

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-556Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use KARBINAL™ ER safely and effectively. See full prescribing information for KARBINAL™ ER.

Karbinal™ ER (carbinoxamine maleate) extended-release oral suspension
Initial U.S. Approval: 1953

INDICATIONS AND USAGE

Karbinal ER (carbinoxamine maleate) Extended-release Oral Suspension is an H₁ receptor antagonist indicated for the symptomatic treatment of:

- Seasonal and perennial allergic rhinitis (1)
- Vasomotor rhinitis (1)
- Allergic conjunctivitis due to inhalant allergens and foods (1)
- Mild, uncomplicated allergic skin manifestations of urticaria and angioedema (1)
- Dermatographism (1)
- As therapy for anaphylactic reactions *adjunctive* to epinephrine and other standard measures after the acute manifestations have been controlled (1)
- Amelioration of the severity of allergic reactions to blood or plasma (1)

DOSAGE AND ADMINISTRATION

Adults and Adolescents 12 years of age and older (2):

7.5 mL to 20 mL (6 to 16 mg) every 12 hours

Children 2-11 years of age (approximately 0.2 to 0.4 mg/kg/day) (2):

2 to 3 years – 3.75 mL to 5 mL (3 to 4 mg) every 12 hours

4 to 5 years – 3.75 mL to 10 mL (3 to 8 mg) every 12 hours

6 to 11 years – 7.5 mL to 15 mL (6 to 12 mg) every 12 hours

DOSAGE FORMS AND STRENGTHS

Extended-Release Oral Suspension: 4 mg carbinoxamine maleate per 5 mL (3)

CONTRAINDICATIONS

- Children younger than 2 years of age (4.1)
- Nursing mothers (4.2)
- Patients with known hypersensitivity to the drug or any of the inactive ingredients (4.3 and 5.3)
- Monoamine oxidase inhibitors (MAOI) (4.4 and 7)

WARNINGS AND PRECAUTIONS

- Activities requiring mental alertness: Avoid engaging in hazardous tasks requiring complete mental alertness such as driving or operating machinery. (5.2)
- Anticholinergic actions: Use with caution in patients with increased intraocular pressure, narrow angle glaucoma, hyperthyroidism, cardiovascular disease, hypertension, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, pyloroduodenal obstruction. (5.3)
- Contains sodium metabisulfite, a sulfite that may cause anaphylaxis including life-threatening or less severe asthmatic episodes in susceptible individuals. (5.4)

ADVERSE REACTIONS

Most common adverse reactions are: sedation, sleepiness, dizziness, disturbed coordination, epigastric distress, and thickening of bronchial secretions. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Tris Pharma, Inc. at 732-940-0358 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Monoamine oxidase inhibitors (MAOIs): Prolong and intensify the anticholinergic (drying) effects. (4.4 and 7)
- Alcohol and CNS depressants (hypnotics sedatives, tranquilizers, etc.): Avoid concomitant use due to additive adverse effects. (7)

USE IN SPECIFIC POPULATIONS

- Because of the higher risk of serious adverse reactions with use of carbinoxamine maleate in infants, Karbinal ER is contraindicated in nursing women. (8.3)
- Contraindicated in children younger than 2 years of age. (8.4)
- May cause sedation or excitation in young children. (8.4)
- May cause dizziness, sedation, and hypotension in elderly patients. Start elderly patients on lower doses and observe closely for confusion and over-sedation. (8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 03/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

1	INDICATIONS AND USAGE
2	DOSAGE AND ADMINISTRATION
3	DOSAGE FORMS AND STRENGTHS
4	CONTRAINDICATIONS
4.1	Children less than 2 years of age
4.2	Nursing mothers
4.3	Hypersensitivity
4.4	Monoamine oxidase inhibitors
5	WARNINGS AND PRECAUTIONS
5.1	Pediatric Mortality
5.2	Activities Requiring Mental Alertness
5.3	Concomitant Medical Conditions
5.4	Allergic Reactions due to Sulfites
5.5	Dosing
6	ADVERSE REACTIONS
7	DRUG INTERACTIONS
8	USE IN SPECIFIC POPULATIONS
8.1	Pregnancy
8.2	Labor and Delivery
8.3	Nursing Mothers
8.4	Pediatric Use
8.5	Geriatric Use
10	OVERDOSAGE
11	DESCRIPTION
12	CLINICAL PHARMACOLOGY
12.1	Mechanism of Action
12.3	Pharmacokinetics
13	NONCLINICAL TOXICOLOGY
13.1	Carcinogenesis, Mutagenesis, Impairment of Fertility
14	CLINICAL STUDIES

16	HOW SUPPLIED/STORAGE AND HANDLING
17	PATIENT COUNSELING INFORMATION
17.1.	Dosing
17.2.	Activities Requiring Mental Alertness
17.3.	Alcohol, Sedatives, and Tranquilizers
17.4.	MAOIs

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Karbinal ER Extended-release Oral Suspension is an H₁ receptor antagonist indicated for the symptomatic treatment of:

- Seasonal and perennial allergic rhinitis
- Vasomotor rhinitis
- Allergic conjunctivitis due to inhalant allergens and foods
- Mild, uncomplicated allergic skin manifestations of urticaria and angioedema
- Dermatographism
- As therapy for anaphylactic reactions *adjunctive* to epinephrine and other standard measures after the acute manifestations have been controlled
- Amelioration of the severity of allergic reactions to blood or plasma

2 DOSAGE AND ADMINISTRATION

The dosage of Karbinal ER should be individualized based on the severity of the condition and the response of the patient. Start with lower doses and increase as needed and tolerated.

Administer Karbinal ER by the oral route only. Measure Karbinal ER with an accurate milliliter measuring device. A household teaspoon is not an accurate measuring device and could lead to overdosage. A pharmacist can provide an appropriate measuring device and can provide instructions for measuring the correct dose. [see [Warnings and Precautions \(5.5\)](#)]

Adults and Adolescents 12 years of age and older:

7.5 mL to 20 mL (6 to 16 mg) every 12 hours

Children 2 to 11 years of age (approximately 0.2 to 0.4 mg/kg/day):

2 to 3 years: 3.75 mL to 5 mL (3 to 4 mg) every 12 hours

4 to 5 years: 3.75 mL to 10 mL (3 to 8 mg) every 12 hours

6 to 11 years: 7.5 mL to 15 mL (6 to 12 mg) every 12 hours

3 DOSAGE FORMS AND STRENGTHS

Extended-release oral suspension containing 4 mg carbinoxamine maleate per 5 mL

4 CONTRAINDICATIONS

4.1 Children less than 2 years of age

Karbinal ER is contraindicated in children younger than 2 years of age because deaths have been reported in this age group [see [Warnings and Precautions \(5.1\)](#)].

4.2 Nursing Mothers

Karbinal ER is contraindicated in nursing mothers because of the risk of mortality in infants given carbinoxamine-containing products [see [Use in Specific Populations \(8.3\)](#)].

4.3 Hypersensitivity

Karbinal ER is contraindicated in patients who are hypersensitive to carbinoxamine maleate or any of the inactive ingredients in Karbinal ER [see [Warnings and Precautions \(5.4\)](#)].

4.4 Monoamine oxidase inhibitors

Karbinal ER is contraindicated in patients who are taking monoamine oxidase inhibitors (MAOI) [see [Drug Interactions \(7\)](#)].

5 WARNINGS AND PRECAUTIONS

5.1 Pediatric Mortality

Deaths have been reported in children less than 2 years of age who were taking carbinoxamine-containing drug products; therefore, Karbinal ER is contraindicated in children younger than 2 years of age.

5.2 Activities Requiring Mental Alertness

Karbinal ER may produce marked drowsiness and impair the mental or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. Advise patients to avoid engaging in hazardous tasks requiring mental alertness and motor coordination after ingestion of Karbinal ER. Avoid concurrent use of Karbinal ER with alcohol or other central nervous system depressants because additional impairment of central nervous system performance may occur.

5.3 Concomitant Medical Conditions

Karbinal ER has anticholinergic (atropine-like) properties and, therefore, should be used with caution in patients with: increased intraocular pressure, narrow angle glaucoma, hyperthyroidism, cardiovascular disease, hypertension, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, or pyloroduodenal obstruction.

5.4 Allergic Reactions due to Sulfites

Karbinal ER contains sodium metabisulfite, a sulfite that may cause allergic-type reactions, including anaphylaxis and life-threatening or less severe asthmatic episodes, in susceptible individuals. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic individuals.

5.5 Dosing

Advise patients to measure Karbinal ER with an accurate milliliter measuring device. A household teaspoon is not an accurate measuring device and could lead to overdose. A pharmacist can recommend an appropriate measuring device and can provide instructions for measuring the correct dose.

6 ADVERSE REACTIONS

Use of Karbinal ER may result in decreased mental alertness with impaired mental or physical abilities [see [Warnings and Precautions \(5.2\)](#)].

The most frequent adverse reactions include: sedation, sleepiness, dizziness, disturbed coordination, epigastric distress, and thickening of bronchial secretions. In clinical use, younger children and older adults may be particularly sensitive to adverse reactions [see [Pediatric Use \(8.4\)](#) and [Geriatric Use \(8.5\)](#)].

The following adverse reactions, listed by body system, have been identified in case reports and during the use of carbinoxamine in observational studies. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Body as a Whole: Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose and throat.

Cardiovascular: Hypotension, headache, palpitations, tachycardia, extrasystoles.

Central Nervous System: Fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions.

Gastrointestinal: Anorexia, nausea, vomiting, diarrhea, constipation.

Hematologic: Hemolytic anemia, thrombocytopenia, agranulocytosis.

Laboratory: Increase in uric acid levels.

Respiratory: Tightness of chest and wheezing, nasal stuffiness.

Urogenital: Urinary frequency, difficult urination, urinary retention, early menses.

7 DRUG INTERACTIONS

Use of Karbinal ER is contraindicated in patients who are taking monoamine oxidase inhibitors (MAOIs), which prolong and intensify the anticholinergic (drying) effects of antihistamines.

Avoid use of Karbinal ER with alcohol and other CNS depressants (hypnotics sedatives, tranquilizers, etc.) due to additive effects.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. Animal reproductive studies have not been conducted with carbinoxamine maleate. It is also not known whether Karbinal ER can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Karbinal ER should be given to a pregnant woman only if clearly needed.

8.2 Labor and Delivery

The effect of Karbinal ER on labor and delivery is not known.

8.3 Nursing Mothers

Because of the risk of mortality in infants given carbinoxamine-containing drugs, use of Karbinal ER is contraindicated in nursing mothers.

8.4 Pediatric Use

Deaths have been reported in children younger than 2 years of age who were taking carbinoxamine-containing drug products. Therefore, Karbinal ER is contraindicated in children younger than 2 years of age and in nursing mothers. Carbinoxamine may diminish mental alertness or produce sedation in children. Paradoxical reactions with excitation are more likely in younger children.

8.5 Geriatric Use

Karbinal ER may cause dizziness, hypotension, confusion, or over-sedation in the elderly. Start elderly patients on lower doses and observed closely.

10. OVERDOSAGE

Overdosage with carbinoxamine may cause central nervous system depression or stimulation, hallucinations, convulsions, and death. Atropine-like signs and symptoms – dry mouth; fixed, dilated pupils; flushing; and gastrointestinal symptoms may also occur.

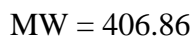
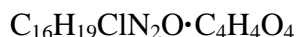
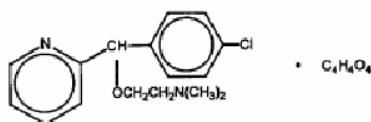
The treatment of overdosage consists of discontinuation of Karbinal ER and institution of symptomatic and supportive therapy. Vital signs (including respiration, pulse, blood pressure, and temperature) and EKG should be monitored. Induction of vomiting is not recommended. Activated charcoal should be given and gastric lavage should be considered after ingestion of a potentially life-threatening amount of drug. In the

presence of severe anticholinergic effects, physostigmine may be useful. Vasopressors may be used to treat hypotension.

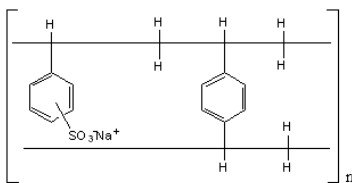
11. DESCRIPTION

Each 5 mL of Karbinal ER Extended-release Oral Suspension contains carbinoxamine complexed with polistirex equivalent to 4 mg carbinoxamine maleate and the following inactive ingredients: citric acid anhydrous, strawberry-banana flavor, glycerin, high fructose corn syrup, methylparaben, modified food starch, polysorbate 80, polyvinyl acetate, povidone, propylparaben, purified water, sodium metabisulfite, sodium polystyrene sulfonate, sucrose, triacetin, and xanthan gum.

Carbinoxamine maleate is freely soluble in water. The chemical name is 2-[(4-chlorophenyl)-2-pyridinylmethoxy]-*N,N*-dimethylethanamine (Z)-2-butenedioate (1:1), which has the following structure:



The drug-polistirex complex is formed with the active ingredient (carbinoxamine maleate, USP) and sodium polystyrene sulfonate, USP, which has the following structure:



12. CLINICAL PHARMACOLOGY

12.1. Mechanism of Action

Carbinoxamine is an H₁ receptor antagonist (antihistamine) that exhibits anticholinergic (drying) and sedative properties.

Antihistamines compete with histamine for receptor sites on effector cells.

12.3 Pharmacokinetics

Karbinal ER after single-dose administration of 16 mg was bioequivalent to the reference carbinoxamine immediate-release oral solution after the administration of two doses of 8 mg six hours apart under fasting conditions. The carbinoxamine mean (SD) peak plasma concentration (C_{max}) was 28.7 (5.3) ng/mL at 6.7 hours after Karbinal ER administration. The plasma half-life of carbinoxamine was 17.0 hours. There was no effect of food on the pharmacokinetic parameters.

Karbinal ER after multiple-dose administration of 16 mg every 12 hours for 8 days was bioequivalent to the reference carbinoxamine immediate-release oral solution after multiple-dose administration of 8 mg every 6 hours. The mean (SD) steady-state C_{max} was 72.9 (24.4) ng/mL at 5.6 hours after Karbinal ER administration. Carbinoxamine mean (SD) minimum plasma concentration at steady-state was 51.8 (20.3) ng/mL.

13. NONCLINICAL TOXICOLOGY

13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies in animals have been performed to determine the possible effects of carbinoxamine on carcinogenesis, mutagenesis, and fertility.

14. CLINICAL STUDIES

The efficacy and safety of Karbinal ER is based on demonstration of bioequivalence to the immediate-release reference product [see [Pharmacokinetics \(12.3\)](#)].

16 HOW SUPPLIED/STORAGE AND HANDLING

Karbinal ER contains 4 mg carbinoxamine maleate per 5 mL. It is a light beige to tan viscous suspension with strawberry banana flavor and is supplied as follows:

NDC 27808-046-02 bottles of 10 fl oz (300 mL)

NDC 27808-046-03 bottles of 16 fl oz (480 mL)

Store at 25°C (77°F); excursions permitted from 15° to 30°C (59° to 86°F). [See USP Controlled Room Temperature.]

Dispense in tight, light-resistant container with child-resistant closure.

17. PATIENT COUNSELING INFORMATION

17.1. Dosing

Advise patients to measure Karbinal ER with an accurate milliliter measuring device. A household teaspoon is not an accurate measuring device and could lead to overdose. [see [Dosage and Administration \(2\)](#)].

17.2. Activities Requiring Mental Alertness

Advise patients to use caution when driving a motor vehicle or operating machinery. Karbinal ER may produce marked drowsiness and impair the mental or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery [see [Warnings and Precautions \(5.2\)](#)].

17.3. Alcohol, Sedatives, and Tranquilizers

Advise patients to avoid the use of alcoholic beverages, sedatives, and tranquilizers while taking Karbinal ER because additional reduction in mental alertness may occur [see [Warnings and Precautions \(5.2\)](#) and [Drug Interactions \(7\)](#)].

17.4. MAOIs

Advise patients to not use MAOIs while taking Karbinal ER. MAOIs may prolong and intensify the anticholinergic (drying) effects [see [Contraindications \(4.4\)](#) and [Drug Interactions \(7\)](#)].

Manufactured by:
Tris Pharma, Inc.
Monmouth Junction, NJ 08852
www.trispharma.com

LB8056
Rev 00
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NDC 27808-046-03

Usual Dosage: See prescribing information.

Pharmacist: Dispense in a tight, light-resistant container with child-resistant closure.

Warning: Keep this and all medications out of the reach of children.

Store at 25°C (77°F); excursions permitted from 15° to 30°C (59° to 86°F) [see USP controlled room temperature].

Mfg by:



Monmouth Junction, NJ 08852
www.trispharma.com

Karbinal™ ER
(carbinoxamine maleate)
Extended-release
Oral Suspension

4 mg/5 mL

Shake Well Before Use

Dose every 12 hours

Dispense with an accurate
milliliter measuring device

Strawberry Banana Flavored

Rx only

16 fl oz (480 mL)



NDC 27808-046-02

Usual Dosage: See prescribing information.

Pharmacist: Dispense in a tight, light-resistant container with child-resistant closure.

Warning: Keep this and all medications out of the reach of children.

Store at 25°C (77°F); excursions permitted from 15° to 30°C (59° to 86°F) [see USP controlled room temperature].

Mfg by:



Monmouth Junction, NJ 08852
www.trispharma.com

Karbinal™ ER
(carbinoxamine maleate)
Extended-release
Oral Suspension

4 mg/5 mL

Shake Well Before Use

Dose every 12 hours

Dispense with an accurate
milliliter measuring device

Strawberry Banana Flavored

Rx only 10 fl oz (300 mL)



LB822
Rev 00
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NDC 27806-046-01

Karbinal™ ER
(carbinoxamine maleate)
Extended-release
Oral Suspension
4 mg/5 mL

Shake Well Before Use

Dose every 12 hours

Dispense with an accurate
milliliter measuring device

Strawberry Banana Flavored

Rx Only 1 fl oz (30 mL)
Physician Sample

Usual Dosage: See prescribing information.

Pharmacist: Dispense in a tight, light-resistant container
with child-resistant closure.

Warning: Keep this and all medications out of the reach
of children.

Store at 25 °C (77 °F); excursions permitted from 15 ° to
30 °C (59 ° to 86 °F) [see USP controlled room temperature].

Mfg by:



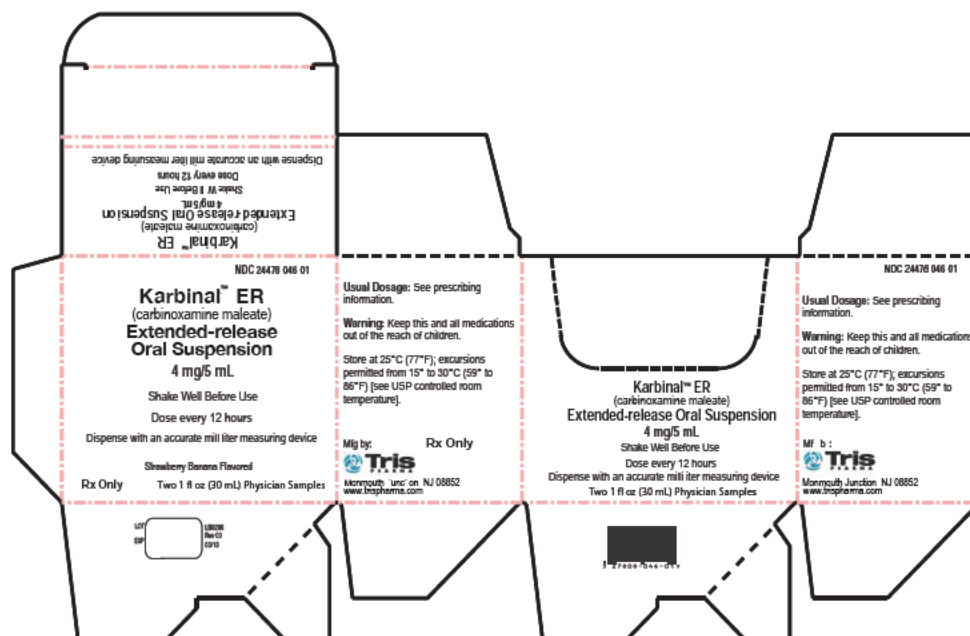
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LOT
EXP



LS8300
Rev 00
02/13



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/s/

LYDIA I GILBERT MCCLAIN
03/28/2013