ACTILOR SYRUP 2.5 MG/ 5 ML

(Desloratadine Syrup 2.5 mg/ 5 ml)
Each ml of syrup contains 0.5 mg desloratadine.

Product Description
Clear, colorless, raspberry flavored solution, free from visible extraneous matter.

Pharmacodynamic properties
Pharmacotherapeutic group: antihistamines – H_1 antagonist, ATC code: R06A X27

Mechanism of action

Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H_1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors because the substance is excluded from entry to the central nervous system.

Desloratadine has demonstrated antiallergic properties. These include inhibiting the release of proinflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 from human mast cells/basophils, as well as inhibition of the expression of the adhesion molecule P-selectin on endothelial cells. The clinical relevance of these observations remains to be confirmed.

Pharmacokinetic properties
Absorption

Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine administration in adults and adolescents. Desloratadine is well absorbed with maximum concentration achieved after approximately 3 hours; the terminal phase half-life is approximately 27 hours. The degree of accumulation of desloratadine was consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. The bioavailability of desloratadine was dose proportional over the range of 5 mg to 20 mg.

The exposure (AUC) to desloratadine was about 6-fold higher and the C_{max} was about 3 to 4 fold higher at 3-6 hours with a terminal half-life of approximately 120 hours. Exposure was the same in adult and paediatric poor metabolisers when treated with age-appropriate doses. The overall safety profile of these subjects was not different from that of the general population. The effects of desloratadine in poor metabolizers < 2 years of age have not been studied.

At the recommended doses, paediatric patients had comparable AUC and C_{max} values of desloratadine to those in adults who received a 5 mg dose of desloratadine syrup.

Distribution

Desloratadine is moderately bound (83 % - 87 %) to plasma proteins. There is no evidence of clinically relevant active substance accumulation following once daily adult and adolescent dosing of desloratadine (5 mg to 20 mg) for 14 days.

The tablet and the syrup formulations were found to be bioequivalent. As Desloratadine oral solution contains the same concentration of desloratadine, no bioequivalence study was required and it is expected to be equivalent to the syrup and tablet.

Biotransformation

The enzyme responsible for the metabolism of desloratadine has not been identified yet, and therefore, some interactions with other medicinal products cannot be fully excluded. Desloratadine does not inhibit CYP3A4 and the medicinal product does not inhibit CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

Elimination

There is no effect of food (high-fat, high caloric breakfast) on the disposition of desloratadine. Grapefruit juice had no effect on the disposition of desloratadine.

Renally impaired patients

The pharmacokinetics of desloratadine in patients with chronic renal insufficiency (CRI), the exposure to desloratadine was approximately 2 and 2.5-fold greater in patients with mild to moderate and severe CRI.

Therapeutic indications
Actilor Syrup is indicated for the rapid relief of symptoms associated with allergic rhinitis, such as sneezing, nasal discharge and itching, congestion/stuffiness, as well as ocular itching, tearing and redness. Actilor Syrup is also indicated for the relief of symptoms associated with urticaria such as the relief of itching and the size and number of hives.

Posology and method of administration
The prescriber should be aware that most cases of rhinitis below 2 years of age are of infections origin and there are no data supporting the treatment of infectious rhinitis with ACTILOR.

Children 1 through 5 years of age: 2.5 ml (1.25 mg) ACTILOR Syrup once a day, with or without a meal for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and urticaria.

Children 6 through 11 years of age: 5 ml (2.5 mg) ACTILOR Syrup once a day, with or without a meal for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and urticaria.

In adults and adolescents (12 years of age and over): 10 ml (5 mg) ACTILOR Syrup once a day, with or without a meal for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and urticaria

Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or less than 4 weeks) should be managed in accordance with the evaluation of patient's disease history and the treatment could be discontinued after symptoms are resolved and reinitiated upon their reappearance. In persistent allergic rhinitis (presence of symptoms for 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during allergen exposure periods.

Method of administration

Oral use.

The dose can be taken with or without food.

Contraindications
Hypersensitivity to the active substance, to any of the excipients, or to loratadine.

Special warnings and precautions for use
Paediatric population

In children below 2 years of age, the diagnosis of allergic rhinitis is particularly difficult to distinguish from other forms of rhinitis. The absence of upper respiratory tract infection or structural abnormalities, as well as patient history, physical examinations, and appropriate laboratory and skin tests should be considered.

Approximately 6 % of adults and children 2- to 11-year old are phenotypic poor metabolisers of desloratadine and exhibit a higher exposure. The safety of desloratadine in children 2-to 11-years of age who are poor metabolisers is the same as in children who are normal metabolisers.

The effects of desloratadine in poor metabolisers < 2 years of age have not been studied.

In the case of severe renal insufficiency, Desloratadine should be used with caution.

Convulsions

Desloratadine should be administered with caution in patients with medical or familial history of seizures, and mainly young children, being more susceptible to develop new seizures under desloratadine treatment. Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

Desloratadine syrup contains sorbitol

Patients with rare hereditary problems of fructose intolerance (HFI) should not take/be given this medicine.

The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

Desloratadine syrup contains sodium

To be taken into consideration by patients on a controlled sodium diet.

Interaction with other medicinal products and other forms of interaction
No clinically relevant interactions were observed with Desloratadine tablets in which erythromycin or ketoconazole were co-administered.

Paediatric population

Interaction studies have only been performed in adults.

Desloratadine tablets taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol. Cases of alcohol intolerance and intoxication have been reported during post-marketing use. Therefore, caution is recommended if alcohol is taken concomitantly.

Pregnancy and lactation
Pregnancy

A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicate no malformative nor foeto/ neonatal toxicity of desloratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of desloratadine during pregnancy.

Breast-feeding

Desloratadine has been identified in breastfed newborns/infants of treated women. The effect of desloratadine on newborns/infants is unknown. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from desloratadine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Effects on ability to drive and use machines
Desloratadine has no or negligible influence on the ability to drive and use machines. Patients should be informed that most people do not experience drowsiness. Nevertheless, as there is individual variation in response to all medicinal products, it is recommended that patients are advised not to engage in activities requiring mental alertness, such as driving a car or using machines, until they have established their own response to the medicinal product.

Undesirable effects
Summary of the safety profile
Paediatric population
In infants and toddlers aged 6 to 23 months, the most frequent adverse events were diarrhoea, fever and insomnia. No adverse events were seen in subjects between 6 and 11 years of age following a single 2.5 mg dose of desloratadine syrup.
In adolescent patients, 12 through 17 years of age, the most common adverse event was headache.

Adults and adolescents
At the recommended dose, in adults and adolescents in a range of indications including allergic rhinitis and chronic idiopathic urticaria, undesirable effects with Desloratadine were fatigue, dry mouth and headache.

Tabulated list of adverse reactions

System Organ Class	**Frequency**	**Adverse reactions seen with Desloratadine**
Metabolism and nutrition disorders	Not known	Increased appetite
Psychiatric disorders	Very rare	Hallucinations
	Not known	Abnormal behaviour, aggression
Nervous system disorders	Common Common (children less than 2 years) Very rare	Headache Insomnia Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures
Cardiac disorders	Very rare Not known	Tachycardia, palpitations QT prolongation

Gastrointestinal disorders	Common Common (children less than 2 years) Very rare	Dry mouth Diarrhoea Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea
Hepatobiliary disorders	Very rare Not known	Elevations of liver enzymes, increased bilirubin, hepatitis Jaundice
Skin and subcutaneous tissue disorders	Not known	Photosensitivity
Musculoskeletal and connective tissue disorders	Very rare	Myalgia
General disorders and administration site conditions	Common Common (children less than 2 years) Very rare Not known	Fatigue Fever Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria) Asthenia
Investigations	Not known	Weight increased

Paediatric population
Other undesirable effects reported during the post-marketing period in paediatric patients with an unknown frequency included QT prolongation, arrhythmia, and bradycardia, weight increased and increased appetite.

Overdose

The adverse event profile associated with overdosage, as seen during post-marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher.

Treatment

In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended.

Desloratadine is not eliminated by haemodialysis; it is not known if it is eliminated by peritoneal dialysis.

Symptoms

In adults and adolescents, in which up to 45 mg of desloratadine was administered (nine times the clinical dose), no clinically relevant effects were observed.

Paediatric population

The adverse event profile associated with overdosage, as seen during post-marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher.

Storage condition

Store below 30°C

Shelf life

3 Years

Dosage form and packaging available

120ml filled in 150ml amber glass bottle labelled and fitted with child resistant cap and plastic measuring cup, packed in a printed carton along with the pack insert.

Manufacturer

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