



October 4, 2004

**OVERNIGHT COURIER October 4, 2004**

Dockets Management Branch  
Food and Drug Administration  
Department of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

**CITIZEN'S PETITION**

The undersigned submits this petition in quadruplicate under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("the FDC Act"), 21 U.S.C. § 355(j)(2)(C), and 21 C.F.R. §§ 10.20, 10.30, and 314.93 to request that the Commissioner of Food and Drugs make a determination that an Abbreviated New Drug Application (ANDA) may be submitted for Carbinoxamine Maleate 4 mg Chewable Tablets.

***A. Action Requested***

The petitioner requests that the Commissioner of Food and Drugs make a determination that a Carbinoxamine Maleate chewable tablet drug product, in a 4 mg per tablet strength, is suitable for submission as an ANDA. The reference-listed drug products which contain the identical active ingredient and upon which this petition is based are Carbinoxamine Maleate Oral Tablet 4mg, NDA number 40-442 and Carbinoxamine Maleate 4mg/5ml Oral Solution, NDA number 40-458, both held by Mikart, Inc. Therefore, this petition requests a new dosage form of the drug product, same in strength as the approved 4mg oral tablet and 4mg/5ml solution.

**B. Statement of Grounds**

Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act provides for the submission of an ANDA for a new drug that differs in dosage form from a listed drug, provided that the FDA has approved a petition seeking permission to file such an application. This petition requests a new dosage form from the reference listed drug products, Carbinoxamine Maleate 4mg oral tablet, and 4mg/5ml oral solution. The same strength of the active component, Carbinoxamine Maleate 4 mg per dosage unit, is proposed.

The listing of Carbinoxamine Maleate 4mg Oral Tablet and 4mg/5ml Oral Solution can be found on the "Prescription Drug Products" list in the CDER's Electronic Orange Book Query.

Please see Attachment A.

According to the approved labeling of the reference listed drug products, Carbinoxamine Maleate is administered to adults in a dosage given as 4 to 8 mg, 3 to 4 times daily, and in children from 2 to 4 mg, 3 to 4 times daily. This dose may be increased according to the patient's needs to a maximum of 24 mg daily in adults. The approved product labeling for Carbinoxamine Maleate 4mg Oral Tablet as marketed under the brand name "Palgic", and the Carbinoxamine Maleate 4mg/5ml Oral Solution, also marketed under the brand name "Palgic", is included in Attachment B.

The dosage for the proposed product is consistent with the dosage approved in the reference-listed drug product's labeling. The proposed labeling for Carbinoxamine Maleate 4 mg Chewable Tablets is included as Attachment C. Labeling for the proposed product will be consistent with the approved labeling for the reference listed drugs, Carbinoxamine Maleate 4mg Oral Tablet, and Carbinoxamine Maleate 4mg/5ml Oral Solution, the products upon which this petition is based.

In summary, the proposed new dosage form change from that of the reference-listed drug products, (a 4mg oral tablet, 4mg/5ml oral solution) is consistent with the safety and efficacy of the new product. The indications remain unchanged and the dosing is consistent with that recommended in the labeling of the approved reference listed drug products. Therefore, the Agency should conclude that clinical investigations are not necessary to demonstrate the proposed product's safety or effectiveness.

This petition requests a new dosage form from that of the listed drug. Therefore, the petitioner also requests a full waiver from the pediatric study requirements of the Pediatric Research Equity Act of 2003, per 21 CFR § 314.55 (2)(i) "*The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients ...*", because the approved listed drug product currently contains pediatric dosing. Moreover, we believe the scored chewable tablet will offer additional convenience of dosing to both the adult and pediatric population.

For the aforementioned reasons, the undersigned requests that the Commissioner approve this petition and find that an application for Carbinoxamine Maleate 4 mg Chewable Tablets be suitable for submission as an ANDA.

### **C. Environmental Impact**

The petitioner claims a categorical exclusion under 21 C.F.R. § 25.31.

### D. Economic Impact Statement

According to 21 C.F.R. § 10.30(b), petitioner will, upon request by the Commissioner, submit economic impact information.

### E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

  
Wei-wei Chang, Ph.D.  
President,  
NuTec Incorporated

Attachments:

- A. Electronic Orange Book listing for Carbinoxamine Maleate Oral Tablet 4mg.  
Electronic Orange Book listing for Carbinoxamine Maleate Oral Solution 4mg/5ml
- B. Labeling for Palgic, Carbinoxamine Maleate Oral Tablet 4mg, Revision 04/03.  
Labeling for Palgic, Carbinoxamine Maleate Oral Solution 4mg/5ml, Revision 05/03
- C. Draft Insert Labeling for Proposed Drug Product.

## Attachment A

Electronic Orange Book Listing  
Carbinoxamine Maleate Oral Tablet 4mg  
Carbinoxamine Maleate Oral Solution 4mg/5ml

**Search results from the "OB\_Rx" table for query on "040442."**

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Active Ingredient:	CARBINOXAMINE MALEATE
Dosage Form;Route:	TABLET; ORAL
Proprietary Name:	CARBINOXAMINE MALEATE
Applicant	MIKART
Strength:	4MG
Application Number:	040442
Product Number:	001
Approval Date:	Mar 19, 2003
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: [View](#)

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[Return to Electronic Orange Book Home Page](#)

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FDA/Center for Drug Evaluation and Research  
Office of Generic Drugs  
Division of Labeling and Program Support  
Update Frequency:  
Orange Book Data - **Monthly**  
Orange Book Data Updated Through July, 2004  
Orange Book Patent Data Only - **Daily**  
Patent Data Last Updated: August 31, 2004

[http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl\\_No=040442&TABLE1=OB\\_Rx](http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=040442&TABLE1=OB_Rx)

Search results from the "OB\_Rx" table for query on "040458."

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Active Ingredient:	CARBINOXAMINE MALEATE
Dosage Form,Route:	SOLUTION; ORAL
Proprietary Name:	CARBINOXAMINE MALEATE
Applicant	MIKART
Strength.	4MG/5ML
Application Number:	040458
Product Number:	001
Approval Date:	Apr 25, 2003
Reference Listed Drug	Yes
RX/OTC/DISCN	RX
TE Code:	

Patent and Exclusivity Info for this product. [View](#)

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[Return to Electronic Orange Book Home Page](#)

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FDA/Center for Drug Evaluation and Research  
Office of Generic Drugs  
Division of Labeling and Program Support  
Update Frequency:

Orange Book Data - **Monthly**

Orange Book Data Updated Through July, 2004

Orange Book Patent Data Only - **Daily**

Patent Data Last Updated: September 03, 2004

[http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl\\_No=040458&TABLE1=OB\\_Rx](http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=040458&TABLE1=OB_Rx)

## Attachment B

Approved Product Labeling  
Carbinoxamine Maleate Oral Tablet 4mg  
Carbinoxamine Maleate Oral Solution 4mg/5ml

05256748

# 05256748

## Palgic

Carbinoxamine Maleate  
Tablets USP 4mg

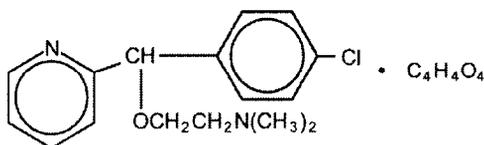
Rx only

Rev 04/03 Code 838B00

### DESCRIPTION:

Carbinoxamine maleate is a histamine-H<sub>1</sub> receptor blocking agent.  
Each tablet contains 4 mg carbinoxamine maleate.

Inactive ingredients: anhydrous lactose, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate  
Carbinoxamine maleate is freely soluble in water. Its structure is:



2-[(4-chlorophenyl)-2-pyridinylmethoxy]-N, N-dimethylethanamine (Z)-2-butenedioate (1:1)

C<sub>16</sub>H<sub>19</sub>ClN<sub>2</sub>O•C<sub>4</sub>H<sub>4</sub>O<sub>4</sub> MW=406.86

### CLINICAL PHARMACOLOGY:

Carbinoxamine maleate is an antihistamine with anticholinergic (drying) and sedative properties.  
Antihistamines appear to compete with histamine for receptor sites on effector cells

The pharmacological effects of carbinoxamine maleate after oral absorption have been shown to last approximately 4 hours

### INDICATIONS AND USAGE:

Carbinoxamine maleate is effective 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

### CONTRAINDICATIONS:

Carbinoxamine maleate is contraindicated in patients who are hypersensitive to the drug or on monoamine oxidase inhibitor therapy (See Drug Interactions section)

Antihistamines such as carbinoxamine maleate should not be used in newborn or premature infants

Antihistamines such as carbinoxamine maleate should not be used to treat lower respiratory tract symptoms, including asthma. Because of the higher risk of antihistamines for infants generally and for newborns and prematures in particular, use of carbinoxamine maleate is contraindicated in nursing mothers.

**WARNINGS:**

Antihistamines should be used with considerable caution in patients with: narrow angle glaucoma, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, pyloroduodenal obstruction

**PRECAUTIONS:**

As with other antihistamines, carbinoxamine maleate has an atropine-like action and, therefore, should be used with caution in patients with: history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension. Antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation. Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients (approximately 60 years or older)

**Information for Patients:** Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating machinery, etc.

**Drug Interactions:** Monoamine oxidase inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines. Carbinoxamine maleate has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.).

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** No long-term studies in animals have been performed to determine the possible effects of carbinoxamine maleate on carcinogenesis, mutagenesis, and fertility.

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

**Nursing Mothers:** (see CONTRAINDICATIONS section)

**ADVERSE REACTIONS:**

The most frequent adverse reactions are underlined:

*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

*Hematologic:* Hemolytic anemia, thrombocytopenia, agranulocytosis.

*Central Nervous System.* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria,

paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions

*Gastrointestinal.* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

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

*Respiratory* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness

**OVERDOSAGE:**

**Manifestations:** Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms - dry mouth, fixed, dilated pupils; flushing; and gastrointestinal symptoms may also occur. Especially in infants and children, antihistamine overdosage may cause hallucinations, convulsions, or death.

The oral LD<sub>50</sub> of carbinoxamine maleate in guinea pigs is 411 mg/kg

**Treatment:** *If vomiting has not occurred spontaneously*, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk, after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

*If the attempt to induce vomiting is unsuccessful*, gastric lavage is indicated within 3 hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or ½ isotonic saline is the lavage solution of choice.

*Saline cathartics*, as milk of magnesia, by osmosis draw water into the bowel and, therefore, are valuable for their action in rapid dilution of bowel content.

*Stimulants* should *not* be used.

Vasopressors may be used to treat hypotension.

**DOSAGE AND ADMINISTRATION:**

DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT. Carbinoxamine maleate dosage should be based on the severity of the condition and the response of the patient. The drug is well tolerated in doses as high as 24 mg daily, in divided doses, over prolonged periods. On the other hand, some patients respond to as little as 4 mg daily.

Clinical experience suggests the following dosage schedules:

Usual Adult Dosage

1 or 2 tablets (4 to 8 mg) 3 to 4 times daily

Usual Child's Dosage (approximately 0.2 – 0.4 mg/kg/day):

One to three years – ½ tablet (2 mg) 3 or 4 times daily

Three to six years – ½ tablet to 1 tablet (2 to 4 mg) 3 or 4 times daily

Over six years – 1 to 1½ tablets (4 to 6 mg) 3 or 4 times daily.



**HOW SUPPLIED:**

Palgic (Carbinoxamine Maleate Tablets USP, 4 mg) is supplied as white, round scored tablets, debossed "PAL" on one side and score "4" on the other side, and are supplied in bottles of 100 tablets, NDC 0525-6748-01 and bottles of 500 tablets, NDC 0525-6748-05.

Store at controlled room temperature, 15°C to 30°C (59°F to 86°F) [See USP]

Dispense in a tight, light-resistant container with a child-resistant closure as defined in the official compendium.

**Manufactured for:**

Pamlab, L L C.  
Covington, LA 70433

**Manufactured by:**

MIKART, INC  
Atlanta, GA 30318

Rev 04/03 Code 838B00

05256752

# 05256752

## Palgic

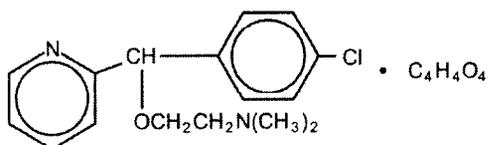
Carbinoxamine Maleate  
Oral Solution 4 mg/5 mL

Rx only

Code 892B00 Rev. 05/03

### DESCRIPTION:

Carbinoxamine maleate is a histamine-H<sub>1</sub> receptor blocking agent. Each 5 mL (teaspoonful) contains 4 mg carbinoxamine maleate. Carbinoxamine maleate is freely soluble in water. Its structure is



2-[(4-chlorophenyl)-2-pyridinylmethoxy]-N, N-dimethylethanamine (Z)-2-butenedioate (1:1)

C<sub>16</sub>H<sub>19</sub>ClN<sub>2</sub>O•C<sub>4</sub>H<sub>4</sub>O<sub>4</sub> MW=406.86

Inactive ingredients: artificial bubblegum flavor, citric acid (anhydrous), glycerin, methylparaben, propylene glycol, propylparaben, purified water, sodium citrate (hydrous) and sorbitol solution.

### CLINICAL PHARMACOLOGY:

Carbinoxamine maleate is an antihistamine with anticholinergic (drying) and sedative properties. Antihistamines appear to compete with histamine for receptor sites on effector cells.

The pharmacological effects of carbinoxamine maleate after oral absorption have been shown to last approximately 4 hours.

### INDICATIONS AND USAGE:

Carbinoxamine maleate is effective 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

#### CONTRAINDICATIONS:

Carbinoxamine maleate is contraindicated in patients who are hypersensitive to the drug or on monoamine oxidase inhibitor therapy (See Drug Interactions section )

Antihistamines such as carbinoxamine maleate should not be used in newborn or premature infants

Antihistamines such as carbinoxamine maleate should not be used to treat lower respiratory tract symptoms, including asthma.

Because of the higher risk of antihistamines for infants generally and for newborns and prematures in particular, use of carbinoxamine maleate is contraindicated in nursing mothers.

#### WARNINGS:

Antihistamines should be used with considerable caution in patients with: narrow angle glaucoma, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, pyloroduodenal obstruction

#### PRECAUTIONS:

As with other antihistamines, carbinoxamine maleate has an atropine-like action and, therefore, should be used with caution in patients with history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension

Antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.

Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients (approximately 60 years or older)

**Information for Patients:** Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating machinery, etc.

**Drug Interactions:** Monoamine oxidase inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines

Carbinoxamine maleate has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc ).

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** No long-term studies in animals have been performed to determine the possible effects of carbinoxamine maleate on carcinogenesis, mutagenesis, and fertility.

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

**Nursing Mothers:** (see CONTRAINDICATIONS section)

#### ADVERSE REACTIONS:

The most frequent adverse reactions are underlined

*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

*Hematologic* Hemolytic anemia, thrombocytopenia, agranulocytosis.

*Central Nervous System:* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions

*Gastrointestinal* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation

*Urogenital* Urinary frequency, difficult urination, urinary retention, early menses

*Respiratory* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

#### OVERDOSAGE:

**Manifestations:** Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms - dry mouth, fixed, dilated pupils; flushing; and gastrointestinal symptoms may also occur

Especially in infants and children, antihistamine overdosage may cause hallucinations, convulsions, or death.

The oral LD<sub>50</sub> of carbinoxamine maleate in guinea pigs is 411 mg/kg

**Treatment:** *If vomiting has not occurred spontaneously*, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk, after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

*If the attempt to induce vomiting is unsuccessful*, gastric lavage is indicated within 3 hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or ½ isotonic saline is the lavage solution of choice

*Saline cathartics*, as milk of magnesia, by osmosis draw water into the bowel and, therefore, are valuable for their action in rapid dilution of bowel content

*Stimulants* should *not* be used.

Vasopressors may be used to treat hypotension

#### DOSAGE AND ADMINISTRATION:

DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT. Carbinoxamine maleate dosage should be based on the severity of the condition and the response of the patient. The drug is well tolerated in doses as high as 24 mg daily, in divided doses, over prolonged periods. On the other hand, some patients respond to as little as 4 mg daily

Clinical experience suggests the following dosage schedules:

Usual Adult Dosage:

1 or 2 teaspoonfuls (4 to 8 mg) 3 to 4 times daily

Usual Child's Dosage (approximately 0.2 – 0.4 mg/kg/day).

One to three years – ½ teaspoonful (2 mg) 3 or 4 times daily

Three to six years – ½ teaspoonful to 1 teaspoonful (2 to 4 mg) 3 or 4 times daily

Over six years – 1 to 1½ teaspoonful (4 to 6 mg) 3 or 4 times daily

**HOW SUPPLIED:**

Palgic (Carbinoxamine Maleate Oral Solution, 4 mg/5 mL) is supplied as clear, colorless liquid with a bubble gum aroma, and is supplied in 4 oz bottles, NDC 0525-6752-04 and 16 oz bottles NDC 0525-6752-16

Store at controlled room temperature, 15°C to 30°C (59°F to 86°F) [See USP]

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

**Manufactured for:**

Pamlab, L L C  
Covington, LA 70433

**Manufactured by:**

MIKART, INC  
Atlanta, GA 30318

Code 892B00 Rev 05/03

## Attachment C

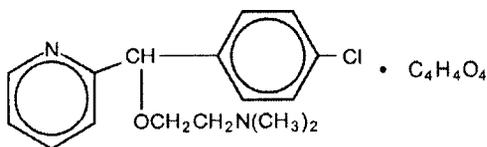
### Proposed Product Labeling Carbinoxamine Maleate 4mg Chewable Tablets

# Carbinoxamine Maleate 4 mg Chewable Tablets

Rx only

## DESCRIPTION:

Carbinoxamine maleate is a histamine-H<sub>1</sub> receptor blocking agent. Each scored chewable tablet contains 4 mg carbinoxamine maleate. Carbinoxamine maleate is freely soluble in water. Its structure is:



2-[(4-chlorophenyl)-2-pyridinylmethoxy]-N, N-dimethylethanamine (Z)-2-butenedioate (1:1)

C<sub>16</sub>H<sub>19</sub>ClN<sub>2</sub>O • C<sub>4</sub>H<sub>4</sub>O<sub>4</sub> MW=406.86

Inactive ingredients: artificial strawberry flavor, aspartame, dextrose, FD&C Red #40, microcrystalline cellulose, sodium starch glycolate, stearic acid

## CLINICAL PHARMACOLOGY:

Carbinoxamine maleate is an antihistamine with anticholinergic (drying) and sedative properties. Antihistamines appear to compete with histamine for receptor sites on effector cells.

The pharmacological effects of carbinoxamine maleate after oral absorption have been shown to last approximately 4 hours.

**INDICATIONS AND USAGE:**

Carbinoxamine maleate is effective 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.

**CONTRAINDICATIONS:**

Carbinoxamine maleate is contraindicated in patients who are hypersensitive to the drug or on monoamine oxidase inhibitor therapy. (See Drug Interactions section.)

Antihistamines such as carbinoxamine maleate should not be used in newborn or premature infants.

Antihistamines such as carbinoxamine maleate should not be used to treat lower respiratory tract symptoms, including asthma.

Because of the higher risk of antihistamines for infants generally and for newborns and prematures in particular, use of carbinoxamine maleate is contraindicated in nursing mothers.

**WARNINGS:**

Antihistamines should be used with considerable caution in patients with: narrow angle glaucoma, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, pyloroduodenal obstruction.

**PRECAUTIONS:**

As with other antihistamines, carbinoxamine maleate has an atropine-like action and, therefore, should be used with caution in patients with: history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, hypertension.

Antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.

Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients (approximately 60 years or older).

**Information for Patients:** Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating machinery, etc.

**Drug Interactions:** Monoamine oxidase inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

Carbinoxamine maleate has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.).

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

**Nursing Mothers:** (see CONTRAINDICATIONS section)

**ADVERSE REACTIONS:**

The most frequent adverse reactions are underlined:

*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.

*Hematologic:* Hemolytic anemia, thrombocytopenia, agranulocytosis.

*Central Nervous System:* Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions.

*Gastrointestinal:* Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.

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

*Respiratory:* Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

**OVERDOSAGE:**

**Manifestations:** Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms - dry mouth; fixed, dilated pupils; flushing; and gastrointestinal symptoms may also occur.

Especially in infants and children, antihistamine overdosage may cause hallucinations, convulsions, or death.

The oral LD<sub>50</sub> of carbinoxamine maleate in guinea pigs is 411 mg/kg.

**Treatment:** *If vomiting has not occurred spontaneously*, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk, after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

*If the attempt to induce vomiting is unsuccessful*, gastric lavage is indicated within 3 hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or ½ isotonic saline is the lavage solution of choice.

*Saline cathartics*, as milk of magnesia, by osmosis draw water into the bowel and, therefore, are valuable for their action in rapid dilution of bowel content.

*Stimulants* should *not* be used.

Vasopressors may be used to treat hypotension.

**DOSAGE AND ADMINISTRATION:**

DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT. Carbinoxamine maleate dosage should be based on the severity of the condition and the response of the patient. The drug is well tolerated in doses as high as 24 mg daily, in divided doses, over prolonged periods. On the other hand, some patients respond to as little as 4 mg daily.

Clinical experience suggests the following dosage schedules:

Usual Adult Dosage:

1 or 2 chewable tablets (4 to 8 mg) 3 to 4 times daily

Usual Child's Dosage (approximately 0.2 – 0.4 mg/kg/day):

One to three years – ½ chewable tablet (2 mg) 3 or 4 times daily.

Three to six years – ½ chewable tablet to 1 chewable tablet (2 to 4 mg) 3 or 4 times daily

Over six years – 1 to 1½ chewable tablet (4 to 6 mg) 3 or 4 times daily.

**HOW SUPPLIED:**

Carbinoxamine Maleate 4 mg Chewable Tablets are supplied as oval-shaped, pink tablets debossed "E" bisected "5" on one side, debossed "101" on the opposite side. Bottles of 100 tablets, NDC 64376-616-01.

Store at controlled room temperature, 15°C to 30°C (59°F to 86°F) [See USP].

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

500159 Rev 08/04