Summary of Product Characteristic

1. **Name of the medicinal product: CACHCET SYRUP** (Cetirizine HydrochlorideSyrup 5 mg/5 mL)

2. **Qualitative and quantitative composition:**

Each 5ml contains:
Cetirizine hydrochloride BP …5mg
Sucrose……..250 mg
Sodium Benzoate…….25 mg
Methyl Paraben…….2.5 mg

3.**Pharmaceutical form:** Liquid Oral

Description: Light orange colour syrup having sweet taste and pleasant flavour.

4. **Clinical particulars:**

4.1.Therapeutic indications:

Seasonal Allergic Rhinitis: Cetirizine is indicated for the relief of symptoms associated with seasonal allergic rhinitis due to allergens such as ragweed, grass and tree pollens in adults and children 2 years of age and older. Symptoms treated effectively include sneezing, rhinorrhea, nasal pruritus, ocular pruritus, tearing, and redness of the eyes.

Perennial Allergic Rhinitis: Cetirizine is indicated for the relief of symptoms associated with perennial allergic rhinitis due to allergens such as dust mites, animal dander and molds in adults and children 6 months of age and older. Symptoms treated effectively include sneezing, rhinorrhea, postnasal discharge, nasal pruritus, ocular pruritus, and tearing.

Chronic Urticaria: Cetirizine is indicated for the treatment of the uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older. It significantly reduces the occurrence, severity, and duration of hives and significantly reduces pruritus.

4.2.Posology and method of administration:

Posology

10 mg once daily (10 ml oral solution (2 full spoons)).Special population

Elderly

Data do not suggest that the dose needs to be reduced in elderly subjects provided that the renal function is normal.

Renal impairment

$$CL_{cr} = \frac{[140 - age(years)]\, x\, weight\,(kg)}{72\, x\, serum\, creatinine\,(mg/dl)} (x0.85\ for\ women)$$

There are no data to document the efficacy/safety ratio in patients with renal impairment. Since cetirizine is mainly eliminated via renal route , in cases no alternative treatment can be used, the dosing intervals must be individualized according to renal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (CL_{cr}) in ml/min is needed. The CL_{cr} (ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:

Dosing adjustments for adult patients with impaired renal function

Group	Creatinine clearance (ml/ min)	Dosage and frequency
Normal	≥80	10 mg once daily
Mild	50 – 79	10 mg once daily
Moderate	30 – 49	5 mg once daily
Severe	<30	5 mg once every 2 days
End-stage renal disease Patients undergoing dialysis	<10	Contraindicated

Hepatic impairment

No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of the dose is recommended (see Renal impairment above).

Paediatric population

Children aged from 2 to 6 years: 2.5 mg twice daily (2.5 ml oral solution twice daily (a half spoon twice daily)).

Children aged from 6 to 12 years: 5 mg twice daily (5 ml oral solution twice daily (a full spoon twice daily).

Adolescents over 12 years of age: 10 mg once daily (10 ml oral solution (2 full spoons)). In paediatric patients suffering from renal impairment, the dose will have to be adjusted on an individual basis taking into account the renal clearance, age and body weight of the

patient.

Method of administration:

The solution can be swallowed as such.

4.3. Contraindications

Hypersensitivity to the active substance, to any of the excipients, to hydroxyzine or toany piperazine derivatives

Patients with severe renal impairment at less than 10 ml/min creatinine clearance.

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.

Caution is recommended in epileptic patients and patients at risk of convulsions. Methylparahydroxybenzoate and propylparahydroxybenzoate may cause allergic reactions (possibly delayed).

Patients with rare hereditary problems of fructose intolerance should not take cetirizine 1 mg/ml oral solution.

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

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.

Paediatric population

Due to the amount of some excipients in the formulation, the use of the product is not recommended in children aged less than 2 years.

4.5. Interaction with other medicinal products and other forms of interaction

Due to the 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).

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.

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

Concomitant use of cetirizine with other CNS depressants should be avoided as reduction in alertness and impairment of performance may occur.

4.6. Fertility, pregnancy and lactation

Pregnancy

For cetirizine, very rare clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

Breast-feeding

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

4.7. Effects on ability to drive and use machines

Objective measurements of driving ability, sleep latency and assembly line performance have not demonstrated any clinically relevant effects at the recommended dose of 10 mg. However, patients who experience somnolence should refrain from driving, engaging in potentially hazardous activities or operating machinery. They should not exceed the recommended dose and should take their response to the medicinal product into account.

4.8. Undesirable effects

Autonomic Nervous System: anorexia, flushing, increased salivation, urinary retention.

Cardiovascular: cardiac failure, hypertension, palpitation, tachycardia.

Central and Peripheral Nervous Systems: abnormal coordination, ataxia, confusion, dysphonia, hyperesthesia, hyperkinesia, hypertonia, hypoesthesia, leg cramps, migraine, myelitis, paralysis, paresthesia, ptosis, syncope, tremor, twitching, vertigo, visual field defect.

Gastrointestinal: abnormal hepatic function, aggravated tooth caries, constipation, dyspepsia, eructation, flatulence, gastritis, hemorrhoids, increased appetite, melena, rectal hemorrhage, stomatitis including ulcerative stomatitis, tongue discoloration,

tongue edema.

Genitourinary: cystitis, dysuria, hematuria, micturition frequency, polyuria, urinary incontinence, urinary tract infection.

Hearing and Vestibular: deafness, earache, ototoxicity, tinnitus. Metabolic/Nutritional: dehydration, diabetes mellitus, thirst.

Musculoskeletal: arthralgia, arthritis, arthrosis, muscle weakness, myalgia. Psychiatric: abnormal thinking, agitation, amnesia, anxiety, decreased libido, depersonalization, depression, emotional lability, euphoria, impaired concentration, insomnia, nervousness, paroniria, sleep disorder.

Respiratory System: bronchitis, dyspnea, hyperventilation, increased sputum, pneumonia, respiratory disorder, rhinitis, sinusitis, upper respiratory tract infection. Reproductive: dysmenorrhea, female breast pain, intermenstrual bleeding, leukorrhea, menorrhagia, vaginitis.

Reticuloendothelial: lymphadenopathy.

Skin: acne, alopecia, angioedema, bullous eruption, dermatitis, dry skin, eczema, erythematous rash, furunculosis, hyperkeratosis, hypertrichosis, increased sweating, maculopapular rash, photosensitivity reaction, photosensitivity toxic reaction, pruritus, purpura, rash, seborrhea, skin disorder, skin nodule, urticaria.

Special Senses: parosmia, taste loss, taste perversion.

Vision: blindness, conjunctivitis, eye pain, glaucoma, loss of accommodation, ocular hemorrhage, xerophthalmia.

Body as a Whole: accidental injury, asthenia, back pain, chest pain, enlarged abdomen, face edema, fever, generalized edema, hot flashes, increased weight, leg edema, malaise, nasal polyp, pain, pallor, periorbital edema, peripheral edema, rigors.

Occasional instances of transient, reversible hepatic transaminase elevations have occurred during cetirizine therapy. Hepatitis with significant transaminase elevation and elevated bilirubin in association with the use of Cetirizine has been reported.

4.7 Overdose

Drowsiness can be a 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. To date there is no specific antidote. Cetirizine is not effectively removed by dialysis

5. Pharmacological properties PHARMACOLOGICAL ACTION

Cetirizine, a human metabolite of hydroxyzine, is an antihistamine; its principal effects are mediated via selective inhibition of peripheral H1 receptors. The antihistaminic activity of cetirizine has been clearly documented in a variety of animal and human models. In vivo and ex vivo animal models have shown negligible anticholinergic and 2 antiserotonergic activity. In clinical studies, however, dry mouth was more common with cetirizine than with placebo. In vitro receptor binding studies have shown no measurable affinity for other than H1 receptors. Autoradiographic studies with radiolabeled cetirizine in the rat have shown negligible penetration into the brain. Ex vivo experiments in the mouse have shown that systemically administered cetirizine does not significantly occupy cerebral H1 receptors.

5.1. Pharmacodynamic properties

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

Mechanism of action

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H1-receptors. In vitro receptor binding studies have shown no measurable affinity for other than H1-receptors.

Pharmacodynamic effects

In addition to its anti-H1 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

lifeof 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 histaminewithin 3 days.

5.2.Pharmacokinetic properties

Cetirizine is absorbed with small inter-individual variations. Cetirizine has not been given intravenously, therefore the bioavailability, clearance and volume of distribution (Vd) are unknown. Maximum plasma concentration is achieved within 1 hour and the terminal half-life is about 10 hours in adults and 6 hours in children between the age of6-12 years. The grade of protein binding in plasma is about 93%. Cetirizine is metabolised to a small extent with a known inactive main metabolite. 60% of a dose ofcetirizine 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. In cases of impaired kidney function, the elimination is slower and the half- life is prolonged. Elimination will also be decreased in cases of hepatic impairment.

There is no evidence that the pharmacokinetics of cetirizine is altered in elderly patients unless renal or hepatic function is reduced.

5.3.Preclinical safety data

There are no pre-clinical data of relevance

6. Pharmaceutical particulars

6.1.List of excipients:

Sucrose
Sodium Benzoate
Methyl Paraben
E.D.T.A Sodium
Propylene glycol
Colour Sunset Yellow FCF
Flavour Pineapple (Ronak)
Purified Water

6.2.Incompatibilities

-Not Applicable

6.3.Shelf life

24 months from the date of manufacturing

6.4. Special precautions for storage

Store in a dry place, below 30° C. Protect from Light.

Use the bottle within 6 days of first opening the bottle.

This medicine does not require any special storage conditions.

6.5. Nature and contents of container

Primary: 60 ml Amber coloured Pet Bottle sealed with 25 mm EPE WAD Cap Secondary: 10 ml Measuring cups & Sticker Label as per text matter.
Such one bottle in a printed carton along with Pack insert.

6.6. Special precautions for disposal and other handling

No special requirements

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

Cachet Pharmaceuticals Pvt. Limited,

415, Shah Nahar, Worli, Mumbai 400 018. **India**

Manufacturer
Cachet Pharmaceuticals Private Limited,

Village: Thana, Baddi,

Himachal Pradesh-173 205,
India.

8. Marketing authorization number(s)

TAN 21 HM 0127

9. Date of first authorization/renewal of the authorization

29th March, 2021

10. Date of revision of the text