PROPOSED CLEAN PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF MEDICINE

ALLERMINE TABLETS 10 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg Cetirizine dihydrochloride.

Excipient(s) with known effect

Each tablet contains 74,30 mg Lactose monohydrate.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

White film-coated, capsule-shaped tablet with a break line on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Allergic processes responding to a histamine H_1 receptor antagonist.

- Respiratory: Allergic rhinitis, hay fever
- Cutaneous: Allergic skin conditions associated with pruritis e.g. urticaria.

4.2 Posology and method of administration

Adults or children 12 years of age or older:

One 10 mg tablet once daily.

Children 6 to 12 years old:

One 10 mg tablet once daily or 5 mg (half a tablet) twice daily.

No dose adjustment is necessary in healthy elderly patients with normal renal function.

Dosage in Renal impairment:

In patients with renal impairment, where the creatinine clearance is less than 40 ml/min, the recommended daily dose of cetirizine should be halved.

Dosage in Hepatic impairment:

In moderate to severe hepatic impairment, half the recommended daily dose should be used.

Paediatric population

ALLERMINE is contraindicated in children under the age of two years, as safety and efficacy have not been demonstrated (see section 4.3).

Method of administration

For oral administration

4.3 Contraindications

- Hypersensitivity to any of the ingredients.
- Hypersensitivity to hydroxyzine or to any piperazine derivatives.
- Lactating women, since the active ingredient is excreted in breast milk. (See section 4.6).
- Pregnancy, as safety has not been established (See section 4.6).
- Children under the age of two years, as safety and efficacy have not been demonstrated.
- Severe renal impairment with creatinine clearance of less than 30 ml/min.

4.4 Special warnings and precautions for use

This medicine may lead to drowsiness and impaired concentration, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressant agents (see section 4.5). The patient's ability to perform hazardous activities requiring mental alertness or physical coordination such as driving or operating machinery may be impaired. (See Section 4.7)

Porphyria: Use with caution.

Although ALLERMINE is relatively free of anticholinergic activity, being a selective antagonist of peripheral H_1-receptors, caution is advised in patients with urinary retention, prostatic hyperplasia, closed-angle glaucoma and pyloroduodenal obstruction. There have been reports of micturition difficulty, eye accommodation disorders and dry mouth (see section 4.8).

Caution should be taken in patients with predisposition factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as cetirizine may increase the risk of urinary retention.

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

ALLERMINE should be stopped several days (at least 3 days is recommended) before skin allergy tests as it may suppress positive skin test results.

Pruritus and/or urticaria may occur when ALLERMINE is stopped, even if those symptoms were not present before treatment initiation. The symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

ALLERMINE contains lactose. Patients with rare hereditary problems of galactose intolerance, e.g. galactosaemia, total lactase deficiency or glucose-galactose malabsorption should not take ALLERMINE.

Paediatric population

The use of ALLERMINE in tablet form is not recommended in children younger than 6 years of age as the suitable dose adjustments to be made are not possible.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of alcohol and other sedating agents should be avoided.

To date there is no known interactions between ALLERMINE with other medicines. Studies with diazepam, glipizide, pseudoephedrine, antipyrine, ketoconazole, azithromycin, erythromycin and cimetidine have revealed no evidence of pharmacokinetic interactions.

ALLERMINE may enhance the sedative effects of central nervous system depressants including anxiolytics, neuroleptics, opioid analgesics, hypnotics, barbiturates and alcohol. Other antimuscarinic medicines, such as atropine and tricyclic antidepressants and MAOI's may enhance the antimuscarinic effects of ALLERMINE if used concomitantly.

It has been suggested that antihistamines, such as ALLERMINE could possibly mask the warning signs of otic damage caused by ototoxic drugs such as aminoglycoside antibiotics.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Some antihistamines have been associated with foetal abnormalities when taken during pregnancy, but a number of large studies have failed to demonstrate any strong associations. Since the safety of cetirizine dihydrochloride in pregnancy has not been established, ALLERMINE is contraindicated in pregnancy (see section 4.3).

Breastfeeding

ALLERMINE is contraindicated in lactating women since cetirizine is excreted in breast milk (see section 4.3).

Fertility

Limited data is available on human fertility, but no safety concern has been identified. Animal data show no safety concern for human reproduction.

4.7 Effects on ability to drive and use machines

ALLERMINE lack significant sedative effects. Patients should be warned, however, that a small number of individuals may experience sedation. It is therefore advisable to determine individual response before driving or performing complicated tasks, (see section 4.4). This effect may be compounded by simultaneous intake of alcohol or other central nervous system depressants, (see section 4.5).

4.8 Undesirable effects

a. Summary of the safety profile

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.

There have been reports of isolated cases of micturition difficulty and eye accommodation disorders (see section 4.4).

Cases of abnormal hepatic function with elevated hepatic enzymes accompanied by elevated bilirubin have been reported. Cessation of the treatment with cetirizine dihydrochloride, mostly resolves this.

b. Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Undesirable effect**
Blood and lymphatic system disorders	Less frequent	Leucopoenia, haemolytic anaemia, agranulocytosis
Psychiatric disorders	Frequent	Somnolence
Nervous system disorders	Frequent	Dizziness, headache
	Less Frequent	Drowsiness, fatigue
	Frequency unknown	Anxiety, nervousness
Ear and labyrinth Disorders	Less frequent	Tinnitus, vertigo
Vascular disorders	Less frequent	Hypotension
Respiratory, thoracic and mediastinal disorders	Frequent	Pharyngitis
	Less frequent	Thickening of mucous, bronchospasm
Gastrointestinal disorders	Frequent	Dry mouth, nausea, gastrointestinal discomfort
	Less frequent	Abdominal pain, diarrhoea, constipation
Hepatobiliary disorders	Less frequent	Jaundice
Skin and subcutaneous tissue disorders	Less frequent	Photosensitivity, hair loss, sweating

System Organ Class	Frequency	Undesirable effect
General disorders and administration site conditions	Frequent	Fatigue

c. Description of selected adverse reactions

Skin reactions occurring after discontinuation of ALLERMINE:

After discontinuation of ALLERMINE, pruritus (intense itching) and/or urticaria have been reported (see section 4.4).

d. Paediatric population

System Organ Class	Frequency	Undesirable effect
Psychiatric disorders	Frequent	Somnolence
Respiratory, thoracic and mediastinal disorders	Frequent	Rhinitis
Gastrointestinal disorders	Frequent	Diarrhoea
General disorders and administration site conditions	Frequent	Fatigue

Post-marketing experience

System Organ Class	Frequency	Undesirable effect
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia
Immune system disorders	Less frequent	Hypersensitivity, Anaphylactic shock
Metabolism and nutrition disorders	Frequency unknown	Increased appetite

System Organ Class	**Frequency**	**Undesirable effect**
Psychiatric disorders	Less frequent	Agitation, aggression, confusion, depression, hallucination, insomnia, tics
	Frequency unknown	Suicidal ideation, nightmare
Nervous system disorders	Less frequent	Paraesthesia, convulsions, dysgeusia, syncope, tremor, dystonia, dyskinesia
	Frequency unknown	Amnesia, memory impairment
Eye disorders	Less frequent	Accommodation disorder, blurred vision, oculogyric crisis
Ear and labyrinth disorders	Frequency unknown	Vertigo
Cardiac disorders	Less frequent	Tachycardia
Gastrointestinal disorders	Less frequent	Diarrhoea
Hepato-biliary disorders	Less frequent	Hepatic function abnormal (increased transaminases, alkaline phosphatase, γ -GT and bilirubin)
	Frequency unknown	Hepatitis
Skin and subcutaneous tissue disorders	Less frequent	Pruritus, rash, urticaria, angioneurotic oedema, fixed drug eruption
	Frequency unknown	Acute generalized exanthematous pustulosis
Musculoskeletal and connective tissue disorders	Frequency unknown	Arthralgia, myalgia
Renal and urinary disorders	Less frequent	Dysuria, enuresis

System Organ Class	Frequency	Undesirable effect
	Frequency unknown	Urinary retention
General disorders and administration site conditions	Less frequent	Asthenia, malaise, oedema
Investigations	Less frequent	Weight increased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms

Symptoms observed after an overdose of ALLERMINE 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 ALLERMINE.

Should overdose occur, symptomatic or supportive treatment is recommended. Gastric lavage may be considered shortly after ingestion of the drug.

Cetirizine is not effectively removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamines for systemic use, Piperazine derivatives ATC code: R06AE07

Mechanism of action

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H_1-receptors. In vitro receptor binding studies have shown no measurable affinity for other than H_1-receptors, without any significant anticholinergic or antiserotonergic effects.

Pharmacodynamic effects

In addition to its anti-H_1 effect, cetirizine was shown to display anti-allergic activities: at a dose of 10 mg once or twice daily, it inhibits the late phase recruitment of eosinophils, in the skin and conjunctiva of atopic subjects submitted to allergen challenge.

Clinical efficacy and safety

Studies in healthy volunteers show that cetirizine, at doses of 5 and 10 mg strongly inhibits the wheal and flare reactions induced by very high concentrations of histamine into the skin, but the correlation with efficacy is not established. In a six-week, placebo-controlled study of 186 patients with allergic rhinitis and concomitant mild to moderate asthma, cetirizine 10 mg once daily improved rhinitis symptoms and did not alter pulmonary function. This study supports the safety of administering cetirizine to allergic patients with mild to moderate asthma. In a placebo-controlled study, cetirizine given at the high daily dose of 60 mg for seven days did not cause statistically significant prolongation of QT interval. At the recommended dosage, cetirizine has demonstrated that it improves the quality of life of patients with perennial and seasonal allergic rhinitis.

Paediatric population

In a 35-day study in children aged 5 to 12, no tolerance to the antihistaminic effect (suppression of wheal and flare) of cetirizine was found. When a treatment with cetirizine is stopped after repeated administration, the skin recovers its normal reactivity to histamine within 3 days.

5.2 Pharmacokinetic properties

Absorption

Cetirizine reaches peak blood levels of 300 ng/ml within one hour after administration of oral doses. Food delays the time to peak plasma concentrations but does not decrease the amount of cetirizine absorbed. The extent of bioavailability is similar when cetirizine is given as solutions or tablets.

The distribution of pharmacokinetic parameters such as peak plasma concentration (Cmax) and area under curve (AUC), is unimodal.

Distribution

The apparent volume of distribution is 0,50 l/kg. Plasma protein binding of cetirizine is 93 ± 0,3 %. Cetirizine does not modify the protein binding of warfarin.

Biotransformation

Cetirizine does not undergo extensive first pass metabolism.

Elimination

In adults, the terminal half-life is approximately 10 hours. This data is consistent with the urinary excretion half-life of cetirizine. The cumulative urinary excretion represents two thirds

of the dose given in both adults and children. The apparent plasma clearance is higher in children compared to adults.

No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days.

Linearity / non-linearity

There is a linear relationship between the dosage given and the plasma levels reached by cetirizine, over the range of 5 to 60 mg.

Pharmacokinetics in specific patient groups

Elderly

Following a single 10 mg oral dose in elderly patients, half-life increases by about 50 % and clearance decreases by 40 % compared to younger patients. The decrease in cetirizine clearance in these elderly patients appears to be related to their decreased renal function.

Renally impaired patients

The pharmacokinetics of the drug are similar in patients with mild impairment (creatinine clearance higher than 40 mL/min) and patients with normal renal function. Patients with moderate renal impairment have a 3-fold increase in half-life and 70 % decrease in clearance compared to patients with normal renal function.

Patients on haemodialysis (creatinine clearance less than 7 mL/min) given a single oral 10 mg dose of cetirizine have a 3-fold increase in half-life and a 70 % decrease in clearance compared to patients with normal renal function. Cetirizine is poorly cleared by haemodialysis. Dosing adjustment is necessary in patients with moderate or severe renal impairment (see section 4.2).

Hepatically impaired patients

Patients with chronic liver diseases (hepatocellular, cholestatic and biliary cirrhosis) given 10

or 20 mg of cetirizine as a single dose have a 50 % increase in half-life along with a 40 % decrease in clearance compared to healthy patients.

Dosing adjustment is only necessary in hepatically impaired patients if concomitant renal impairment is present.

Paediatric population

The half-life of cetirizine was about 6 hours in children of 6-12 years and 5 hours in children 2-6 years. In infants and toddlers aged 6 to 24 months, it is reduced to 3.1 hours

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:

Lactose monohydrate

Magnesium Stearate

Povidone K 29/32

Pregelatinised Maize Starch

Tablet Coating

Opadry White Y-1-7000

Hydroxypropylmethylcellulose 5 cP (E464)

Polyethylene Glycol 400

Talc

Titanium Dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25 ºC in well-closed containers, protected from light. Do not remove the blister from the carton until required for use.

6.5 Nature and contents of container

PVC/Aluminium foil blister strips of 10 tablets, packed in unit cartons of 10 or 30 tablets.

White, opaque polypropylene securitainers containing 30 tablets. Amber glass containers containing 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDERS OF CERTIFICATE OF REGISTRATION

Trinity Pharma (Pty) Ltd.

3 Gwen Lane, 4th Floor

Sandton

2031

Email: pv@trinitypharma.co.za

Contact number: +27 (0)10 594 5610

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2 July 2004

10 DATE OF REVISION OF THE TEXT

14 August 2025.