PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF THE MEDICINE

TRINICET 10 soft gelatine capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 10 mg cetirizine dihydrochloride.

Contains sugar: Sorbitol 44 mg

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

TRINICET 10 soft capsules are clear transparent, oval shaped soft gelatine capsules containing colourless to pale yellow coloured liquid.

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 pruritus e.g. urticaria.

4.2 Posology and method of administration

Posology

Adults or children 12 years of age or older: One 10 mg soft capsule daily.

Paediatric population

Children 6 to 12 years old: One 10 mg soft capsule daily.

The use of **TRINICET** is not recommended in children less than 6 years since this formulation does not allow for appropriate dose adaptation.

4.3 Contraindications

- Hypersensitivity to cetirizine, hydroxyzine, any piperazine or to any of the excipients of **TRINICET** (**see section 6.1**).
- Patients with severe renal impairment at less than 30 ml/min creatinine clearance.
- Pregnancy and lactation since safety has not been established during pregnancy and cetirizine is excreted in breastmilk. (**see section 4.6**).
- In children under 2 years of age.
- The use of **TRINICET** is not recommended in children less than 6 years since this formulation does not allow for appropriate dose adaptation.

4.4 Special warnings and precautions for use

Avoid alcohol consumption.

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

General

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported with cetirizine-containing products. This acute pustular eruption may exhibit an early or delayed onset with numerous small, mostly non-follicular pustules arising on a widespread edematous erythema mainly localised on the skin folds, trunk, and upper extremities, which may be accompanied by fever. Patients should be carefully monitored.

If symptoms persist or worsen, or if new symptoms occur, the patient should discontinue use and consult a doctor.

Studies have shown no effect of cetirizine hydrochloride on cognitive function, motor performance or sleep latency in healthy volunteers. However, in clinical trials the appearance

of some CNS effects, particularly somnolence, have been observed. If drowsiness occurs, patients should be advised not to drive or operate machinery and to avoid concurrent use of **TRINICET** with sedating substances because additional reductions in alertness and additional impairment of CNS performance may occur (**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 as in **TRINICET** may increase the risk of urinary retention.

Pruritus and/or urticaria may occur when cetirizine as in **TRINICET** 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.

Occasional instances of liver function test (transaminase) elevations have occurred during **TRINICET** therapy. This incidence was 1,6 % in the short-term trials and 4,4 % in the 6-month trials. These liver enzyme elevations, mainly ALT, were generally reversible. There was no evidence of jaundice or hepatitis, and the clinical significance is presently unknown. Consequently, **TRINICET** should be used with caution in patients with pre-existing liver disease.

Special populations:

Pregnant Women: TRINICET should not be used during pregnancy (**see section 4.6**).

Use in asthmatics: TRINICET has been safely administered to patients with mild to moderate asthma. **TRINICET** did not cause exacerbation of asthma symptoms.

Paediatric population: TRINICET should not be administered to children below 2 years of age (**see section 4.2**).

Elderly: TRINICET was well tolerated by patients aged 65 and over. Clearance of **TRINICET** is reduced in proportion to creatinine clearance.

4.5 Interaction with other medicines and other forms of interaction

To date there are no known interactions between cetirizine with other medicines. Studies with

diazepam, glipizide, pseudoephedrine, antipyrine, ketoconazole, azithromycin, erythromycin and cimetidine have revealed no evidence of pharmacokinetic interactions.

No clinically significant interactions have been found with theophylline and cimetidine. Epidemiologic data suggests that there also would not be interaction with other macrolide antibiotics or imidazole antifungals. In clinical trials, cetirizine hydrochloride has been safely administered with beta-agonists, non-steroidal anti-inflammatory drugs, oral contraceptives, narcotic analgesics, corticosteroids, H_2-antagonists, cephalosporins, penicillins, thyroid hormones and thiazide diuretics.

Allergy skin tests are inhibited by antihistamines such as **TRINICET** and a wash-out period of 3 days is recommended before performing them.

4.6 Fertility, pregnancy and lactation

TRINICET is contra-indicated in pregnancy and lactation (**see section 4.3**).

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. This effect may be compounded by simultaneous intake of alcohol or other central nervous system depressant. If drowsiness occurs, patients should be advised not to drive or operate machinery and to avoid concurrent use of **TRINICET** with sedating substances because additional reductions in alertness and additional impairment of CNS performance may occur (**see section 4.4**).

4.8 Undesirable effects

a. Summary of the safety profile

TRINICET has potential adverse eflects on the CNS, including somnolence, fatigue, dizziness and headache. In some cases, paradoxical CNS stimula[ł]tions has been reported.

TRINICET is a selective antagonist of peripheral H_3,-receptors and is relatively free of anticholinergic activity.

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.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Blood and lymphatic disorders	Frequency unknown	Thrombocytopenia
Immune system disorders	Frequency unknown	Hypersensitivity, anaphylactic shock
Metabolism and nutrition disorders	Frequency unknown	Increased appetite
Psychiatric disorders	Frequent	Somnolence
	Frequency unknown	Agitation, aggression, confusion, depression, hallucination, insomnia, tics, suicidal ideation, nightmare
Nervous system disorders	Frequent	Headache, dizziness
	Frequency unknown	Paraesthesia, convulsions, dysgeusia, dyskinesia, dystonia, syncope, tremor, amnesia, memory impairment
Eye disorders	Frequency unknown	Accommodation disorder, blurred vision, oculogyration
Ear and labyrinth disorder	Frequency	Vertigo

MedDRA system organ class	**Frequency**	**Adverse reactions**
	unknown	
Cardiac disorders	Frequency unknown	Tachycardia
Respiratory, thoracic and mediastinal disorders	Frequent	Pharyngitis, rhinitis
Gastrointestinal disorders	Frequent	Dry mouth, nausea, diarrhoea
	Less frequent	Abdominal pain
Hepatobiliary disorders	Frequency unknown	Hepatic function abnormal (increased transaminases, alkaline phosphatase, y-GT and bilirubin)
Skin and subcutaneous tissue disorders	Frequency unknown	Pruritus, rash, urticaria, angioneurotic oedema, fixed drug eruption
Musculoskeletal and connective tissue disorders	Frequency unknown	Arthralgia
Renal and urinary disorders	Frequency unknown	Dysuria, enuresis, urinary retention
General disorders and administration site conditions	Frequent	Fatigue
	Frequency unknown	Asthenia, malaise, oedema
Investigations	Frequency unknown	Weight Increased.

c. Description of selected adverse reactions

After discontinuation of cetirizine, pruritus (intense itching) and/or urticaria have been

reported.

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 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

The applicant can be reached at the following contact number: 010 045 2500.

4.9 Overdose

Symptoms: Symptoms observed after an overdose of **TRINICET** are mainly associated with CNS effects or with effects that suggest an anticholinergic effect.

Adverse events reported after an intake of at least 5 times the recommended daily dose is: 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 **TRINICET**.

Should overdose occur, symptomatic or supportive treatment is recommended.

Cetirizine is not effectively removed by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamine for systemic use, piperazine derivatives, ATC code: R06A E07

Mechanism of action

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

effects as demonstrated in experimental and clinical pharmacology.

At the present stage of research into the mode of action of cetirizine, the anti-allergic activity seems to be exerted mainly via its effects on the release of certain mediators, such as histamine, together with a selective action on the H_1-receptors. Cetirizine reduces eosinophil recruitment induced by an antigen-antibody reaction.

5.2 Pharmacokinetic properties

Absorption: In adults, cetirizine is absorbed after oral administration. Peak plasma levels after a 10 mg dose are approximately 300 ng/ml and occur at about 1 hour. Co-administration of cetirizine with food does not affect bioavailability as measured by AUC but absorption is delayed by about 1 hour, with 23 % lower C_{max}.

Distribution: Plasma protein binding is 93 % in the concentration range observed in clinical studies.

Metabolism: Cetirizine does not undergo extensive first pass metabolism.

Excretion: The cumulative urinary excretion represents about two thirds of the dose given in both adults and children. The apparent plasma clearance in children is higher than that measured in adults.

Linearity/non-linearity

Cetirizine exhibits linear kinetics over the range of 5 to 60 mg.

Special populations and conditions

Renal impairment: In patients with impaired renal clearance (less than 40 ml/min) an increase in half-life and decrease in total clearance occurs.

Hepatic impairment: In patients with hepatic insufficiency, an increase in half-life and decrease in total clearance occurs.

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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol,

Sodium hydroxide,

Gelatine,

Partially dehydrated liquid sorbitol

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years. Store at or below 25 °C.

6.4 Special precautions for storage

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

White, opaque HDPE container with white opaque HDPE screw cap with induction sealing.

Pack sizes of 25's, 40's and 84's.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Strides Pharma SA (Pty) Ltd.

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1685

Tel: 010 045 2500

8 REGISTRATION NUMBER(S)

54/5.7.1/0824.823

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13 September 2022

10 DATE OF REVISION OF THE TEXT