Clean Professional Information for Medicines for Human Use:

CETIRIZINE 5 mg AUSTELL

CETIRIZINE 10 mg AUSTELL

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

CETIRIZINE 5 mg AUSTELL film-coated tablets

CETIRIZINE 10 mg AUSTELL film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CETIRIZINE 5 mg AUSTELL film-coated tablets:

Each film coated tablet contains cetirizine dihydrochloride 5 mg.

Contains sugar: lactose monohydrate 68,00 mg.

CETIRIZINE 10 mg AUSTELL film-coated tablets:

Each film coated tablet contains cetirizine dihydrochloride 10 mg.

Contains sugar: lactose monohydrate 65,00 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

CETIRIZINE 5 mg AUSTELL film-coated tablets:

White to creamish white, capsule shaped film coated tablets with breakline and ‘B’ & ‘L’ embossed on either side of the breakline and ‘5’ embossing on the other side.

CETIRIZINE 10 mg AUSTELL film-coated tablets:

White to creamish white, capsule shaped film coated tablets with scoreline and ‘B’ & ‘L’ debossed on either side of the scoreline and ‘10’ debossing on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CETIRIZINE AUSTELL is indicated for the symptomatic relief of:

- Respiratory: Allergic rhinitis, hay fever.
- Cutaneous: Allergic skin conditions associated with pruritus such as urticaria.

4.2 Posology and method of administration

Posology

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 twice daily.

Special populations

Elderly population

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

Cetirizine 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

CETIRIZINE AUSTELL is for oral use.

Missed dose:

Doctors should advice patients who forget to take CETIRIZINE AUSTELL to take a dose as soon as possible and then to continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- Hypersensitivity to cetirizine, hydroxyzine, any piperazine derivative or to any of the excipients listed in section 6.1.
- Patients with severe renal impairment at less than 30 mL/min creatinine clearance.
- Asthma, as it may cause airway obstruction in patients who have previously experienced adverse reactions to antihistamines
- Pregnancy and lactation, 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.

4.4 Special warnings and precautions for use

This medicine may lead to drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants.

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.

Patients with kidney disease are instructed to consult a health care provider before use. The health care provider should determine if a different dose is needed (see section 4.2).

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.

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported very rarely with cetirizine containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of this medicine should be discontinued and appropriate measures taken if needed.

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

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

Porphyria: Use with caution.

Excipient lactose monohydrate

This medicine contains lactose:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of alcohol and other central nervous system depressants should be avoided.

There is no evidence of an interaction between cetirizine and cimetidine, ketoconazole, erythromycin, azithromycin, diazepam, glipizide and pseudoephedrine.

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

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established. (see section 4.3)

Pregnancy

Prospectively collected data on pregnancy outcomes do not suggest potential for maternal or foetal/embryonic toxicity above background rates. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. CETIRIZINE AUSTELL should not be used during pregnancy.

Breastfeeding

Cetirizine is excreted in breast milk. Cetirizine is excreted in human milk at concentrations representing 25 % to 90 % those measured in plasma, depending on sampling time after

administration. CETIRIZINE AUSTELL should not be used when breastfeeding.

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

CETIRIZINE AUSTELL lacks significant sedative effects**.** Patients should be warned, however, that a small number of individuals may experience sedation. This effect may be compounded by the

simultaneous intake of alcohol or other central nervous system depressants (see section 4.5).

The patient's ability to perform hazardous activities requiring mental alertness or physical co-ordination such as driving or operating machinery may be impaired. It is therefore advisable to determine individual response before driving or performing complicated tasks.

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.

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.

b) Tabulated list of adverse reactions

Clinical trials

Double blind controlled clinical 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 3 200 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:

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Psychiatric disorders	Somnolence		

Nervous system disorders	Dizziness, headache		
Respiratory system disorders	Pharyngitis		
Gastrointestinal disorders	Dry mouth, nausea	Abdominal pain	
General disorders	Fatigue		

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

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Psychiatric disorders	Somnolence		
Respiratory system disorders	Rhinitis		
Gastrointestinal disorders	Diarrhoea		
General disorders	Fatigue		

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and post-marketing spontaneous reports with cetirizine.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Blood and lymphatic system		Thrombocytopenia	

disorders			
Immune system disorders		Hypersensitivity reactions, anaphylactic shock	
Metabolism and nutrition disorders			Increased appetite
Psychiatric disorders		Agitation, aggression, confusion, depression, hallucinations, insomnia, tics	Suicidal ideation
Nervous system disorders	Headache, dizziness, anxiety	Paraesthesia, convulsions, dysgeusia, dystonia, dyskinesia, syncope, tremor	Drowsiness, nervousness, amnesia, memory impairment
Eye disorders		Accommodation disorder, vision blurred, oculogyration	Eye pain
Ear and labyrinth disorders			Vertigo
Cardiac disorders		Tachycardia	
Respiratory, system disorders			Thickening of mucous
Gastrointestinal disorders	Dry mouth, nausea	Diarrhoea	Gastrointestinal discomfort
Hepatobiliary disorders		Hepatic function abnormal (increased	Hepatitis

		transaminases, alkaline phosphatase, y-GT and bilirubin)	
Skin and subcutaneous tissue disorders		Pruritus, skin rash, urticaria, angioneurotic oedema, fixed drug eruption	Acute generalized exanthematous pustulosis (AGEP)
Musculoskeletal, bone and connective tissue disorders			Arthralgia
Renal and urinary disorders		Dysuria, enuresis	Urinary retention
Reproductive system and breast disorders			Erectile dysfunction
General disorders and administration site conditions		Asthenia, malaise, oedema	Pruritus on withdrawal
Investigations		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.

Suspected adverse reactions can also be reported directly to the HCR via medsafety@austell.co.za.

4.9 Overdose

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.

Drowsiness is an expected symptom of overdosage. Overdosage in children may produce agitation, somnolence, pruritus, rash, urinary retention, fatigue, tremor and tachycardia.

Treatment

In the case of overdosage, symptomatic and supportive measures is recommended. There is no specific antidote. Cetirizine is not effectively removed by dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class:

A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamine for systemic use, piperazine derivatives,

ATC Code: R06A E07

Mechanism of action

CETIRIZINE AUSTELL is a metabolite of hydroxyzine. It is a second – generation, non-sedating, reversible, competitive inhibitor of histamine at the histamine-1 (H_1)

receptor, devoid of any significant anticholinergic and antiserotonergic effects. Cetirizine competes with histamine for the H_1 receptor site. Cetirizine prevents but does not reverse, pharmacological responses mediated by histamine, at the H_1 receptor. Cetirizine inhibits the late phase recruitment of eosinophils, in the skin and conjunctiva of atopic subjects submitted to allergen challenge.

5.2 Pharmacokinetic properties

Absorption

Cetirizine is well absorbed from the gastro-intestinal tract and peak plasma concentrations are reached within 1 hour after oral administration. The steady state peak plasma concentrations is approximately 300 ng/mL. The distribution of pharmacokinetic parameters such as peak plasma concentration (C_{max}) and area under curve (AUC), is unimodal. Food decreases the rate but not the extent of absorption.

Distribution

The apparent volume of distribution is 0,50 L/kg. Cetirizine is highly bound to plasma proteins, however, does not modify the protein binding of warfarin.

Biotransformation

Cetirizine is only marginally affected by first pass metabolism in the liver.

Elimination

The terminal half-life in adults is approximately 10 hours.

Cetirizine is eliminated faster in children, and slower in patients with hepatic or renal impairment (creatinine clearance < 40 mL/min), with a resultant increase in half-life

and decrease in clearance. Cetirizine does not undergo extensive first-pass metabolism. The cumulative urinary excretion represents about two thirds of the dose given in both adults and children. No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days.

Linearity/non-linearity

Pharmacokinetics are linear, with plasma concentrations increasing proportionately with increasing doses.

Special populations

Renal impairment

The pharmacokinetics of cetirizine was similar in patients with mild impairment (creatinine clearance higher than 40 mL/min) and healthy volunteers. Patients with moderate renal impairment had a 3-fold increase in half-life and 70 % decrease in clearance compared to healthy volunteers. Patients on haemodialysis (creatinine clearance less than 7 mL/min) given a single oral 10 mg dose of cetirizine had a 3-fold increase in half-life and a 70 % decrease in clearance compared to patients with normal renal function. Cetirizine was poorly cleared by haemodialysis. Dosing adjustment is necessary in patients with renal impairment (see section 4.2).

Hepatic impairment

Patients with chronic liver diseases (hepatocellular, cholestatic, and biliary cirrhosis) given 10 or 20 mg of cetirizine as a single dose had a 50 % increase in half-life along with a 40 % decrease in clearance compared to healthy subjects.

Elderly

Following a single 10 mg oral dose, half-life increased by about 50 % and clearance decreased by 40 % in 16 elderly subjects compared to younger subjects. The decrease in cetirizine clearance in these elderly volunteers appeared to be related to their decreased renal function.

Paediatric population

The half-life of cetirizine in children was about 6 hours in children aged 6 to 12 years and 5 hours in children aged 2 to 6 years.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate

Maize starch

Pregelatinised starch

Dried maize starch

Purified talc

Magnesium stearate

Film-coating:

Hydroxypropyl methylcellulose (hypromellose)

Macrogol 6000

Titanium dioxide

Purified talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Keep tablets in a dry place. Protect from light.

Keep the blister packs in the outer carton until required for use.

Keep the securipack tightly closed.

6.5 Nature and contents of container

CETIRIZINE 5 mg AUSTELL film-coated tablets are supplied in:

- Blister packs (Clear PVC/Aluminium foil) of 1 x 10, 3 x 10 and 10 x 10 tablets.

  Pack sizes of 10, 30 or 100 film-coated tablets.
- Bulk packs (White HDPE Jars) of 250, 500 and 1 000 film-coated tablets.

CETIRIZINE 10 mg AUSTELL film-coated tablets are supplied in:

- Blister packs (Clear PVC/Aluminium foil) of 1 x 10, 3 x 10 and 10 x 10 tablets.

  Pack sizes of 10, 30 or 100 film-coated tablets.
- Bulk packs (White HDPE Jars) of 250, 500 and 1 000 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

1 Sherborne Road

Parktown

Johannesburg

2193

South Africa

Tel: +27 11 611 1400 or +27 860 287 835

8. REGISTRATION NUMBERS

CETIRIZINE 5 mg AUSTELL film-coated tablets: 37/5.7.1/0579

CETIRIZINE 10 mg AUSTELL film-coated tablets: 37/5.7.1/0580

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 September 2004

10. DATE OF REVISION OF THE TEXT

15 July 2026