CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

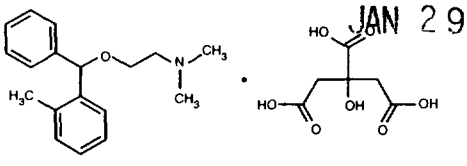
40249

DRAFT FINAL PRINTED LABELING

Orphenadrine Citrate
Extended-release Tablets

DESCRIPTION:
Orphenadrine citrate is the citrate salt of orphenadrine. It occurs as a white, crystalline powder having a bitter taste. It is practically odorless; sparingly soluble in water, slightly soluble in alcohol.

The chemical name for orphenadrine citrate is (±) -N,N-Dimethyl-2-[(*o*-methyl-α-phenylbenzyl)oxy]ethylamine citrate (1:1). Orphenadrine citrate's molecular weight is 461.51. The molecular formula is $C_{18}H_{23}NO \cdot C_6H_8O_7$ and the structural formula is:



Each tablet, for oral administration contains 100 mg orphenadrine citrate. In addition, each tablet contains the following inactive ingredients: Calcium stearate, ethylcellulose and lactose monohydrate.

CLINICAL PHARMACOLOGY:
Orphenadrine citrate is a centrally acting (brain stem) compound which in animals selectively blocks facilitatory functions of the reticular formation. Orphenadrine does not produce myoneural block, nor does it affect crossed extensor reflexes. Orphenadrine prevents nicotine-induced convulsions but not those produced by strychnine.

The mode of therapeutic action has not been clearly identified but may be related to its analgesic properties. Orphenadrine citrate also possesses anti-cholinergic actions.

INDICATIONS AND USAGE:
Orphenadrine Citrate Extended-release Tablets are indicated as adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute painful musculo skeletal conditions. The mode of action of the drug has not been clearly identified, but may be related to its analgesic properties.

Orphenadrine citrate does not directly relax tense skeletal muscles in man.

CONTRAINDICATIONS
Orphenadrine citrate Extended-release Tablets are contraindicated in patients with glaucoma, pyloric or duodenal obstruction, stenosing peptic ulcers, prostatic hypertrophy or obstruction of the bladder neck, cardio-spasm (megaesophagus) and myasthenia gravis.

Contraindicated in patients who have demonstrated a previous hypersensitivity to the drug.

WARNINGS:
Some patients may experience transient episodes of lightheadedness, dizziness or syncope. Orphenadrine Citrate Extended-release Tablets may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; ambulatory patients should therefore be cautioned accordingly.

Pregnancy:
Safe use of orphenadrine has not been established with respect to adverse effects upon fetal development. Therefore, orphenadrine citrate should be used in women of childbearing potential and particularly during early pregnancy only when in the judgment of the physician the potential benefits outweigh the possible hazards.

Usage in children:
Safety and effectiveness in children have not been established; therefore, this drug is not recommended for use in the pediatric age group.

PRECAUTIONS:
Confusion, anxiety and tremors have been reported in few patients receiving propoxyphene and orphenadrine concomitantly. As these symptoms may be simply due to an additive effect, reduction of dosage and/or discontinuation of one or both agents is recommended in such cases.

Orphenadrine citrate should be used with caution in patients with tachycardia, cardiac decompensation, coronary insufficiency, or cardiac arrhythmias.

Safety of continuous long term therapy with orphenadrine has not been established. Therefore, if orphenadrine is prescribed for prolonged use, periodic monitoring of blood, urine and liver function values is recommended.

ADVERSE REACTIONS:
Adverse reactions of orphenadrine are mainly due to the mild anticholinergic action of orphenadrine, and are usually associated with higher dosage. Dryness of the mouth is usually the first adverse effect to appear. When the daily dose is increased, possible adverse effects include: tachycardia, palpitation, urinary hesitancy or retention, blurred vision, dilatation of pupils, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, drowsiness, hypersensitivity reactions, pruritus, hallucinations, agitation, tremor, gastric irritation, and rarely urticaria and other dermatoses. Infrequently, an elderly patient may experience some degree of mental confusion. These adverse reactions can usually be eliminated by reduction in dosage. Very rare cases of aplastic anemia associated with the use of Orphenadrine Citrate Extended-release Tablets have been reported. No causal relationship has been established.

DOSAGE AND ADMINISTRATION:
Adults – Two tablets per day; one in the morning and one in the evening.

HOW SUPPLIED:
Orphenadrine Citrate Extended-release Tablets 100 mg are supplied as white, round, unscored tablets with "KL-111" imprinted on one side. Bottles of 100 (NDC 59743-201-01) and 250 (NDC 59743-201-25) tablets. Each tablet contains 100 mg of orphenadrine citrate.

Dispense in a tight, light resistant container.

Store at controlled room temperatures 15° – 30°C (59° – 86°F).

Rx only.

Distributed by
Alphagen Laboratories, Inc.
Alpharetta, GA 30201

Manufactured by
Kiel Laboratories, Inc.
Gainesville, GA 30504

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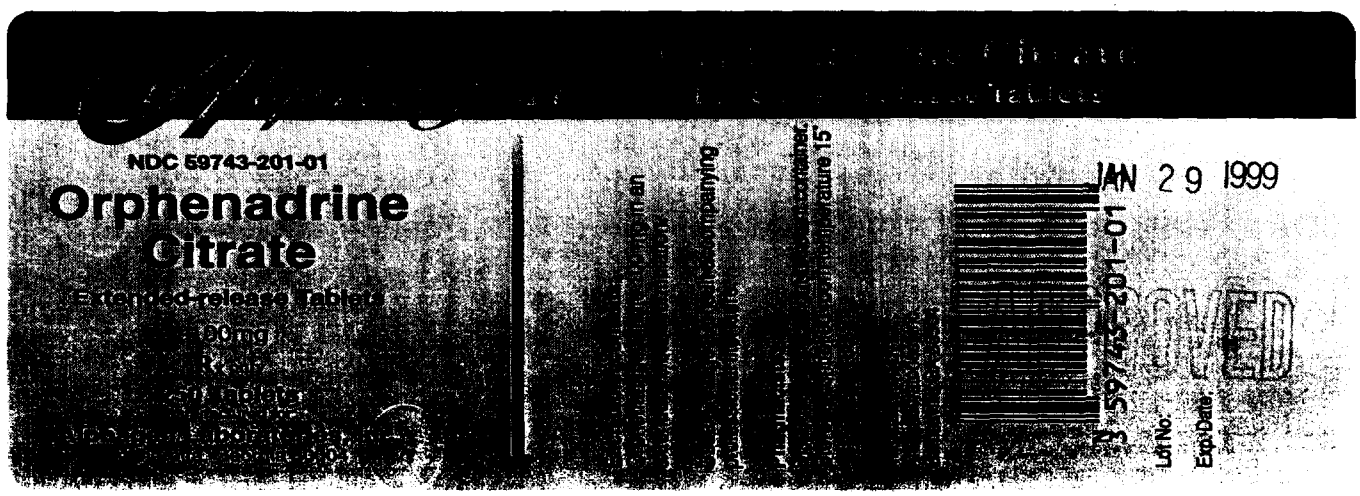
NDC 59743-201-01
Orphenadrine
Citrate
Extended-release Tablets
100mg
Rx only
JAN 29 1999
APPROVED
59743-201-01
Lot No.
Exp. Date

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