DICYCLOMINE HYDROCHLORIDE- dicyclomine hydrochloride tablet
Rebel Distributors Corp

Dicyclomine Hydrochloride

Rx Only

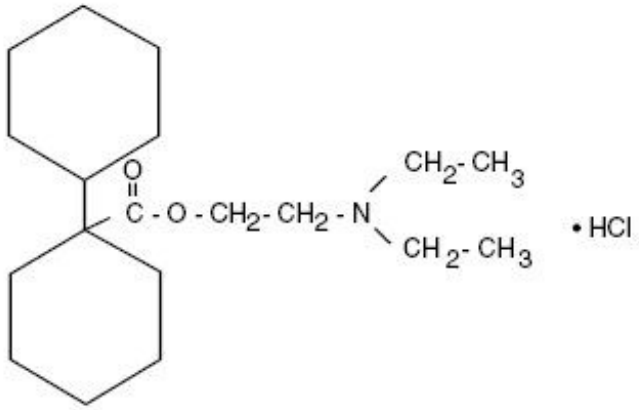
DESCRIPTION

Dicyclomine hydrochloride is an antispasmodic and anticholinergic (antimuscarinic) agent available in the following forms:

1. Dicyclomine Hydrochloride Tablets USP, for oral administration, contain 20 mg dicyclomine hydrochloride, USP. In addition, each tablet contains the following inactive ingredients: acacia, pregelatinized starch, anhydrous lactose, compressible sugar, dicalcium phosphate, colloidal silicon dioxide, magnesium stearate, stearic acid, and FD & C Blue #1 Aluminum Lake.

2. Dicyclomine Hydrochloride Capsules USP, for oral administration, contain 10 mg of dicyclomine hydrochloride, USP. In addition, each capsule contains the following inactive ingredients: lactose monohydrate, calcium sulfate, magnesium stearate; and the capsules shells contain: gelatin, FD&C Blue # 1, and FD&C Red # 3.

Chemically, dicyclomine hydrochloride is 2-(Diethylamino)ethyl [bicyclohexyl]-1-carboxylate hydrochloride with the structural formula:



$C_{19}H_{35}NO_2 \bullet HCl$ MW 345.95

Dicyclomine hydrochloride occurs as a fine, white, crystalline, practically odorless powder with a bitter taste. It is soluble in water, freely soluble in alcohol and chloroform, and very slightly soluble in ether.

CLINICAL PHARMACOLOGY

Dicyclomine relieves smooth muscle spasm of the gastrointestinal tract. Animal studies indicate that this action is achieved via a dual mechanism: (1) a specific anticholinergic effect (antimuscarinic) at the acetylcholine-receptor sites with approximately 1/8 the milligram potency of atropine (*in vitro*, guinea pig ileum); and (2) a direct effect upon smooth muscle (musculotropic) as evidenced by dicyclomine's antagonism of bradykinin- and histamine-induced spasms of the isolated guinea pig ileum. Atropine did not affect responses to these two agonists. *In vivo* studies in cats and dogs showed dicyclomine to be equally potent against acetylcholine (ACh)- or barium chloride ($BaCl_2$)- induced intestinal spasm while

atropine was at least 200 times more potent against effects of ACh than $BaCl_2$. Tests for mydriatic effects in mice showed that dicyclomine was approximately 1/500 as potent as atropine; antisialagogue tests in rabbits showed dicyclomine to be 1/300 as potent as atropine.

In man, dicyclomine is rapidly absorbed after oral administration, reaching peak values within 60-90 minutes. The principal route of elimination is via the urine (79.5% of the dose). Excretion also occurs in the feces, but to a lesser extent (8.4%). Mean half-life of plasma elimination in one study was determined to be approximately 1.8 hours when plasma concentrations were measured for 9 hours after a single dose. In subsequent studies, plasma concentrations were followed for up to 24 hours after a single dose, showing a secondary phase of elimination with a somewhat longer half-life. Mean volume of distribution for a 20 mg oral dose is approximately 3.65 L/kg suggesting extensive distribution in tissues.

In controlled clinical trials involving over 100 patients who received drug, 82% of patients treated for functional bowel/irritable bowel syndrome with dicyclomine hydrochloride at initial doses of 160 mg daily (40 mg q.i.d.) demonstrated a favorable clinical response compared with 55% treated with placebo ($p<.05$). In these trials, most of the side effects were typically anticholinergic in nature (see table) and were reported by 61% of the patients.

Side Effect	Dicyclomine Hydrochloride (40 mg q.i.d.) %	Placebo %
Dry Mouth	33	5
Dizziness	29	2
Blurred Vision	27	2
Nausea	14	6
Light-Headedness	11	3
Drowsiness	9	1
Weakness	7	1
Nervousness	6	2

Nine percent (9%) of patients were discontinued from the drug because of one or more of these side effects (compared with 2% in the placebo group). In 41% of the patients with side effects, side effects disappeared or were tolerated at the 160 mg daily dose without reduction. A dose reduction from 160 mg daily to an average daily dose of 90 mg was required in 46% of the patients with side effects who then continued to experience a favorable clinical response; their side effects either disappeared or were tolerated. (See **ADVERSE REACTIONS.**)

INDICATIONS AND USAGE

Dicyclomine hydrochloride tablets and capsules are indicated for the treatment of functional bowel/ irritable bowel syndrome.

CONTRAINDICATIONS

1. Obstructive uropathy
2. Obstructive disease of the gastrointestinal tract
3. Severe ulcerative colitis (See **PRECAUTIONS**)
4. Reflux esophagitis
5. Unstable cardiovascular status in acute hemorrhage
6. Glaucoma
7. Myasthenia gravis
8. Evidence of prior hypersensitivity to dicyclomine hydrochloride or other ingredients of these

formulations
9. Infants less than 6 months of age (See **WARNINGS** and **PRECAUTIONS: Information for Patients.**)
10. Nursing Mothers (See **WARNINGS** and **PRECAUTIONS: Information for Patients**.)

WARNINGS

In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). If symptoms occur, the drug should be discontinued and supportive measures instituted.

Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance, treatment with this drug would be inappropriate and possibly harmful.

Dicyclomine hydrochloride may produce drowsiness or blurred vision. The patient should be warned not to engage in activities requiring mental alertness, such as operating a motor vehicle or other machinery or performing hazardous work while taking this drug.

Psychosis has been reported in sensitive individuals given anticholinergic drugs. CNS signs and symptoms include confusion, disorientation, short-term memory loss, hallucinations, dysarthria, ataxia, coma, euphoria, decreased anxiety, fatigue, insomnia, agitation and mannerisms, and inappropriate affect. These CNS signs and symptoms usually resolve within 12 to 24 hours after discontinuation of the drug.

There are reports that administration of dicyclomine hydrochloride syrup to infants has been followed by serious respiratory symptoms (dyspnea, shortness of breath, breathlessness, respiratory collapse, apnea, asphyxia), seizures, syncope, pulse rate fluctuations, muscular hypotonia, and coma. Death has been reported. No causal relationship between these effects observed in infants and dicyclomine administration has been established. DICYCLOMINE IS CONTRAINDICATED IN INFANTS LESS THAN 6 MONTHS OF AGE AND IN NURSING MOTHERS. (See **CONTRAINDICATIONS** and **PRECAUTIONS: Nursing Mothers** and **Pediatric Use**.)

Safety and efficacy of dicyclomine hydrochloride in pediatric patients has not been established.

PRECAUTIONS

General

Use with caution in patients with:
1. Autonomic neuropathy
2. Hepatic or renal disease
3. Ulcerative colitis - large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon (see **CONTRAINDICATIONS**)
4. Hyperthyroidism
5. Hypertension
6. Coronary heart disease
7. Congestive heart failure
8. Cardiac tachyarrhythmia
9. Hiatal hernia (see **CONTRAINDICATIONS: Reflux esophagitis**)
10. Known or suspected prostatic hypertrophy.

Investigate any tachycardia before administration of dicyclomine hydrochloride, since it may increase the heart rate.

With overdosage, a curare-like action may occur (i.e., neuromuscular blockade leading to muscular

weakness and possible paralysis).

Information for Patients

Dicyclomine hydrochloride may produce drowsiness or blurred vision. The patient should be warned not to engage in activities requiring mental alertness, such as operating a motor vehicle or other machinery or to perform hazardous work while taking this drug.

Dicyclomine is contraindicated in infants less than 6 months of age and in nursing mothers. (See **CONTRAINDICATIONS**, **WARNINGS**, and **PRECAUTIONS: Nursing Mothers** and **Pediatric Use.**)

In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). If symptoms occur, the drug should be discontinued and a physician contacted.

Drug Interactions

The following agents may increase certain actions or side effects of anticholinergic drugs: amantadine, antiarrhythmic agents of Class I (e.g., quinidine), antihistamines, antipsychotic agents (e.g., phenothiazines), benzodiazepines, MAO inhibitors, narcotic analgesics (e.g., meperidine), nitrates and nitrites, sympathomimetic agents, tricyclic antidepressants, and other drugs having anticholinergic activity.

Anticholinergics antagonize the effects of antiglaucoma agents. Anticholinergic drugs in the presence of increased intraocular pressure may be hazardous when taken concurrently with agents such as corticosteroids. (See also **CONTRAINDICATIONS.**)

Anticholinergic agents may affect gastrointestinal absorption of various drugs, such as slowly dissolving dosage forms of digoxin; increased serum digoxin concentrations may result. Anticholinergic drugs may antagonize the effects of drugs that alter gastrointestinal motility, such as metoclopramide. Because antacids may interfere with the absorption of anticholinergic agents, simultaneous use of these drugs should be avoided. The inhibiting effects of anticholinergic drugs on gastric hydrochloric acid secretion are antagonized by agents used to treat achlorhydria and those used to test gastric secretion.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There are no known human data on long-term potential for carcinogenicity or mutagenicity.

Long-term studies in animals to determine carcinogenic potential are not known to have been conducted. In studies in rats at doses of up to 100 mg/kg/day, dicyclomine hydrochloride produced no deleterious effects on breeding, conception, or parturition.

Pregnancy

Teratogenic Effects

Pregnancy Category B

Reproduction studies have been performed in rats and rabbits at doses up to 33 times the maximum recommended human dose based on 160 mg/day (3 mg/kg) and have revealed no evidence of impaired fertility or harm to the fetus due to dicyclomine. Epidemiologic studies in pregnant women with products containing dicyclomine hydrochloride (at doses up to 40 mg/day) have not shown that dicyclomine increases the risk of fetal abnormalities if administered during the first trimester of pregnancy. There are, however, no adequate and well-controlled studies in pregnant women at the recommended doses (80-160 mg/day). Because animal reproduction studies are not always predictive of human response, dicyclomine hydrochloride as indicated for functional bowel/irritable bowel syndrome should be used during pregnancy only if clearly needed.

Nursing Mothers

Since dicyclomine hydrochloride has been reported to be excreted in human milk, DICYCLOMINE HYDROCHLORIDE IS CONTRAINDICATED IN NURSING MOTHERS. (See **CONTRAINDICATIONS**, **WARNINGS**, **PRECAUTIONS: Pediatric Use** and **ADVERSE REACTIONS**.)

Pediatric Use

(See **CONTRAINDICATIONS**, **WARNINGS**, and **PRECAUTIONS: Nursing Mothers**.) DICYCLOMINE HYDROCHLORIDE IS CONTRAINDICATED IN INFANTS LESS THAN 6 MONTHS OF AGE.

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Clinical studies of dicyclomine hydrochloride did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. (See **DOSAGE AND ADMINISTRATION**).

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

Controlled clinical trials have provided frequency information for reported adverse effects of dicyclomine hydrochloride listed in a decreasing order of frequency. (See **CLINICAL PHARMACOLOGY.**)

Not all of the following adverse reactions have been reported with dicyclomine hydrochloride. Adverse reactions are included here that have been reported for pharmacologically similar drugs with anticholinergic/antispasmodic action.

Gastrointestinal: dry mouth, nausea, vomiting, constipation, bloated feeling, abdominal pain, taste loss, anorexia

Central Nervous System: dizziness, light-headedness, tingling, headache, drowsiness, weakness, nervousness, numbness, mental confusion and/or excitement (especially in elderly persons), dyskinesia, lethargy, syncope, speech disturbance, insomnia

Ophthalmologic: blurred vision, diplopia, mydriasis, cycloplegia, increased ocular tension

Dermatologic/Allergic: rash, urticaria, itching, and other dermal manifestations; severe allergic reaction or drug idiosyncrasies including anaphylaxis

Genitourinary: urinary hesitancy, urinary retention

Cardiovascular: tachycardia, palpitations

Respiratory: dyspnea, apnea, asphyxia (see **WARNINGS**)

Other: decreased sweating, nasal stuffiness or congestion, sneezing, throat congestion, impotence, suppression of lactation (see **PRECAUTIONS: Nursing Mothers**)

DRUG ABUSE AND DEPENDENCE

Abuse of and/or dependence on dicyclomine for anticholinergic effects have been rarely reported.

OVERDOSAGE

Signs and Symptoms

The signs and symptoms of overdosage are headache; nausea; vomiting; blurred vision; dilated pupils; hot, dry skin; dizziness; dryness of the mouth; difficulty in swallowing; and CNS stimulation. A curare-like action may occur (i.e., neuromuscular blockade leading to muscular weakness and possible paralysis).

A 37-year-old female reported numbness on the left side, cold fingertips, blurred vision, abdominal and flank pain, decreased appetite, dry mouth, and nervousness following ingestion of 320 mg daily (four 20 mg tablets QID) for four days. These events resolved after discontinuing the dicyclomine.

Oral LD_{50}

The acute oral LD_{50} of the drug is 625 mg/kg in mice.

Minimum Human Lethal Dose/Maximum Human Dose Recorded

The amount of drug in a single dose that is ordinarily associated with symptoms of overdosage or that is likely to be life threatening, has not been defined. The maximum human oral dose recorded was 600 mg by mouth in a 10-month-old child and approximately 1500 mg in an adult, each of whom survived. In three of the infants who died following administration of dicyclomine hydrochloride (see **WARNINGS**), the blood concentrations of drug were 200, 220, and 505 ng/mL, respectively.

Dialysis

It is not known if dicyclomine hydrochloride is dialyzable.

Treatment

Treatment should consist of gastric lavage, emetics, and activated charcoal. Sedatives (e.g., short-acting barbiturates, benzodiazepines) may be used for management of overt signs of excitement. If indicated, an appropriate parenteral cholinergic agent may be used as an antidote.

DOSAGE AND ADMINISTRATION

DOSAGE MUST BE ADJUSTED TO INDIVIDUAL PATIENT NEEDS (See **CLINICAL PHARMACOLOGY**.)

Adults-Oral

The only oral dose clearly shown to be effective is 160 mg per day (in 4 equally divided doses). Since this dose is associated with a significant incidence of side effects, it is prudent to begin with 80 mg per day (in 4 equally divided doses). Depending upon the patient's response during the first week of therapy, the dose should be increased to 160 mg per day unless side effects limit dosage escalation. If efficacy is not achieved within 2 weeks or side effects require doses below 80 mg per day, the drug should be discontinued. Documented safety data are not available for doses above 80 mg daily for periods longer than 2 weeks.

Elderly

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of

concomitant disease or other drug therapy. (See **PRECAUTIONS: Geriatric Use**).

HOW SUPPLIED

Dicyclomine Hydrochloride Tablets USP, 20 mg are blue, round, flat-faced, beveled edge tablets, debossed LAN over 1282, supplied in bottles of 100, 500 and 1000 tablets.

Bottles of 20 Tablets NDC 21695-219-20

Bottles of 30 Tablets NDC 21695-219-30

To prevent fading, avoid exposure to direct sunlight. Store at 20° - 25°C (68° - 77°F) [See USP Controlled Room Temperature]. Dispense in a well-closed container as defined in the USP.

Store at 20° - 25°C (68° - 77°F) [See USP Controlled Room Temperature]. Dispense in a well-closed container as defined in the USP.

Rx Only

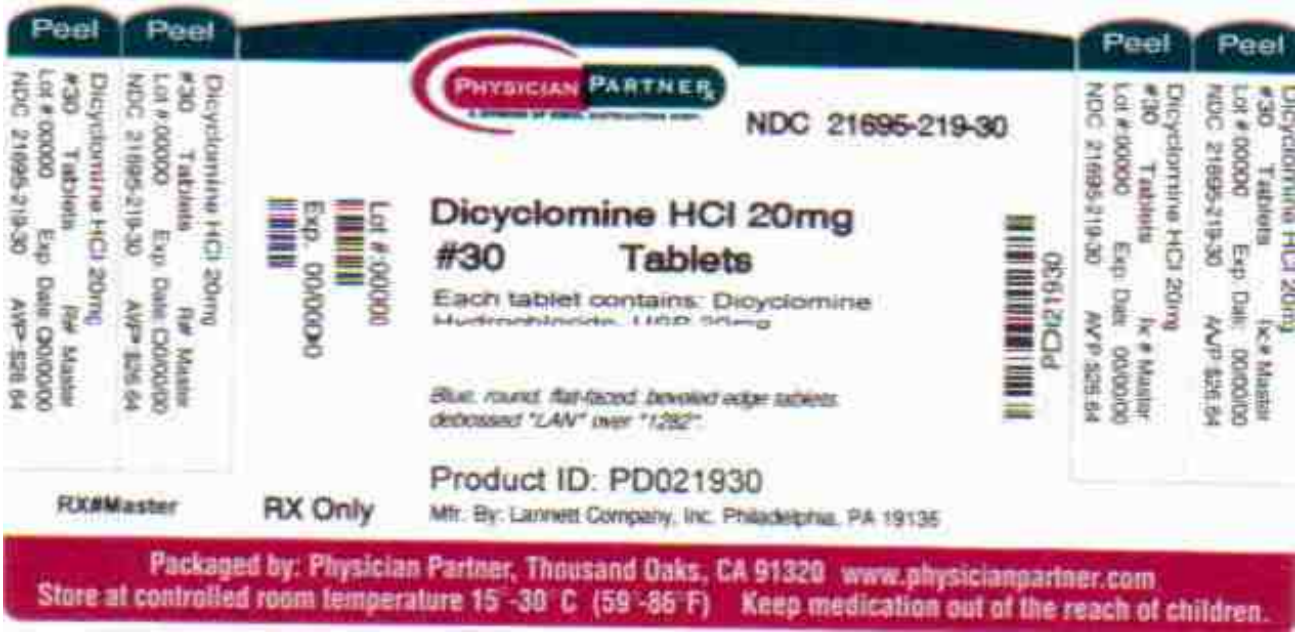
MANUFACTURED BY
LANNETT CO., INC.
PHILADELPHIA, PA 19136

REPACKAGED BY:

REBEL DISTRIBUTORS CORP

THOUSAND OAKS, CA 91320

Principal Display Panel



DICYCLOMINE HYDROCHLORIDE

dicyclomine hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:21695-219(NDC:0527-1282)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Dicyclomine Hydrochloride (UNII: CQ903KQA31) (Dicyclomine - UNII:4KV4X8IF6V)	Dicyclomine Hydrochloride	20 mg

Inactive Ingredients

Ingredient Name	Strength
ACACIA (UNII: 5C5403N26O)	
STARCH, CORN (UNII: O8232NY3SJ)	
anhydrous lactose (UNII: 3SY5LH9PMK)	
SUCROSE (UNII: C151H8M554)	
ANHYDROUS DIBASIC CALCIUM PHOSPHATE (UNII: L11K75P92J)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
magnesium stearate (UNII: 70097M6I30)	
stearic acid (UNII: 4ELV7Z65AP)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	

Product Characteristics

Color	BLUE	**Score**	no score
Shape	ROUND	**Size**	7mm
Flavor		**Imprint Code**	LAN;1282
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:21695-219-20	20 in 1 BOTTLE		
2	NDC:21695-219-30	30 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040230	02/26/1999	

Labeler - Rebel Distributors Corp (118802834)

Establishment

Name	Address	ID/FEI	Business Operations
Rebel Distributors Corp		118802834	RELABEL, REPACK

Revised: 9/2010 Rebel Distributors Corp