CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION

PL 04917/0068

UKPAR

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CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION

PL 04917/0068

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Pinewood Laboratories Limited a Marketing Authorisation (licence) for the medicinal product Cetirizine Hydrochloride 5 mg/5 ml Oral Solution (Product Licence number: 04917/0068). This product is available without prescription from pharmacies.

Cetirizine hydrochloride is an anti-histamine, which means that it blocks the action of histamine, a natural substance found in the body that can cause the symptoms of some allergies. Cetirizine Hydrochloride 5 mg/5 ml Oral Solution is used to treat hayfever and pet, dust and skin allergies in adults and children aged 6 years and over, and to treat hay fever in children aged between 2 and 5 years.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Cetirizine Hydrochloride 5 mg/5 ml Oral Solution outweigh the risks, hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Cetirizine Hydrochloride 5 mg/5 ml Oral Solution (PL 04917/0068) to Pinewood Laboratories Limited on 3 January 2007. This product holds a Pharmacy Licence (P).

The application was submitted as an abridged application according to Article 10.1 of EC Directive 2001/83. The cross reference product is Zirtek Solution (PL 08972/0033), granted to UCB S.A on 19 July 1993, changing ownership to UCB Pharma Ltd on 5 May 2000. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) was generated for it.

Cetirizine Hydrochloride 5 mg/5 ml Oral Solution contains the active substance cetirizine hydrochloride and is used in the treatment of perennial rhinitis, seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria in adults and children aged 6 years and over, and for seasonal rhinitis (hay fever) in children aged between 2 to 5 years.
I. REQUESTS FOR INSPECTION ACTION PRIOR TO AUTHORISATION

Suitably qualified manufacturers are responsible for the manufacture of the drug product; one of these manufacturing sites is also the sole batch release site. Each manufacturer has a valid Manufacturer’s Licence, confirming the suitability of the site for preparation of multidose liquids.

II. INTRODUCTION

This is an abridged application for Marketing Authorisation in the UK, submitted under Article 10.1 of Directive 2001/83/EC for a product claiming essential similarity to Zirtek Solution (formerly PL 05221/0002, currently PL 08972/0033). The cross-referenced product was originally granted a licence on 19 July 1993 to UCB S.A and, therefore, the required 10 years have passed since authorisation. UCB Pharma Ltd has been the MA holder for the reference product in the UK since 5 May 2000.

III. DRUG SUBSTANCE

The active ingredient, cetirizine dihydrochloride, is the subject of a Ph. Eur. monograph. The applicant refers to the active ingredient manufacturer’s Drug Master File (DMF). A letter of access naming the applicant is provided. This DMF had been assessed as satisfactory for use in oral licensed products. In view of this, the named source is considered acceptable.

IV. DRUG PRODUCT

IV.1 Description and Composition of the Drug Product

The qualitative composition of the solution is shown in table 1.

Table 1 Composition of Drug Product

<table>
<thead>
<tr>
<th>Name of Ingredient</th>
<th>Function</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACTIVE INGREDIENT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetirizine hydrochloride</td>
<td>Active</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td><strong>OTHER INGREDIENTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sorbitol solution 70%</td>
<td>Sweetener</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Glycerol</td>
<td>Solvent</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>Solvent</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Sodium acetate</td>
<td>Buffering agent</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Methyl Paraben</td>
<td>Anti-microbial Preservative</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Propyl paraben</td>
<td>Anti-microbial Preservative</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Saccharin sodium</td>
<td>Sweetener</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Acetic acid 5N</td>
<td>Buffering agent</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Banana flavour</td>
<td>Flavouring</td>
<td>In-House</td>
</tr>
<tr>
<td><strong>Purified Water</strong> (Qs to 1ml)</td>
<td>Solvent/vehicle</td>
<td>Ph.Eur</td>
</tr>
</tbody>
</table>
The solution is packed into amber type III glass bottles of various sizes with a tamper evident closure.

The product is supplied with a 5ml measuring spoon or oral syringe.

**IV.2 Pharmaceutical Development**
The proposed product is designed to be comparable to the innovator’s product. The active substance is water soluble. The choice of formulation and the functions of ingredients are justified.

A study on product/container-closure compatibility has also been carried out with bottles closed with polyethylene caps. No degradation was noted, indicating a stable product.

**IV.3 Manufacture**

**IV.3.1 Manufacturer(s)**
A suitably qualified manufacturer is responsible for making the finished product.

**IV.3.2 Batch Formula**
The batch formula has been provided and is acceptable.

**IV.3.3 Description of Manufacturing Process and Process Controls**
The manufacturing process is given both in a descriptive and flow chart form.

**IV.3.4 Control of Critical Steps and Intermediates**
Details of the in-process controls are provided and are acceptable for a product of this type.

**IV.3.5 Process Validation and/or Evaluation**
Validation data for three batches of the syrup manufactured at Pinewood are provided. These are acceptable. Confirmation has been given that validation will be performed on the first three production scale batches.

**IV.4 Control of Excipients**

**IV.4.1 Specifications**
All the excipients comply with a monograph of the Ph. Eur, with the exception of the banana flavour and acetic acid. Representative certificates of analysis are provided for these starting materials and the finished product manufacturer, on receipt of new batches, performs an identity test.

The non-compendial excipients are supported by in-house specifications.

**IV.4.2 Excipients of Human or Animal Origin**
As glycerol is prepared from tallow, data are provided that confirm the suitability of the material in relation to TSE guidelines.

**IV.5 Control of Drug Product**

**IV.5.1 Specification(s)**
The proposed specifications at release and end of shelf life are provided.

IV.5.2 Analytical Procedures
Suitable analytical procedures are used to control this drug product.

IV.5.3 Validation of Analytical Procedures
Satisfactory data confirming the validity of the analytical procedures have been provided.

IV.5.4 Batch Analyses
Certificates of analysis are provided for three validation batches, showing full compliance with the finished product specification.

IV.5.5 Characterisation of Impurities
The impurities have been appropriately characterised by the active substance manufacturer. The finished production specification includes suitable impurity limits.

IV.5.6 Justification of Specification(s)
The proposed tests and specifications are appropriate for a product of this type.

IV.6 Reference Standards or Materials
Specifications are provided for reference standards for the active and related substances and these are satisfactory.

IV.7 Container Closure System
The solution is filled into amber type III glass bottles, which comply with the Ph. Eur. monograph. A diagrammatic representation of the bottles used is provided. The dimensions of the bottles are routinely checked.
Relevant information in relation to the bottle closure, measuring spoon and oral dosing syringe are also provided.

IV.8 Stability

IV.8.1 Stability Summary and Conclusion
The data provided support the shelf life of 18 months before opening and the shelf life of 6 months after opening.

IV.8.2 Post-approval Stability Protocol and Stability Commitment
A commitment has been given by finished product manufacturer that accelerated and real time stability studies will be performed on the first three consecutive production scale batches and that any anomalous results will be reported to the MHRA.

IV.8.3 Stability Data
The data show that there were no significant deviations from initial values (within the capabilities of the analytical method) and the product remained within the proposed specification.
The in-use stability study shows little change to the physical and chemical parameters over a 6-month period.

V ASSESSOR’S COMMENTS ON THE SPC, LABELS AND PACKAGE LEAFLET
The SPC, PIL and packaging for this product are satisfactory.

VI OTHER INFORMATION

VI.1 Bioanalytical methods
Not applicable. No clinical studies were required.

VI.2 Bioavailability, bioequivalence
No clinical trials have been performed. This is consistent with the current guidelines relating to bioequivalence/bioavailability for such preparations where it is considered that the excipients will not interfere with bioavailability of the drug. In this instance there are no concerns as the same excipients are used in this formulation compared to that of the innovator.

VI.3 Essential similarity
Comparative impurity profiles for two batches of the proposed product (development scale) and one batch of the innovator product (Zirtek – UCB) are provided. Although the impurity profiles differ between the innovator and the proposed product, all impurities are controlled within ICH limits for an oral solution administered to a maximum daily dose of 10mg. Therefore, these data support the conclusion that the proposed product is essentially similar to the innovator product with respect to impurities.

VII. ADMINISTRATIVE

VII.1 Comment on Expert report
An appropriately qualified pharmacist has written the report. It is acceptable.

VIII ASSESSOR’S OVERALL CONCLUSIONS ON QUALITY AND ADVICE
A grant of a marketing authorisation is acceptable.
PRECLINICAL ASSESSMENT

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

1. INTRODUCTION

This is an abridged application for Marketing Authorisation in the UK submitted under Article 10.1 of Directive 2001/83/EC (as amended) for a product claiming essential similarity to Zirtek Solution 1mg/ml.

The active substance, cetirizine dihydrochloride, is an antihistamine and is used in the treatment of perennial rhinitis, seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria.

2. BACKGROUND

The applicant claims essential similarity, under Article 10.1, to Zirtek Solution 1mg/ml, which contains the same amount of active substance in the same pharmaceutical form. UCB Pharma Ltd. was granted a licence for this product in the UK (PL 05221/0002, changed to 08972/0033) on 19 July 1993; thus the 10-year rule has been fulfilled.

3. INDICATIONS

The applicant has submitted the following:

‘For the treatment of perennial rhinitis, seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria in adults and children aged 6 years and over, and for seasonal rhinitis (hayfever) in children aged between 2 to 5 years.’

This is consistent with the indications for Zirtek.

4. DOSE & DOSE SCHEDULE

The applicant has submitted the following:

‘For oral use only.

Adults and children 6 years and above: 10mg daily.
Adults and children aged 12 years and above: 10ml once daily.
Children aged between 6 to 11 years: Either 5ml twice daily or 10ml once daily.

Children aged between 2-5 years: 5mg daily.
Either 5ml once daily or 2.5ml twice daily.

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

There is no data to suggest that the dose should be reduced in elderly patients.
In patients with renal insufficiency the dosage should be reduced to half the normal recommended daily dose.’
This is consistent with the dose and dose schedule for Zirtek.

5. **TOXICOLOGY**

No formal toxicological data have been provided for this application and none are required.

6. **CLINICAL PHARMACOLOGY**

6.1 **Bioequivalence**

As the formulation is an oral liquid and so is the essentially similar product; no formal bioequivalence studies are required.

7. **EFFICACY**

No formal efficacy data have been provided for this application and none are required.

8. **SAFETY**

No formal safety data derived from studies of patients have been provided for this application and none are required. The adverse events that have been documented for the originator product are listed in the Summary of Product Characteristics.

9. **EXPERT REPORT**

There is a clinical expert report written by a consultant to the pharmaceutical industry; he concludes that cetrizine is well established and is efficacious, with a good safety profile with regard to the proposed indications.

10. **SUMMARY OF PRODUCT CHARACTERISTICS (SPC)**

The Summary of Product Characteristics for this product is satisfactory.

11. **PATIENT INFORMATION LEAFLET (PIL)**

The PIL for this product is satisfactory.

12. **LABELLING**

All labelling for this product is satisfactory.

13. **MAA**

The MAA form is satisfactory.

14. **DISCUSSION**
This is an abridged application for Marketing Authorisation in the UK submitted under Article 10.1 of Directive 2001/83/EC (as amended) for a product claiming essential similarity to Zirtek Solution 1mg/ml.

The active drug, cetirizine dihydrochloride, is an antihistamine and is used in the treatment of perennial rhinitis, seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria.

As the formulation is a liquid, and so is the essentially similar product, no formal bioequivalence studies are required.

The clinical expert has made a fair appraisal of the data derived from the published papers. His overall conclusion, including the risk/benefit assessment, appears to be well judged. The data presented here are sufficient to establish the efficacy and safety of Cetirizine Oral Solution for use in the proposed indications.

15. RECOMMENDATIONS

The efficacy and safety of Cetirizine Hydrochloride 5 mg/5 ml Oral Solution are satisfactory for the grant of a Marketing Authorisation.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of the product are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

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

EFFICACY AND SAFETY

The efficacy of cetirizine dihydrochloride products has been well documented in the past. No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The risk benefit ratio is considered to be positive.
CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION

PL 04917/0068

**STEPS TAKEN FOR ASSESSMENT**

<table>
<thead>
<tr>
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<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 31 October 2003</td>
</tr>
<tr>
<td>2</td>
<td>Following assessment of the application the MHRA requested further information relating to the clinical dossier on 19 February 2004</td>
</tr>
<tr>
<td>3</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 31 March 2004</td>
</tr>
<tr>
<td>4</td>
<td>Following assessment of the response the MHRA requested further information relating to the clinical and quality dossiers on 23 August 2004</td>
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<td>5</td>
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<td>6</td>
<td>Following assessment of the response the MHRA requested further information relating to the clinical and quality dossiers on 4 May 2005</td>
</tr>
<tr>
<td>7</td>
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<tr>
<td>8</td>
<td>Following assessment of the response the MHRA requested further information relating to the quality dossier on 10 August 2005</td>
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<td>9</td>
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<td>10</td>
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<td>11</td>
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<td>12</td>
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</tr>
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<td>13</td>
<td>The applicant responded to the MHRA’s request, providing further information on 10 July 2006.</td>
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<tr>
<td>14</td>
<td>Following assessment of the response the MHRA requested further information relating to the quality dossier on 10 August 2006.</td>
</tr>
<tr>
<td>15</td>
<td>The applicant responded to the MHRA’s request, providing further information on 12 December 2006.</td>
</tr>
<tr>
<td>16</td>
<td>The application was determined on 22 January 2007</td>
</tr>
</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cetirizine Hydrochloride 5 mg/5 ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml spoonful contains 5mg Cetirizine hydrochloride. Each 5ml spoonful also contains the following excipients:
- 250 mg Propylene glycol
- 6.75 mg Methyl parahydroxybenzoate (E218)
- 0.75 mg Propyl parahydroxybenzoate (E216)
- 2250 mg Liquid Sorbitol (E420)
For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Oral Solution
Clear or almost clear, colourless solution with taste and odour of banana.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the treatment of perennial rhinitis, seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria in adults and children aged 6 years and over, and for seasonal rhinitis (hay fever) in children aged between 2 to 5 years.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

For oral use only.
Adults and children 6 years and above: 10mg daily.
Adults and children aged 12 years and above: 10ml once daily.
Children aged between 6 to 11 years: Either 5ml twice daily or 10ml once daily.
Children aged between 2-5 years: 5mg daily.
Either 5ml once daily or 2.5ml twice daily.
At present there is insufficient clinical data to recommend the use of cetirizine in children under 2 years of age.
There is no data to suggest that the dose should be reduced in elderly patients.
In patients with renal insufficiency the dosage should be reduced to half the normal recommended daily dose.
4.3 CONTRAINDICATIONS

Cetirizine is contra-indicated in patients who are hypersensitive to cetirizine, hydroxyzine or any constituent of the product.
Cetirizine has been reported to be excreted in human breast milk. Due to lack of evidence of safety, cetirizine is therefore contra-indicated in lactating women.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

(See also section 4.7 Effects on Ability to Drive and Use Machines).
Dosage adjustment is necessary in patients with moderate or severe renal impairment (see section 4.2 Posology and Method of Administration).
This medicinal product contains propylene glycol which may cause alcohol-like symptoms.
This medicinal product also contains Methyl parahydroxybenzoate and Propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).
Patients with rare hereditary problems of fructose intolerance should not take this medicinal product as it contains Liquid Sorbitol (E420).
For patients whose symptoms persist, it is advised to consult a doctor or pharmacist.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No evidence of interactions with psuedoephedrine, antipyrine, ketoconazole, erythromycin, azithromycin, diazepam and cimetidine has been reported.
Theophylline decreases the clearance of cetirizine although the disposition of theophylline is not affected.
In common with other antihistamines it is not recommended that excessive alcohol consumption be avoided. Concurrent use of cetirizine with other CNS depressants should also be avoided as reduction in alertness and impairment of performance may occur.

4.6 PREGNANCY AND LACTATION

Animal studies have not revealed any undesirable effects.
Use of cetirizine in human pregnancy has been limited. Although cetirizine does not appear to be associated with increased teratogenic risk, it is recommended that the use of cetirizine be avoided in pregnancy except where clearly needed.
As cetirizine has been reported to be excreted in breast milk, its use is contra-indicated in lactating women (See also section 4.3 Contra-indications).

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Studies in healthy volunteers at daily doses of 20 and 25 mg/day have not revealed adverse effects on alertness or reaction time. However, patients are advised not to exceed the recommended dose if driving or operating machinery.
Please refer also to section 4.8 Undesirable effects.
4.8 UNDESIRABLE EFFECTS

Mild and transient side effects such as headache, dizziness, drowsiness/fatigue, agitation, rash, nausea, palpitations, dry mouth and gastro-intestinal discomfort have been reported occasionally. Affected patients may divide their daily dose, i.e. take as 5 mg in the morning and 5 mg in the evening.
The incidence of sedation has been reported to be similar cetirizine and placebo. Convulsions have very rarely been reported.

4.9 OVERDOSE

Symptoms of overdosage may include drowsiness in adults and initially agitation or restlessness, followed by drowsiness, in children.
Treatment of overdose should be symptomatic and supportive. Gastric lavage should be performed in the case of massive overdosage. There is no known specific antidote, and cetirizine is not effectively removed by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic classification:
R06A E07 (ATC classification system)
Cetirizine is a potent antihistamine, selective H1 receptor antagonist. The histamine-mediated ‘early’ phase of the allergic reaction is inhibited by cetirizine, which also reduces the migration of inflammatory cells and the release of mediators associated with the ‘late’ allergic responses. Effects on other receptors are negligible and consequently cetirizine is unlikely to cause undesirable anti-cholinergic and anti-serotonin effects. At the recommended therapeutic dose of 10 mg daily, impairment of CNS function has not been found to be greater than with the placebo.

5.2 PHARMACOKINETIC PROPERTIES

Cetirizine is rapidly absorbed from the gastrointestinal tract; absorption is not reduced by food, though the rate may be decreased slightly. Peak blood levels in the order of 0.3 micrograms/ml are attained between 30 and 60 minutes following administration of a 10 mg oral dose of cetirizine. Apparent plasma clearance is greater in children than in adults: the terminal elimination half-life in healthy adult volunteers ranges between 6.7 – 10.7 hours; in children 6.1 – 7.1 hours; and in children aged under 4 years 5.55 hours. Cetirizine is mainly excreted unchanged in the urine (approximately 70% over 5 days compared with 10% in the faeces). The half-life is increased in renal dysfunction: half lives of 19 and 21 hours in patients with mild to moderate renal impairment respectively have been reported. This may have implications for elderly patients. Cetirizine binds strongly to plasma proteins.

5.3 PRECLINICAL SAFETY DATA

No relevant information additional to that contained elsewhere in the SPC.
6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Propylene glycol
- Glycerol
- Methyl parahydroxybenzoate (E218)
- Propyl parahydroxybenzoate (E216)
- Sodium acetate
- Acetic acid
- Saccharin sodium
- Liquid Sorbitol (E420)
- Banana flavour
- Purified water

6.2 INCOMPATIBILITIES

None known.

6.3 SHELF LIFE

Shelf life before opening – 18 months
Shelf life after opening – 6 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Type III amber glass bottles with a tamper evident screw cap having a polypropylene outer layer and a polyethylene inner layer.
Polystyrene/polyethylene measuring device.
60ml, 75ml, 80ml, 100ml, 150ml and 200 ml

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

None

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited,
Ballymacarbry,
Clonmel,

MHRA PAR; CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION, PL 04917/0068
Co. Tipperary,
Ireland.

8 MARKETING AUTHORISATION NUMBER(S)
PL 04917/0068

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
22/01/2007

10 DATE OF REVISION OF THE TEXT
22/01/2007
PATIENT INFORMATION LEAFLET
Cetirizine Hydrochloride 5 mg/5 ml Oral Solution

Read all of 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 Cetirizine Hydrochloride 5 mg/5 ml Oral Solution carefully to get the best results.
• Keep this leaflet. You may need to read it again.
• Ask your pharmacist if you need more information or advice.
• You must see a doctor if your symptoms worsen or do not improve.

In this leaflet:
1. What Cetirizine Hydrochloride 5 mg/5 ml Oral Solution is and what it is used for
2. Before you take/use Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
3. How to take/use Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
4. Possible Side Effects
5. Storing Cetirizine Hydrochloride 5 mg/5 ml Oral Solution

The name of your medicine is Cetirizine Hydrochloride 5 mg/5 ml Oral Solution. It is a clear or almost clear, colourless banana flavoured oral solution.
• The active substance is: Cetirizine Hydrochloride.
• Other ingredients: liquid sorbitol (E420), glycerol, propylene glycol, sodium acetate, acetic acid, saccharin sodium, methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), banana flavour and purified water.

Marketing Authorisation Holder and Manufacturer:
Pinewood Laboratories Ltd., Ballymacarbry, Clonmel, Co. Tipperary, Ireland.
Product Licence number: PL 04917/0068

1. What Cetirizine Hydrochloride 5 mg/5 ml Oral Solution is
• This medicine belongs to a group of medicines called antihistamines.
• The product is available in pack sizes of 60 ml, 75 ml, 80 ml, 100 ml, 150 ml and 200 ml.

and what it is used for:
It is used to relieve the symptoms of:
- In children aged 2-5 years:
  • hayfever (seasonal rhinitis) the symptoms of which include: sneezing, irritated, runny and blocked up nose, itchy, red and watering eyes.
- In children aged 6 years and older and adults:
  • hayfever (seasonal rhinitis) the symptoms of which include: sneezing, irritated, runny and blocked up nose, itchy, red and watering eyes.
  • runny and itchy nose (non-seasonal rhinitis).
  • other allergies e.g. pet or house dust mite allergies and,
  • skin allergies such as rash, itching and urticaria. (hives).

2. Before you take/use Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
Do not take/use if you:
• Are sensitive to any of the ingredients in your medicine.
• Are breast-feeding.
Consult your doctor if you:
• Have had an allergic reaction to antihistamines in the past.
• If you are pregnant.
• If you have kidney problems.
You should avoid excessive alcohol consumption when taking this medicine.

Driving and using machines
Cetirizine Hydrochloride does not normally cause drowsiness at the recommended dose. However, individuals react differently so if affected, do not drive or operate machinery.

Important information about some of the ingredients of Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
Methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216), may cause allergic reactions, (possibly delayed).
Liquid sorbitol (E420): If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
3. How to take/use Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
   For oral use only. Use 5 ml spoon provided. The measuring spoon provided is two sided. The larger side of the spoon is capable of delivering a 5 ml dose whilst the opposite smaller side is capable of delivering a 2.5 ml dose.

   Adults, elderly and children aged 12 years and above: 10 ml (10 mg) once daily.
   Children aged between 6 to 11 years: Either 5 ml (5 mg) twice daily or 10 ml (10 mg) once daily.
   Children aged 2 - 5 years: Either 5 ml (5 mg) once daily or 2.5 ml (2.5 mg) twice daily.
   Children under 2 years of age: Not recommended unless under medical supervision.

   In patients with kidney (on haemodialysis) impairment, the dose should be reduced to half the normal recommended daily dose, or as recommended by a doctor.

   Remember to take your medicine.
   If you have the impression that the effect of Cetirizine Hydrochloride 5 mg/5 ml Oral Solution is too strong or too weak, talk to your doctor or pharmacist.

   If you take/use more Cetirizine Hydrochloride 5 mg/5 ml Oral Solution than you should:
   If you or your child may have taken/used more Cetirizine Hydrochloride 5 mg/5 ml Oral Solution than you should, talk to a doctor or pharmacist immediately. You or the child may feel drowsy or dizzy. In children agitation may also occur.

   If you forget to take Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
   If you forget to take a dose, take it as soon as you remember, but wait at least 24 hours before taking the next dose.

4. Possible side effects
   Like all medicines, Cetirizine Hydrochloride 5 mg/5 ml Oral Solution can have side effects.
   Tell your doctor if you notice any of the following:
   • nausea (feeling sick),
   • abdominal cramps or stomach pains,
   • headache,
   • dizziness,
   • become agitated,
   • get a dry mouth,
   • drowsiness/fatigue,
   • rash,
   • palpitations,
   These are all mild side effects. If you feel unwell or notice anything unusual or have other unexpected effects, stop taking the medicine and tell your doctor.
   • convulsions (fits) have very rarely been reported.

5. Storing Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
   Do not store above 25°C.
   Keep this medicine out of the reach and sight of children.
   Shelf life after opening - 6 months.

   Use by date: Do not use after the expiry date shown on the label/carton.
   Do not use if you notice any defects or signs of deterioration, please consult your pharmacist.
   Return all unused medicines to your pharmacist for safe disposal.

   This leaflet was approved:
   This leaflet was updated: March 2006

PINEWOOD
HEALTHCARE
Clonmel, Ireland.

3LF
LABELLING

75 ml:

Bottle label

Cetirizine Hydrochloride 5 mg/5 ml Oral Solution
(as Cetirizine hydrochloride)

Once Daily Allergy Relief
Adults and children over 6 years
- Hayfever
- Pet allergy
- Dust allergy
- Skin allergy

Children 2 - 5 years
- Hayfever

The active ingredient is: Cetirizine hydrochloride.
Other ingredients: Glycerol, polyethylene glycol 400, propyl parahydroxybenzoate (E216), isopropyl parahydroxybenzoate (E213), sodium hydroxide, water (aqueous).

Warning: Consult your doctor if you are pregnant or have kidney problems before taking this medicine. Do not use if breast-feeding. Do not take if sensitive to any of the ingredients. Avoid excessive alcohol. Warning: Do not exceed the stated dose. Cetirizine hydrochloride does not normally cause drowsiness at the recommended dose. However, individuals react differently, so if affected, you should not drive or operate machinery.

This product should only be used when clearly necessary. If symptoms persist consult your doctor. Keep out of the reach and sight of children. Do not store above 25°C. Shelf life after opening - 6 months.

Manufactured by: Pinewood Healthcare, Dunsany, Co. Meath, Ireland. PL: 04917/0068

BP: EXP:
CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION

This medicine is used to relieve the following symptoms: Adults & children over 6 years: Hayfever, pet or house dust mite allergies, and year round allergy rhinitis (itching, irritated, runny and blocked nose, itchy, red and watering eyes). Other allergies e.g. skin allergies such as rash, itching and urticaria (hives). Children aged between 2-5 years: Hayfever.

Dosage: For oral use only.
Adults, elderly and children aged 12 years and above: 10 ml once daily.
Children aged between 6 - 11 years: 5 ml once daily.
Children aged between 2 - 5 years: 2.5 ml once daily.
Children under 2 years of age: Not recommended.

Children 2 - 5 years: Hayfever

The active substance is: CETIRIZINE HYDROCHLORIDE.

Other ingredients: Lactic acid (E260), methylparaben (E218), propylparaben (E216) (see leaflet).

Warnings:
Consult your doctor if you are pregnant or have kidney problems before taking this medicine.
Do not use if breast-feeding.
Do not use if sensitive to any of the ingredients.
Avoid excessive alcohol.
Do not exceed the stated dose.

Cetirizine hydrochloride does not normally cause drowsiness at the recommended dose. However, individuals react differently so if affected, you should not drive or operate machinery.

PINEWOOD HEALTHCARE
Clonmel, Ireland,
cetirizine hcl
5 mg/5 ml
oral solution
**Cetirizine Hydrochloride**

**5 mg/5 ml Oral Solution** (as Cetirizine hydrochloride)

**Once Daily Allergy Relief**
- Adults and children over 6 years
- Hayfever
- Pet allergy
- Dust allergy
- Skin allergy

**Children 2 - 5 years**
- Hayfever

**Dosage**
- Adults, elderly and children aged 12 years and above: 10 ml once daily.
- Children aged between 6 - 11 years: 5 ml twice daily or 10 ml once daily.
- Children aged between 2 - 5 years: 5 ml once daily or 2.5 ml twice daily.
- Children under 2 years of age: Not recommended.

**Bottle label**

**MHRA PAR; CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION, PL 04917/0068**
MHRA PAR; CETIRIZINE HYDROCHLORIDE 5 MG/5 ML ORAL SOLUTION, PL 04917/0068

200 ml:

Bottle label

<table>
<thead>
<tr>
<th>Dosage:</th>
<th>200 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults, elderly and children aged 12 years and above:</td>
<td>10 ml once daily.</td>
</tr>
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</tbody>
</table>

Cetirizine Hydrochloride 5 mg/5 ml Oral Solution (as Cetirizine hydrochloride)

Once Daily Allergy Relief
Adults and children over 6 years:
- Hay Fever
- Pet Allergy
- Dust Allergy
- Skin Allergy

Children 2 - 5 years:
- Hay Fever

The active ingredient is: Cetirizine hydrochloride. Other ingredients: Liquid sorbitol (E420), methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216) (see leaflet).

Warnings: Consult your doctor if you are pregnant or have kidney problems before taking this medicine. Do not use if breastfeeding. Do not use if sensitive to any of the ingredients. Avoid excessive alcohol. Warning: Do not exceed the stated dose. Cetirizine hydrochloride does not normally cause drowsiness at the recommended dose. However, individuals react differently so if affected, you should not drive or operate machinery. This product should only be used when clearly necessary. If symptoms persist consult your doctor. Keep all medicines out of the reach and sight of children.

Marketing Authorisation Holder:
Pine Wood Laboratories Ltd., Ballymacarbery, Cork, Co. Tipperary, Ireland, PL 04917/0088 3LL