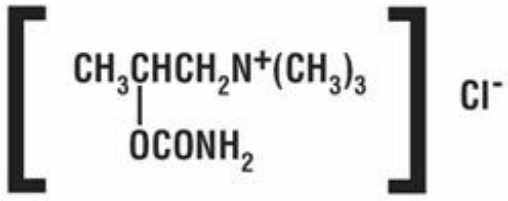
BETHANECHOL CHLORIDE- bethanechol chloride tablet
Rising Pharmaceuticals Inc.

Bethanechol Chloride Tablets USP

DESCRIPTION

Bethanechol chloride, a cholinergic agent, is a synthetic ester which is structurally and pharmacologically related to acetylcholine.

It is designated chemically as 2-[(aminocarbonyl)oxy]-*N*, *N*, *N*-trimethyl-1-propanaminium chloride. Its molecular formula is $C_7H_{17}ClN_2O_2$ and its structural formula is:



It is a white, hygroscopic crystalline powder having a slight amine-like odor, freely soluble in water, and has a molecular weight of 196.68.

Each tablet for oral administration contains 5 mg, 10 mg, 25 mg or 50 mg bethanechol chloride, USP. Tablets also contain the following inactive ingredients: lactose monohydrate, silicon dioxide, magnesium stearate, microcrystalline cellulose, sodium starch glycolate, and povidone.

CLINICAL PHARMACOLOGY

Bethanechol chloride acts principally by producing the effects of stimulation of the parasympathetic nervous system. It increases the tone of the detrusor urinae muscle, usually producing a contraction sufficiently strong to initiate micturition and empty the bladder. It stimulates gastric motility, increases gastric tone and often restores impaired rhythmic peristalsis.

Stimulation of the parasympathetic nervous system releases acetylcholine at the nerve endings. When spontaneous stimulation is reduced and therapeutic intervention is required, acetylcholine can be given, but it is rapidly hydrolyzed by cholinesterase and its effects are transient. Bethanechol chloride is not destroyed by cholinesterase and its effects are more prolonged than those of acetylcholine.

Effects on the GI and urinary tracts sometimes appear within 30 minutes after oral administration of bethanechol chloride, but more often 60 to 90 minutes are required to reach maximum effectiveness. Following oral administration, the usual duration of action of bethanechol is one hour, although large doses (300 to 400 mg) have been reported to produce effects for up to six hours. Subcutaneous injection produces a more intense action on bladder muscle than does oral administration of the drug.

Because of the selective action of bethanechol, nicotinic symptoms of cholinergic stimulation are usually absent or minimal when orally or subcutaneously administered in therapeutic doses, while muscarinic effects are prominent. Muscarinic effects usually occur within 5 to 15 minutes after subcutaneous injection, reach a maximum in 15 to 30 minutes, and disappear within two hours. Doses that stimulate micturition and defecation and increase peristalsis do not ordinarily stimulate ganglia or voluntary muscles. Therapeutic test doses in normal human subjects have little effect on heart rate, blood pressure or peripheral circulation.

Bethanechol chloride does not cross the blood-brain barrier because of its charged quaternary amine

moiety. The metabolic rate and mode of excretion of the drug have not been elucidated.

A clinical study (Diokno, A.C.; Lapides, J.; Urol 10: 23-24, July 1977) was conducted on the relative effectiveness of oral and subcutaneous doses of bethanechol chloride on the stretch response of bladder muscle in patients with urinary retention. Results showed that 5 mg of the drug given subcutaneously stimulated a response that was more rapid in onset and of larger magnitude than an oral dose of 50 mg, 100 mg, or 200 mg. All the oral doses, however, had a longer duration of effect than the subcutaneous dose. Although the 50 mg oral dose caused little change in intravesical pressure in this study, this dose has been found in other studies to be clinically effective in the rehabilitation of patients with decompensated bladders.

INDICATIONS AND USAGE

Bethanechol chloride is indicated for the treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention.

CONTRAINDICATIONS

Hypersensitivity to bethanechol chloride tablets, hyperthyroidism, peptic ulcer, latent or active bronchial asthma, pronounced bradycardia or hypotension, vasomotor instability, coronary artery disease, epilepsy and parkinsonism.

Bethanechol chloride should not be employed when the strength or integrity of the gastrointestinal or bladder wall is in question, or in the presence of mechanical obstruction; when increased muscular activity of the gastrointestinal tract or urinary bladder might prove harmful, as following recent urinary bladder surgery, gastrointestinal resection and anastomosis, or when there is possible gastrointestinal obstruction; in bladder neck obstruction, spastic gastrointestinal disturbances, acute inflammatory lesions of the gastrointestinal tract, or peritonitis; or in marked vagotonia.

PRECAUTIONS

General

In urinary retention, if the sphincter fails to relax as bethanechol contracts the bladder, urine may be forced up the ureter into the kidney pelvis. If there is bacteriuria, this may cause reflux infection.

Information for Patients

Bethanechol chloride tablets should preferably be taken one hour before or two hours after meals to avoid nausea or vomiting. Dizziness, lightheadedness or fainting may occur, especially when getting up from a lying or sitting position.

Drug Interactions

Special care is required if this drug is given to patients receiving ganglion blocking compounds because a critical fall in blood pressure may occur. Usually, severe abdominal symptoms appear before there is such a fall in the blood pressure.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the effects upon fertility, mutagenic or carcinogenic potential of bethanechol chloride.

Pregnancy

Teratogenic effects: Pregnancy Category C

Animal reproduction studies have not been conducted with bethanechol chloride. It is also not known whether bethanechol chloride can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Bethanechol chloride should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk and because of the potential for serious adverse reactions from bethanechol chloride in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Adverse reactions are rare following oral administration of bethanechol, but are more common following subcutaneous injection. Adverse reactions are more likely to occur when dosage is increased.

The following adverse reactions have been observed: *Body as a Whole:* malaise; *Digestive:* abdominal cramps or discomfort, colicky pain, nausea and belching, diarrhea, borborygmi, salivation; *Renal:* urinary urgency; *Nervous System:* headache; *Cardiovascular:* a fall in blood pressure with reflex tachycardia, vasomotor response; *Skin:* flushing producing a feeling of warmth, sensation of heat about the face, sweating; "*Respiratory*:" bronchial constriction, asthmatic attacks; *Special Senses:* lacrimation, miosis.

Causal Relationship Unknown: The following adverse reactions have been reported, and a causal relationship to therapy with bethanechol has not been established: *Body as a Whole:* malaise; *Nervous System:* seizures.

To report SUSPECTED ADVERSE REACTIONS, contact Rising Pharmaceuticals at 1-866-562-4579 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

Early signs of overdosage are abdominal discomfort, salivation, flushing of the skin ("hot feeling"), sweating, nausea, and vomiting.

Atropine Sulfate is a specific antidote. The recommended dose for adults is 0.6 mg. Repeat doses can be given every two hours, according to clinical response. The recommended dosage in infants and children up to 12 years of age is 0.01 mg/kg (to a maximum single dose of 0.4 mg) repeated every two hours as needed until the desired effect is obtained or adverse effects of atropine preclude further usage. Subcutaneous injection of atropine is preferred except in emergencies when the intravenous route may be employed.

The oral LD_{50} of bethanechol chloride is 1510 mg/kg in the mouse.

DOSAGE AND ADMINISTRATION

Dosage must be individualized, depending on the type and severity of the condition to be treated.

Preferably give the drug when the stomach is empty. If taken soon after eating, nausea and vomiting may occur.

The usual adult oral dose ranges from 10 to 50 mg three or four times a day. The minimum effective

dose is determined by giving 5 to 10 mg initially and repeating the same amount at hourly intervals until satisfactory response occurs, or until a maximum of 50 mg has been given. The effects of the drug sometimes appear within 30 minutes and are usually maximal within 60 to 90 minutes. The drug effects persist for about one hour.

If necessary, the effects of the drug can be abolished promptly by atropine (see **OVERDOSAGE**).

HOW SUPPLIED

Bethanechol ChlorideTablets USP

5 mg – White, round, scored tablets in bottles of 100.

Debossed EP 118 on one side and plain on reverse side.

NDC 64980-160-01 Bottles of 100

10 mg – White, round, scored tablets in bottles of 100.

Debossed EP 119 on one side and plain on reverse side.

NDC 64980-161-01 Bottles of 100

25 mg – White, round, scored tablets in bottles of 100.

Debossed EP 120 on one side and plain on reverse side.

NDC 64980-162-01 Bottles of 100

50 mg -White, round, scored tablets in bottles of 100.

Debossed EP 121 on one side and plain on reverse side.

NDC 64980-163-01 Bottles of 100

Dispense in a tight container as defined in the USP.

Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature].

Manufactured for:

Rising®

Rising Pharmaceuticals, Inc.

Allendale, NJ 07401

Manufactured by:

Heritage Pharma Labs Inc.

East Brunswick, NJ 08816

51U000000056US02

Revised: 08/2015

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Bethanechol Chloride Tablets, 5 mg

100 Tablets

Rx only

NDC 64980-160-01

Each Tablet Contains:

Bethanechol Chloride, USP 5 mg

Usual Dosage: See package insert.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

WARNING: KEEP THIS AND ALL THE DRUGS OUT OF THE REACH OF CHILDREN.

Dispense in a tight container as defined in the USP.

Manufactured for:

Rising Pharmaceuticals, Inc.

Allendale, NJ 07401

Manufactured by:

Heritage Pharma Labs Inc.

East Brunswick, New Jersey 08816, USA

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Bethanechol Chloride Tablets, 50 mg

100 Tablets

Rx only

NDC 64980-163-01

Each Tablet Contains:

Bethanechol Chloride, USP 50 mg

Usual Dosage: See package insert.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

WARNING: KEEP THIS AND ALL THE DRUGS OUT OF THE REACH OF CHILDREN.

Dispense in a tight container as defined in the USP.

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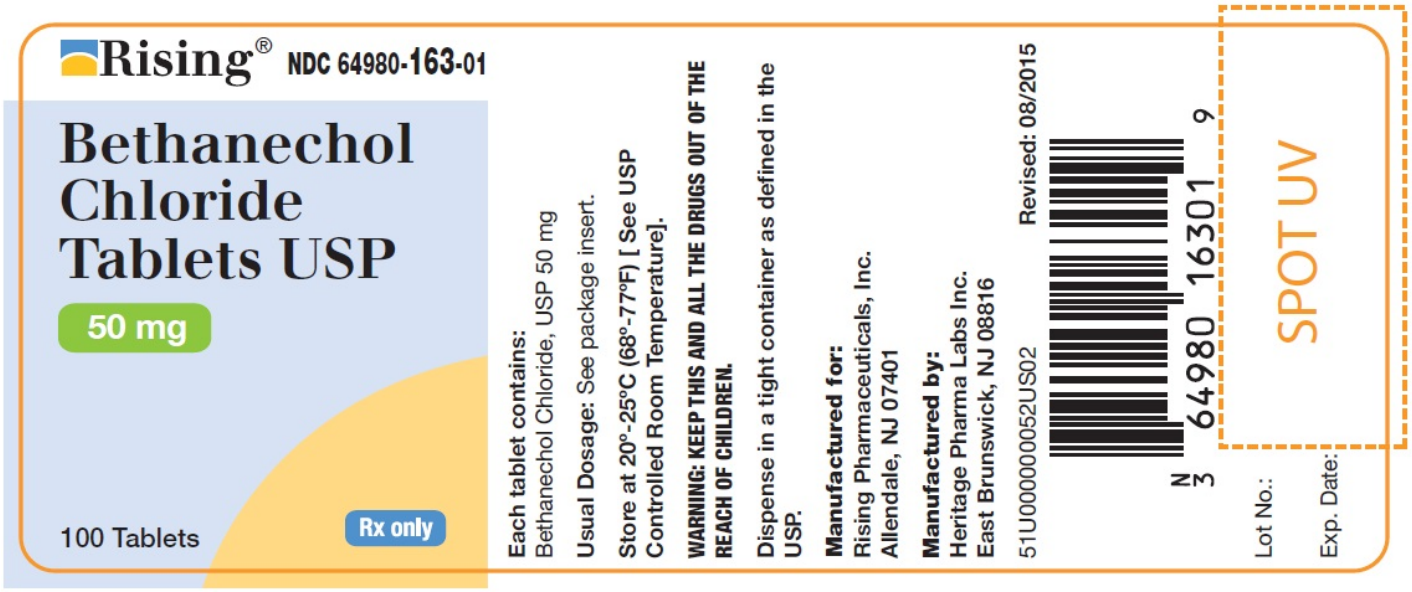

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Bethanechol Chloride Tablets, 25 mg

100 Tablets

Rx only

NDC 64980-162-01

Each Tablet Contains:

Bethanechol Chloride, USP 25 mg

Usual Dosage: See package insert.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

WARNING: KEEP THIS AND ALL THE DRUGS OUT OF THE REACH OF CHILDREN.

Dispense in a tight container as defined in the USP.

Manufactured for:

Rising Pharmaceuticals, Inc.

Allendale, NJ 07401

Manufactured by:

Heritage Pharma Labs Inc.

East Brunswick, New Jersey 08816, USA

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Bethanechol Chloride Tablets, 10 mg

100 Tablets

Rx only

NDC 64980-161-01

Each Tablet Contains:

Bethanechol Chloride, USP 10 mg

Usual Dosage: See package insert.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]

WARNING: KEEP THIS AND ALL THE DRUGS OUT OF THE REACH OF CHILDREN

Dispense in a tight container as defined in the USP.

Manufactured for:

Rising Pharmaceuticals, Inc.

Allendale, NJ 07401

Manufactured by:

Heritage Pharma Labs Inc.

East Brunswick, New Jersey 08816, USA

BETHANECHOL CHLORIDE

bethanechol chloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64980-160
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
BETHANECHOL CHLORIDE (UNII: H4QBZ2LO84) (BETHANECHOL - UNII:004F72P8F4)	BETHANECHOL CHLORIDE	5 mg

Inactive Ingredients	
Ingredient Name	**Strength**
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
POVIDONE (UNII: FZ989GH94E)	

Product Characteristics			
Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	EP118
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:64980-160-01	100 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091256	08/24/2010	

BETHANECHOL CHLORIDE

bethanechol chloride tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64980-161
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BETHANECHOL CHLORIDE (UNII: H4QBZ2LO84) (BETHANECHOL - UNII:004F72P8F4)	BETHANECHOL CHLORIDE	10 mg

Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
POVIDONE (UNII: FZ989GH94E)	

Product Characteristics

Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	EP119
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64980-161-01	100 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091256	04/06/2010	

BETHANECHOL CHLORIDE

bethanechol chloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64980-162
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
BETHANECHOL CHLORIDE (UNII: H4QBZ2LO84) (BETHANECHOL - UNII:004F72P8F4)	BETHANECHOL CHLORIDE	25 mg

Inactive Ingredients	
Ingredient Name	**Strength**
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
POVIDONE (UNII: FZ989GH94E)	

Product Characteristics			
Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	9mm
Flavor		**Imprint Code**	EP120
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:64980-162-01	100 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091256	04/06/2010	

BETHANECHOL CHLORIDE

bethanechol chloride tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64980-163
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BETHANECHOL CHLORIDE (UNII: H4QBZ2LO84) (BETHANECHOL - UNII:004F72P8F4)	BETHANECHOL CHLORIDE	50 mg

Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
POVIDONE (UNII: FZ989GH94E)	

Product Characteristics

Color	WHITE	**Score**	no score
Shape	ROUND	**Size**	11mm
Flavor		**Imprint Code**	EP121
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64980-163-01	100 in 1 BOTTLE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091256	04/06/2010	

Labeler - Rising Pharmaceuticals Inc. (041241766)

Registrant - Emcure Pharmaceuticals Limited (916921919)

Establishment

Name	Address	ID/FEI	Business Operations
Heritage Pharma Labs, Inc		189630168	analysis(64980-160, 64980-161, 64980-162, 64980-163) , label(64980-160, 64980-161, 64980-162, 64980-163) , manufacture(64980-160, 64980-161, 64980-162, 64980-163) , pack(64980-160, 64980-161, 64980-162, 64980-163)