XYZAL

Levocetirizine dihydrochloride

NAME OF THE MEDICINAL PRODUCT

XYZAL, 5 mg, film-coated tablet

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg levocetirizine dihydrochloride.

Excipients

Excipients: 63,50 mg lactose monohydrate per tablet.

Other excipients are colloidal anhydrous silica, magnesium stearate, and microcrystalline cellulose.

The tablet is coated with Opadry® Y-1-7000 consisting of hypromellose, titanium dioxide, and macrogol 400.

PHARMACEUTICAL FORM

White to off-white, oval, film-coated tablet with a Y logo on one side.

CLINICAL INFORMATION

Indications

For the symptomatic treatment of:

- allergic rhinitis (including persistent allergic rhinitis),
- urticaria.

Dosage and Administration

XYZAL tablets must be taken orally, swallowed whole with liquid and may be taken with or without food. It is recommended to take the daily dose in one single intake.

Duration of use

Intermittent allergic rhinitis (symptoms < 4 days/week or for less than 4 weeks a year) has to be treated according to the disease and its history; it can be stopped once the symptoms have disappeared and can be restarted again when symptoms reappear.

In case of persistent allergic rhinitis (symptoms > 4 days/week or for more than 4 weeks a year), continuous therapy can be proposed to the patient during the period of exposure to allergens.
There is clinical experience with the use of levocetirizine for treatment periods of at least 6 months. In chronic urticaria and chronic allergic rhinitis, there is clinical experience of use of cetirizine (racemate) for up to one year.

Route of Administration

For oral use.

Adults and adolescents 12 years and above:

The daily recommended dose is 5 mg (1 film-coated tablet).

Children

Children aged less than 2 years
The administration of levocetirizine to infants and toddlers aged less than 2 years is not recommended *(see Section Warnings and Precautions)*.

Children aged 2 to 6 years

XYZAL, 5 mg, film-coated tablet
For children aged 2 to 6 years no adjusted dosage is possible with the film-coated tablet formulation. It is recommended to use a paediatric formulation of levocetirizine *(see Section Warnings and Precautions)*.

Children aged 6 to 12 years
The daily recommended dose is 5 mg (1 film-coated tablet).

Elderly

Adjustment of the dose is recommended in elderly patients with moderate to severe renal impairment *(see Renal impairment).*

Renal impairment

The dosing intervals must be individualised 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 (CLcr) in ml/min is needed. The CLcr (ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:

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

Dosing Adjustments for Patients with Impaired Renal Function:

Group	**Creatinine clearance (ml/min)**	**Dosage and frequency**
Normal	≥ 80	5 mg once daily
Mild	50 – 79	5 mg once daily
Moderate	30 – 49	5 mg once every 2 days
Severe	< 30	5 mg once every 3 days
End-stage renal disease – Patients undergoing dialysis	< 10	Contraindicated

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 and his body weight. There are no specific data for children with renal impairment.

Hepatic impairment

No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of the dose is recommended *(see Renal impairment)*.

Contraindications

Levocetirizine is contraindicated in:

- hypersensitivity to levocetirizine, to cetirizine, to hydroxyzine, to any piperazine derivatives or to any of the excipients *(see Section Warnings and Precautions),*

- severe renal impairment at less than 10 ml/min creatinine clearance.

Warnings and Precautions

Alcohol

Precaution is recommended with concurrent intake of alcohol *(see Section Interactions).*

Risk of urinary retention

Caution should be taken in patients with predisposing factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as levocetirizine may increase the risk of urinary retention.

Risk of seizure aggravation

Caution should be taken in patients with epilepsy and patients at risk of convulsion as levocetirizine may cause seizure aggravation.

Allergy skin tests

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

Withdrawal syndrome

Pruritus may occur when levocetirizine is stopped even if those symptoms were not present before treatment initiation (see Section Adverse Reactions). The symptoms may resolve spontaneously. In some
cases, the symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

Infants and children under 2 years

Even if some clinical data are available in children aged 6 months to 12 years (see Section Adverse Reactions), these data are not sufficient to support the administration of levocetirizine to infants and toddlers aged less than 2 years. Therefore the administration of levocetirizine to infants and toddlers aged less than 2 years is not recommended.

Children aged less than 6 years

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. It is recommended to use a paediatric formulation of levocetirizine.

Lactose

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

Interactions

No interaction studies have been performed with levocetirizine (including no studies with CYP3A4 inducers); studies with the racemate compound cetirizine demonstrated that there were no clinically relevant adverse interactions (with antipyrine, pseudoephedrine, cimetidine, ketoconazole, erythromycin, azithromycin, glipizide and diazepam).

Theophylline

A small decrease in the clearance of cetirizine (16%) was observed in a multiple dose study with theophylline (400 mg once a day); while the disposition of theophylline was not altered by concomitant cetirizine administration.

Ritonavir

In a multiple dose study of ritonavir (600 mg twice daily) and cetirizine (10 mg daily), the extent of exposure to cetirizine was increased by about 40% while the disposition of ritonavir was slightly altered (-11%) further to concomitant cetirizine administration.

Food

The extent of absorption of levocetirizine is not reduced with food, although the rate of absorption is decreased.

Alcohol

In sensitive patients the concurrent administration of cetirizine or levocetirizine and alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

Pregnancy and Lactation

Fertility

There are no relevant data available.

Pregnancy

The use of levocetirizine may be considered during pregnancy, if necessary. There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of levocetirizine in pregnant women. However, for cetirizine, the racemate of levocetirizine, a large amount of data (more than 1000 pregnancy outcomes) on pregnant women indicate no malformative or feto/neonatal toxicity. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Lactation

Caution should be exercised when prescribing to lactating women. Cetirizine, the racemate of levocetirizine has been shown excreted in human. Therefore, the excretion of levocetirizine in human milk is likely. Adverse reactions associated with levocetirizine may be observed in breastfed infants.

Ability to perform tasks that require judgement, motor or cognitive skills

Comparative clinical trials have revealed no evidence that levocetirizine at the recommended dose impairs mental alertness, reactivity or the ability to drive. Nevertheless, some patients could experience somnolence, fatigue and asthenia under therapy with levocetirizine. Therefore, patients intending to drive, engage in potentially hazardous activities or operate machinery should take their response to the medicinal product into account.

Adverse Reactions

Clinical Trial Data

Adults and adolescents above 12 years of age

In therapeutic studies in women and men aged 12 to 71 years, 15.1% of the patients in the levocetirizine 5 mg group had at least one adverse drug reaction compared to 11.3% in the placebo group. 91.6 % of these adverse drug reactions were mild to moderate.
In therapeutic trials, the dropout rate due to adverse events was 1.0% (9/935) with levocetirizine 5 mg and 1.8% (14/771) with placebo. Clinical therapeutic trials with levocetirizine included 935 subjects exposed to the drug at the recommended dose of 5 mg daily.

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency.

Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100
Rare ≥1/10000 to <1/1000
Very rare <1/10000
Not known (cannot be estimated from the available data).

Nervous system disorders
Common: headache, somnolence

Gastrointestinal disorders
Common: dry mouth
Uncommon: abdominal pain

General disorders and administration site conditions
Common: fatigue
Uncommon: asthenia

The incidence of sedating adverse drug reactions such as somnolence, fatigue, and asthenia was altogether more common (8.1 %) under levocetirizine 5 mg than under placebo (3.1%).

Paediatric Patients
In children aged 6-12 years double blind placebo controlled studies were performed where 243 children were exposed to 5 mg levocetirizine daily for variable periods ranging from less than 1 week to 13 weeks. The following incidence of adverse drug reactions was reported.

Nervous system disorders
Common: somnolence
Uncommon: headache

Post Marketing Data

Immune system disorders

Not known: hypersensitivity including anaphylaxis

Metabolism and nutrition disorders

Not known: increased weight, increased appetite

Psychiatric disorders

Not known: aggression, agitation, hallucination, depression, insomnia, suicidal ideation, nightmares

Nervous system disorders

Not known: convulsions, paraesthesia, dizziness, syncope, tremor, dysgeusia

Eye disorders

Not known: visual disturbances, blurred vision

Ear and labyrinth disorders

Not known: vertigo

Cardiac disorders

Not known: palpitations, tachycardia

Respiratory, thoracic and mediastinal disorders

Not known: dyspnoea

Gastrointestinal disorders

Not known: nausea, vomiting, diarrhoea

Hepatobiliary disorders

Not known: hepatitis, abnormal liver function test

Skin and subcutaneous tissue disorders

Not known: angioneurotic oedema, fixed drug eruption, pruritus, rash, urticaria

Musculoskeletal and connective tissue disorders

Not known: myalgia, arthralgia

Renal and urinary disorders
Not known: dysuria, urinary retention

General disorders and administration site conditions
Not known: oedema

Skin reactions occuring after discontinuation of levocetirizine
After levocetirizine discontinuation, pruritus has been reported (see Section Warnings and Precautions).

Overdosage

Symptoms and signs

Symptoms of overdose may include drowsiness in adults. In children agitation and restlessness may initially occur, followed by drowsiness.

Treatment

There is no known specific antidote to levocetirizine. Should overdose occur, symptomatic or supportive treatment is recommended. Levocetirizine is not effectively removed by haemodialysis.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

Clinical Pharmacology

Pharmacodynamics

Pharmacotherapeutic group

Antihistamine for systemic use, piperazine derivative.

ATC Code
R06A E09

Mechanism of Action/Pharmacodynamic effects

Levocetirizine, the (R) enantiomer of cetirizine, is a potent and selective antagonist of peripheral H_1-receptors.

Binding studies revealed that levocetirizine has high affinity for human H_1- receptors (K_i = 3.2 nmol/l). Levocetirizine has an affinity 2-fold higher than that of cetirizine (K_i = 6.3 nmol/l). Levocetirizine dissociates from H_1- receptors with a half-life of 115 ± 38 min.

After single administration, levocetirizine shows a receptor occupancy of 90% at 4 hours and 57% at 24 hours.

Pharmacodynamic studies in healthy volunteers demonstrate that, at half the dose, levocetirizine has comparable activity to cetirizine, both in the skin and in the nose.

The pharmacodynamic activity of levocetirizine has been studied in randomised, controlled trials:

In a study comparing the effects of levocetirizine 5mg, desloratadine 5mg, and placebo on histamine-induced wheal and flare, levocetirizine treatment resulted in significantly decreased wheal and flare formation which was highest in the first 12 hours and lasted for 24 hours, ($p<0.001$) compared with placebo and desloratadine.

The onset of action of levocetirizine 5 mg in controlling pollen-induced symptoms has been observed at 1 hour post drug intake in placebo controlled trials in the model of the allergen challenge chamber.

In vitro studies (Boyden chambers and cell layers techniques) show that levocetirizine inhibits eotaxin-induced eosinophil transendothelial migration through both dermal and lung cells. A pharmacodynamic experimental study *in vivo* (skin chamber technique) showed three main inhibitory effects of levocetirizine 5 mg in the first 6 hours of pollen-induced reaction, compared with placebo in 14 adult patients: inhibition of VCAM-1 release, modulation of vascular permeability and a decrease in eosinophil recruitment.

Pharmacokinetics

The pharmacokinetics of levocetirizine are linear with dose - and time-independent with low inter-subject variability. The pharmacokinetic profile is the same when given as the single enantiomer or when given as cetirizine. No chiral inversion occurs during the process of absorption and elimination.

Absorption

Levocetirizine is rapidly and extensively absorbed following oral administration. In adults, peak plasma concentrations are achieved 0.9 h after dosing. Steady state is achieved after two days. Peak concentrations are typically 270 ng/ml and 308 ng/ml following a single and a repeated 5 mg once daily dose, respectively. The extent of absorption is dose-independent and is not altered by food, but the peak concentration is reduced and delayed.

Distribution

No tissue distribution data are available in humans, neither concerning the passage of levocetirizine through the blood-brain-barrier. In rats and dogs, the highest tissue levels are found in liver and kidneys, the lowest in the CNS compartment. In humans, levocetirizine is 90% bound to plasma proteins. The distribution of levocetirizine is restrictive, as the volume of distribution is 0.4 l/kg.

Metabolism

The extent of metabolism of levocetirizine in humans is less than 14% of the dose and therefore differences resulting from genetic polymorphism or concomitant intake of enzyme inhibitors are expected to be negligible. Metabolic pathways include aromatic oxidation, N- and O- dealkylation and taurine conjugation. Dealkylation pathways are primarily mediated by CYP 3A4 while aromatic oxidation involved multiple and/or unidentified CYP isoforms. Levocetirizine had no effect on the activities of CYP isoenzymes 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 at concentrations well above peak concentrations achieved following a 5 mg oral dose.
Due to its low metabolism and absence of metabolic inhibition potential, the interaction of levocetirizine with other substances, or vice-versa, is unlikely.

Elimination

The plasma half-life in adults is 7.9 ± 1.9 hours. The half-life is shorter in small children. The mean apparent total body clearance in adults is 0.63 ml/min/kg. The major route of excretion of levocetirizine and metabolites is via urine, accounting for a mean of 85.4% of the dose. Excretion via faeces accounts for only 12.9% of the dose. Levocetirizine is excreted both by glomerular filtration and active tubular secretion.

Special patient populations

Children

Data from a paediatric pharmacokinetic study with oral administration of a single dose of 5 mg levocetirizine in 14 children age 6 to 11 years with body weight ranging between 20 and 40 kg show that C_{max} and AUC values are about 2-fold greater than that reported in healthy adult subjects in a cross-study comparison. The mean C_{max} was 450 ng/mL, occurring at a mean time of 1.2 hours, weight-normalised, total body clearance was 30% greater, and the elimination half-life 24% shorter in this paediatric population than in adults. Dedicated pharmacokinetic studies have not been conducted in paediatric patients younger than 6 years of age. A retrospective population pharmacokinetic analysis was conducted in 323 subjects (181 children 1 to 5 years of age, 18 children 6 to 11 years of age, and 124 adults 18 to 55 years of age) who received single or multiple doses of levocetirizine ranging from 1.25 mg to 30 mg. Data generated from this analysis indicated that administration of 1.25 mg once daily to children 6 months to 5 years of age is expected to result in plasma concentrations similar to those of adults receiving 5 mg once daily.

Elderly

Limited pharmacokinetic data are available in elderly subjects. Following once daily repeat oral administration of 30 mg levocetirizine for 6 days in 9 elderly subjects (65–74 years of age), the total body clearance was approximately 33% lower compared to that in younger adults. The disposition of racemic cetirizine has been shown to be dependent on renal function rather than on age. This finding would also be applicable for levocetirizine, as levocetirizine and cetirizine are both predominantly excreted in urine. Therefore, the levocetirizine dose should be adjusted in accordance with renal function in elderly patients.

Renal impairment

The apparent body clearance of levocetirizine is correlated to the creatinine clearance. It is therefore recommended to adjust the dosing intervals of levocetirizine, based on creatinine clearance in patients with moderate and severe renal impairment. In anuric end stage renal disease subjects, the total body clearance is decreased by approximately 80% when compared to normal subjects. The amount of levocetirizine removed during a standard 4- hour hemodialysis procedure was < 10%.

Hepatic impairment

The pharmacokinetics of levocetirizine in hepatically impaired subjects have not been tested. Patients with chronic liver diseases (hepatocellular, cholestatic, and biliary cirrhosis) given 10 or 20 mg of the racemic compound cetirizine as a single dose had a 50% increase in half life along with a 40% decrease in clearance compared to healthy subjects.

Other patient characteristics

Gender

Pharmacokinetic results for 77 patients (40 men, 37 women) were evaluated for potential effect of gender. The half-life was slightly shorter in women (7.08 ± 1.72 hr) than in men (8.62 ± 1.84 hr); however, the body weight-adjusted oral clearance in women (0.67 ± 0.16 mL/min/kg) appears to be comparable to that in men (0.59 ± 0.12 mL/min/kg). The same daily doses and dosing intervals are applicable for men and women with normal renal function.

Race

The effect of race on levocetirizine has not been studied. As levocetirizine is primarily renally excreted, and there are no important racial differences in creatinine clearance, pharmacokinetic characteristics of levocetirizine are not expected to be different across races. No race-related differences in the kinetics of racemic cetirizine have been observed.

Clinical Studies

The efficacy and safety of levocetirizine has been demonstrated in several double-blind, placebo controlled, clinical trials performed in adult patients suffering from seasonal allergic rhinitis, perennial allergic rhinitis, or persistent allergic rhinitis. Levocetirizine has been shown to significantly improve symptoms of allergic rhinitis, including nasal obstruction in some studies.

A 6-month clinical study in 551 adult patients (including 276 levocetirizine-treated patients) suffering from persistent allergic rhinitis (symptoms present 4 days a week for at least 4 consecutive weeks) and sensitized to house dust mites and grass pollen, demonstrated that levocetirizine 5 mg was clinically and statistically significantly more potent than placebo on the relief from the total symptom score of allergic rhinitis throughout the whole duration of the study, without any tachyphylaxis. During the whole

duration of the study, levocetirizine significantly improved the quality of life of the patients.

In a placebo-controlled clinical trial including 166 patients suffering from chronic idiopathic urticaria, 85 patients were treated with placebo and 81 patients with levocetirizine 5mg once daily over six weeks. Treatment with levocetirizine resulted in significant decrease in pruritus severity over the first week and over the total treatment period as compared to placebo. Levocetirizine also resulted in a larger improvement of health-related quality of life as assessed by the Dermatology Life Quality Index as compared to placebo.

Chronic idiopathic urticaria was studied as a model for urticarial conditions. Since histamine release is a causal factor in urticarial diseases, levocetirizine is expected to be effective in providing symptomatic relief for other urticarial conditions, in addition to chronic idiopathic urticaria.

ECGs did not show relevant effects of levocetirizine on QT interval.

Pharmacokinetic / pharmacodynamic relationship:
The action on histamine-induced skin reactions is out of phase with the plasma concentrations.

Paediatric population
The paediatric safety and efficacy of levocetirizine tablets has been studied in two placebo controlled clinical trials including patients aged 6 to 12 years and suffering from seasonal and perennial allergic rhinitis, respectively. In both trials, levocetirizine significantly improved symptoms and increased health-related quality of life.

NON-CLINICAL INFORMATION

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.

PHARMACEUTICAL INFORMATION

Shelf-Life

The expiry date is indicated on the packaging.

Storage

Store at or below 30 °C.

Protect from moisture.

Keep out of reach of children.

Nature and Contents of Container

XYZAL film-coated tablets are packaged in blisters (polyamide/aluminium/PVC complex with a push through aluminium lidding foil or polyamide/aluminium/PVC complex with lidding material of paper backed aluminium foil) of 7 or 10 tablets. 1 strip (7 or 10 tablets) or 3 strips (30 tablets) are packed into cardboard boxes.

Not all pack sizes are available in every country.

Incompatibilities

There are no relevant data available.

Use and Handling

There are no special requirements for use or handling of this product.

Name and address of the holder of the certificate of registration

GlaxoSmithKline South Africa (Pty) Ltd
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Bryanston, 2021
South Africa

Manufacturer

UCB Farchim SA

Z.I. de Planchy, 10, Chemin de Croix Blanche

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Switzerland

Registration details

Botswana: Reg No BOT0700949	S2

Namibia: Reg No 04/5.7.1/1709 NS1

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PATIENT LEAFLET

XYZAL

Levocetirizine dihydrochloride

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to take XYZAL carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 3 days.
- If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.
- Always read the label to make sure the product is appropriate for your child's age.

In this leaflet

1. What XYZAL is and what it is used for

The active substance in XYZAL is levocetirizine. Levocetirizine belongs to a group of antiallergic medicines called antihistamines.

XYZAL is used to treat symptoms such as sneezing, a runny nose and watery eyes associated with allergic rhinitis (including persistent allergic rhinitis).

XYZAL is also used to relieve the rashes and itching of chronic urticaria (*hives*).

2. Before you take XYZAL

Don't take XYZAL

- if you are **allergic** (*hypersensitive*) to levocetirizine, cetirizine, hydroxyzine, any piperazine derivatives (closely related active substances of other medicines) or any other ingredients of XYZAL (listed in Section 6)
- if you have **severe kidney disease** (severe impairment of kidney function with creatinine clearance below 10 ml/min)
- if you use other antiallergic medicines

➔ If you think any of these apply to you, **don't take XYZAL** until you have checked with your doctor.

Take special care with XYZAL

Talk to your doctor or pharmacist before using XYZAL:

- if you have **difficulty passing urine** or you have conditions that make you more likely to be unable to empty your bladder, such as **spinal cord injury** or **enlarged prostate**
- if you have **kidney problems** (your doctor may lower your dose of XYZAL)
- if you have **epilepsy** or you are at risk of convulsions (fits)
- if you are pregnant ~~of~~ or breast-feeding *(see Pregnancy and breast-feeding later in Section 2)*

➔ **Check with your doctor** if you think any of these may apply to you**.**

XYZAL is not recommended for children under 6 years, as this formulation does not allow for appropriate dose adaptation.

While you are taking XYZAL

- Avoid alcohol while you are taking XYZAL (see 'Food and drink with XYZAL' in Section 2).
- XYZAL may affect your allergy test result. If you are scheduled for allergy testing ask your doctor if you should stop taking XYZAL for several days before testing.
- Contact you doctor if you have high temperature (fever), shivering or chills, as you may require other type of treatment.

Conditions you need to look out for
XYZAL can make some existing conditions worse, or cause **severe allergic reactions or urinary retention**. Some people may have suicidal thoughts when taking XYZAL. You must look out for certain symptoms while you are taking XYZAL, to reduce the risk of any problems. See 'Conditions you need to look out for' in Section 4.

Other medicines and XYZAL

Tell your doctor or pharmacist if you're taking any other medicines, if you've taken any recently, or if you start taking new ones. This includes medicines bought without a prescription.

Some medicines may affect how XYZAL works, or make it more likely that you'll have side effects. XYZAL can also affect how some other medicines work. These include:

- **theophylline** (used to treat respiratory diseases such as **asthma**)
- **ritonavir** (used to treat **HIV/AIDS**)
- medicines acting on the brain, for example **other antihistamines** such as hydroxizine, clemastine, **medicines used to treat anxiety** such as diazepam or **sleeping pills** such as zolpidem (concurrent administration of XYZAL with other agents acting on the brain may cause additional reductions in alertness and impairment of performance, *see 'Food and drink with* XYZAL*' later in Section 2*).

➔ **Tell your doctor or pharmacist** if you are taking any of these.

Food and drink with XYZAL

Caution is advised if you take XYZAL at the same time as alcohol. In sensitive patients, the concurrent administration of XYZAL and alcohol may cause additional reductions in alertness and impairment of performance.

Pregnancy and breast-feeding

There is only limited information about the safety of XYZAL in pregnant women. XYZAL should therefore be avoided in pregnant women. It can only be administered if necessary and after medical advice.

- **Tell your doctor if you are pregnant** or planning to become pregnant.
- **If you do become pregnant during treatment** with XYZAL, tell your doctor.

The ingredients XYZAL can pass into breast milk. **If you are breast-feeding, you must check with your doctor** before you take XYZAL.

Driving and using machines

XYZAL at the recommended dose is unlikely to affect your ability to drive or use machines. However, some patients being treated with **XYZAL may feel drowsy, tired or weak** (see 'Possible side effects' in Section 4).

➔ **Don't drive or use machines** unless you are sure you're not affected.

3. How to take XYZAL

How much to take

Always take XYZAL exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

Don't take more than the recommended dose.

Don't take XYZAL for longer than **7 days**, without advice of your doctor or pharmacist.

➔ **Contact your doctor** if your symptoms worsen or do not improve after 3 days.

Adults and adolescents 12 years and above

The usual dose of XYZAL is one 5 mg tablet once a day.

Children

Always read the label to make sure the product is appropriate for your child's age.

- **Children aged 2 to 6 years**

XYZAL film-coated tablets are **not suitable for children under 6 years**.

- **Children aged 6 to 12 years**

The usual dose of XYZAL is one 5 mg tablet once a day.

Patients with kidney and liver disease
If you have kidney problems, you should talk to your doctor or pharmacists before taking XYZAL. Your doctor will decide on the correct dose of XYZAL depending on the illness and the results of blood tests carried out before treatment. Patients who have severe impairment of kidney function must not take XYZAL (see 'Don't take XYZAL', in section 2).

How to take

Swallow the tablet whole, with some water.
Take XYZAL once daily, with or without food.
It is best to take XYZAL at bedtime as it can make you feel drowsy.

If you forget to take XYZAL

Don't take an extra dose to make up for a missed dose. Just take your next dose at the usual time.

If you take too much XYZAL

If you take more XYZAL than you should **contact your doctor or pharmacist for advice.** If possible, show them the XYZAL pack.
Symptoms of overdose in adults may include **drowsiness**. Children may initially show **agitation** and **restlessness**, followed by **drowsiness**.

If you stop taking XYZAL

Rarely pruritus (intense itching) may occur if you stop taking XYZAL, even if those symptoms were not present before treatment initiation. The symptoms may resolve spontaneously. In some cases, the symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

4. Possible side effects

Like all medicines, XYZAL can cause side effects, but not everybody gets them.

Conditions you need to look out for

Severe allergic reactions. These have occurred in a small number of people, but their exact frequency is unknown. Signs include:
- raised and itchy rash (*hives*)
- swelling, sometimes of the face or mouth (*angioedema*), causing difficulty in swallowing or breathing
- collapse or loss of consciousness

Suicidal thoughts. Some people had suicidal thoughts when taking XYZAL.

Urinary retention. Signs include:
- pain when passing urine or inability to pass urine

➔ **Contact a doctor immediately** if you get any of these symptoms**. Stop taking XYZAL.**

➔ Common side effects

These may affect **up to 1 in 10** people:
- headache, feeling drowsy
- dry mouth
- lack of energy
- sleep disorders, diarrhoea, constipation (in children)

Uncommon side effects

These may affect **up to 1 in 100** people:
- stomach pain
- feeling weak
- vomiting, headache (in children)

Other side effects

Other side effects have occurred in a very small number of people but their exact frequency is unknown:

- allergic reactions (*hypersensitivity*) including severe allergic reactions (see 'Severe allergic reactions' earlier in Section 4)
- increased weight, increased appetite
- aggression, agitation, seeing or hearing things that are not really there, depression, difficulty in sleeping, nightmares, suicidal thoughts
- fits (seizures), tingling or numbness of the hands or feet, dizziness, fainting, tremor, taste disturbance
- visual disturbances, blurred vision, oculogyration (eyes having uncontrolled circular movements)
- spinning sensation
- fast or irregular heart beats, heart beating faster
- shortness of breath
- feeling sick (*nausea*), vomiting, diarrhoea
- inflammation of the liver
- small patches of swelling and redness of the skin, which may blister
- itching, rash
- itchy, bumpy rash (*hives)* (see 'Severe allergic reactions' earlier in Section 4)
- muscle and joint pain
- pain when passing urine, inability to pass urine (see 'Urinary retention' earlier in Section 4)
- swelling caused by fluid
- intense itching (pruritus) upon discontinuation.

Other side effects that may show up in blood tests:

- abnormal liver function test (increased amounts of liver enzymes in the blood)

➔ **Talk to your doctor or pharmacist** if you have any of the side effects listed above or if you notice any side effects not listed in this leaflet.

5. How to store XYZAL

Keep out of the sight and reach of children.
Don't take XYZAL after the expiry date shown on the pack.

Store at or below 30 °C.

Protect from moisture.

Don't dispose of medicines in wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. This will help to protect the environment.

6. Further information

What XYZAL contains

The active substance is levocetirizine dihydrochloride.

Each tablet contains 5 mg levocetirizine dihydrochloride.

Each tablet contains 63,50 mg lactose monohydrate per tablet.

The other ingredients are: colloidal anhydrous silica, magnesium stearate, and microcrystalline cellulose.

The tablet is coated with Opadry® Y-1-7000 consisting of hypromellose, titanium dioxide, and macrogol 400.

What XYZAL looks like and contents of the pack

XYZAL film-coated tablets are white to off-white, oval, film-coated tablet with a Y logo on one side.

XYZAL are packaged in blisters (polyamide/aluminium/PVC complex with a push through aluminium lidding foil or polyamide/aluminium/PVC complex with lidding material of paper backed aluminium foil) of 7 or 10 tablets. 1 strip (7 or 10 tablets) or 3 strips (30 tablets) are packed into cardboard boxes.

Not all pack sizes are available in every country.

Name and address of the holder of the certificate of registration

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South Africa

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Registration details

Botswana: Reg No BOT0700949 S2

Namibia: Reg No 04/5.7.1/1709 NS1

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