For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

This package insert is continually updated: Please read carefully before using a new pack.

R_x
Cetirizine Hydrochloride Tablets I.P. 10mg
Avil® NU 10mg

COMPOSITION

Each film coated tablet contains:
Cetirizine hydrochloride I.P. 10mg
Colour: Titanium Dioxide I.P.
Excipients q.s.

INDICATION

Avil® NU is indicated in the seasonal rhinitis and conjunctivitis, perennial allergic rhinitis, pruritis and urticaria.

DOSAGE AND ADMINISTRATION

Children aged from 6 to 12 years: 5 mg twice daily (a half tablet twice daily).
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.

Pediatric patients

Elderly patients

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

Hepatic impairment

No dose adjustment is needed in patients with solely hepatic impairment.

Moderate to severe renal impairment

There are no data to document the efficacy/safety ratio in patients with renal impairment. Since cetirizine is mainly excreted via renal route (see section 10.2), 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:

$$CL_{CR} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}} \quad (\times 0.85 \text{ for women})$$

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 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, his age and his body weight.

Hepatic impairment and renal impairment

Adjustment of the dose is recommended (see Moderate to severe renal impairment above).

CONTRAINDICATIONS

Avil® NU is contraindicated in -
- Hypersensitivity to the active substance, 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.

SPECIAL WARNINGS AND PRECAUTIONS

In some patients, long term treatment with cetirizine tablets may lead to an increased risk of caries due to mouth dryness. The patients should therefore be informed about the importance of oral hygiene.

At impaired hepatic function and renal function, the elimination of cetirizine may be impaired. Caution should be exercised when administering cetirizine to these patients.

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 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.

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.

Acute Generalized Exanthematous Pustulosis (AGEP) has been reported in association with Avil NU treatment. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely.
Treatment should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of skin hypersensitivity.

Paediatric population
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.

Cetirizine contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

DRUG INTERACTIONS

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).
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).

PREGNANCY

For cetirizine prospectively collected data on pregnancy outcomes do not suggest potential for maternal or foetal/embryonic toxicity above background rates.
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.

LACTATION

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

FERTILITY

Limited data is available on human fertility but no safety concern has been identified. Animal data show no safety concern for human reproduction.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Cetirizine may have minor or moderate influence on the patient's ability to drive and use machines. This should be considered when extra alertness is required e.g., when driving. Cetirizine may potentiate the effects of alcohol and CND depressants

ADVERSE REACTIONS

The following CIOMS frequency rating is used, when applicable:

Very common ≥ 10%; Common ≥ 1 and < 10%; Uncommon ≥ 0.1 and < 1%;

Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%; Not known (cannot be estimated from available data).

Clinical studies

Overview

Clinical studies have shown that cetirizine at the recommended dosage has minor adverse 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.

a) 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 reactions 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%
Gastrointestinal system disorders		
Abdominal pain	0.98%	1.08%
Dry mouth	2.09%	0.82%
Nausea	1.07%	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 reaction (WHO-ART)	Cetirizine 10 mg (n=1656)	Placebo (n=1294)
Gastrointestinal 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%

b) Post-marketing experience
In addition to the adverse reactions reported during clinical studies and listed above, the following undesirable effects have been reported in post-marketing experience.

Blood and lymphatic disorders:
Very rare: Thrombocytopenia.

Immune system disorders:
Rare: Hypersensitivity.
Very rare: Anaphylactic shock.
Metabolism and nutrition disorders:
Not known: Increased appetite.

Psychiatric disorders:
Uncommon: Agitation.
Rare: Aggression, confusion, depression, hallucination, insomnia.
Very rare: Tics.
Not known: Suicidal ideation.

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.

Ear and labyrinth disorder
Not known: Vertigo.

Cardiac disorders:
Rare: Tachycardia.

Gastrointestinal disorders:
Uncommon: Diarrhoea.

Hepatobiliary disorders:
Rare: Hepatic function abnormal (increased transaminases, alkaline phosphatase, γ-GT and bilirubin).

Skin and subcutaneous tissue disorders:
Uncommon: Pruritus, rash.
Rare: Urticaria.
Very rare: Angioneurotic oedema, fixed drug eruption.
Not known: Acute generalised exanthematous pustulosis

Renal and urinary disorders:
Very rare: Dysuria, enuresis.
Not known: Urinary retention.

General disorders and administration site conditions:
Uncommon: Asthenia, malaise.
Rare: Oedema.

Investigations:
Rare: Weight increased.

Description of selected adverse reactions
After discontinuation of cetirizine, pruritus (intense itching) and/or urticaria have been reported.

DRUG ABUSE AND DEPENDANCE
There is no information to indicate that abuse or dependency occurs with cetirizine.

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 haemodialysis.

Manufactured by:
Sanofi India Limited, Plot No. L-121, Phase III, Verna Industrial Estate, Verna Goa - 403722

Marketed by:
Sanofi India Limited, Sanofi House, CTS No. 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai - 400072

Updated: Jan 2022

Sources:

1. CCDS V2 LRC dated 9th Dec 2021
2. UKPAR Cetirizine Hydrochloride 10mg Film-Coated tablets https://mhraproducts4853.blob.core.windows.net/docs/92f0b151160d66cc95a1184385b28601dc92724f (as accessed on 5th January 2022)