PRESCRIBING INFORMATION

RIVA-DICYCLOMINE

Dicyclomine Hydrochloride Capsules USP

10 mg

ANTISPASMODIC

LABORATOIRE RIVA INC.
660 Boul. Industriel
Blainville, Québec
J7C 3V4

www.labriva.com

Date of Revision:
December 8, 2017

Submission Control No: 198804

PRESCRIBING INFORMATION

RIVA-DICYCLOMINE

(dicyclomine hydrochloride USP)

10 mg Capsules

Antispasmodic

ACTION AND CLINICAL PHARMACOLOGY

RIVA-DICYCLOMINE (dicyclomine hydrochloride capsules USP) 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 (ACh)-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. Animal studies showed dicyclomine to be equally potent against ACh - or barium chloride ($BaCl_2$) -induced intestinal spasm while atropine was at least 200 times more potent against the effects of ACh than against $BaCl_2$. 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.

After a single oral 20 mg dose of dicyclomine in volunteers, peak plasma concentration reached a mean value of 58 ng/mL in 1 to 1.5 hours. The principal route of elimination is via the urine.

INDICATIONS AND CLINICAL USE

RIVA-DICYCLOMINE (dicyclomine hydrochloride capsules USP) is indicated for the treatment of functional gastrointestinal tract conditions involving smooth muscle spasm such as irritable colon (mucous colitis, spastic colon, irritable bowel syndrome) and spastic constipation. It can also be used as adjunctive therapy in organic gastrointestinal conditions to relieve associated smooth muscle spasm such as in colitis, diverticulitis, regional enteritis, gastritis, and peptic ulcer.

CONTRAINDICATIONS

Known idiosyncrasy to **RIVA-DICYCLOMINE** (dicyclomine hydrochloride capsules USP).

Infants less than 6 months of age **(See WARNINGS)** and in nursing mothers **(See PRECAUTIONS).**

Should not be used in patients with:

- obstructive uropathy
- obstructive disease of the gastrointestinal tract
- paralytic ileus and intestinal atony
- severe ulcerative colitis
- myasthenia gravis
- reflux esophagitis
- glaucoma
- unstable cardiovascular status in acute hemorrhage

WARNINGS

Use in infants: There are reports of infants who, in their first 3 months of life, were given dicyclomine hydrochloride syrup and evidenced respiratory symptoms (breathing difficulty, shortness of breath, breathlessness, respiratory collapse, apnea), as well as seizures, syncope, asphyxia, pulse rate fluctuations, muscular hypotonia, and coma. In some instances, these symptoms occurred within minutes of ingestion and lasted up to 20 to 30 minutes. The symptoms were reported in association with dicyclomine syrup therapy but a proven cause and effect relationship has not been established.

Worldwide, a few deaths have been reported in infants three months of age or less who had been given dicyclomine syrup. Two of these were reported to have been associated with excessively high dicyclomine blood levels.

Although no causal relationship between these effects observed in infants and dicyclomine administration has been established, dicyclomine is contraindicated in infants 6 months of age or less. **(See CONTRAINDICATIONS)**

Other: 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 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 and Delirium have been reported in sensitive individuals (elderly patients and/or patients with mental illness) given anticholinergic drugs. CNS signs and symptoms include confusional state, disorientation, amnesia, 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.

PRECAUTIONS

General: **RIVA-DICYCLOMINE** (dicyclomine hydrochloride capsules USP) should be used with caution in any patient with, or suspected of having:

- prostatic hypertrophy
- hiatal hernia associated with reflux esophagitis because anticholinergic drugs may aggravate the condition
- autonomic neuropathy
- hepatic or renal disease
- hyperthyroidism
- hypertension
- coronary heart disease
- congestive heart failure
- cardiac tachyarrhythmia

Use in Pregnancy: Epidemiologic studies in pregnant women with products containing dicyclomine (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 to 160 mg/day). Animal reproduction studies have revealed no evidence of impaired fertility or harm to the fetus due to dicyclomine. Because animal reproduction studies are not always predictive of human response, **RIVA-DICYCLOMINE** (dicyclomine hydrochloride capsules USP) should be used during pregnancy only if required.

Nursing Mothers: Since dicyclomine has been reported to be excreted in human milk, **RIVA-DICYCLOMINE** is contraindicated in nursing mothers **(See CONTRAINDICATIONS).**

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.

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 to test gastric secretion.

ADVERSE REACTIONS

Most adverse reactions reported in clinical trials conducted with dicyclomine were typically anticholinergic in nature and included, in decreasing order of frequency: dry mouth, dizziness, blurred vision, nausea, light-headedness, drowsiness, weakness and nervousness.

The following adverse reactions, presented by system organ class in alphabetical order, have been identified during post approval use of **RIVA-DICYCLOMINE** (dicyclomine hydrochloride capsules USP) and pharmacologically similar drugs, e.g., other anticholinergics and antispasmodics. Since 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.

Cardiac disorders: palpitations, tachyarrhythmias.
Eye disorders: cyclopedia, mydriasis, vision blurred.
Gastrointestinal disorders: abdominal distension, abdominal pain, constipation, dry mouth, dyspepsia, nausea, vomiting.
General disorders and administration site conditions: fatigue, malaise.
Immune System Disorders: drug hypersensitivity including face oedema, angioedema, anaphylactic shock.
Nervous system disorders: dizziness, headache, somnolence, syncope.
Psychiatric disorders: As of the other cholinergic drugs, cases of delirium or symptoms of delirium such as amnesia (or transient global amnesia), agitation, confusional state, delusion, disorientation, hallucination (including visual hallucination) as well as mania, mood altered and pseudodementia, have been reported with the use of Dicyclomine. Nervousness and insomnia have also been reported.
Reproductive system and breast disorders: suppressed lactation (see Precautions).
Respiratory, thoracic and mediastinal disorders: dyspnoea, nasal congestion
Skin and subcutaneous tissue disorder: dermatitis allergic, erythema, rash.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Signs and symptoms of **RIVA-DICYCLOMINE** (dicyclomine hydrochloride capsules USP) overdosage are headache; nausea; vomiting; blurred vision; dilated pupils; hot, dry skin; dizziness; dry mouth; difficulty in swallowing; and CNS stimulation. A curare-like action may occur (i.e., neuromuscular blockage leading to muscular weakness and possible paralysis).

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.

Dialysis: It is not known if dicyclomine is dialyzable.

For management of a suspected drug overdose, contact your regional **Poison Control Centre.**

DOSAGE AND ADMINISTRATION

DOSAGE SHOULD BE ADJUSTED TO INDIVIDUAL PATIENT NEEDS.

Oral Dosage Forms (Capsules):

Adults: 10 to 20 mg 3 to 4 times daily. Depending upon the patient's response during the first week of therapy, the dose should be increased to 160 mg/day unless side effects limit dose escalation. If efficacy is not achieved within 2 weeks or side effects require doses below 80 mg/day, the drug should be discontinued. Documented safety data are not available for doses above 80 mg daily for periods longer than 2 weeks.

Children (2 to 12 Years): 10 mg 3 to 4 times daily.

AVAILABILITY OF DOSAGE FORMS

Capsules 10 mg: #4 size transparent blue bodied and cap hard gelatine capsule with a number "10" marked on it. Available in bottles of 100 and 500 capsules.

Non-medicinal ingredients: Brillant Blue FCF Sodium Salt (FD&C Blue No. 1), Colloidal Silicon Dioxide, Gelatin, Lactose, Magnesium Stearate, Phloxine B Sodium Salt (D&C Red No. 28), Water and White ink (Ammonium Hydroxide, Denatured Alcohol, Isopropyl Alcohol, n-Butyl Alcohol, Propylene Glycol, Shellac, Simethicone, Titanium Dioxide).

Store between 15 and 30°C. Protect from excessive heat and moisture.

REFRENCES

Prescribing Information Bentylol® (dicyclomine hydrochloride USP), Aptalis Pharma Canada Inc. Control No.: 156699, Date of Revision: July 16, 2012.