PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

CETIRIZINE-HEXAL® 10 mg TABLETS

CETIRIZINE-HEXAL® 1 mg/ml ORAL SOLUTION

CETIRIZINE HEXAL® 10 mg/ml ORAL DROPS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg cetirizine dihydrochloride.

Each 1 ml oral solution contains 1 mg cetirizine dihydrochloride.

Each 1 ml oral drop contains 10 mg cetirizine dihydrochloride.

Excipients with known effect:

CETIRIZINE-HEXAL® 10 mg TABLETS contains sugar (lactose monohydrate 80,0 mg) (see section 4.4).

CETIRIZINE-HEXAL® 1 mg/ml ORAL SOLUTION contains sorbitol solution 70 % (see section 4.4).

CETIRIZINE-HEXAL® 10 mg/ml ORAL DROPS: Sugar free

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral administration.

CETIRIZINE-HEXAL 10 mg TABLETS: White, oblong, film-coated tablet, notch on one side.

CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION: Clear, colourless liquid with banana flavour. The solution must be free of any visible particulate matter.

CETIRIZINE-HEXAL 10 mg/ml ORAL DROPS: Clear colourless liquid free from undissolved foreign matter.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

CETIRIZINE-HEXAL is indicated for symptomatic relief of allergic conditions such as allergic rhinitis, and allergic skin conditions such as urticaria.

4.2. Posology and method of administration

Posology

Tablets:

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.

Oral solution:

Adults or children 12 years of age or older: 10 mg (10 ml) once daily.

Children 6 to 12 years old: 10 mg (10 ml) daily, either as a single dose or as divided doses of 5 ml in the morning and 5 ml in the evening.

Children 2 to 6 years old: 5 mg (5 ml) daily, either as a single dose or as divided doses of 2,5 ml in the morning and 2,5 ml in the evening.

Oral drops:

Adults or children 12 years of age or older: 10 mg (20 drops) once daily.

Children 6 to 12 years old: 10 mg (20 drops) daily, either as a single dose or as divided doses of 10 drops in the morning and 10 drops in the evening.

Children aged 2-6 years: 5 mg (10 drops) may be given as a single dose or divided into two doses of 5 drops in the morning and 5 drops in the evening.

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.

4.3. Contraindications

- Hypersensitivity to the active substance, to any of the excipients, to hydroxyzine or to any piperazine derivatives.
- Patients with severe renal impairment at less than 10 ml/min creatinine clearance.
- Lactating women, since the active ingredient is excreted in breastmilk.
- Pregnancy, as safety has not been established.
- Children under the age of two years, as safety and efficacy have not been demonstrated.

4.4 Special warnings and precautions for use

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 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 (see section 4.8).

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

Methyl-parahydroxybenzoate and propyl-parahydroxybenzoate may cause allergic reactions (possibly delayed).

Pruritus and/or urticaria may occur when cetirizine is stopped, even if those symptoms were not present before treatment initiation (see section 4.8). In some cases, the symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

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

Lactose intolerance:

CETIRIZINE-HEXAL 10 mg TABLETS contains lactose monohydrate. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take CETIRIZINE-HEXAL 10 mg TABLETS.

CETIRIZINE-HEXAL 10 mg TABLETS contains lactose monohydrate which may have an effect on the glycaemic control of patients with diabetes mellitus.

CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION contains sorbitol. Patients with the rare hereditary condition of sorbitol intolerance should not take CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of alcohol and other sedating medicines should be avoided. There is no evidence of an interaction between cetirizine and cimetidine, ketoconazole, erythromycin, azithromycin, diazepam, glipizide, and pseudoephedrine.

Due to 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.

Alcohol and other CNS depressants

In sensitive patients, the concurrent use of alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance, although cetirizine does not potentiate the effect of alcohol (see section 4.4).

4.6 Fertility, pregnancy and lactation

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

Breastfeeding

Caution should be exercised when prescribing cetirizine to lactating women. Cetirizine is excreted in human milk at concentrations representing 25 % to 90 % of those measured in plasma, depending on sampling time after administration.

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

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. The patient's ability to perform hazardous activities requiring mental alertness or physical co-ordination such as driving or operating machinery may be impaired.

4.8 Undesirable effects

Blood and lymphatic system disorders:

Less frequent: Thrombocytopenia

Metabolism and nutrition disorders:

Frequency unknown: Increased appetite

Psychiatric disorders:

Less frequent: Agitation, aggression, confusion, depression, hallucination, insomnia, tics

Frequency unknown: Suicidal ideation, nightmare

Nervous system disorders:

Frequent: Headache, drowsiness, somnolence

Less frequent: Dizziness, paraesthesia, convulsions, movement disorders, syncope, dysgeusia, tremor, dystonia, dyskinesia

Frequency unknown: Anxiety, nervousness, amnesia, memory impairment

Eye disorders:

Less frequent: Accommodation disorder, blurred vision, oculogyric crisis, especially in children

Ear and labyrinth disorders:

Frequency unknown: Vertigo

Cardiac disorders:

Less frequent: Tachycardia

Respiratory system:

Frequency unknown: Thickening of mucus

Gastrointestinal disorders:

Frequent: Dry mouth

Less frequent: Abdominal complaints such as abdominal pains, nausea, diarrhoea, digestive disorders

Frequency unknown: Increased appetite, gastrointestinal discomfort

Hepatobiliary disorders:

Less frequent: Abnormal hepatic function (increased transaminases, alkaline phosphatase, gamma-GT and bilirubin), hepatitis

Skin and subcutaneous tissue disorders:

Less frequent: Rash, pruritus**,** urticaria, angioneurotic oedema, erythema multiforme

Frequency unknown: Acute generalized exanthematous pustulosis (AGEP)

Musculoskeletal and connective tissue disorders:

Frequency unknown: Arthralgia

Renal and urinary disorders:

Less frequent: Dysuria, enuresis, micturition difficulties

Frequency unknown: Urinary retention (see section 4.4)

General disorders and administration site conditions:

Frequent: Fatigue

***Less frequent*:** Asthenia, malaise, oedema

Investigations:

Less frequent: Increased weight

Immune system disorders:

Less frequent: Hypersensitivity, anaphylactic shock

Skin reactions occurring after discontinuation of cetirizine:

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

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 medicinal product. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

4.9 Overdose

Toxicity:

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

a) 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.

b) Management

There is no known specific antidote to cetirizine.

Should overdose occur, symptomatic or supportive treatment is recommended. Cetirizine is not effectively removed by dialysis.

Drowsiness is an expected symptom of overdosage. Overdosage in children may produce agitation, somnolence, pruritus, rash, urinary retention, fatigue, tremor, and tachycardia. In the case of massive overdosage, gastric lavage should be performed together with the usual supportive measures. There is no specific antidote. Cetirizine is not effectively removed by dialysis.
FURTHER TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Piperazine derivatives, ATC code: R06A E07

CETIRIZINE-HEXAL is a metabolite of hydroxyzine. It is a second-generation reversible, competitive inhibitor of histamine at the histamine-1 (H_1) receptor.
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.

5.2 Pharmacokinetic properties

Cetirizine is well absorbed from the gastrointestinal tract and peak plasma concentrations are reached within 1 hour after oral administration.

Pharmacokinetics are linear, with plasma concentrations increasing proportionately with increasing doses. The terminal half-life in adults is approximately 10 hours; in children aged 6 to 12 years, 6 hours; in children aged 2 to 6 years, 5 hours. Cetirizine is metabolised to a small extent with a known inactive main metabolite. 60 % of a dose of cetirizine is eliminated in unchanged form via the kidneys within 96 hours. Repeated administration does not lead to any accumulation, nor is the absorption or elimination affected. 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.

6. Pharmaceutical particulars

6.1 List of excipients

CETIRIZINE-HEXAL 10 mg TABLETS:

Colloidal anhydrous silica, hypromellose, lactose monohydrate, macrogol 4000, magnesium stearate, microcrystalline cellulose, opadry white and titanium dioxide.

CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION:

Acetic acid 20 %, banana flavour, glycerol 85 %, methyl-parahydroxybenzoate (0,117 % *m/v*), propylene glycol, propyl-parahydroxybenzoate (0,013 % *m/v*), purified water, saccharin sodium, sodium acetate, sorbitol 70 %.

The oral solution contains methyl-parahydroxybenzoate (0,117 % *m/v)* and propyl-parahydroxybenzoate (0,013 % *m/v)* as preservatives.

CETIRIZINE-HEXAL 10 mg/ml ORAL DROPS:

Acetic acid, glycerol 85 %, methyl-parahydroxybenzoate (0,198 % *m/v*), propylene glycol, purified water, saccharin sodium, sodium acetate trihydrate.

The oral drops contain benzoic acid 0,198 % *m/v* as a preservative.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION:

36 months

CETIRIZINE-HEXAL 10 mg TABLETS and CETIRIZINE-HEXAL 10 mg/ml ORAL DROPS:

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

No special precautions for storage.

6.5 Nature and contents of container

CETIRIZINE-HEXAL 10 mg TABLETS: Polyvinylchloride/aluminium blister packs of 30’s.

CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION**:** 75 ml or 150 ml round brown glass bottles containing 75 or 150 ml oral solution respectively. A 5 ml measuring spoon is provided.

CETIRIZINE-HEXAL 10 mg/ml ORAL DROPS: 20 ml brown glass bottles containing 20 ml oral drops.

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

Not applicable

7. HOLDER OF CERTIFICATE OF REGISTRATION

Sandoz SA (Pty) Ltd[1]

Waterfall 5-lr

Magwa Crescent West

Waterfall City

Jukskei View

2090

8. REGISTRATION NUMBER(S)

CETIRIZINE-HEXAL® 10 mg TABLETS: 37/5.7.1/0497

CETIRIZINE-HEXAL® 1 mg/ml ORAL SOLUTION: A39/5.7.1/0103

CETIRIZINE-HEXAL® 10 mg/ml ORAL DROPS: 37/5.7.1/0498

9. DATE OF FIRST AUTHORISATION

CETIRIZINE-HEXAL 10 mg TABLETS:

Date of registration*:* 17 September 2004

CETIRIZINE-HEXAL 1 mg/ml ORAL SOLUTION:

Date of registration*:* 07 July 2006

CETIRIZINE-HEXAL 10 mg/ml ORAL DROPS:

Date of registration*:* 17 September 2004

10. DATE OF REVISION OF THE TEXT

03 February 2021

Additional country registration details:

Country	*Product name*	*Scheduling status (or Category of distribution)*	*Registration number*
Namibia	Cetirizine-Hexal 1,0 mg / ml oral solution	NS1	12/5.7/0133
	Cetirizine-Hexal 10	NS1	12/5.7/0134
Botswana	Cetirizine-Hexal 1,0 mg / ml oral solution	S2	BOT1302469A/B
	Cetirizine-Hexal 10	S2	BOT1703202
Zambia	Cetirizine-Hexal 10	P	039/053

ATC Code: R06AE07 - Piperazine derivatives

Name and address of manufacturer:

(Oral solution)
Lichtenheldt GmbH
Pharmazeutische Fabrik,
Justus-Liebig-Weg 1 and
Industriestraße 7 - 10
D-23812 Wahlstedt,
Germany

or

(Oral solution and film-coated tablets)
Salutas Pharma GmbH
Otto-von-Guericke-Allee 1,
D-39179 Barleben,
Germany

or

(Film-coated tablets)
Ilaclari Sanayi ve Ticaret A.S.
GOSB Ihsan Dede Cad. 900. sok.
TR-41480 Gebze – Kocaeli,
Turkey

[1]Company Reg. No.: 1990/001979/07