SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Benadryl One A Day Relief
Benadryl Allergy One A Day 10mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 10 mg cetirizine dihydrochloride

Excipients: one film-coated tablet contains 66.40 mg lactose-monohydrate

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets

White oblong film-coated tablets, with the letters 'CTZ' on one side and the characters '10 MG' on the other side with a break-line between '10' and 'MG'.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Benadryl Allergy One a Day 10mg Tablets are indicated in children aged 12 years and above, adolescents and adults:

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

4.2 Posology and method of administration

Adults and adolescents over 12 years of age: 10 mg 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 in patients with renal impairement. Since cetirizine is mainly

excreted via renal route (see section 5.2), 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:

$$CL_{cr} = \frac{[140 - age(years)]\, x\, weight\,(kg)}{72\, x\, serum\, creatinine\,(mg\,/\,dl)} \left(x\, 0.85\ for\ women\right)$$

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	Contra-indicated

In pediatric 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, his age and his 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 dihydrochloride, to hydroxyzine, to any piperazine derivatives, or to any of the excipients listed in section 6.1.

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.

Patients with kidney disease are instructed to consult a physician before use. The physician should determine if a different dose is needed (see section 4.2).

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.

Severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) have been reported very rarely with cetirizine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of this medicine should be discontinued and appropriate measures taken if needed.

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

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

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose- galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Paediatric Population

The use of the film-coated tablet formulation is not recommended in children aged less than 12 years.

4.5. Interactions 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).

In sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance (see section 4.7).

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/fetal 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. 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.

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.

In sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance (see section 4.5).

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 dihydrochloride.

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 10 mg in the placebo
controlled trials at rates of 1.0 % or greater:

Adverse event (WHO-ART)	**Cetirizine 10 mg (n = 3260)**	**Placebo (n = 3061)**
Body as a whole – general disorders Fatigue	1,63 %	0,95 %
Central and peripheral nervous system disorders Dizziness	1,10 %	0,98 %

Headache	7,42 %	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 usual
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 drug reactions (WHO-ART)	**Cetirizin 10 mg (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 reactions reported during clinical studies and listed above, the following undesirable effects have been reported in postmarketing experience.
Undesirable effects are described according to MEDdra System Order 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 1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

System organ class	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not Known**
Blood and lymphatic disorders:				Thrombocytopenia	
Immune system disorders:			Hypersensitivity	Anaphylactic shock	

System organ class	Common	Uncommon	Rare	Very rare	Not Known
Metabolism and nutrition disorders:					Increased appetite
Psychiatric disorders:		Agitation	Aggression, confusion, depression, hallucination, insomnia	Tics	Suicidal ideation
Nervous system disorders:		Paraesthesia	Convulsions	Dysgeusia, dystonia, dyskinesia, syncope, tremor	Amnesia, memory impairment
Eye disorders:				Accommodation disorder, vision blurred, oculogyration	Eye pain
Ear and labyrinth disorders:					Vertigo
Cardiac disorders:			Tachycardia		
Gastro-intestinal disorders:		Diarrhoea			
Hepatobiliary disorders:			Hepatic function abnormal (increased transaminases, alkaline phosphatase, γ-GT and bilirubin)		Hepatitis
Skin and subcutaneous tissue disorders:		Pruritus, rash	Urticaria	Angioneurotic oedema, fixed drug eruption	Acute generalised exanthematous pustulosis (AGEP)
Musculoskeletal and connective tissue disorders:					Arthralgia
Renal and urinary disorders:				Dysuria, enuresis	Urinary retention
Reproductive system and breast disorders:					Erectile dysfunction
General disorders and administration site conditions:		Asthenia, malaise	Oedema		Pruritus on withdrawal
Investigations:			Weight increased		

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It
allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare
professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: *www.mhra.gov.uk/yellowcard* or search for MHRA Yellow Card in the Google Play or Apple App Store.

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.
Cetirizine is not effectively removed by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Piperazine derivatives, ATC code: R06A E07

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H_1-receptors. *In vitro* receptor binding studies have shown no measurable affinity for other than H_1-receptors.

In addition to its anti-H_1 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 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 histamine within 3 days.

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 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 (C_{max}) 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 third 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.

Special populations

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 diseases (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

Microcrystalline cellulose
Lactose monohydrate
Colloidal Silicon Dioxide
Magnesium stearate
Crosscarmellose sodium
Opadry® White (YS-2-7063)
- Hydroxypropylmethylcellulose (E464)
- Titanium dioxide (E171)
- Polyethylene glycol (PEG3350)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The tablets are packed in blister PVDC/PE/PVC laminate film with lidding foil heat seal lacquer/alu foil/primer or paper/PET/alu foil/heat seal lacquer in a cardboard box which also contains the patient information leaflet.

Boxes of 7, 14 or 30 tablets.

Not all the packs may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
Foundation Park
Roxborough Way
Maidenhead
Berkshire

SL6 3UG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0118

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/11/2008

10 DATE OF REVISION OF THE TEXT

05/02/2025