1.17 **Summary Product Characteristics (SPC)**

1. NAME OF DRUG PRODUCT:

1.1. (Trade) name of product: **MYDAWA Cetirizine 10mg**

(Cetirizine Tablets BP 10mg)

1.2. Strength (Formula): Each film coated tablet contains

Sr. No.	Ingredients	Spec.	Quantity /tab (mg)	Over-ages (%)	Quantity /tab with Overages (mg)	Category
1.	Cetirizine Hydrochloride	BP	10.00	4.0%	10.40	Active
2.	Lactose monohydrate	USP/NF	60.00	NA	60.00	Diluent
3.	Maize Starch	BP	88.00	NA	88.00	Excipient
4.	Calcium Hydrogren phosphate	BP	126.60	NA	126.60	Diluent
5.	Maize Starch	BP	12.00	NA	12.00	Binder
6.	Povidone	USP	2.000	NA	2.000	Binder
7.	Purified water	BP	0.090ml	NA	0.090ml**	Binder
8.	Purified Talc	BP	5.00	NA	5.00	Lubricant
9.	Magnesium stearate	BP	4.00	NA	4.00	Lubricant
10.	Sodium starch glycolate	BP	12.00	NA	12.00	Disintegrant
11.	Ready Mix Of Titanium Dioxide Elegance Coat EL-W-1001 (White)	IHS	8.00	NA	8.00	Coating Agent
12.	Isopropyl Alcohol	BP	80.00	NA	80.00**	Solvent
13.	Di Chloromethane	BP	120.00	NA	120.00**	Solvent

Note: *** Evaporating during manufacturing process.

1.3. Pharmaceutical dosage form: Film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

2.1. Qualitative Declaration: Cetirizine Hydrochloride BP 10mg

2.2. Quantitative Declaration: Each film coated tablet contains:

Cetirizine Hydrochloride BP 10 mg
Excipients q. s.
Colour: Titanium Dioxide

3. PHARMACEUTICAL FORM:

White, oblong shaped, biconvex coated tablet with breakline on one side & plain on other sides.

4. CLINICAL PARTICULARS:

4.1. Therapeutic indications:

In adults and paediatric patients 6 years and above:

- Cetirizine is indicated for the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis.
- Cetirizine is indicated for the relief of symptoms of chronic idiopathic urticaria.

4.2. Posology and Method of Administration:

Children aged from 6 to 12 years: 5mg twice daily (a half tablet twice daily).
Adults and adolescents over 12 years of age: 10mg once daily (1 tablet)
The tablets need to be swallowed with a glass of liquid.
Elderly subjects: data do not suggest that the dose needs to be reduced in elderly subjects provided that the renal function is normal.
Patients with moderate to severe renal impairment: there are no data to document the efficacy/safety ratio patients with renal impairment. Since cetirizine is mainly excreted via renal route (see section 5.2), in cases where 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 the dosing table, an estimate of the patient's creatinine clearance (CLcr) in ml/min is needed. The CLcr (ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:
Dosing adjustment 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	Contra- indicated

In paediatric patients suffering from renal impairment, the dose will have to be adjusted on an individual basis taking into account the renal clearance of the patient, their age and body weight.
Patients with hepatic impairment: no dose adjustment is needed in patients with solely hepatic impairment.
Patients with hepatic impairment and renal impairment: dose adjustment is recommended (see Patients with moderate to severe renal impairment above).

4.3 Contraindications

Hypersensitivity to cetirizine hydrochloride, 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.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 in epileptic patients and patients who are at risk of convulsions is recommended.

The use of the film-coated tablet formulation is not recommended in children aged less than 6 years since this formulation does not allow for appropriate dose adaptation.

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

4.5 Interaction with other medicinal products and other forms of interaction

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.

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 post natal development. Caution should be exercised when prescribing to pregnant women.

Lactation

Cetirizine is excreted in human milk at concentrations representing 0.25 to 0.90 those measured in plasma, depending on sampling time after administration. Therefore, caution 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.

Patients intending to drive, engaging in potentially hazardous activities or operating machinery should not exceed the recommended dose and should take their response to the medicinal product into account.

In sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

4.8 Undesirable effects

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 hydrochloride.

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 3200 subjects exposed to cetirizine. From this pooling, the following adverse events were reported for cetirizine 10mg in the placebo-controlled trials at rates of 1.0% or greater.

Adverse event (WHOART)	Cetirizine 10mg (n = 3260)	Placebo (n = 3061)
Body as a whole = general disorders		
Fatigue	1.63%	0.95%
Central and peripheral nervous system disorders		
Dizziness Headache	1.10% 7.42%	0.98% 8.07%
Gastro-intestinal system disorders		
Abdominal pain Dry mouth Nausea	0.98% 2.09% 1.07%	1.08% 0.82% 1.14%
Psychiatric disorders		
Somnolence	9.63%	5.00%
Respiratory system disorders		
Pharyngitis	1.29%	1.34%

Although statistically more common than under placebo, somnolence was mild to moderate in the majority of cases. Objective tests as demonstrated by other studies have demonstrated that usually daily activities are unaffected at the recommended daily dose in healthy young volunteers.

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:

Adverse event (WHOART)	Cetirizine 10mg (n = 1656)	Placebo (n = 1294)
Gastro-intestinal system disorders		
Diarrhoea	1.0%	0.6%
Psychiatric disorders		
Somnolence	1.8%	1.4%
Respiratory system disorders		
Rhinitis	1.4%	1.1%
Body as a whole – general disorders		
Fatigue	1.0%	0.3%

Post marketing experience

In addition to the adverse effects reported during clinical studies and listed above, the following undesirable effects have been reported in post-marketing experience. Undesirable effects are described according to MedDRA System Organ Class and by estimated frequency based on post-marketing experience.

Frequencies are defined as follows: Very common (≥1/10); common (≥1/100 to<1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to<1/1000); very rare (<1/10000), not known (cannot be estimated from the available data)

Blood and lymphatic disorders:

Very rare: thrombocytopenia

Immune system disorders:
Rare: hypersensitivity
Very rare: anaphylactic shock
Psychiatric disorders:
Uncommon: agitation
Rare: aggression, confusion, depression, hallucinations, insomnia
Very rare: tics
Nervous system disorders:
Uncommon: paraesthesia
Rare: convulsions
Very rare: dysgeusia, syncope, tremor, dystonia, dyskinesia
Not known: amnesia, memory impairment
Eye disorders:
Very rare: accommodation disorder, blurred vision, oculogyration
Cardiac disorders:
Rare: tachycardia
Gastro-intestinal disorders:
Uncommon: diarrhoea
Hepatobiliary disorders:
Rare: hepatic function abnormal (increased transaminases, alkaline phosphatises, γ- GT and bilirubin)
Skin and subcutaneous tissue disorders:
Uncommon: pruritis, rash
Rare: urticaria
Very rare: angioneurotic oedema, fixed drug eruption
Renal and urinary disorders:
Very rare: dysuria, enuresis
General disorders and administration site conditions:
Uncommon: asthenia, malaise Rare: oedema
Investigations:
Rare: weight increased

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.

Management

There is no known specific antidote to cetirizine. Should overdose occur symptomatic or supportive treatment is recommended. Gastric lavage should be considered following ingestion of a short occurrence. Alternatively consider activated charcoal. Cetirizine is not effectively removed by dialysis**.**

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:. Piperazine derivatives.

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.
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.
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 35-day study in children aged 5 to 12, no tolerance to the antihistamine 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 histamine within 3 days.
In a six-week, placebo-controlled study of 186 patients with allergic rhinitis and concomitant mild to moderate asthma, cetirizine 10mg 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 life of patients with perennial and seasonal allergic rhinitis.

5.2 Pharmacokinetic properties

The steady-state peak plasma concentrations is approximately 300 ng/ml and is achieved within 1.0 ± 0.5 h. No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days. The distribution of pharmacokinetic parameters such as peak plasma concentration (Cmax) and area under curve (AUC) is unimodal in human volunteers.
The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased. The extent of bioavailability is similar when cetirizine is given as solutions, capsules or tablets.
The apparent volume of distribution is 0.50 l/kg. Plasma protein binding of cetirizine is 93 ± 0.3%. Cetirizine does not modify the protein binding of warfarin.
Cetirizine does not undergo extensive first pass metabolism. About two thirds of the dose are excreted unchanged in urine. The terminal half-life is approximately 10 hours.
Cetirizine exhibits linear kinetics over the range of 5 to 60 mg.
<u>Special populations</u>
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 the normal subjects. The decrease in cetirizine clearance in these elderly volunteers appeared to be related to their decreased renal function.
Children, infants and toddlers: The half-life of cetirizine was about 6 hours in children of 6 – 12 years and 5 hours in children 2 – 6 years. In infants and toddlers aged 6 to 24 months, it is reduced to 3.1 hours.
Renally impaired patients: The pharmacokinetics of the drug were 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 hemodialysis (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 normals. Cetirizine was poorly cleared by haemodialysis. Dosing adjustment is necessary in patients with moderate or severe renal impairment (see section 4.2).
Hepatically impaired patients: Patients with chronic liver disease (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.
Dosing adjustment is only necessary in hepatically impaired patients if concomitant renal impairment is present.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate, Maize Starch, Calcium hydrogen phosphate, Purified water, Povidone, Magnesium Stearate & Purified Talc, sodium Starch Glycolate.
Film coat contains:
Ready mix of Titanium Dioxide Elegance coat EL-W-1001 (White), isopropyl alcohol, Di chloromethane.

6.2 Incompatibilities : None

6.3 Shelf life : 3 years

6.4 Special precautions for storage:

Store at temperatures not exceeding 30°C, Protected from light.

6.5 Nature and contents of container

10 Tablets in one Blisters.

7 MARKETING AUTHORISATION HOLDER

MYDAWA TRADING LIMITED

8 MARKETING AUTHORISATION NUMBER(S)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

- Date of first authorization :
- Date of renewal of authorization :

10 DATE OF REVISION OF THE TEXT: 01 Jan 2016