CETIRIZINE HYDROCHLORIDE 10 MG FILM-COATED TABLETS
PL 36390/0043

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency granted STD Chemicals Ltd, a Marketing Authorisation for the medicinal product, Cetirizine Hydrochloride 10 mg Film-Coated Tablets (PL 36390/0043) on 15 November 2011. The product is a pharmacy only medicine (P) medicine and can be purchased at pharmacies under the supervision of a pharmacist.

Cetirizine Hydrochloride 10 mg Film-Coated Tablets contains the active ingredient cetirizine hydrochloride belongs to a group of medicines called antihistamines. These are used to relieve the symptoms of seasonal allergic rhinitis (e.g. hay fever), perennial allergic rhinitis (e.g. year round allergies often due to house dust mites or animal allergies) and urticaria (itchy, red, swollen skin). These symptoms include itchy skin rashes; sneezing, tichy, runny blocked nose, red, itchy and watering eyes.

This application is considered to be identical to a previously granted licence for Cetirizine Hydrochloride 10 mg Film-Coated Tablets (PL 08137/0053) on 17 June 2002 to NeoLab Ltd. Holder.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Cetirizine Hydrochloride 10 mg Film-Coated Tablets outweigh the risks; hence a Marketing Authorisation has been granted.
CETIRIZINE HYDROCHLORIDE 10 MG FILM-COATED TABLETS
PL 36390/0043

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted STD Chemicals Ltd., a Marketing Authorisation for the medicinal product, Cetirizine Hydrochloride 10 mg Film-Coated Tablets (PL 36390/0043), on 15 November 2011. The product is a Pharmacy-Only (P) licensed medicine.

This is a simple, abridged, ‘informed consent’ application submitted according to Article 10(c) of EC Directive 2001/83 (as amended), cross-referencing the Marketing Authorisation for Cetirizine Hydrochloride 10 mg Film-Coated Tablets (PL 08137/0053), licensed to Neolab Ltd on 17 June 2002. The reference product cross-refers to the innovator product Zirtek Tablets 10 mg mg (PL 05221/0001) granted on 16 August 1988 to UCB S.A. However this licence underwent a change of ownership on 5 May 2000 and is licensed to UCB Pharma Limited (PL 08972/0032). The innovator product has been authorised in the EEA for over 10 years.

Cetirizine hydrochloride is a piperizine derivative and metabolite of hydroxyzine. It is a potent antihistamine with a low potential for drowsiness at the usual doses, and with additional anti-allergic properties. It is a selective H1 antagonist with negligible effects on other receptors and is therefore virtually free from anti-cholinergic and anti-serotonin effects.

Cetirizine Hydrochloride 10 mg Film-Coated Tablets is indicated for the treatment of perennial rhinitis, seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria in adults and children over 6 years of age.

No new data were submitted nor were they necessary for this simple application, as the data is identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated for it.
1. INTRODUCTION
This is a simple, informed consent application for Cetirizine Hydrochloride 10 mg Film-Coated Tablets submitted under Article 10c of Directive 2001/83/EC. The proposed Marketing Authorisation Holder is STD Chemicals Ltd, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW, UK.

The application cross-refers to Cetirizine Hydrochloride 10 mg Film-Coated Tablets, PL 08137/0053 authorised to Neolab Ltd since 17 June 2002. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name
The proposed name of the product is for Cetirizine Hydrochloride 10 mg Film-Coated Tablets. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
One film-coated tablet contains the 10 mg of the active ingredient, cetirizine hydrochloride. The medicinal product is licensed for marketing in polyethylenevinylcholride (PVC)/aluminium blister strips, which are packed with the Patient Information Leaflet (PIL) into cardboard outer cartons, in pack sizes of 7, 10, 14, 28, 30, 60 and 100 tablets. The container closure systems and pack sizes are identical to those for the reference products.

The approved shelf-life (3 years) with no special storage conditions is identical to the details registered for the cross-reference product.

2.3 Legal status
This product is a pharmacy-only medicine.

2.4 Marketing authorisation holder/Contact Persons/Company
The proposed Marketing Authorisation Holder is STD Chemicals Ltd, Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW, UK.

The Quality Person (QP) responsible for pharmacovigilance is stated and their curriculum vita has been included.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of 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
With the exception of lactose monohydrate, none of the other excipients contained or used in the manufacturing process for the proposed product contain material derived from animal or human origin. The applicant has provided a declaration that milk used in the production of lactose is sourced from healthy animals under the same conditions as that for human consumption. None of the excipients are sourced from genetically modified organisms. This is consistent with the cross-reference product.

3. EXPERT REPORT
A satisfactory quality overall summary has been prepared by an appropriately qualified expert. The CV of the expert was provided.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product (white coloured, circular, bioconvex, film-coated tablet; marked with ‘A’ on one side and a break-line on the other) is identical to that of the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The approved SmPC is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL)/CARTON
PIL
The PIL is satisfactory and in line with the approved SmPC and has been prepared in the user-tested format.

To support the proposed patient leaflet, a user testing report has been provided for the approved reference product, Cetirizine Hydrochloride 10 mg Film-Coated Tablets, PL 08137/0053 authorised to Neolab Ltd. The patient leaflet for the reference product met all criteria for successful user testing. The proposed layout and content of the proposed patient leaflet is identical to that of the approved reference product. As a result, bridging justification is accepted for the proposed product without the need for further user testing.

Carton and label
Mock-ups of the labelling have been provided and are satisfactory. The approved 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 included the name of the product in Braille on the outer packaging.
7. **CONCLUSIONS**
The data submitted with this application is acceptable. A Marketing Authorisation was, therefore, granted.
NON-CLINICAL ASSESSMENT

This is a simple, abridged, ‘informed consent’ application made under Article 10c of EC Directive 2001/83 (as amended). This application is identical to the reference product Cetirizine Hydrochloride 10 mg Film-Coated Tablets, PL 08137/0053 authorised to Neolab Ltd on 17 June 2002 in the UK, therefore, no new non-clinical data has been supplied with this application and none are required. A non-clinical overview report has been written by a suitably qualified person and is satisfactory. The CV of the non-clinical expert has been supplied.

The marketing authorisation holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As this application is identical to an already authorised reference product, it is not expected that the environmental exposure to ibuprofen will increase following the marketing approval of the proposed product.
CLINICAL ASSESSMENT

This is a simple, abridged, ‘informed consent’ application made under Article 10(c) of EC Directive 2001/83 (as amended), cross-referring to Cetirizine Hydrochloride 10 mg Film-Coated Tablets, PL 08137/0053 authorised to Neolab Ltd on 17 June 2002 in the UK.

No new clinical data has been supplied with this application and none are required. A clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the clinical expert has been supplied.

The marketing authorisation holder (MAH) has provided adequate justification for not submitting a Risk Management Plan (RMP). As this application is identical to 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. The reference product has been in use for many years and the safety profile of the active is well-established.

The MAH has provided a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the MAH 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.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application is consistent with those previously assessed for the cross-reference product and as such has 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 considered identical to the previously granted licence for Cetirizine Hydrochloride 10 mg Film-Coated Tablets, PL 08137/0053, authorised to Neolab Ltd on 17 June 2002 in the UK.

No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The approved SmPC, PIL and labelling are satisfactory, and consistent with those for the cross-reference product.

A user testing report has been provided for the approved reference product, Cetirizine Hydrochloride 10 mg Film-Coated Tablets, PL 08137/0053. The patient leaflet for the reference product met all criteria for successful user testing. The proposed layout and content of the proposed patient leaflet is identical to that of the approved reference product. As a result, bridging justification is accepted for the proposed product without the need for further user testing.

Mock-ups of the labeling have been provided and are satisfactory. The approved labeling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging. The MAH has committed to submitting mock-ups for currently mock-ups for currently unmarketed packs to the UK regulatory authority for approval before those packs are commercially marketed.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. The risk benefit is, therefore, considered to be positive.
CETIRIZINE HYDROCHLORIDE 10 MG FILM-COATED TABLETS
PL 36390/0043

STEPS TAKEN FOR ASSESSMENT

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<table>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 28 January 2011.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 16 February 2011.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the quality dossier on 26 April 2011.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 22 August 2011.</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 15 November 2011.</td>
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## STEPS TAKEN AFTER ASSESSMENT

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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</table>
CETIRIZINE HYDROCHLORIDE 10 MG FILM-COATED TABLETS
PL 36390/0043

SUMMARY OF PRODUCT CHARACTERISTICS
The UK Summary of Product Characteristics (SmPC) for Cetirizine Hydrochloride 10 mg Film-Coated Tablets (PL 36390/0043) is as follows:

1 NAME OF THE MEDICINAL PRODUCT
Cetirizine hydrochloride 10 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One film-coated tablet contains cetirizine hydrochloride 10 mg.

Excipients:
One film-coated tablet contains lactose monohydrate 101.83 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablet (tablet).

White coloured, circular, biconvex film coated tablet. Marked with ‘A’ on one side and a break-line on the other.

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.

4.2 Posology and method of administration
Adults and adolescents over 12 years of age: 1 tablet (10 mg) once daily.

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

Children 6-12 years:
1 tablet (10 mg) once daily or ½ tablet (5mg) taken twice daily (morning and evening)

For children weighing less than 30 kg:
½ tablet (5mg) taken once daily.

Clinical trials in children have not exceeded four weeks.

Elderly subjects: data do not suggest that the dose needs to be reduced in elderly subjects provided that the renal function is normal. The duration of the treatment may vary depending on the symptoms.

Cetirizine is contraindicated in patients with severe renal impairment.

Patients with moderate to severe renal impairment: the dosing intervals must be individualized according to renal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient’s creatinine clearance (CLcr) in ml/min is needed. The CLcr
(ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:

\[ \text{CL}_{\text{cr}} = \frac{(140 - \text{age [years]}) \times \text{weight [kg]}}{72 \times \text{serum creatinine [mg / dl]}} (x 0.85 \text{ for women}) \]

Dosing adjustments for adult patients with impaired renal function

<table>
<thead>
<tr>
<th>Group</th>
<th>Creatinine clearance (ml/min)</th>
<th>Dosage and frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥80</td>
<td>10 mg once daily</td>
</tr>
<tr>
<td>Mild</td>
<td>50 – 79</td>
<td>10 mg once daily</td>
</tr>
<tr>
<td>Moderate</td>
<td>30 – 49</td>
<td>5 mg once daily</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;30</td>
<td>5 mg once every 2 days</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>&lt;10</td>
<td>Contra-indicated</td>
</tr>
<tr>
<td>Patients undergoing dialysis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In pediatric patients suffering from renal impairment, the dose will have to be adjusted on an individual basis taking into account the renal clearance of the patient, his age and his body weight.

Patients with hepatic impairment: no dose adjustment is needed in patients with solely hepatic impairment.

Patients with hepatic impairment and renal impairment: dose adjustment is recommended (see Patients with moderate to severe renal impairment above).

**4.3 Contraindications**

Cetirizine hydrochloride 10 mg Film Coated Tablets are contraindicated in

- patients with a history of hypersensitivity to any of the constituents of the formulation, to hydroxyzine or to any piperazine derivatives.
- Patients with severe renal impairment at less that 10ml/min creatine clearance

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose- galactose malabsorption should not take Cetirizine Film-Coated Tablets.

**4.4 Special warnings and precautions for use**

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

At 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).

At therapeutic doses, no clinically significant interactions have been demonstrated with alcohol (for a blood alcohol level of 0.5 g/L). Nevertheless, precaution is recommended if alcohol is taken concomitantly.

Caution is recommended with concomitant use of CNS depressants.

Caution in epileptic patients and patients at risk of convulsions is recommended.

The use of the film-coated tablet formulation is not recommended in children aged less than 6 years since this formulation does not allow for appropriate dose adaptation.

Allergy skin tests are inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them.

**4.5 Interaction with other medicinal products and other forms of interaction**

Due to the pharmacokinetic, pharmacodynamic and tolerance profile of cetirizine, no interactions are expected with this antihistamine. Actually, neither pharmacodynamic nor significant
pharmacokinetic interaction was reported in drug-drug interactions studies performed, notably with pseudoephedrine or theophylline (400 mg/day).

The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased.

Caution is recommended with the concomitant use of CNS depressants.

4.6 Fertility, Pregnancy and Lactation

For cetirizine very rare clinical data on exposed pregnancies are available. The data indicates no adverse effects of cetirizine on pregnancy or on the health of the 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.

Lactation

No data concerning the excretion of cetirizine into human milk are available. Cetirizine is excreted in human milk at concentrations representing 0.25 to 0.90 those measured in plasma, depending on sampling time after administration. Therefore, caution should be exercised when prescribing cetirizine to lactating women.

4.7 Effects on ability to drive and use machines

Objective measurements of driving ability, sleep latency and assembly line performance have not demonstrated any clinically relevant effects at the recommended dose of 10 mg.

Patients intending to drive, engaging in potentially hazardous activities or operating machinery should not exceed the recommended dose and should take their response to the medicinal product into account. In these sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

4.8 Undesirable effects

Clinical studies have shown that cetirizine at the recommended dosage has minor undesirable effects on the CNS, including somnolence, fatigue, dizziness and headache. In some cases, paradoxical CNS stimulation has been reported.

Although cetirizine is a selective antagonist of peripheral H1-receptors and is relatively free of anticholinergic activity, isolated cases of micturition difficulty, eye accommodation disorders and dry mouth have been reported.

Instances of abnormal hepatic function with elevated hepatic enzymes accompanied by elevated bilirubin have been reported. Mostly this resolves upon discontinuation of the treatment with cetirizine dihydrochloride.

Clinical trials

Double blind controlled clinical or pharmacoclinical trials comparing cetirizine to placebo or other antihistamines at the recommended dosage (10 mg daily for cetirizine), of which quantified safety data are available, included more than 3200 subjects exposed to cetirizine.

From this pooling, the following adverse events were reported for cetirizine 10 mg in the placebo-controlled trials at rates of 1.0 % or greater:

<table>
<thead>
<tr>
<th>Adverse event (WHO-ART)</th>
<th>Cetirizine 10 mg (n= 3260)</th>
<th>Placebo (n = 3061)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a whole – general disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.63 %</td>
<td>0.95 %</td>
</tr>
<tr>
<td>Central and peripheral nervous system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.10 %</td>
<td>0.98 %</td>
</tr>
<tr>
<td></td>
<td>7.42 %</td>
<td>8.07 %</td>
</tr>
</tbody>
</table>
Although statistically more common than under placebo, somnolence was mild to moderate in the majority of cases. Objective tests as demonstrated by other studies have demonstrated that usual daily activities are unaffected at the recommended daily dose in healthy young volunteers.

Adverse drug reactions at rates of 1% or greater in children aged from 6 months to 12 years, included in placebo-controlled clinical or pharmacoclinical trials are:

<table>
<thead>
<tr>
<th>Adverse drug reactions (WHO-ART)</th>
<th>Cetirizine (n=1656)</th>
<th>Placebo (n =1294)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal system disorders</td>
<td>1.0 %</td>
<td>0.6 %</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somnolence</td>
<td>1.8 %</td>
<td>1.4 %</td>
</tr>
<tr>
<td>Respiratory system disorders</td>
<td>1.4 %</td>
<td>1.1 %</td>
</tr>
<tr>
<td>Rhinitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body as a whole – general disorders</td>
<td>1.0 %</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Post-marketing experience

In addition to the adverse effects reported during clinical studies and listed above, isolated cases of the following adverse drug reactions have been reported in post-marketing experience.

Undesirable effects are described according to MedDRA System Organ Class and by estimated frequency based on post-marketing experience.

Frequency estimates: Very common (≥1/10); Common (≥1/100, <1/10); Uncommon (≥1/1,000, <1/100); Rare (≥1/10,000, <1/1,000); Very rare (<1/10,000), not known (cannot be estimated from the available data):

Blood and lymphatic system disorders:
Very rare: thrombocytopenia

Immune system disorders:
Rare: hypersensitivity, allergic reactions (see Skin and subcutaneous disorders)
Very rare: anaphylactic shock

Psychiatric disorders:
Uncommon: agitation
Rare: aggression, confusion, depression, hallucination, insomnia
Very rare: tics

Nervous system:
Uncommon: paraesthesia.
Rare: convulsions
Very rare: dysgeusia, dyskinesia, dystonia, syncpe, tremor
Not known: amnesia, memory impairment
Eye disorders:
Rare: abnormal involuntary eye movements.
Very rare: accommodation disorder, blurred vision, oculogyration

Cardiac disorders:
Rare: tachycardia

Gastrointestinal disorders:
Uncommon: diarrhoea

Hepatobiliary disorders:
Rare: abnormal hepatic function (increased transaminases, alkaline phosphatase, γ-GT and bilirubin)

Skin and subcutaneous tissue disorders:
Uncommon: skin rash, pruritus
Rare: urticaria
Very rare: angioedema, erythema multiforme, fixed drug eruption

Renal and urinary disorders:
Very rare: dysuria, enuresis, micturition difficulties

General disorders:
Uncommon: asthenia, malaise
Rare: oedema

Investigations:
Rare: weight increased

4.9 Overdose
There is 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 to 500 mg to an adult gave no symptoms at all.

Symptoms
Symptoms observed after an overdose of cetirizine are mainly associated with CNS effects or with effects that could suggest an anticholinergic effect. Adverse events reported after an intake of at least 5 times the recommended daily dose are: confusion, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, restlessness, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention.

Management
There is no known specific antidote to cetirizine. Should overdose occur, symptomatic or supportive treatment is recommended. The patient should be kept under clinical observation for at least four hours after ingestion, and the blood pressure, heart rate and vital signs monitored until stable. In symptomatic cases, ECG should be performed.

Gastric lavage should be considered following ingestion of a short occurrence. Oral activated charcoal (50 g for an adult, 10-15 g for a child) should be considered if more than 2.5 mg/kg cetirizine has been ingested within one hour.

There is no specific antidote.

Cetirizine is not effectively removed by dialysis

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
ATC code: R06AE07

Pharmacotherapeutic group: Antihistamine for systemic use, piperazine derivative.
Cetirizine hydrochloride is a racemate and an anti-allergic with specific histamine H1-receptor blocking characteristics.

Cetirizine inhibits cutaneous reactions in allergic individuals by VIP (Vasoactive Intestinal Polypeptide) and the P substance, neuropeptides that are considered 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 eosinophiles after simulation with allergens and unselective histamine liberators, by a mechanism that is not primarily explained by the H1-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 distribution volume (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 ages 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. Cetirizine is eliminated to 60% in unchanged form via the kidneys within 96 hours. At repeated administration there is no accumulation at hand, nor is absorption or elimination affected. With 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
Tablet core
Lactose monohydrate
Microcrystalline cellulose
Colloidal anhydrous silica
Maize starch
Talc
Magnesium stearate

Coating
Titanium dioxide (E171)
Hypermellose (E464)
Lactose monohydrate
Macrogol
Sodium citrate (E331)

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
Blister comprising of PVC/Aluminium foil with 7, 10, 14, 28, 30, 60 and 100 tablets.

Not all packs may be marketed.

6.6 Special precautions for disposal
No special requirements.
MARKETING AUTHORISATION HOLDER
STD Chemicals Ltd,
Hillbrow House,
Hillbrow Road,
Esher,
Surrey,
KT10 9NW

MARKETING AUTHORISATION NUMBER(S)
PL 36390/0043

DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
15/11/2011

DATE OF REVISION OF THE TEXT
15/11/2011
PATIENT INFORMATION LEAFLET

CETIRIZINE HYDROCHLORIDE 10 mg FILM-COATED TABLETS
(cetirizine hydrochloride)

The name of this medicine is CETIRIZINE HYDROCHLORIDE 10 mg Film-Coated Tablets, which will be referred to as CETIRIZINE Tablets throughout this leaflet.

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- Do not pass this medicine on to others; it may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

1. WHAT CETIRIZINE TABLETS ARE AND WHAT THEY ARE USED FOR

The active ingredient in your tablets is cetirizine hydrochloride, which belongs to a group of medicines called antihistamines. These are used to relieve the symptoms of seasonal allergic rhinitis (e.g. hay fever), perennial allergic rhinitis (e.g. year round allergies often due to house dust mites or animal allergies) and urticaria (itchy, red, swollen skin). These symptoms include itchy skin rash, sneezing, itchy, runny or blocked nose, red, itchy and watering eyes.

2. BEFORE YOU TAKE CETIRIZINE TABLETS

Do not take CETIRIZINE Tablets if you:
- are allergic (hypersensitive) to cetirizine hydrochloride, hydroxyzine, pipazetine derivatives or any of the other ingredients in CETIRIZINE Tablets (see section 6. Further Information)
- have a severe kidney disease (severe renal failure with creatinine clearance below 10 ml/min)
- have hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

Take special care with CETIRIZINE Tablets

If you are a patient with renal insufficiency, please ask your doctor for advice; if necessary, you will take a lower dose. The new dose will be determined by your doctor.
If you are an epileptic patient or a patient at risk of convulsions, you should ask your doctor for advice.

No interactions susceptible to be noticeable impact have been observed between alcohol at the blood level of 0.5% (ml) corresponding to one glass of wine and cetirizine used at the normal doses. However, as is the case with all antihistamines, it is recommended to avoid concurrent consumption of alcohol.

CETIRIZINE Tablets can affect the results of allergy skin tests. If you require an allergy test you should stop taking CETIRIZINE Tablets three days before you have the test.

Taking other medicines

Please tell your doctor if you are taking or have recently taken any of the following medicines, as they may decrease or increase the effect of CETIRIZINE Tablets and vice versa.
- medication for anxiety or stress (CNS depressants)

It may still be alright for you to take CETIRIZINE Tablets and your doctor will be able to decide what is suitable for you. Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking your medicine with food and drink

CETIRIZINE Tablets can be taken with or without food.

Pregnancy and breast-feeding

Tell your doctor if you are pregnant, think you might be pregnant, or are planning to become pregnant. As with other drugs, the use of CETIRIZINE Tablets should be avoided in pregnant women.

Adolescent use of the drug by a pregnant woman should not produce any harmful effects on the fetus. Nevertheless, the administration of the medicine should be discontinued.

You should not take CETIRIZINE Tablets during breast-feeding because cetirizine passes into your breast milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Clinical studies have produced no evidence of impaired attention, alertness and driving capabilities after taking CETIRIZINE Tablets at the recommended dose.

If you are intending to drive, engage in potentially hazardous activities or operate machinery, you should not exceed the recommended dose. You should closely observe your response to the drug. If you are a sensitive patient, you may find that the simultaneous use of alcohol or other nervous depressant agents may additionally affect your attention and ability to read.

Important information about some of the ingredients of CETIRIZINE Tablets

This product contains lactose. 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 CETIRIZINE TABLETS

Always take CETIRIZINE Tablets exactly as your doctor or pharmacist has told you to do so. You should check with your doctor or pharmacist if you are not sure.

Dosage

The usual dosage is:
- Adults, elderly and children over 12 years: Take one tablet (10 mg) once daily.
- Children aged 4 - 12 years: Take one tablet (10 mg) once daily or half a tablet (5 mg) twice daily (morning and evening).
- Children weighing less than 30 kg: Half a tablet (5 mg) should be taken once daily.

Patients with moderate to severe renal impairment: Patients with moderate or severe renal impairment are recommended to take 5 mg once daily.

If drowsiness occurs, your tablet can be taken in the evening.

Method of administration: For oral use.
If you take more Cetirizine Tablets than you should
If you have accidentally taken more than the recommended dose, contact your nearest hospital casualty department or tell your doctor or pharmacist immediately. Remember to take the pack and any remaining tablets with you.

The most common signs and symptoms of overdose may include feeling unwell, confused, restless, shaky, dizzy, tired or very sleepy. You may also notice a rapid heart beat, having dilated pupils or blurred vision, and experience headache, itching, diarrhoea, or difficulty urinating.

If you forget to take Cetirizine Tablets
If you have forgotten to take your tablet, take it as soon as you remember and then wait 24 hours before taking your next dose.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cetirizine Tablets can cause side effects, although not everybody gets them. If you get any of the following symptoms after taking these tablets you should contact your doctor or pharmacist immediately:

- any sudden wheeziness, difficulty in breathing
- dizziness
- swelling of the eyelids, face, lips or throat

The following side effects have also been reported:

Common side effects (seen in less than 1 in 10 patients but in more than 1 in 100 patients):
- dryness, fatigue
- dry mouth, nausea, diarrhoea
- dizziness, headache
- sore or irritable throat, swelling and irritation of the lining of the nose

Uncommon side effects (seen in less than 1 in 100 patients but in more than 1 per 1000 patients):
- agitation
- paraesthesia (feeling of pins and needles)
- stomach ache
- rash, itching
- feelings of weakness and/or extreme tiredness; feeling unwell.

Rare side effects (seen in less than 1 in 10,000 patients):
- allergic reactions, some severe (very rare)
- feelings of aggression, confusion and depression
- hallucinations, difficulty in sleeping
- convulsions, movement disorders
- abnormal eye movements
- rapid heart beat
- oedema (swelling of the feet or ankles)
- eczema
- unusual weight gain
- changes in liver function tests, indicating the possibility of damage to the liver

Very rare side effects (seen in less than 1 in 10,000 patients):
- serious allergic reaction which causes difficulty in breathing or dizziness
- fits, shaking
- distorted sense of taste
- fainting

- blurred vision, eyes having uncontrolled circular movements (oculogyration)
- swelling of the face, lips or throat
- severe blistering skin rash
- difficult and/or painful urination
- loss of urinary control
- an increased tendency to bruise or bleed easily

Side effects of unknown frequency
- forgetfulness, memory impairment

Long term treatment with Cetirizine Tablets can lead to a dry mouth; it is therefore important that adequate oral hygiene is maintained.

If any of these side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE CETIRIZINE TABLETS

Keep out of the reach and sight of children.

Do not take this medicine after the expiry date (Exp.) stated. The expiry date refers to the last day of that month. The medicinal product does not require any special storage conditions.

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

6. FURTHER INFORMATION

What Cetirizine Tablets contain:
The active ingredient is cetirizine hydrochloride. Each tablet contains 10 mg of cetirizine hydrochloride.

The other ingredients are: lactose monohydrate, microcrystalline cellulose, colloidal anhydrous silica, maize starch, talc, magnesium stearate, titanium dioxide (E171), hypromellose, macrogol, sodium citrate

What Cetirizine Tablets look like and the contents of the pack:
Cetirizine Tablets are white coloured, circular, biconvex film coated tablets. They are marked with ‘A’ on one side and a break-line on the other.

Your medicine is available in packs containing 7, 10, 14, 20, 30, 60 and 100 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:
The Product Licence holder is STD Chemicals Ltd, Hillrow House, Hillrow Road, Essh, Surrey, KT10 9NW.
The manufacturer responsible for batch release is Neshal Ltd, 57 High Street, Oxted, Surrey, RH8 1NF.

This leaflet was last revised in August 2011.
CETIRIZINE HYDROCHLORIDE 10 MG FILM-COATED TABLETS
PL 36390/0043

LABELLING

CARTON

Cetirizine Hydrochloride 10 mg Tablets
Relief of the symptoms of hay fever and allergic rhinitis (e.g. dust and pet allergies), such as runny or blocked nose, itchy and watery eyes. Also relieves urticaria (swelling, red itchy skin). DOSE: Adults: Take one tablet (10mg) once daily. Children aged 6-12 years: Take one tablet (10mg) once daily or half a tablet (5mg) twice daily (morning and evening).
Not recommended for children under 6 years of age. If symptoms persist consult your doctor. DO NOT TAKE if you are pregnant or breastfeeding. This medicine does not usually cause drowsiness when taken at the recommended dose; however, if affected do not drive or operate machinery. Please read the leaflet enclosed carefully before taking this medicine.
No special precautions for storage. For oral administration.

Each tablet contains: cetirizine hydrochloride 10 mg.
Also contains lactose (see enclosed leaflet).
KEEP THIS MEDICINE OUT OF THE REACH AND SIGHT OF CHILDREN

Distributor:
Novab Ltd, 57 High Street, Ockham,
Hants, RG29 1LF.

PL 36390/0043
MA Holder: STD Chemicals Ltd
Hillbow House, Hillbow Road, Esher,
Surrey, KT10 9NW.
Cetirizine Hydrochloride 10 mg Tablets

Relief of the symptoms of hay fever and allergic rhinitis (e.g. dust and pet allergies), such as runny or blocked nose, itchy and watery eyes. Also relieves urticaria (swollen, red, itchy skin). DOSE: Adults, the elderly and children over 12 years: Take one tablet (10mg) once daily. Children aged 6-12 years: Take one tablet (10mg) once daily or half a tablet (5mg) twice daily (morning and evening). Not recommended for children under 6 years of age. If symptoms persist consult your doctor. DO NOT TAKE if you are pregnant or breastfeeding. This medicine does not usually cause drowsiness when taken at the recommended dose, however, if affected do not drive or operate machinery. Please read the leaflet enclosed carefully before taking this medicine. No special precautions for storage. For oral administration.

Each tablet contains: cetirizine hydrochloride 10 mg. Also contains lactose (see enclosed leaflet).

KEEP THIS MEDICINE OUT OF THE REACH AND SIGHT OF CHILDREN.

WARNING: DO NOT EXCEED THE STATED DOSE.

Distributor:
Neoslab Ltd, 57 High Street, Oldham, Lancs, OL2 5LF.

PL 36390/0043
MA Holder: STD Chemicals Ltd.
Hillbrow House, Hillbrow Road, Esher, Surrey, KT10 9NW.
Cetirizine Hydrochloride 10 mg Tablets

Relief of the symptoms of hay fever and allergic rhinitis (e.g. dust and pet allergies), such as runny or blocked nose, itchy and watery eyes. Also relieves urticaria (swollen, red itchy skin). DOSE: Adults, the elderly and children over 12 years: Take one tablet (10mg) once daily. Children aged 6-12 years: Take one tablet (10mg) once daily or half a tablet (5mg) twice daily (morning and evening). Not recommended for children under 6 years of age. If symptoms persist consult your doctor. DO NOT TAKE if you are pregnant or breastfeeding. This medicine does not usually cause drowsiness when taken at the recommended dose, however, if affected do not drive or operate machinery. Please read the leaflet enclosed carefully before taking this medicine.

No special precautions for storage. For oral administration.

Each tablet contains: cetirizine hydrochloride 10 mg.
Also contains lactose (see enclosed leaflet).

KEEP THIS MEDICINE OUT OF THE REACH AND SIGHT OF CHILDREN

WARNING: DO NOT EXCEED THE STATED DOSE.

Distributor: 
NeoLab Ltd, 57 High Street, Odiham, 
Hants, RG29 1LF.

PL 36390/0043

MA Holder: STD Chemicals Ltd.
Hill brow House, Hill brow Road, Esher, 
Surrey, KT10 9NW.