Applicant/PHRC: ***Hetero Drugs South Africa (Pty) Ltd***

Product proprietary name: ***ZIALDEL***

Dosage form and strength: Oral solution, Each 5 ml contains 5 mg cetirizine dihydrochloride

CLEAN PROFESSIONAL INFORMATION FOR ZIALDEL

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

ZIALDEL ORAL SOLUTION 5 mg/5 mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 5 mg cetirizine dihydrochloride.

Excipients:

Each ml contains 2,7 g sorbitol (sugar) and 2,5 mg sucralose (sweetener).

For a full list of excipients, see Section 6.1.

Preservative:

Sodium benzoate 0,2 % m/v

3. PHARMACEUTICAL FORM

Oral solution

ZIALDEL is a clear, colourless to yellow grape-flavoured liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZIALDEL is indicated for the treatment of allergic processes which respond to histamine H_1 receptor antagonists:

- Respiratory: Allergic rhinitis, hay fever.

- Cutaneous: Allergic skin conditions associated with pruritus e.g., urticaria.

4.2 Posology and method of administration

Posology

Adults and children over the age of 12 years:

Take 10 mL (10 mg) once daily.

Children 6 to 12 years of age:

Take 10 ml (10 mg) daily, either as a single dose or as divided doses of 5 ml (5 mg) in the morning and 5 ml (5 mg) in the evening.

Children 2 to 6 years of age:

Take 5 ml (5 mg) daily, either as a single dose or as divided doses of 2,5 ml (2,5 mg) in the morning and 2,5 ml (2,5 mg) in the evening.

Special populations

Elderly patients:

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

Renal impairment:

In patients with renal insufficiency (creatinine clearance less than 40 ml/min), the dose should be reduced to half the recommended daily dose.

Hepatic impairment:

In patients with moderate to severe hepatic impairment the dose should be reduced to half the recommended daily dose.

Method of administration

For oral use only

4.3 Contraindications

- Hypersensitivity to cetirizine dihydrochloride, hydroxyzine, any piperazine derivatives or to any of the excipients listed in section 6.1
- Patients with severe renal impairment where the creatinine clearance is less than 30 ml/min.
- ZIALDEL is contra-indicated in lactating women since the active ingredient is excreted in breast milk (see section 4.6).
- ZIALDEL is contra-indicated in pregnancy as the safety has not been established (see section 4.6)
- Asthma, as it may cause airway obstruction in patients who have previously experienced adverse reactions to antihistamines.
- In children under 2 years of age, as safety and efficacy have not been demonstrated.

4.4 Special warnings and precautions for use

ZIALDEL lacks significant sedative effects. Patients should be warned, however, that a small number of individuals may experience sedation.

Renal and hepatic impairment:

The daily dose of ZIALDEL should be reduced in patients with renal insufficiency and patients with moderate to severe hepatic impairment (see section 4.2)

Epilepsy:

ZIALDEL should be used with caution in patients with epilepsy or patients at risk of convulsions.

Alcohol:

Avoid alcohol intake while taking ZIALDEL.

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.

Elderly patients are more susceptible to many of the adverse effects of cetirizine.

ZIALDEL contains propylene glycol which may cause alcohol-like symptoms.

Allergy skin tests are inhibited by antihistamines such as ZIALDEL and a wash-out period of 3 days is recommended before performing them (see section 4.5)

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

Patients with hereditary fructose intolerance, should not take ZIALDEL.

Sorbitol may cause gastrointestinal discomfort and have a mild laxative effect.

The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

The content of sorbitol in medicines for oral use may affect the bioavailability of other medicines for oral use administered concomitantly.

4.5 Interaction with other medicines and other forms of interaction

- There are no known interactions between ZIALDEL and other medicines. Due to pharmacokinetic, pharmacodynamic and tolerance profile of cetirizine, no interactions are expected with this medicine. Neither pharmacodynamic nor significant pharmacokinetic interaction was reported in interaction studies performed, notably with pseudoephedrine or theophylline (400 mg/day).

- There is no evidence of an interaction between cetirizine and cimetidine, ketoconazole, erythromycin, azithromycin, diazepam and glipizide.
- The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased.
- 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 (0,5 g/l blood levels) (see section 4.7).

4.6 Fertility, pregnancy and lactation

Pregnancy

ZIALDEL is contraindicated in pregnancy as the safety has not been established (see section 4.3)

Breastfeeding

ZIALDEL is contraindicated in lactating women since the active ingredient is excreted in breast milk (see section 4.3).

Fertility

Limited data is available on human fertility but no safety concern has been identified.

4.7 Effects on ability to drive and use machines

Patients should be warned that some individuals may experience sedation. It is therefore advisable to determine individual response before driving or performing complicated tasks.

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 (0.5 g/l blood levels) (see section 4.5).

4.8 Undesirable effects

a. Summary of the safety profile

ZIALDEL has potential adverse effects on the CNS, including somnolence, fatigue, dizziness and headache.

b. Tabulated summary of adverse reactions

Blood and lymphatic system disorders:	
Less frequent	thrombocytopenia, leucopenia, haemolytic anaemia, agranulocytosis.
Immune system disorders:	
Less frequent	Hypersensitivity (including bronchospasm and angioedema), anaphylactic shock.
Metabolism and nutrition disorders:	
Frequency unknown	Increased appetite.
Psychiatric disorders:	
Frequent	Somnolence.
Less frequent:	Confusion, depression, insomnia, agitation, aggression, hallucinations.
Frequency unknown	Suicidal ideation, nightmares.
Nervous system disorders:	
Frequent	Dizziness, headache.

Less frequent	Paraesthesia, convulsions, tremor, tics.
Frequency unknown	Anxiety, nervousness, movement disorders, dysgeusia, syncope, dystonia, dyskinesia, amnesia, memory impairment.
Eye disorders	
Less frequent	accommodation disorder, blurred vision, oculogyration
Ear and labyrinth disorders:	
Frequent unknown:	Tinnitus,vertigo.
Cardiac disorders:	
Less frequent	Tachycardia, dysrhythmias, palpitations
Vascular disorders	
Less frequent	Hypotension
Respiratory, thoracic and mediastinal disorders:	
Frequent	Rhinitis, pharyngitis.
Less frequent	Thickening of mucous
Gastrointestinal disorders:	
Frequent	Diarrhoea, dry mouth, nausea.
Less frequent	Gastrointestinal discomfort, constipation.
Hepatobiliary disorders:	
Less frequent	abnormal hepatic function (increased transaminases, alkaline

	phosphatase, gamma-GT and bilirubin), jaundice.
Frequency not known	hepatitis
Skin and subcutaneous tissue disorders:	
Less frequent	pruritus, rash, urticaria, angioedema, fixed drug eruption, photosensitivity, hair loss, sweating.
Frequency unknown	Acute generalized exanthematous pustulosis
Musculoskeletal, connective tissue and bone disorders:	
Less frequent	Myalgia
Frequency unknown	arthralgia
Renal and urinary disorders:	
Less frequent	Dysuria, enuresis, urinary retention.
General disorders and administration site conditions:	
Frequent	Fatigue, malaise, asthenia.
Investigations:	
Less frequent	Weight increased

c. Description of selected adverse reactions

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

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 asked to report any suspected adverse to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publication https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/

or to the Holder of certificate of registration through the mail: pvg.cdma@heterogroups.com.

4.9 Overdose

Symptoms:

Symptoms after an overdose of ZIALDEL are mainly associated with CNS effects or with effects that suggest an anticholinergic effect. Drowsiness is an expected symptom of overdosage.

Adverse events associated with overdosage include 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 ZIALDEL. Should overdose occur, symptomatic or supportive treatment is recommended. Cetirizine is not effectively removed by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamine for systemic use, Piperazine derivatives

ATC code: R06A E07

Pharmacological classification: A 5.7.1 Antihistaminics

Cetirizine dihydrochloride, a metabolite of hydroxyzine, is an anti-allergic medicine, with selective histamine H_1 receptor antagonism devoid of any significant anticholinergic and anti-serotonin effects.

The anti-allergic activity is exerted mainly via its effect on the release of mediators (such as histamine) combined with its selective H_1 receptor-blocking action. Cetirizine reduces eosinophil recruitment caused by an antigen-antibody reaction.

5.2 Pharmacokinetic Properties

- **Absorption:**

Cetirizine is rapidly absorbed from the gastrointestinal tract; absorption is not reduced by food, though the rate may be decreased slightly. Peak blood levels of 300 ng/ml are reached within one hour after oral administration of cetirizine.

- **Distribution:**

Cetirizine binds strongly to plasma proteins. The apparent volume of distribution is 0,5 l/kg.

- **Biotransformation:**

Cetirizine is not subjected to extensive first pass metabolism.

- **Elimination:**

The terminal half-life is about 5 hours in children aged 2 to 6 years, 6 hours in children aged 6 to 12 years and 10 hours in adults. This is consistent with the urinary excretion half-life of cetirizine. Approximately two thirds of the doses given to both children and adults are excreted via urinary excretion. The apparent plasma clearance is higher in children than in adults.

- **Linearity/ non-linearity:**

Plasma levels are linear to the dose administered.

Characteristics in specific groups of patients

An increase in half-life and a decrease in total clearance occur in patients with impaired renal clearance (less than 40 mL/min) and hepatic deficiency (see section 4.2).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetirizine Hydrochloride

Propylene glycol

Sodium benzoate

Sucralose

Non crystallizing sorbitol solution

Anhydrous citric acid

Purified water

ART Grape FL # 10273 composition

Propylene glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Keep in the original container until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

150 ml white, opaque, round PP bottle with a white, opaque PP child-resistant ribbed, plastic cap with opening illustrations embossed on the top, packed in an outer cardboard carton with 118mL fill volume.

6.6 Special precautions for disposal

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER(S)

53/5.7.1/0404

9 DATE OF FIRST AUTHORISATION

12 March 2024

10 DATES OF REVISION OF THE TEXT

07 February 2025