Safeguarding public health

MHRA

Public Assessment Report

Care Hayfever and Allergy 1mg/ml Solution

(cetirizine hydrochloride)

PL 00240/0138

CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

PL 00240/0138

UKPAR

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CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

PL 00240/0138

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) has granted Thornton & Ross Limited a Marketing Authorisation (licence) for the medicinal product Care Hayfever and Allergy 1mg/ml Solution (PL 00240/0138). This is a pharmacy [P] medicine for the relief of the symptoms of hayfever and other allergies.

The product contains the active ingredient cetirizine hydrochloride which belongs to a group of drugs called antihistamines.

This is a simple application that cross-refers to a previously granted licence for Cetirizine Hydrochloride 1mg/1ml Oral Solution (PL 00289/0416).

No new or unexpected safety concerns arose from this simple application and it was therefore judged that the benefits of using Care Hayfever and Allergy 1mg/ml Solution outweigh the risks, hence a Marketing Authorisation has been granted.

CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

PL 00240/0138

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Care Hayfever and Allergy 1mg/ml Solution (PL 00240/0138) to Thornton & Ross Limited on 16 October 2006. The product is a pharmacy [P] medicine.

This application was submitted as a simple abridged application according to Article 10.1(a)(i) of Directive 2001/83/EC, as amended, cross-referring to Cetirizine Hydrochloride 1mg/1ml Oral Solution (PL 00289/0416, approved on 13 November 2002).

The product contains cetirizine hydrochloride. Cetirizine hydrochloride is a racemate and an anti-allergic with specific histamine H_1-receptor blocking characteristics. Cetirizine inhibits cutaneous reactions in allergic individuals through VIP (Vasoactive Intestinal Polypeptide) and substance P, neuropeptides that are considered to be involved in the allergic reaction. Effect is reached within 2 hours with a maximum effect after 4 hours, and remains for at least 24 hours. In allergic individuals, cetirizine inhibits the recruitment of eosinophils after stimulation with allergens and non selective histamine liberators, by a mechanism that is not primarily explained by the H_1-receptor blocking characteristics of the pharmaceutical.

No new data were submitted for this simple application, nor were any necessary, as the data are identical to that of the previously granted cross-referenced product. As the cross-referenced product was granted prior to the introduction of current legislation, no public assessment report was generated for it.

Care Hayfever and Allergy 1mg/ml Solution is used: in adults and adolescents over 12 years of age, for the symptomatic treatment of allergic rhinitis (seasonal and perennial), associated allergic conjunctivitis, and chronic idiopathic urticaria; in children aged 6-12 years, for the symptomatic treatment of allergic rhinitis (seasonal and perennial), and chronic idiopathic urticaria; and in children aged 2–6 years, for the symptomatic treatment of seasonal allergic rhinitis.

PHARMACEUTICAL ASSESSMENT

LICENCE NO:	**PL 00240/0138**
PROPRIETARY NAME:	**Care Hayfever and Allergy 1mg/ml Solution**
ACTIVE(S):	**Cetirizine hydrochloride**
COMPANY NAME:	**Thornton & Ross Limited**
E.C. ARTICLE:	**10.1(a)(i)**
LEGAL STATUS:	**P**

INTRODUCTION

Legal basis

This is a simple abridged application for Care Hayfever and Allergy 1mg/ml Solution (P status), containing cetirizine hydrochloride 1mg per ml.

The applicant claims essential similarity, under article 10.1(a)(i), to Cetirizine hydrochloride 1mg/ml Oral Solution. The reference product PL 00289/0416 was held by Approved Prescription Services (APS) Limited, UK, granted 13 November 2002 (Current MA holder: Teva UK Limited).

Letters of access

Satisfactory letters of consent/access are provided by the finished product and active substance manufacturers.

Confirmation that the manufacturer is prepared to manufacture the product on the applicant's behalf is provided.

The applicant has also provided satisfactory written confirmation that they have access to all the data supporting the application, and that Module III of the data is in their possession.

REFERENCE PRODUCT

There were no outstanding variations and renewal issues.

TSE

The Marketing Authorisation Application form indicates no ingredients in the product that are TSE susceptible.

A suitable TSE statement has been provided for the glycerol, confirming the non-animal origin of the excipient.

QUALITY OVERALL SUMMARIES

Satisfactory Summaries (Quality, Pre-clinical and Clinical) are provided for the proposed product, confirming similarities to the reference product.

MODULE I

Product name

Acceptable

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
PATIENT INFORMATION LEAFLET (PIL)
LABELLING

Satisfactory.

CONCLUSION

Marketing authorisation may be granted for this product.

PRECLINICAL ASSESSMENT

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

CLINICAL ASSESSMENT

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

OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT

QUALITY

The data for this application are consistent with those previously assessed for the cross-referenced 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 Cetirizine Hydrochloride 1mg/1ml Oral Solution (PL 00289/0416).

No new or unexpected safety concerns arose from this application.

The SPC, PIL and labelling are satisfactory and consistent with those of the cross-referenced product.

RISK-BENEFIT 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-referenced product. The risk-benefit assessment is therefore considered to be favourable.

CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

PL 00240/0138

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application for Care Hayfever and Allergy 1mg/1ml Solution on 1 July 2004.
2	The MHRA's assessment of the submitted data was completed on 6 January 2005.
3	Further information was requested from the company on 12 January 2005.
4	The applicant's response to further information request was received on 27 April 2005.
5	Further information was requested from the company on 12 January 2006.
6	The applicant's response to further information request was sent in a letter dated 27 February 2006.
7	Additional information was requested from the company on 9 May 2006.
8	The applicant's response to additional information request was sent on 19 June 2006 and 27 September 2006.
9	The MHRA completed its assessment of the application on 13 October 2006.
10	The application was determined on 16 October 2006.

CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

PL 00240/0138

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Care Hayfever and Allergy 1mg/mL Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution contains 1mg of cetirizine hydrochloride.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Oral solution.
Clear colourless solution .

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adults and adolescents over 12 years of age:
Symptomatic treatment of allergic rhinitis (seasonal and perennial), associated allergic conjunctivitis, and chronic idiopathic urticaria.

Children 6-12 years:
Symptomatic treatment of allergic rhinitis (seasonal and perennial), and chronic idiopathic urticaria.

Children 2–6 years
Symptomatic treatment of seasonal allergic rhinitis

4.2. Posology and method of administration

Adults and adolescents over 12 years of age: 2 x 5 ml once daily.

If drowsiness occurs, the solution can be administered in the evening.

Children 6-12 years:
2 x 5 ml once daily or 5 ml taken twice daily (morning and evening).

Children 2-6 years or weighing less than 30 Kg:
5 ml taken once daily or 2.5 ml twice daily.

At present there is insufficient clinical data to recommend the use of cetirizine in children under 2 years of age.

Cetirizine is contraindicated in patients with severe renal impairment. In patients with moderate renal impairment the dose should be adjusted to 5 ml. Caution should be exercised in patients with mild to moderate renal impairment or impaired liver function (see 4.4 Special warnings and precautions for use).

There is no evidence that the dose needs to be modified for healthy elderly patients. The duration of the treatment may vary depending on the symptoms.

4.3. Contraindications

Hypersensitivity to any component of the preparation.

Patients with severe renal impairment.

4.4. Special warnings and precautions for use

In some patients, long term treatment with Cetirizine Solution may lead to an increased risk of caries due to mouth dryness. The patients should therefore be informed about the importance of oral hygiene.

In cases of impaired hepatic function and renal function, the elimination of cetirizine may be impaired. Caution should be exercised when administering cetirizine to these patients. (see section 4.2 posology and section 4.3 contraindications).

Cetirizine may potentiate the effects of alcohol. Therefore caution is recommended during concomitant use of alcohol.

Caution is recommended with concomitant use of CNS depressants.

Contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5. Interactions with other medicinal products and other forms of interaction

Allergy testing: Use of cetirizine must be discontinued three days before allergy tests. Cetirizine may potentiate the effects of alcohol. Therefore caution is recommended during concomitant use of alcohol. Caution is recommended during concomitant use of CNS depressants.

4.6. Pregnancy and lactation

Data on a limited number of exposed pregnancies indicate no adverse effects of cetirizine on pregnancy or on health of foetus/new born child. To date no other relevant epidemiological data are available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post natal development (see 5.3*)*. Caution should be exercised when prescribing to pregnant women.

Breast feeding
No data concerning the excretion of cetirizine into human milk are available. Cetirizine should be avoided during lactation.

4.7. Effects on ability to drive and use machines

Cetirizine may have minor or moderate influence on the patient's ability to react. This should be considered when extra alertness is required e.g. when driving. Cetirizine may potentiate the effects of alcohol and CNS depressants.

4.8. Undesirable effects

Mouth dryness, headache, dizziness, drowsiness, somnolence in children and adults, agitation, abdominal complaints and digestive disorders.
Exceptionally, cases of allergic reactions such as cutaneous reactions and angioedema (Quincke's Oedema) have been reported.

4.9. Overdose

Toxicity: Limited experience of overdosing. 20 mg to a 2 year old, 30 mg to a 3 year old and 40 mg to an 11 year old did not give any symptoms. 60 mg to a 4 year old gave mild intoxication, 400 mg to a 14 year old gave mild symptoms while 400-500 mg to an adult gave no symptoms at all.

Symptoms of overdosage reported with antihistamine substances: Somnolence, unconsciousness and/or excitation (principally in children). Ataxia, tremor, headache, hallucinations, seizures, dry mouth, flush, hyperthermia, mydriasis, urine retention tachycardia and in the case of massive doses, possible fall in blood pressure and arrhythmias. Nausea and vomiting. Also extrapyramidal symptoms are possible. Cetirizine has a low sedative and anticholinergic effect. Sedation can be a symptom of overdose , it can occur after a single dose of less than 50 mg.

Treatment: At the present time there is no specific antidote. Experience of overdosing is limited and no severe intoxication has been reported to date. Primary treatment should be gastric lavage, if justified and charcoal. Symptomatic treatment should be

instituted in the case of acute intoxication, such as diazepam for seizures or acute dystonias.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ATC code: R06AE07
Pharmacotherapeutic group: Antihistamines for systemic use
Cetirizine hydrochloride is a racemate and an anti-allergic with specific histamine H_1-receptor blocking characteristics.

Cetirizine inhibits cutaneous reactions in allergic individuals through VIP (Vasoactive Intestinal Polypeptide) and substance P, neuropeptides that are considered to be involved in the allergic reaction. Effect is reached within 2 hours with a maximum effect after 4 hours, and remains for at least 24 hours. In allergic individuals, cetirizine inhibits the recruitment of eosinophils after stimulation with allergens and non selective histamine liberators, by a mechanism that is not primarily explained by the H_1-receptor blocking characteristics of the pharmaceutical.

5.2. Pharmacokinetic properties

Cetirizine is absorbed with small inter-individual variations. Cetirizine has not been given intravenously, therefore the bioavailability, clearance and volume of distribution (Vd) are unknown. Maximum plasma concentration is achieved within 1 hour and the terminal half-life is about 10 hours in adults and 6 hours in children between the age of 6-12 years. The grade of protein binding in plasma is about 93%. Cetirizine is metabolised to a small extent with a known inactive main metabolite. 60% of a dose of cetirizine is eliminated in unchanged form via the kidneys within 96 hours. Repeated administration does not lead to any accumulation, nor is the absorption or elimination affected. In cases of impaired kidney function, the elimination is slower and the half-life is prolonged. Elimination will also be decreased in cases of hepatic impairment.

There is no evidence that the pharmacokinetics of cetirizine is altered in elderly patients unless renal or hepatic function is reduced.

5.3. Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction, genotoxicity or carcinogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Glycerol
Propylene glycol
Sorbitol
Sodium Methylparaben
Propylparaben
Sodium acetate
Acetic acid
Saccharin sodium
Banana flavour
Purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

No special precautions for storage.

6.5. Nature and contents of container

100 ml fill bottles.

Amber glass bottle with child-resistant polypropylene screw cap incorporating a tamper evident seal (yellow polyethylene).

Measuring device: 5 ml plastic PP measuring spoon graduated at 2.5 ml

6.6 Special disposal precautions

Not applicable

ADMINISTRATIVE DATA

7. MARKETING AUTHORISATION HOLDER

Thornton & Ross Limited
Linthwaite
Huddersfield
HD7 5QH

8. MARKETING AUTHORISATION NUMBER

PL 00240/0138

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/10/2006

10 DATE OF REVISION OF THE TEXT

16/10/2006

Patient Information Leaflet

CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

PL 00240/0138

Hayfever and Allergy 1mg/mL Solution

Cetirizine Hydrochloride

Patient Information Leaflet

Please read this leaflet carefully because it contains important information for you. This medicine is available without a prescription for you to treat a mild illness without a doctor's help. Nevertheless, you still need to use Care Hayfever and Allergy 1mg/mL Solution 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 see your doctor if your symptoms worsen or do not improve.

In this leaflet:

1. Care Hayfever and Allergy 1mg/mL Solution; what it is and what it's used for
2. Before you take this product
3. How to take this product
4. Possible side effects
5. Storing this product

The name of your medicine is Care Hayfever and Allergy 1mg/mL Solution.

- The active ingredient is cetirizine hydrochloride.
- Other ingredients are glycerol (E422), propylene glycol, liquid sorbitol (E420), methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), sodium acetate, acetic acid, saccharin sodium, banana flavour and purified water.

Marketing Authorisation Holder: Thornton & Ross Ltd., Huddersfield, HD7 5QH, UK. Company responsible for manufacture: Approved Prescription Services Limited, Eastbourne, BN22 9AG, England.

1. Care Hayfever and Allergy 1mg/mL Solution; what it is and what it's used for

- Each 1 mL of solution contains 1mg of cetirizine hydrochloride. Cetirizine belongs to a group of drugs called antihistamines which help to relieve the symptoms of some allergies.
- The product is available in bottles of 100mL.
- Your medicine is used to relieve the symptoms of hayfever, non-seasonal rhinitis (runny and itchy nose) and other allergies e.g. pet or house dust mite allergies. Also for allergic eye infection (conjunctivitis) in adults and children over 12, and for skin allergies such as rash, itching and urticaria (hives) in adults and children over 6. This medicine may be given to children aged 2 – 6 years to relieve hayfever symptoms.

2. Before you take this product

Do not take this product if you:

- Are sensitive to any of the ingredients in your medicine.
- Have severe kidney problems.

Take special care with this product if you have:

- Liver problems.
- Mild or moderate kidney problems.

Tell your doctor if you are taking any of the following:

- Sedatives e.g. nitrazepam, as their effects may be increased by this product.

Taking this medicine with food and drink:

- Avoid drinking large amounts of alcohol.

Pregnancy and Breast-feeding:

- Talk to your doctor before taking this product if you are pregnant.
- Do not take if you are breast-feeding.

Driving and using machines:

- This medicine at the recommended dose does not cause drowsiness in the majority of people. However, as with all antihistamines, rare cases of drowsiness have been reported. If affected do not drive or operate machinery. As with all antihistamines you should avoid excessive alcohol consumption when taking this medicine.

Other precautions you should take:

- This product must be discontinued 3 days before any allergy testing.
- If you take this product for a long time there is an increased risk of tooth decay due to mouth dryness. It is important to brush your teeth regularly.

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Important information about some of the ingredients of this medicine:

- This product contains Sorbitol: if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
- It also contains Propyl Parahydroxybenzoate (E216) and Methyl Parahydroxybenzoate (E218): These may cause allergic reactions (possibly delayed).

3. How to take this product

If your doctor has prescribed this medicine, always follow your doctor's instructions. Otherwise follow the instructions below. If you do not understand these instructions, or you are in any doubt, ask your doctor or pharmacist.

Use the spoon provided to make sure you have the correct dose.

For oral administration.

Adults and children aged 12 years and over: Two 5mL spoonfuls once daily.
If drowsiness occurs, take your medicine in the evening.

Children aged 6 – 12 years: Either two 5mL spoonfuls once daily, or one 5mL spoonful morning and evening.

Children aged 2 – 6 years: Either one 5mL spoonful daily, or half a spoonful (2.5mL) morning and evening.

Children under 2 years of age: Not recommended.

If you have kidney problems, you may only need half the recommended dose.

If you take more than you should

If you (or someone else) swallow a lot of the solution all together, or if you think a child has accidentally swallowed any of the solution, contact your nearest hospital casualty department or your doctor immediately.

Overdose can cause drowsiness, unconsciousness, dry mouth, loss of co-ordination, shaking, headache, dilated pupils, feeling flushed, a very high temperature, hallucinations, fits, tics, dizziness or fainting, problems urinating, changes in heart rhythm, feeling and being sick. In children, agitation may occur.

If you forget to take this product

If you forget to take a dose, take one as soon as you remember, unless it is nearly time to take the next one. Never take two doses together. Take the remaining doses at the correct time.

4. Possible side effects

Like all medicines, this product can have side effects.

Tell your doctor if you notice any of the following:

- Headache.
- Dizziness.
- Agitation.
- Dry Mouth.
- Drowsiness.
- Stomach or intestinal discomfort.

These are all temporary, mild side effects of this product.

If the following happens, stop taking this product and tell your doctor immediately or go to the casualty department at your nearest hospital:

- a severe allergic reaction (swelling of the face, lips, mouth or throat which may cause difficulty swallowing or breathing, hives).

This is a very serious but rare side effect. You may need urgent medical attention or hospitalisation.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. Storing this product

Keep this medicine out of the reach and sight of children. Do not transfer to another container. Do not use this product after the expiry date shown on the outer packaging. Return all unused medicines to your pharmacist for safe disposal.

Revised: October 2005

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Labelling

CARE HAYFEVER AND ALLERGY 1MG/ML SOLUTION

(CETIRIZINE HYDROCHLORIDE)

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