Approved Date: October 20th, 2008
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Package Insert of Loratadine and Pseudoephedrine Sulfate Sustained Release Tablets

Please read the package insert carefully and use according to doctor's instructions.

[Drug Name]
Generic Name: Loratadine and Pseudoephedrine Sulfate Sustained Release Tablets
Chinese Pinyin: Lüleiweima Huanshi Pian

[Active Ingredients]

Active ingredient (in each tablet)	*Purpose*
Loratadine 5 mg	Antihistamine
Pseudoephedrine sulfate 120 mg	Nasal decongestant

[Inactive Ingredients]
Low-substituted Hydroxypropyl Cellulose, Polyvinylpyrrolidone, Purified Water, Alcohol, Magnesium Stearate, Hydroxypropylmethylcellulose, Iron(III) Oxide.

[Properties]
This product is a double-layered tablets, one layer is white or off-white the other layer is dark red.

[Indications]
1. temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: sneezing
2. itchy, watery eyes
3. runny nose
4. itching of the nose or throat
5. temporarily relieves nasal congestion due to the common cold, hay fever or other upper respiratory allergies reduces swelling of nasal passages
6. temporarily relieves sinus congestion and pressure temporarily restores freer breathing through the nose.

[Dosage and Administration]

adults and children 12 years and over	1 tablet every 12 hours; not more than 2 tablets in 24 hours
children under 12 years of age	ask a doctor
consumers with liver or kidney disease	ask a doctor

[Adverse Reactions]
The most frequently reported adverse reactions (incidences greater than 5%) in clinical studies are insomnia, dry mouth, headache, neurotisim, and lethargy. The incidence of sleepiness and headache was reported to be the same as placebo.
The rare side effects of this product are (according to the incidence) tension, dizziness, fatigue, nausea, abdominal discomfort, anorexia, thirst, tachycardia, pharyngitis, rhinitis, hemorrhoids, itching, rash, urticaria, joint pain, confusion, difficulty in pronunciation, hyperactivity, loss of sensation, loss of libido, feeling disorder, tremor, dizziness, flushing, orthostatic hypotension, hyperhidrosis, eye discomfort, earache, tinnitus, abnormal taste, agitation, apathy, depression Symptoms, euphoria, nightmares, increased appetite, changes in bowel habits, indigestion, hernias, tongue color changes, tongue discomfort, vomiting, transient liver abnormal function, dehydration, weight gain, high blood pressure, migraine, bronchospasm, cough, difficulty breathing, nosebleed, nasal congestion, sneezing, nose stimulation, dysuria, dysuria, nocturia, frequent urination, urinary retention, fatigue, back pain, cramps in the lower leg, discomfort and chills.

The following adverse reactions can occur with pseudoephedrine alone:
Pseudoephedrine is a sympathomimetic drug, which may be blurred, headache, irritability, insomnia, nausea, vomiting, thirst, palpitations, and frequent urination increases. There may be illusions and hallucinations, and some can develop into arrhythmia, circulatory failure, convulsions, coma and respiratory failure. For patients with high sensitivity, it may cause mild central nervous system symptoms such as nervousness, insomnia, blurred vision, excitement, dizziness, and fatigue, there have been reports of headache, nausea, drowsiness, palpitations, blood pressure fluctuations, arrhythmia, etc., while sympathomimetic drugs may also appear as hallucinations, adverse reactions such as nervousness, trepidation, difficulty breathing, difficulty urinating, and circulatory failure.

The following adverse reactions can occur with loratadine alone:
1. The incidence rate is higher than 2%: headache, lethargy, fatigue, dry mouth.
2. The incidence is less than 2%:
(1) Cardiovascular system: high blood pressure, hypotension, palpitations, supraventricular tachyarrhythmia, syncope, tachycardia, etc. No elevated QT interval found so far
(2) Central nervous system: agitation, bad memory, anxiety, confusion, depression, insomnia, irritability, dizziness, epilepsy, tremor, etc.
(3) Respiratory system: bronchitis, bronchospasm, cough, difficult breathing, nosebleeds, hemoptysis, laryngitis, nasal dryness, pharyngitis, Sinusitis, sneezing, etc.
(4) Musculoskeletal system: leg muscle spasm, joint pain, muscle pain, etc.
(5) Genitourinary system: frequent urination, urine appearance color change, urinary incontinence, urinary retention, breast pain, breast hyperplasia, dysmenorrhea, menorrhagia, vaginitis, impotence, decreased sexual desire, etc.
(6) Digestive system: Abnormal liver function (including jaundice, hepatitis and liver necrosis), bloating, taste changes, loss of appetite, constipation, diarrhea, hiccup, increased appetite, nausea, vomiting, spit, toothache, etc.
(7) Skin and appendages: dermatitis, dry hair, dry skin, itchy skin, cyanosis, rash, rubella, polymorphous erythema, etc.
(8) Others: hair loss, eyelids, tearing, salivation, flushing, sweating, tinnitus, angioedema, blurred vision, chest pain, earache, eye pain, weight gain, allergic reactions, photosensitivity reactions, viral infections, etc.

[Contraindications]
Do not use this product if patient is allergic or have idiosyncratic reactions to the ingredients contained in this product and adrenaline drugs or other drugs with similar chemical structures. This product is contraindicated in patients who are receiving treatment with a monoamine oxidase inhibitor or who have received such treatment within 14 days or who have just stopped such treatment. This product is also contraindicated in patients with narrow-angle glaucoma, urinary retention, severe hypertension, or severe coronary artery disease.

[Precautions]
1. Athletes use with caution.
2. Peptic ulcer, pyloric duodenal obstruction, prostatic hypertrophy, bladder neck obstruction, cardiovascular disease, glaucoma, increased intraocular pressure, Hyperthyroidism. Patients with hyperactivity, liver and kidney dysfunction, and diabetes should be used with caution; patients receiving digitalis should be used with caution.
3. Sympathomimetic drugs may cause central nervous system excitement, convulsions, and/or accompanied by hypotension, circulatory collapse. For 60 years old or older patients, sympathomimetic drugs are more likely to cause adverse reactions such as confusion, hallucinations, convulsions, central nervous system depression and death, and thus for older patients should be careful when co-administrated with the same pharmacology mechanism drugs.
4. Patients under sympathomimetic drugs medication co-administrated with monoamine oxidase (MAO) inhibitors may develop hypertensive reactions, including hypertensive crisis. The antihypertensive effects of methyldopa, mecamylamine, reserpine and veratrum alkaloids may be reduced by sympathomimetic drugs. Beta-adrenergic blocker
can interact with sympathomimetic drugs. When pseudoephedrine and digitalis are used simultaneously, the

activity of the ectopic pacemaker may be increased. Antacid will increase the absorption rate of pseudoephedrine.
5. Pseudoephedrine has been abused like other central nervous system stimulants. High doses can produce euphoria, loss of appetite and increased physical strength. Feeling excited, but also accompanied by anxiety and irritability. Continuing use of any central nervous system stimulant can produce tolerance, increasing doses and eventually causing poisoning, abruptly stop the drug can cause depression.
6. Loratadine can prevent or reduce the positive result of the skin drug antigen reaction test, so the drug should be discontinued 48 hours before the skin test. Patients driving vehicles, boats, high-altitude operations, mechanical operations and precision instruments should use with caution.
7. If there is an allergic reaction such as rash, itchy skin, nausea, vomiting during medication, stop the drug immediately and switch to other drugs. Patients should strictly follow the recommended agent dosage and dosing interval should not be exceeded or shortened. For 7 days, if the symptoms are not relieved, please consult your physician or pharmacist. Do not take this drug with other anti-allergic or anti-cold medicines similar to the ingredients in this product.
8. This product is a double-layer sustained-release tablet. It must be swallowed as a whole and should not be crushed or dissolved. Otherwise, it will affect the safety and effectiveness of this product.

[Use in Pregnant and Lactation]
There is no information about the safety use of this product during pregnancy, only use this product if the benefits to the fetus are greater than the disadvantages. Due to both pseudoephedrine and loratadine can be secreted from the milk, so breastfeeding women should consider stopping breastfeeding or stopping taking the drug.

[Pediatric Use]
There is no safety and effectiveness data in pediatric patients under 12 years old. This product is not recommended for pediatric patient under 12 years old.

[Geriatric Use]
Patients with 60 years of age or older are more likely to cause confusion, hallucinations, convulsions, central nervous system depression, death and other adverse reaction with sympathomimetic drugs.

[Drug Interactions]
1. Pseudoephedrine combination with monoamine oxidase inhibitors (rasagiline, furazolidone, moclobemide, nicotinamide, phenelzine, procarbazine, selegiline) can cause severe hypertension, high fever, headache, due to norepinephrine effect is enhanced. Therefore, the combination of pseudoephedrine and monoamine oxidase inhibitors are prohibited, and pseudoephedrine should be used after 14 days of stopping monoamine oxidase inhibitor.
2. Antacids (such as omeprazole, etc.) can increase the absorption rate of pseudoephedrine. Pseudoephedrine combined with sodium bicarbonate can cause pseudoephedrine toxicity (excitement, high blood pressure, heart palpitations), when combined with two drugs, it is necessary to monitor the possible adverse reactions, if necessary, reduce the dose, patients who need to alkalinize their urine may need to reduce the dose of both.
3. The combination of pseudoephedrine and dihydroergotamine can cause a sharp rise in blood pressure, so it is forbidden to use the two drugs together. Pseudoephedrine combined with morpholinone can cause blood pressure
increase, because the latter can inhibit the metabolism of the former, need to be cautious when used together. Sympathomimetic drugs combined with Fructus Aurantii can cause hypertensive crisis (headache, high fever, high
blood pressure), the mechanism is the additive sympathetic effect, so the sympathomimetic should be avoided in combination with Fructus Aurantii. Pseudoephedrine can enhance the pressure of midodrine, should be used with caution, and monitor blood pressure. Pseudoephedrine combined with methyldopa can cause elevated blood pressure and arrhythmia, and blood pressure should be monitored when used together. In the case of high blood pressure, pseudoephedrine is discontinued and phentolamine is given in severe cases. Pseudoephedrine combined with guanethidine can lead to elevated blood pressure and arrhythmia. Pseudoephedrine can antagonize the central nervous effect of the guanethidine, blood pressure and heart rhythm should be monitored two of them combined, and pseudoephedrine should be stopped if adverse reactions occur. Sympathomimetic

drug can reduce the antihypertensive effects of mecamylamine, reserpine and veratrum alkaloids. Beta-adrenergic blockers (eg propranolol, metoprolol, labetalol, etc.) may interact with sympathomimetic drugs.
4. The combination of pseudoephedrine and iobenguane (I-131) can lead to false negative results during scanning, because the former can reduce the absorption of the latter. Pseudoephedrine should be stopped before using iobenguane (I-131). Pseudoephedrine and digitalis may increase the activity of ectopic pacemakers when applied together.
5. Loratadine combined with ketoconazole, macrolide antibiotics (such as erythromycin), cimetidine, theophylline, etc., can inhibit the metabolism of loratadine, increase plasma concentration of loratadine and its metabolite decarboxylated ethoxylated loratadine (blood concentration of cimetidine and ketoconazole is not affected, erythromycin is increased by about 15%).
6. Loratadine combined with isocarbopurine, pegillin, phenelzine, tranylcypromine and other drugs can increase the adverse reactions of loratadine. Loratadine combined with central nervous system inhibitors (such as barbiturates, benzodiazepine sedatives, phenothiazine sedatives, tricyclic antidepressants, muscle relaxants, anesthetics, painkillers) can cause severe sleepiness.

[Over-Dosage]
After the large dose of pseudoephedrine, the following symptoms may occur: blurred vision, irritability, insomnia, headache, nausea, vomiting, excessive sweating, thirst, tachycardia, pain in the precordial area, palpitations, urinary urgency, muscle weakness, muscle tension, anxiety, irritability, insomnia, many patients may also have psychotoxic effect such as illusions and hallucinations, and some may also have arrhythmia, circulatory failure, convulsions, coma and respiratory failure.
Adults who take excessive loratadine (40-180 mg) can develop symptoms such as lethargy, tachycardia and headache; children take this medicine excessively (> 10 mg) might have extrapyramidal signs, palpitations and other symptoms. If the above symptoms occur, measures such as vomiting, gastric lavage, and activated carbon adsorption may be used. Also consider using salt laxatives (such as sodium sulphate) to stop the drug absorption in the intestines. It is strictly forbidden to use histamine as a rescue drug when the drug is overdose.

[Pharmacology and Toxicology]

Pseudoephedrine hydrochloride is an adrenergic drug that can contract blood vessels in the nasal mucosa and relieve symptoms of nasal congestion and runny nose. Loratadine is a long-acting tricyclic antihistamine. A drug that relieves nasal or non-nasal symptoms of seasonal allergic rhinitis by selectively antagonizing peripheral H1 receptors.

Toxicological research

Genotoxicity: In the Ames test, forward-mutation test, DNA damage test, chromosome aberration test, no carcinogenic effect has been found for loratadine. In the mouse lymphoma assay, a positive result occurred in the non-activated state and negative result in the activated state.

Reproductive toxicity: Male rats were orally administered with loratadine at a dose of 64 mg/kg (according to the body surface, the dose is 50 times more than the maximum recommended clinical daily dose intake.), the fertility will be reduced, which is manifested by a decrease in the conception rate of females. Oral administration of loratadine at a dose of 24 mg/kg (according to the body surface, the dose is 20 times more than the maximum recommended clinical daily dose intake.), has no effect on the fertility of male and female rats. Rats and rabbits were given oral loratadine 96 mg/kg (according to the body surface, the dose is 75, 150 times more than the maximum recommended clinical daily dose intake respectively.)

and there was no teratogenic effect.

Carcinogenicity: Mice were given oral loratadine for consecutive 18 months at the dose of 40 mg/kg. In male mice, the incidence of hepatocellular carcinoma (including adenomas and carcinomas) increased significantly; the rats were given loratadine orally for 2 consecutive years. In male rats with the given dose of 10 mg/kg and the female rats with the given dose of 25 mg/kg, the incidence of hepatocellular carcinoma (including adenomas and carcinomas) increased significantly. The clinical significance of the above findings is not clear when people take loratadine for a long time.

[Pharmacokinetics]
Food has no significant effect on the pharmacokinetics of pseudoephedrine. Pseudoephedrine has 1% to 7% convert to pseudoephedrine. The half-life of pseudoephedrine is 6.0 hr. According to reports, about 0.4% to 0.7% of pseudoephedrine is secreted by milk after a single dose. The pseudoephedrine concentration is about 2 to 3 times more than the plasma concentration. Loratadine is rapidly absorbed from the gastrointestinal mucosa after oral administration, with a plasma half-life of about 10 hours and the plasma protein binding rate of 98%. Most drugs are metabolized by liver, this product also has first pass effect and is metabolized to descarboethoxyloratadine, which still has antihistaminic activity. Both loratadine and its metabolites are difficult to pass the blood-brain barrier. Its metabolites are excreted in the urine, feces, sweat, and milk. Patients with chronic alcoholic liver disease take this medicine, the plasma half-life of loratadine and descarboethoxyloratadine increases, depending on the degree of liver damage. For chronic renal insufficiency and healthy elderly patients, the area under curve (AUC) and C_{max} of loratadine and descarboethoxyloratadine increases. Food can increase the AUC of loratadine about 40%, and delay the peak concentration of blood concentration about 1 hour, but the food does not affect the peak concentration of loratadine and descarboethoxyloratadine.

[Storage]
Seal and store under 2°C~30°C. Prevent from moisture

[Packaging]
Aluminum-aluminum blister packaging, 6 tablets/plate, one plate/carton

[Shelf-Life]
36 months

[Executive Standard]
National Medical Products Agency standard YBH12662008

[Approval Number]
Guo Yao Zhun Zi H20080709

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