CIRRUS®

TRADE NAME OF THE MEDICINAL PRODUCT

Cirrus®

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged release tablet contains 5 mg cetirizine dihydrochloride and 120 mg pseudoephedrine hydrochloride

Excipients: Hydroxypropylmethylcellulose, microcrystalline cellulose, silica colloidal anhydrous, magnesium stearate, lactose monohydrate, croscarmellose sodium, hydroxypropylmethyl cellulose, Titanium dioxyde (E171), Polyethylene glycol 400

PHARMACEUTICAL FORM

Prolonged release tablet. White to off-white, round, biconvex tablet

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Antiallergic agent; antihistamine with vasoconstrictor

Mechanism of action

Cirrus® combines the action of an antihistamine with that of an oral vasoconstrictor.

Pharmacodynamic effects

The pharmacodynamic property of Cirrus® lies in the additional effect of the two constituents.

Cetirizine is an antihistamine with antiallergic properties. As a selective H1-antagonist with a limited action on the other receptors, it is essentially free from anticholinergic and antiserotoninergic properties. Cetirizine inhibits the histamine-related early phase of allergic reaction and reduces the migration of cells and the release of mediators associated with the late allergic response. In allergic patients, it prevents the histamine- or pollen- induced reactions in nasal provocation tests. The effect of cetirizine lasts 24 hours.

Pseudoephedrine is an oral active sympathomimetic agent with principally alpha-mimetic properties.

The substance shows vasoconstrictor, nasal mucosa decongestant and bronchodilator effects. Pseudoephedrine – the pharmacological activity of which is similar to that of ephedrine, although with a smaller influence on blood pressure and the central nervous system – diffuses in the peripheral sympathetic ways and decongests the mucosa in the upper respiratory ways.

Pharmacokinetic properties

Absorption:

After oral administration cetirizine is readily and almost completely absorbed. Maximum plasma concentration is reached after 1 hour under fasting conditions. Absorption is not influenced by the concomitant intake of food, although the maximum plasma concentration reduces and is reached after 3 hours only.

Resorption of pseudoephedrine in the gastro-intestinal tract occurs readily. Maximum plasma concentration after intake of Cirrus® prolonged release tablets is reached after 3 – 5 hours. The absorption rate is not influenced by the concomitant intake of food.

Distribution:

Cetirizine is 93% bound to plasma proteins. The pharmaceutical form of Cirrus® prolonged release tablets allows the blood levels to remain longer above the minimum active concentrations.

The volume of distribution of cetirizine is 0.5 l/kg, that of pseudoephedrine is + 3 l/kg. Both cetirizine and pseudoephedrine cross the placental barrier and are found in breastmilk.

Metabolism:

Cetirizine does not undergo a significant first-pass effect. Pseudoephedrine is hardly metabolised after oral administration. Less than 1% is N-demethylated to the active metabolite norpseudoephedrine.

Elimination:

After repeated oral administration of cetirizine, the daily urinary excretion of unchanged cetirizine is appoximately 65% of the dose. The plasma half-life is approximately 9 hours.

Pseudoephedrine and the active metabolite are mainly eliminated via the kidneys. The rate of elimination is reduced when the pH value of urine rises and rises when the pH value is reduced. The effective half-life in steady-state condition (administration of the corresponding tablet formulation every 12 hours) is 9 hours.

Kinetics in special clinical situations:

In case of renal insufficiency, the area under the curve (AUC) of cetirizine rises, elimination half-time is prolonged and renal and total clearance reduced.

Cetirizine can only be very restrictedly dialysed. In patients with hepatic function impairment, elimination half-life is prolonged and extra-renal clearance, which is about 30% of total clearance, is reduced. In patients with hepatic function impairment and renal insufficiency, both renal clearance and extra-renal clearance reduce.

Since pseudoephedrine is 90% eliminated in urine in unchanged form, attention is required in patients with renal insufficiency.

A dose reduction of Cirrus® is recommended in patients above 60 years with low creatinine clearance and in patients with renal and hepatic impairment (see "Special precautions for use").

CLINICAL PARTICULARS

Therapeutic indications

Cirrus® is indicated in the treatment of seasonal and perennial allergic rhinitis in adults and children above 12 years.

Posology and method of administration

Usual daily dose:

Adults and children above 12 years: 2 times per day (morning and evening) one tablet (not to be chewed) with a sufficient amount of liquid. The tablet can be taken during a meal or outside meals.

Duration of therapy:

The duration of the therapy should not exceed 2-3 weeks.

After relief from the nasal symptoms, treatment can be prolonged with cetirizine (Zyrtec), if necessary.

Patients with impaired renal function:

Patients with light renal function impairment should take only half the usual daily dose. The product should not be used in case of moderate or severe renal insufficiency.

Contraindications

Cirrus® is contra-indicated in case of known hypersensitivity to one of the constituents, to ephedrine or other piperazines.

Cirrus® is not to be administered in case of

- severe hypertension
- severe cardiovascular disease
- glaucoma
- urinary retention

Do not administer simultaneously with MAO inhibitors nor during the 2 weeks following their discontinuation.

Cirrus® is not to be administered to children below 12 years.

Special warnings and special precautions for use

Basically, attention is required when Cirrus® is administered in case of: diabetes mellitus, hyperactivity of the thyroid gland, high blood pressure, tachycardia and arrhythmia, hepatic- or renal insufficiency, prostate hyperplasia, as well as when administered to the elderly.

The concomitant administration of sympathomimetics (vasoconstrictors, anorexic agents or psychostimulants such as amphetamines), tricyclic antidepressants, digitalis preparations and antiemetics such as phenothiazines, has to be avoided.

As for other centrally acting stimulants, there is with pseudoephedrine a danger of abuse.

Patients suffering from impaired renal function: The product should not be used in case of moderate or severe renal insufficiency. Patients with a mild renal function impairment should take only half the daily recommended dose.

Interaction with other medicinal products and other forms of interaction

For cetirizine and pseudoephedrine, no relevant pharmacokinetic interactions have been found. No interaction is known up to now between cetirizine and other substances.

The concomitant use of pseudoephedrine and MAO inhibitors or b-adrenergic blockers induces the increase of the effect of sympathomimetics. An interaction with MAO inhibitors is still possible during the14 days following their discontinuation. Sympathomimetics can reduce the antihypertensive effect of methyldopa, guanethidine and reserpine. The concomitant treatment of patients with digitalis and Cirrus® is to be avoided, since it provokes an increase of ectopic activity due to pseudoephedrine.The absorption of pseudoephedrine is increased by the concomitant use of antacids; kaolin reduces this. The combination of Cirrus® with tricyclic antidepressants has to be avoided.

Antihistamines can interfere with cutaneous tests for allergies and an appropriate wash-out period is required before conducting such tests.

Pregnancy and lactation

There are no controlled studies performed with Cirrus® in pregnant women.

Animal experimental studies have not allowed any direct conclusion on safety in man.

The product should not be used during pregnancy.

No harmfull effect to the foetus is foreseen if the medicinal product is taken by inadvertence during pregnancy.

Cetirizine and pseudoephedrine are excreted in breast milk and should not be taken by women who are breast-feeding.

Effects on ability to drive and use machines

No pharmacodynamic interaction studies have been performed on vigilance (i.e. cognitive tests, effects on reaction times or behaviour while driving).

This is why the patients driving a car or operating a machine have to be warned against incorrect use and be explained the possible effects of Cirrus®.

Undesirable effects

In controlled clinical trials, adverse reactions reported in more than 1% of the patients receiving the combination cetirizine/pseudoephedrine were not different from those reported for cetirizine or pseudoephedrine alone.

Common (> 1%):

Nervous system disorders: headache, sleeplessness, somnolence, nervousness, vertigo, imbalance, dry mouth

Cardiological disorders: tachycardia

Body as a whole-general disorders: asthenia, nausea

Sympathomimetics are also related to the following adverse reactions: hypertension, hot flushes, anxiety, feeling tense, restlessness, tremor, weakness, pallor, respiratory distress, hallucinations, convulsions, CNS depression, arrhytmia, cardiovascular collapse with hypotension and dysuria.

Hypersensitivity reactions such as skin reactions and angioedema can occur.

Overdose

There are no data available on overdosage when cetirizine and pseudoephedrine are administered in combination.

The following data are based on the administration of cetirizine or pseudoephedrine as single preparations.

Symptoms:

An acute overdose with the association cetirizine / pseudoephedrine can induce the following symptoms : often nausea, vomiting, CNS depression (sommolence, coma), CNS stimulation (restlessness, tremor, agitation, hallucinations, psychosis, cerebral seizures, headache; rarely intracranial bleeding; often tachycardia, arterial hypertension; very rarely cardiac arrythmia, bradycardia, arterial hypotension, myocardial infarction.

Measures to be taken in case of overdose:

All the children under 12 years exposed as well as the adults suffering from an overdose should be clinically controlled. The additional measures to be taken depend on the expected severity of the intoxication, the symptoms observed and the latent period since the administration of the product. The risk factors for a severe issue are cardiovascular history, hypertension, renal insufficiency and increased predisposition to convulsions.

For the primary detoxication within 1-2 hours after an overdose, it is appropriate to administer a suspension of activated charcoal at a dosage of 1 g/kg of body weight.

In patients suffering from late overdose with this prolonged release combination, detoxication may also consist in an orthograde intestinal lavage. For this purpose, a non absorbable, iso-osmotic macrogol/electrolyte solution should be used.

Secondary detoxication measures, such as hemodialysis, do not give satisfactory results.

There are no known specific antidotes.

Cerebral seizures are treated with benzodiazepines administered intravenously.

In case of agitation, benzodiazepines are emergency measures.

In patients who need to be treated for arterial hypertension, a sufficient sedation should be induced. Should the decrease in blood pressure not be enough despite sufficient sedation, the alpha-blocker pentolamine or the vasodilator nitroprusside may be used.

INCOMPATIBILITIES Not applicable

STORAGE CONDITIONS AND EXPIRY DATE

Store below 30°C. Keep out of the reach and sight of children. Do not use after the expiry date stated on the carton box and blister

NATURE AND CONTENTS OF THE CONTAINER

The tablets are packed in PVC-Aclar Rx 160/Aluminium foil blisters placed in a cardboard box containing 14 tablets.

MARKETING AUTHORIZATION HOLDER

UCB Farchim S.A.
Bulle - Switzerland

MANUFACTURER

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(ان هـــذا الـــدواء)

- الدواء مستحضر يؤثر على صحتك واستهلاكه خلافا للتعليمات يعرضك للخطر
- اتبع بدقه وصفة الطبيب وطريقة الاستعمال المنصوص عليها وتعليمات الصـــيدلانى الـذى صرفها لك .
- فالطبيب والصيدلانى هما الخبيران بالدواء وبنفعه وضرره .
- لاتقطع مدة العلاج المحدده لك من تلقاء نفسك .
- لاتكرر صرف الدواء بدون وصفه طبيه .

لاتترك الادويه فى متناول ايدى الاطفال

مجلس وزراء الصحة العرب
واتحاد الصيادلة العرب