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Clarityn-D® 24 Hour Extended Release

Brand of loratadine and pseudoephedrine sulfate

Extended-Release, Non-Sedating Antihistamine / Decongestant Tablets

Product Description
Each Clarityn-D® 24 Hour Extended Release Tablet contains 10 mg loratadine and 240 mg pseudoephedrine sulfate.
The loratadine component is released immediately, whereas the pseudoephedrine component is released slowly from the core allowing for once daily dosing.

Also contains: Hydroxypropyl Methylcellulose, Ethylcellulose, Calcium Hydrogen Phosphate, Polyvidone, Silicon Dioxide, Magnesium Stearate, Hydroxypropyl Methylcellulose, Polyethylene Glycol, White Color Dispersion and Macrogol 400.

Clarityn-D® 24 Hour Extended Release is available in blister packs of 10 tablets.

What is Clarityn-D® 24 Hour Extended Release and what is it used for?
Clarityn-D® 24 Hour Extended Release relieves symptoms associated with allergic rhinitis and the common cold, including
- nasal congestion
- sneezing
- runny, itchy nose,
- watery, itchy eyes

Clarityn-D® 24 Hour Tablets Extended Release Tablet contains a combination of two medicines, loratadine (an antihistamine) and pseudoephedrine (a decongestant).
Antihistamines help reduce allergic symptoms by preventing the effects of a substance called histamine. Histamine is produced by the body in response to foreign substances which the body is allergic to. Decongestants clear stuffy or blocked nose.

How to take Clarityn-D® 24 Hour Extended Release?
The recommended dose for Clarityn-D® 24 Hour Extended Release in adults and children over 12 years is one tablet once daily. It does not matter if you take Clarityn-D® 24 Hour Extended Release before or after food.

Swallow the tablet whole with a glass of water. Do not crush, break or chew the tablet before swallowing.

If you have severe liver and/or kidney problems, use should generally be avoided.

Be sure to take Clarityn-D® 24 Hour Extended Release exactly as your doctor or pharmacist has told you to. If you do not follow their instructions, you may not get relief from your symptoms.

When should Clarityn-D® 24 Hour Extended Release not be taken?
Do not take Clarityn-D® 24 Hour Extended Release if:
- you are allergic to loratadine, pseudoephedrine or any of its other ingredients
- you are on monoamine oxidase inhibitors, medicines used to treat depression, or within two weeks of discontinuing such treatment
- with narrow angle glaucoma
- with urinary retention
- with severe high blood pressure
- with severe coronary artery disease (heart disease)
- who have hyperthyroidism (overactive thyroid gland)
- you have a history of difficulty in swallowing tablets, or have had known upper gastrointestinal narrowing or abnormal esophageal peristalsis

Do not give this medicine to a child under the age of 12 years.

Pregnancy and breast-feeding
Safe use of Clarityn-D® 24 Hour Extended Release during pregnancy has not been established. Therefore, the product is not recommended for use during pregnancy.

Since loratadine and pseudoephedrine sulfate are excreted in breast milk, the product is not recommended for use during breast-feeding. Please speak to your doctor or pharmacist if you are breastfeeding and intend to take Clarityn-D® 24 Hour Extended Release Tablet.

What are the precautionary measures to be observed when taking Clarityn-D® 24 Hour Extended Release?
Clarityn-D® 24 Hour Extended Release should be used with caution in patients with
- glaucoma or increased intraocular pressure
- prostate or urinary bladder problems
- heart disease
- diabetes
- 60 years of age or older, because older adults maybe more sensitive to the effects of the medicines
- liver or kidney disease
- stomach ulcer
- intestinal obstruction
- hypertension
- hyperthyroidism
- prostatic hypertrophy

Laboratory tests
If you are scheduled to have any skin tests for allergies, you should not take Clarityn-D® 24 Hour Extended Release for two days before.

Acute generalized exanthematous pustulosis (AGEP), a form of severe skin reaction, may occur in isolated cases. If you have signs and symptoms such as fever, redness, or small (generalized) pustules, you should stop taking Clarityn-D® 24Hour Extended Release and consult your doctor.

Possible side effects
Like all medicines, Clarityn-D® 24 Hour Extended Release can cause side effects, although not everybody gets them.
The most commonly reported side effects (i.e.,>5% incidence in clinical studies) include headache and dry mouth. Less commonly reported events were drowsiness and inability to sleep. Rarely reported side effects include dizziness, fatigue, lack of appetite for food, nervousness, nausea, nosebleed, runny nose, tear gland disorder, lack of strength, muscle spasm, constipation, indigestion, palpitation, rapid heart rate, thirst, agitation, irritability, coughing, shortness of breath, nasal irritation, and sore throat. Isolated cases of acute generalized exanthematous pustulosis (AGEP), a form of skin reaction, have also been reported with pseudoephedrine-containing products. Pseudoephedrine use has been associated with increased heart rate and increased blood pressure.

If you experience any of these side effects or you notice any not listed in this leaflet, stop taking the medicine and contact your pharmacist or doctor at once.

What other medicine should be avoided whilst taking Clarityn-D® 24 Hour Extended Release?
Tell your doctor or pharmacist if you are taking any other medicines, including medicines that are obtained without a prescription. Some medicines should not be taken with Clarityn-D® 24 Hour Extended Release. These medicines include:
- Some heart or blood pressure medicines
- monoamine oxidase inhibitors, medicines used to treat depression
- digitalis

These medicines may be affected by Clarityn-D® 24 Hour Extended Release, or may affect how well it works. You may need different amounts of your medicine, or you may need to take different medicines. Your doctor or pharmacist will advise you.

Signs and symptoms of overdose
Signs and symptoms of overdose may vary from CNS depression (sedation, apnea, diminished mental alertness, cyanosis, coma, cardiovascular collapse) to stimulation (insomnia, hallucination, tremors or convulsions) which may be fatal. Other signs and symptoms may be headache, euphoria, excitement, rapid heart rate, palpitations, thirst, perspiration, nausea, dizziness, tinnitus (ringing in the ears), ataxia (lack of muscle coordination), blurred vision and hypertension (high blood pressure) or hypotension (low blood pressure). Stimulation is particularly likely in children, as are atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing; hyperthermia (elevated body temperature); and gastrointestinal symptoms).

What should you do in case of an overdose?
In the event of overdose, seek medical help immediately.

How do I store Clarityn-D® 24 Hour Extended Release
Keep the tablets out of reach of children.
Store the tablets at or below 25°C. Protect blister packs from excessive moisture.

For the shelf-life, please refer to labels.

For further information, ask a doctor or pharmacist.

Section Below is meant for Healthcare Professionals

Clarityn-D® 24 Hour Extended Release

Brand of loratadine and pseudoephedrine sulfate

Extended-Release, Non-Sedating Antihistamine / Decongestant Tablets

Description
Each Clarityn-D® 24 Hour Extended Release Tablet contains 10 mg loratadine and 240 mg pseudoephedrine sulfate.
The loratadine component is released immediately, whereas the pseudoephedrine component is released slowly from the core allowing for once daily administration.
Excipients: Hydroxypropyl Methylcellulose, Ethylcellulose, Calcium Hydrogen Phosphate, Polyvidone, Silicon Dioxide, Magnesium Stearate, Hydroxypropyl Methylcellulose, Polyethylene Glycol, White Color Dispersion and Macrogol 400.

Actions
Loratadine
Loratadine is a potent long-acting tri-cyclic antihistamine with selective peripheral H_1-receptor antagonistic activity.

Pseudoephedrine
Pseudoephedrine sulfate, one of the naturally occurring alkaloids of Ephedra and an orally administered vasoconstrictor, produces a gradual but sustained decongestant effect facilitating shrinkage of congested mucosa in upper respiratory areas. The mucous membrane of the respiratory tract is decongested through the action on the sympathetic nerves.
The combination of loratadine and pseudoephedrine sulfate controls histamine mediated symptoms and relieves the nasal congestion associated with allergic rhinitis and the common cold.

Pharmacodynamic Properties
Loratadine
During studies of its effects on the CNS, loratadine has exhibited no depressant activity and no acute anticholinergic activity. Loratadine has exhibited a very low affinity for membrane receptors from the cerebral cortex and does not readily penetrate into the CNS. Whole body autoradiographic studies in rats and monkeys, radiolabeled tissue distribution studies in mice and rats, and *in vivo* radioligand studies in mice have shown that neither loratadine nor its metabolites readily cross the blood-brain barrier. Radioligand binding studies with guinea pig pulmonary and brain H_1-receptors indicate that there was preferential binding to peripheral versus central nervous system H_1-receptors.
The sedation profile of loratadine, 10 mg daily, is comparable to that of placebo and, during long term treatment, there were no clinically significant changes in vital signs, laboratory test values, physical examinations or electrocardiograms. In studies with loratadine tablets at doses two to four times higher than the recommended dose of 10 mg, a dose-related increase in the incidence of somnolence was observed.
Loratadine has no significant H_2-receptor activity, does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity. In a study in which loratadine tablets were administered at four times the clinical dose for 90 days, no clinically significant increase in the QTc was seen on ECGs.

Pseudoephedrine
Pseudoephedrine acts directly on both α- and to a lesser degree, β-adrenergic receptors. It is believed that α-adrenergic effects result from the inhibition of the production of cyclic adenosine-3',5'-monophosphate (AMP) by inhibition of the enzyme adenyl cyclase, whereas β-adrenergic effects result from stimulation of adenyl cyclase activity. Like ephedrine, pseudoephedrine also has an indirect effect by releasing norepinephrine from its storage sites.
Pseudoephedrine acts directly on α-adrenergic receptors in the mucosa of respiratory tract producing vasoconstriction which results in shrinkage of swollen nasal mucous membranes, reduction of tissue hyperemia, edema and nasal congestion, and in an increase in nasal airway patency. Drainage of sinus secretions is increased and obstructed eustachian ostia may be opened.
Pseudoephedrine may relax bronchial smooth muscle by stimulation of β_2-adrenergic receptors; however, substantial bronchodilation has not been demonstrated consistently following oral administration of the drug.
Oral administration of usual doses of pseudoephedrine to normotensive patients usually produces negligible effect on blood pressure. Pseudoephedrine may increase the irritability of the heart muscle and may alter the rhythmic function of the ventricles, especially in large doses or after administration to patients such as those with cardiac disease who are hypersensitive to the myocardial effects of sympathomimetic drugs. Tachycardia, palpitation, and/or multifocal premature ventricular contractions may occur.
Pseudoephedrine may cause mild CNS stimulation, especially in patients who are sensitive to the effects of sympathomimetic drugs.

Pharmacokinetics
Loratadine
After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism. In normal subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours, respectively. Initial data in normal subjects demonstrated a mean elimination half-life of 12.4 hours for loratadine and 19.6 hours for the active metabolite.
Subsequent data in normal adult subjects demonstrated mean elimination half-lives of 8.4 hours (range=3 to 20 hours) for loratadine and 28 hours (range=8.8 to 92 hours) for the major active metabolite. In nearly all patients, exposure (AUC) to the metabolite was greater than exposure to the parent compound.
Loratadine is highly bound (97% to 99%) and its active metabolite moderately bound (73% to 76%) to plasma proteins.
The bioavailability parameters of loratadine and of the active metabolite are dose proportional. Approximately 40% of the dose is excreted in the urine and 42% in the feces over a 10-day period and that, mainly in the form of conjugated metabolites. Approximately 27% of the dose is eliminated in the urine during the first 24 hours. Traces of unchanged loratadine and of its active metabolite were found in the urine. The pharmacokinetic profile of loratadine and its metabolites is comparable in healthy adult volunteers and in healthy geriatric volunteers.

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In patients with chronic renal impairment, both the AUCs and peak plasma levels (C_{max}) increased for loratadine and its metabolite as compared to the AUCs and peak plasma levels (C_{max}) of patients with normal renal function. The mean elimination half-lives of loratadine and its metabolite were not significantly different from that observed in normal subjects. Hemodialysis does not have an effect on the pharmacokinetics of loratadine or its active metabolite in subjects with chronic renal impairment.
In patients with chronic alcoholic liver disease, the AUC and peak plasma levels (C_{max}) of loratadine were double while the pharmacokinetic profile of the active metabolite was not significantly changed from that in patients with normal liver function. The elimination half-lives of loratadine and its metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.
Loratadine and its active metabolite are excreted in the breast milk of lactating women. Forty-eight hours after dosing, only 0.029% of the loratadine dose is detected in the milk as unchanged loratadine and its active metabolite.

Pseudoephedrine
Absorption - After oral administration of 60 mg of pseudoephedrine hydrochloride as tablets or oral solution, nasal decongestion occurs within 30 minutes and persists for 4-6 hours. Nasal decongestion may persist for 8 hours following oral administration of 60 mg and up to 12 hours following 120 mg of the drug in extended-release preparations.
Distribution - Although specific information is lacking, pseudoephedrine is presumed to cross the placenta and to enter CSF. The drug may also be distributed into milk.
Elimination - Pseudoephedrine is incompletely metabolized in the liver by N-demethylation to an inactive metabolite. The drug and its metabolite are excreted in urine; 55-75% of a dose is excreted unchanged. The rate of urinary excretion of pseudoephedrine is accelerated when urine is acidified to a pH of about 5 by prior administration of ammonium chloride. When the urine is alkalinized to a pH of about 8 by prior administration of sodium bicarbonate, some of the drug is reabsorbed in the kidney tubule and the rate of urinary excretion is slowed.

Indications and usage
Clarityn-D® 24 Hour Extended Release is indicated for the relief of symptoms associated with allergic rhinitis and the common cold, including nasal congestion, sneezing, rhinorrhea, pruritus and lacrimation.
Clarityn-D® 24 Hour Extended Release is recommended when both the antihistaminic properties of loratadine and the decongestant effect of pseudoephedrine sulfate are desired.

Dosage and Administration
Adults and Children 12 years of age and over: One Clarityn-D® 24 Hour Extended Release Tablet once daily. Clarityn-D® 24 Hour Extended Release may be taken without regard to meal time.
Patients who have a history of difficulty in swallowing tablets or who have known upper gastrointestinal narrowing or abnormal esophageal peristalsis should not use this product (see Precautions and Adverse Reactions).

Drug interactions
When administered concomitantly with alcohol, loratadine has no potentiating effect as measured by psychomotor performance studies.
Increase in plasma concentrations of loratadine has been reported after concomitant use with ketoconazole, erythromycin (inhibitors of CYP3A4) or cimetidine (inhibitor of CYP3A4 and CYP2D6) in controlled clinical trials, but without clinically significant changes (including electrocardiographic). Other drugs known to inhibit hepatic metabolism should be coadministered with caution until definitive interaction studies can be completed.
When sympathomimetic drugs are given to patients receiving monoamine oxidase (MAO) inhibitors, hypertensive reactions, including hypertensive crisis may occur. This interaction is still possible two weeks after MAO inhibitor therapy is stopped. The antihypertensive effects of methyldopa, guanethidine, mecamylamine, and reserpine may be reduced by sympathomimetics. Beta-adrenergic blocking agents also may interact with sympathomimetics. Increased ectopic pacemaker activity can occur when pseudoephedrine sulfate is used concomitantly with digitalis.

Drug/Laboratory Test Interactions: Antihistamines should be discontinued approximately 48 hours prior to skin testing procedures since these drugs may prevent or diminish otherwise positive reactions to dermal reactivity indicators.
The *in vitro* addition of pseudoephedrine to sera containing the cardiac isoenzyme MB of serum creatine phosphokinase progressively inhibits the activity of the enzyme. The inhibition becomes complete over six hours.

Adverse reactions
In controlled clinical studies, the incidence of adverse effects (i.e., >5% incidence) was similar to that of placebo, with the exception of insomnia and dry mouth. Other reported adverse reactions included headache and somnolence.
Rarely reported events in decreasing order of frequency included dizziness, fatigue, anorexia, nervousness, nausea, epistaxis, rhinitis, lacrimal gland disorder, asthenia, hyperkinesia, constipation, dyspepsia, palpitation, tachycardia, thirst, agitation, irritability, coughing, dyspnea, nasal irritation, and pharyngitis.
With the exception of headache, which was occasionally severe, most of the adverse events associated with Clarityn-D® 24 Hour Extended Release Tablet were mild to moderate in severity.
During the marketing of loratadine, alopecia, anaphylaxis (including angioedema), abnormal hepatic function, dizziness and convulsion have been reported rarely.
There have been rare postmarketing reports of mechanical upper gastrointestinal tract obstruction in patients taking Clarityn-D® 24 Hour Extended Release Tablets. In most of these cases, patients have had a history of difficulty in swallowing tablets, or have had known upper gastrointestinal narrowing or abnormal esophageal peristalsis.

Isolated cases of acute generalized exanthematous pustulosis (AGEP), a form of severe skin reaction, have been reported post-market with pseudoephedrine-containing products. Pseudoephedrine use has been associated with increased heart rate and increased blood pressure.

Contraindications
Clarityn-D® 24 Hour Extended Release Tablets are contraindicated in those who have shown sensitivity or idiosyncrasy to their components or to adrenergic agents. Clarityn-D® 24 Hour Extended Release Tablets also are contraindicated in patients receiving MAO inhibitor therapy or within two weeks of discontinuing such treatment and in patients with narrow angle glaucoma, urinary retention, severe hypertension, severe coronary artery disease and hyperthyroidism.

Precautions
Sympathomimetic agents should be used with caution in patients with hypertension, hyperthyroidism, glaucoma, stomach ulcer, intestinal obstruction, prostatic hypertrophy or bladder neck obstruction, cardiovascular disease, increased intraocular pressure or diabetes mellitus.
Sympathomimetics should be used with caution in patients receiving digitalis.
Sympathomimetics may cause central nervous system (CNS) stimulation, excitability, convulsions, and/or cardiovascular collapse with accompanying hypotension.
In patients 60 years of age or older, sympathomimetics also are more likely to cause adverse reactions such as confusion, hallucination, convulsions, CNS depression and death. Consequently, caution should be exercised when administering a long-acting formulation to elderly patients.
Acute generalized exanthematous pustulosis (AGEP), a form of severe skin reaction, may occur with pseudoephedrine-containing products in isolated cases. If signs and symptoms such as fever, erythema, or small (generalized) pustules are observed, patients should discontinue the drug and consult their physician.
Because the doses of this combination product cannot be individually titrated, it should generally be avoided in patients with severe hepatic impairment and in patients with severe renal impairment or renal tubular acidosis.
Patients who have a history of difficulty in swallowing tablets, or have had known upper gastrointestinal narrowing or abnormal esophageal peristalsis should not use this product.

Drug Abuse and Dependence
No data are available to indicate that abuse or dependency occurs with loratadine.
Like other CNS stimulants, pseudoephedrine sulfate has a potential for abuse, and increased doses may ultimately produce toxicity. Depression may follow rapid withdrawal.

Pediatric usage
Safety and efficacy of C larityn-D® 24 Hour Extended Release in children younger than 12 years of age have not yet been established.

Fertility, usage during pregnancy and in nursing mothers
Safe use of Clarityn-D® 24 Hour Extended Release during pregnancy has not been established. There was no evidence of animal teratogenicity in reproduction studies performed on rats and rabbits up to 30 times human daily dose. Because animal reproduction studies are not always predictive of human response, it is not recommended for use during pregnancy.
Since loratadine and pseudoephedrine sulfate are excreted in breast milk, the use of the product during breast-feeding is not recommended. There are no animal or laboratory data on male and female fertility. However, no significant findings have been noted for the loratadine and pseudoephedrine sulfate.

Overdosage Information
In the event of overdosage, general symptomatic and supportive treatment should be started immediately and maintained for as long as necessary.

Manifestations
These may vary from CNS depression (sedation, apnea, diminished mental alertness, cyanosis, coma, cardiovascular collapse) to stimulation (insomnia, hallucination, tremors or convulsions) to death. Other signs and symptoms may be euphoria, excitement, tachycardia, palpitations, thirst, perspiration, nausea, dizziness, tinnitus, ataxia, blurred vision and hypertension or hypotension. Stimulation is particularly likely in children, as are atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing; hyperthermia; and gastrointestinal symptoms).
In large doses sympathomimetics may give rise to giddiness, headache, nausea, vomiting, sweating, thirst, tachycardia, precordial pain, palpitations, difficulty in micturition, muscular weakness, tenseness, anxiety, restlessness and insomnia. Some patients present a toxic psychosis with delusions and hallucinations. Some may develop cardiac arrhythmias, circulatory collapse, convulsions, coma and respiratory failure.
The Oral LK_{50} values for loratadine and pseudoephedrine sulfate in combination product were approximately 600 mg/kg in mice and 2000 mg/kg in rats. Cynomolgus monkeys tolerated single doses of up to 240 mg/kg.

Treatment
The patient should be induced to vomit, even if emesis has occurred spontaneously. Pharmacologically-induced vomiting by the administration of ipecac syrup is a preferred method. However, vomiting should not be induced in patients with impaired consciousness. The action of ipecac is facilitated by physical activity and by the administration of 240 to 360 milliliters of water. If emesis does not occur within 15 minutes, the dose of ipecac should be repeated. Precautions against aspiration must be taken, especially in children. Following emesis, adsorption of any drug remaining in the stomach may be attempted by the administration of activated charcoal as a slurry with water. If vomiting is unsuccessful, or contraindicated, gastric lavage should be performed. Physiologic saline solution is the lavage solution of choice, particularly in children. In adults, tap water can be used; however, as much as possible of the amount administered should be removed before the next instillation. Saline cathartics draw water into the bowel by osmosis and therefore may be valuable for their action in rapid dilution of bowel content. Loratadine is not removed by hemodialysis; it is not known if loratadine is removed by peritoneal dialysis.
After emergency treatment, the patient should continue to be medically monitored.
Treatment of the signs and symptoms of overdosage is symptomatic and supportive. Stimulants (analeptic agents) should not be used. Vasopressors may be used to treat hypotension. Short-acting barbiturates, diazepam or paraldehyde may be administered to control seizures. Hyperpyrexia, especially in children, may require treatment with tepid water sponge baths or hypothermic blanket. Apnea is treated with ventilatory support.

End of Section meant for Healthcare Professionals

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