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

LEZYNCET-D

1. Generic Name

Levocetirizine Hydrochloride and Phenylephrine Hydrochloride Tablets

2. Qualitative and quantitative composition

Each film coated tablet contains:
Levocetirizine Hydrochloride I.P. ….2.5 mg
Phenylephrine Hydrochloride I.P. ….10 mg.
Excipients ……..q.s.
Colour: Titanium Dioxide I.P.

The excipients used are Microcrystalline Cellulose, Sodium Starch Glycolate, PVPK-30, Maize Starch, Talcum, Magnesium Stearate, Hydroxy Propyl Methyl Cellulose, Titanium Dioxide, PEG 400, Methylene Chloride and Isopropyl Alcohol.

3. Dosage form and strength

Dosage form: Film coated Tablets

Strength: Levocetirizine hydrochloride 2.5 mg and Phenylephrine hydrochloride 10 mg.

4. Clinical particulars

4.1 Therapeutic indication

For the treatment of allergic rhinitis

4.2 Posology and method of administration

Posology

Adults and adolescents 12 years and above
The daily recommended dose is 1 film-coated tablet.

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

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:

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

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 above).

Method of administration

The film-coated tablet 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.

4.3 Contraindications

Hypersensitivity to the active substance, or to any of the other excipients.

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

Concomitant use of other sympathomimetic decongestants.

Phaeochromocytoma, Closed angle glaucoma

Patients taking tricyclic antidepressants, or beta blocking drugs and those who are taking or who have taken within the last two weeks monoamine oxidase inhibitors.

4.4 Special warnings and precautions for use

Levocetirizine

Precaution is recommended with concurrent intake of alcohol.

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.

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

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

Pruritus may occur when levocetirizine is stopped 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.

Phenylephrine

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) (see interactions).

4.5 Drugs interactions

Levocetirizine

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, azithromycin, cimetidine, diazepam, erythromycin, glipizide, ketoconazole and pseudoephedrine). 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.

In a reported 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.

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

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.

Phenylephrine

Monoamine oxidase inhibitors (including moclobemide): Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine, Oxidase inhibitors.

Sympathomimetic amines: Concomitant use of phenylephrine with other sympathomimetics amines can increase the risk of cardiovascular side effects.

Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa): Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased.

Tricyclic antidepressants (eg amitriptyline): May increase the risk of cardiovascular side effects with phenylephrine.

Digoxin and cardiac glycosides: Concomitant use of phenylephrine with digoxin or cardiac glycosides may increase the risk of irregular heartbeat or heart attack.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

This product is not recommended for use in pregnancy due to phenylephrine. Animal studies are insufficient with respect to reproductive toxicity and teratogenicity. Administration of phenylephrine in late pregnancy or labour may potentially cause fetal hypoxia and bradycardia. The combination with some oxytocic agents can cause severe hypertension.

Breast-feeding

This product should not be used while breast-feeding without medical advice. Small quantities of phenylephrine are excreted into human breast milk and oral bioavalability may be low. Avoid the use of the product during lactation, unless the benefits to the mother outweigh the risks to the infant.

Fertility

There is no available data concerning fertility.

4.7 Effects on ability to drive and use machines

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.

4.8 Undesirable effects

Levocetirizine

Adults and adolescents above 12 years of age

In reported 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.

Reported clinical therapeutic trials with levocetirizine included 935 subjects exposed to the medicinal product at the recommended dose of 5 mg daily. From this pooling, following incidence of adverse drug reactions were reported at rates of 1% or greater (common: ≥1/100 to <1/10) under levocetirizine 5 mg or placebo:

Preferred Term (WHOART)	**Placebo (n =771)**	**Levocetirizine 5 mg (n = 935)**
Headache	25 (3.2%)	24 (2.6%)
Somnolence	11 (1.4%)	49 (5.2%)
Mouth dry	12 (1.6%)	24 (2.6%)
Fatigue	9 (1.2%)	23 (2.5%)

Further uncommon incidences of adverse reactions (uncommon ≥1/1,000 to <1/100) like asthenia or abdominal pain were observed. 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%).

Post-marketing experience

Adverse reactions from post-marketing experience are per System Organ Class and per frequency. The frequency is 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).

• Immune system disorders:

Not known: hypersensitivity including anaphylaxis

• Metabolism and nutrition disorders:

Not known: increased appetite

• Psychiatric disorders:

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

• Nervous system disorders:

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

• Ear and labyrinth disorders:

Not known: vertigo

• Eyes disorders:

Not known: visual disturbances, blurred vision, oculogyration

• 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

• Renal and urinary disorders:

Not known: dysuria, urinary retention

• Skin and subcutaneous tissue disorders:

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

• Musculoskeletal, connective tissues, and bone disorders:

Not known: myalgia, arthralgia

• General disorders and administration site conditions:

Not known: oedema

• Investigations:

Not known: weight increased, abnormal liver function tests

Description of selected adverse reactions

After levocetirizine discontinuation, pruritus has been reported.

Phenylephrine

The following adverse events have been observed in reported clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

Body System	Undesirable effect
Psychiatric disorders	Nervousness
Nervous system disorders	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure
Gastrointestinal disorders	Nausea, vomiting, diarrhoea

Other most common adverse events of phenylephrine are bradycardia and hypertensive episodes. Hypertension is more frequent with high doses.

Adverse reactions identified during post-marketing use are listed below. The frequency of these reactions is unknown.

Body System	Undesirable effect
Immune system disorders	Hypersensitivity, allergic dermatitis, urticaria
Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma
Cardiac disorders	Tachycardia, palpitations
Skin and subcutaneous disorders	Rash
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose

Levocetirizine

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

Phenylephrine

Phenylephrine overdosage is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include, irritability, restlessness, hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However the amount required to produce serious phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.

Treatment: Treatment should be as clinically appropriate. Should overdose occur, symptomatic or supportive treatment is recommended. Gastric lavage may be considered shortly after ingestion of the drug. Severe hypertension may need to be treated with alpha blocking drugs such as phentolamine. If overdose is confirmed or suspected, seek immediate advice nearest Emergency Medical Centre for management and expert treatment.

5. Pharmacological properties

5.1 Mechanism of Action

Levocetirizine

Levocetirizine, the (R) enantiomer of cetirizine, is a potent and selective antagonist of peripheral histamine (H1)-receptors. H1 receptors are activated by the biogenic amine histamine. Levocetirizine prevent binding of histamine to this receptors and this in turn prevent relief from the typical symptoms of allergic rhinitis.

Binding studies revealed that levocetirizine has high affinity for human H1-receptors (Ki = 3.2 nmol/l). Levocetirizine has an affinity 2-fold higher than that of cetirizine (Ki = 6.3 nmol/l). Levocetirizine dissociates from H1-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.

Phenylephrine

Phenylephrine is a potent vasoconstrictor that acts almost exclusively by stimulation of alpha-1-adrenergic receptors. Arterial vasoconstriction is accompanied by venous vasoconstriction which gives an increase in blood pressure and reflex bradycardia. The potent arterial vasoconstriction results in an increase in the resistance which results in reduction of the cardiac output. This is less pronounced in healthy people, but can be exacerbated in the case of previous heart failure.

5.2 Pharmacodynamic properties

Levocetirizine

Pharmacotherapeutic group: antihistamine for systemic use, piperazine derivatives, ATC code: R06A E09.

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

In a reported study comparing the effects of levocetirizine 5 mg, desloratadine 5 mg, 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.

Clinical efficacy and safety

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.

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.

Phenylephrine

Pharmacotherapeutic group: Adrenergic- and dopaminergic drugs. ATC code: C01C A06

Phenylephrine hydrochloride: A sympathomimetic decongestant.

Phenylephrine is a potent vasoconstrictor that acts almost exclusively by stimulation of alpha-1-adrenergic receptors. Arterial vasoconstriction is accompanied by venous vasoconstriction which gives an increase in blood pressure and reflex bradycardia. The potent arterial vasoconstriction results in an increase in the resistance which results in reduction of the cardiac output. This is less pronounced in healthy people, but can be exacerbated in the case of previous heart failure.

5.3 Pharmacokinetic properties

Levocetirizine

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 o.d. 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.

Biotransformation

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.

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 population

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%.

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.

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.

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.

Phenylephrine

Absorption

Phenylephrine is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine thus has reduced bioavailability.

Distribution

Plasma protein binding is unknown.

Elimination and biotransformation

Phenylephrine is primarily excreted by the kidneys as m-hydroxy mandelic acid and phenol conjugates. It is excreted in the urine almost entirely as the sulphate conjugate.

Special patient populations: There are no pharmacokinetic data available in special patient populations.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Levocetirizine

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.

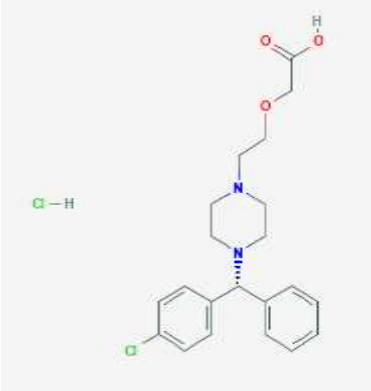
Phenylephrine

There are no pre-clinical data of relevance to the assessment of safety, in addition to that already presented in this prescribing information. Animal studies are insufficient to evaluate the effects on fertility and reproduction.

7. Description

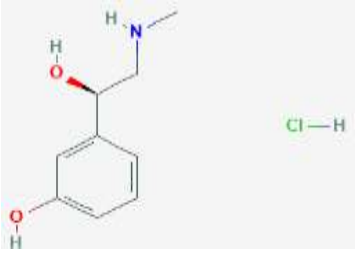
Levocetirizine Hydrochloride

Levocetirizine Hydrochloride is chemically 2-[2-[4-[(R)-(4-chlorophenyl)-phenylmethyl]piperazin-1-yl]ethoxy]acetic acid; hydrochloride having molecular weight of 425.3 g/mol and molecular formula is $C_{21}H_{26}Cl_2N_2O_3$ and the chemical structure is:



Phenylepherine Hydrochloride

Phenylephrine Hydrochloride is chemically 3-[(1R)-1-hydroxy-2-(methylamino)ethyl]phenol; hydrochloride having molecular weight of 203.66 g/mol and molecular formula is $C_9H_{14}ClNO_2$ and the chemical structure is:



Levocetirizine Hydrochloride and Phenylephrine Hydrochloride Tablets are white, circular, biconvex, film coated tablets plain on one side and breakline on the other side. The excipients used are Microcrystalline Cellulose, Sodium Starch Glycolate, PVPK-30, Maize Starch, Talcum, Magnesium Stearate, Hydroxy Propyl Methyl Cellulose, Titanium Dioxide, PEG 400, Methylene Chloride and Isopropyl Alcohol.

8. Pharmaceutical particulars

8.1 Incompatibilities

None stated

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

LEZYNCET-D is available in blister strip of 10 tablets.

8.4 Storage and handing instructions

Store in a cool and dry place, protected from light.
Keep all medicines out of reach of children

9. Patient counselling information

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• **This medicine has been prescribed for you only.** Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

9.1 What LEZYNCET-D is and what it is used for

LEZYNCET-D contains the active substance Levocetirizine Hydrochloride and Phenylephrine Hydrochloride.

LEZYNCET-D is used for the treatment of allergic rhinitis

9.2 What you need to know before you take LEZYNCET-D

Do not take LEZYNCET-D:

– if you are allergic to Levocetirizine Hydrochloride & Phenylephrine, or to any of the other ingredients of this medicine.

– if you have a severe impairment of kidney function (severe renal failure with creatinine clearance below 10 ml/min).

– if you have kidney or liver problems, overactive thyroid, diabetes, high blood pressure or heart disease.

Warnings and precautions

Talk to your doctor before taking LEZYNCET-D:

If you are likely to be unable to empty your bladder (with conditions such as spinal cord injury or enlarged prostate), please ask your doctor for advice.

If you suffer from epilepsy or are at risk of convulsions, please ask your doctor for advice as use of LEZYNCET-D may cause seizure aggravation.

If you are scheduled for allergy testing, ask your doctor if you should stop taking LEZYNCET-D for several days before testing. This medicine may affect your allergy test result.

If you have phaeochromocytoma or glaucoma.

If you are taking tricyclic antidepressants (e.g. imipramine or amitriptyline) or if you are taking or have taken within the last two weeks monoamine oxidase inhibitors (MAOIs) (e.g. moclobemide) prescribed for depression.

If you are taking beta blockers (e.g. atenolol).

Children

The use of LEZYNCET-D is not recommended in children below 12 years of age.

Other medicines and LEZYNCET-D

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

LEZYNCET-D with food, drink and alcohol

Caution is advised if LEZYNCET-D is taken at the same time as alcohol or other agents acting on the brain.

In sensitive patients, the concurrent administration of LEZYNCET-D and alcohol or other agents acting on the brain may cause additional reductions in alertness and impairment of performance. LEZYNCET-D can be taken with or without food.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Some patients being treated with LEZYNCET-D may experience somnolence/drowsiness, tiredness and exhaustion. Use caution when driving or operating machinery untill you know how this medicine affects you. However, special tests have revealed no impairment of mental alertness, the ability to react or the ability to drive in healthy test persons after taking levocetirizine in the recommended dosage.

9.3 How to take LEZYNCET-D

Always take this medicine 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.

The recommended dose is one tablet a day.

Method of administration: The film-coated tablet 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.

Special dosage instructions for specific populations:
Renal and hepatic impairment

Patients with impaired kidney function may be given a lower dose according to the severity of their kidney disease, the dose will be determined by your doctor.

Patients who have severe impairment of kidney function must not take LEZYNCET-D.

Patients who only have impaired liver function should take the usual prescribed dose.

Elderly patients aged 65 years and above

No adaptation of the dose is necessary in elderly patients, provided their renal function is normal.

If you take more LEZYNCET-D than you should

Tell your doctor or pharmacist if you have taken more than the recommended dose. If possible take your medicine and this leaflet with you.

If you forget to take LEZYNCET-D

Do not take a double dose to make up for the forgotten dose. Take your next, normal dose, the next day, at your usual time.

If you have any further questions on the use of this medicine ask your doctor or pharmacist.

9.4 Possible side effects

Levocetirizine

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common: may affect up to 1 in 10 people

Dry mouth, headache, tiredness and somnolence/drowsiness

Uncommon: may affect up to 1 in 100 people

Exhaustion and abdominal pain

Not known: frequency cannot be estimated from the available data

Other side effects such as palpitations, increased heart rate, fits, pins and needles, dizziness, syncope, tremor, dysgeusia (distortion of the sense of taste), sensation of rotation or movement, visual disturbances, blurred vision, oculogyration (eyes having uncontrolled circular movements), painful or difficult urination, inability to completely empty the bladder, oedema, pruritus (itchiness), rash, urticaria (swelling, redness and itchiness of the skin), skin eruption, shortness of breath, weight increase, muscular pain, joint pain, aggressive or agitated behaviour, hallucination, depression, insomnia, recurring thoughts of or preoccupation with suicide, nightmare, hepatitis, abnormal liver function, vomiting, increased appetite, nausea and diarrhoea have also been reported. Pruritus (intense itching) upon discontinuation.

Phenylephrine

Allergic reactions which may be severe such as skin rash and itching sometimes with swelling of the mouth or face or shortness of breath.

Nausea, sudden weight loss, loss of appetite and yellowing of the eyes and skin.

Visual disturbances: This is rare but is more likely in those with glaucoma.

Unusually fast pulse rate or a sensation of an unusually fast or irregular heartbeat.

Raised blood pressure, irregular heartbeat, feeling the heart pumping in the chest, headache, dizziness, difficulty sleeping, nervousness, anxiety, diarrhoea or sickness.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting. By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store LEZYNCET-D

Store in a cool and dry place, protected from light.

9.6 Contents of the pack and other information

What **LEZYNCET-D** contains

The active substances **LEZYNCET-D** is Levocetirizine Hydrochloride and Phenylepherine Hydrochloride.

The excipients used are Microcrystalline Cellulose, Sodium Starch Glycolate, PVPK-30, Maize Starch, Talcum, Magnesium Stearate, Hydroxy Propyl Methyl Cellulose, Titanium Dioxide, PEG 400, Methylene Chloride and Isopropyl Alcohol.

10. Details of manufacturer

Manufactured in India by:

Uni Medicolabs

Plot No. 25-26 Pharmacity, Selaqui, Dehradun, Uttarakhand.

11. Details of permission or licence number with date

Mfg Lic No. 29/UA/2018 issued on 01.12.2018

12. Date of revision

Not Applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/LEZYNCET-D 2.5, 10mg/APR-20/01/PI