mg, menthol 2.5mg.

Also contains: ethanol, glycerol (E422), sucrose.

Alcohol 0.18 vol%, Sucrose 5.07g per 5ml.

See reverse for full list.

MA holder and manufacturer
Thornton and Ross Ltd., Huddersfield, HD7 5OJ, UK.
PL 00240/0365 M697

Overprint Area

150 ml
2. Possible side effects
Like all medicines, Thornton & Ross Bronchial Balsam Syrup can have side effects, although these don’t affect everyone.
Possible side effects: drowsiness • dizziness • sickness or feeling sick • constipation • stomach discomfort.
If you notice these or any other side effects not listed, stop use and tell your doctor or pharmacist.

3. Further information
If you accidentally take too much see a doctor straight away. Take the pack with you to show which medicine you have 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 ingredients per 5ml are: dextromethorphan hydrobromide 7.5mg, menthol 2.5mg.
The other ingredients are: ethanol, glycerol (E422), capsicum tincture (capsicum oleoresin), peppermint oil, anise oil, citric acid (E330), macrogol cetostearyl ether, caramel (E150), diethyl ether, cinnamal, chloroform, sucrose and purified water.
What the medicine looks like
Thornton & Ross Bronchial Balsam Syrup is a brown syrupy liquid.
It is supplied in 150ml bottles.
This label was revised in June 2010
Thornton & Ross Bronchial Balsam Syrup contains dextromethorphan which reduces the desire to cough and menthol which relieves irritation, reduces congestion and helps you breathe more easily.

1. Before you use this medicine
   - Do not use the medicine if you have:
     * An allergy to any of the ingredients listed in section 3
     * Taken MAOIs (monoamine oxidase inhibitors) for depression within the last two weeks
     * Shortage of breath
     * Liver problems
     * An asthma attack
     * A persistent cough or one which produces phlegm
     * Or are under 12 years.
   - Talk to your doctor if you have:
     * A history of asthma.
   - Talk to your doctor or pharmacist if you are taking:
     * Cimetidine for stomach ulcers.
   - Pregnant or breastfeeding:
     Ask your doctor or pharmacist for advice before using if you are pregnant, might be pregnant or are breastfeeding.
   - Driving and using machines:
     This medicine normally works without causing drowsiness, but care should be taken initially as in rare cases drowsiness may occur. If you are affected do not drive or operate machinery.

2. Important ingredient information
   - Contains 3.07g of sucrose per 5ml dose. This should be taken into account in people with diabetes. If you have an intolerance to some sugars, contact your doctor before taking this medicine.
   - It contains small amounts of ethanol (alcohol), less than 100mg per 10ml dose.
Thornton & Ross
Bronchial BALSAM Syrup
Dextromethorphan Hydrobromide
Levomenthol
troublesome dry coughs and irritation in the throat and chest
RAPID IMPACT
Thornton & Ross Bronchial BALSAM Syrup

Dextromethorphan Hydrobromide
Lemomethol

and irritation in the throat and chest

RAPID IMPACT