# NEW ZEALAND DATA SHEET

## 1 PRODUCT NAME

**PRO-BANTHINE** Propantheline bromide tablet 15mg

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 15mg propantheline bromide.

Propantheline bromide powder is a quaternary ammonium compound (2- diisopropy-laminoethyl xanthen-9-carboxylate methobromide) with a melting point 157° to 162°C. At relative humidities of more than 50% it is hygroscopic and it is deliquescent above about 90%.

Propantheline bromide is a white or yellowish-white odourless powder with a very bitter taste. It is very soluble in water, alcohol and chloroform, however, is insoluble in ether.

Propantheline bromide has the molecular formula $C_{23}H_{30}BrNO_3$ (CAS-50-34-0) with a molecular weight of 448.40.

Excipients with known effect: Lactose monohydrate

For the full list of excipients, see Section 6.1 List of excipients.

## 3 PHARMACEUTICAL FORM

A round, pale orange, film-coated tablet, plain on both sides

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

PRO-BANTHINE is indicated as an adjunctive therapy in the treatment of peptic ulcer (gastric and duodenal) and for the relief of the symptoms of gastritis. PRO-BANTHINE is also indicated for the symptomatic treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis, acute enterocolitis, nervous diarrhoea and functional gastrointestinal disorders). Other indications include renal colic, hyperhidrosis, as adjunctive therapy in ulcerative colitis, diverticulitis, cholecystitis and pancreatitis and for certain gastrointestinal diagnostic procedures.

## 4.2 DOSE AND METHOD OF ADMINISTRATION

**ADULTS**

In peptic ulcer cases, one tablet three times a day, 30 minutes before each meal, and two at bedtime is usual (75mg daily). There is considerable variation of individual needs and the dosage may be raised until dryness of the mouth occurs. A dose slightly lower than this amount is optimal. The maximum daily dosage should not exceed 120mg.

For contrast radiology two tablets (30mg) should be given 45 minutes before radiology.

For other indications the dose is one or two tablets (15mg to 30mg) four times daily.

## 4.3 CONTRAINDICATIONS

The medicine is contraindicated in patients with:

- Hypersensitivity to propantheline bromide or other anticholinergic agents, or any of the ingredients in PRO-BANTHINE tablets.
- Tachycardia secondary to cardiac insufficiency or thyrotoxicosis.
- Glaucoma, since mydriasis is to be avoided
- Obstructive disease of the gastrointestinal tract (pyloroduodenal stenosis, achalasia, paralytic ileus, etc)
- Obstructive uropathy (prostatism)
- Intestinal atony of elderly or debilitated patients
- Toxic megacolon complicating ulcerative colitis
- Hiatal hernia associated with reflux oesophagitis
- Unstable cardiovascular adjustment in acute haemorrhage
- Myasthenia gravis

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

- Potential risks or benefits should be carefully considered before using the product.

- PRO-BANTHINE should be used with caution in patients with severe cardiac disease in whom even a slight increase in heart rate is undesirable.

- Propantheline bromide should be used with caution in patients with chronic lung disease, as inspissation and formation of bronchial plugs may occur, due to the reduction in bronchial secretion.

- In some patients, especially those with ileostomy or colostomy, diarrhoea may be a symptom of incomplete intestinal obstruction. PRO-BANTHINE therapy should be avoided in such patients.

- PRO-BANTHINE should be used with caution in the elderly and in all patients with autonomic neuropathy, hepatic or renal disease, hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, mitral stenosis or hypertension.

- Caution is required in patients with ulcerative colitis, since in these patients PRO-BANTHINE may suppress intestinal motility to the point of producing paralytic ileus, thus precipitating or aggravating toxic megacolon.

- Caution is also required in patients with known or suspected gastrointestinal infections such as *Clostridium difficile*- associated diarrhoea and colitis. Gastrointestinal motility may decrease, so continuance of causative toxins and organisms occur, therefore prolonging the infection symptoms.

- Caution is required for those patients with fever or who may be exposed to elevated environmental temperatures, as there may be an increase in the risk of hyperthermia occurring. Fever and possibly heat stroke may occur due to anhidrosis.

### Use in hepatic impairment

PRO-BANTHINE should be used with caution in all patients with hepatic disease.

### Use in renal impairment

PRO-BANTHINE should be used with caution in all patients with renal disease.

**PEDIATRIC USE**

Safety and efficacy of propantheline bromide in children have not been established.

### Use in the elderly

Caution should also be exercised in elderly patients because of the possibility of inducing urinary retention. Urinary retention may be avoided if these patients are advised to micturate at the time of taking medication. Caution should also be exercised in elderly patients due to the danger of precipitating undiagnosed glaucoma.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

- **Antacids or Absorbent Antidiarrhoeals:** May reduce the absorption of propantheline bromide, therefore resulting in a reduction of its therapeutic effectiveness. Therefore, take two to three hours apart from doses of propantheline bromide.

- **Anticholinergics:** May delay absorption of other medication given concomitantly.

- **Antimyasthenics:** Concurrently used with propantheline bromide may further reduce intestinal motility.

- Increased intra-ocular pressure may result from concurrent administration of **anticholinergics** and **corticosteroids**.
- **Cisapride:** Concurrent use of propantheline bromide with cisapride is likely to counteract gastrointestinal motility normally induced by cisapride.

- **Digoxin** tablets concurrently used with propantheline bromide may assist absorption and lead to elevated serum digoxin levels.

- **Haloperidol** concurrently used with propantheline bromide may decrease the effectiveness of haloperidol as an antipsychotic agent.

- **Ketoconazole:** Anticholinergics may decrease gastric acid output and/or increase gastrointestinal pH, possibly resulting in ketoconazole absorption during concurrent use with anticholinergics. Therefore, take propantheline bromide at least two hours after ketoconazole.

- **Levodopa:** Concurrent administration of anticholinergics and levodopa may decrease the extent of absorption of levodopa in the small intestine by causing increased metabolism of levodopa in the stomach. If propantheline bromide is discontinued without a concomitant reduction in levodopa dosage, toxicity may result from the increased absorption of levodopa.

- **Metoclopramide:** Concurrently used with propantheline bromide may cause propantheline bromide to antagonise the gastrointestinal motility effects of metoclopramide.

- **Opioid (narcotic) Analgesics:** Concurrently used with propantheline bromide may cause an increase in the risk of severe constipation. This may lead to urinary retention or paralytic ileus occurring.

- Propantheline bromide may also potentiate the sedative effect of phenothiazines.

- **Potassium chloride, especially wax-matrix preparations:** Concurrent use with propantheline bromide may increase severity of potassium chloride-induced gastrointestinal lesions.

- **Urinary alkalisers** (e.g. antacids, carbonic anhydrase inhibitors and sodium bicarbonate): May cause a delay in urinary excretion, therefore potentiating propantheline bromide's therapeutic and/or side effects.

Excessive cholinergic blockage may occur if propantheline bromide is given concomitantly with antihistamines; Type 1 antiarrhythmic agents (e.g. disopyramide, procainamide or quinidine); synthetic and semisynthetic anticholinergic agents; Belladonna alkaloids; narcotic analgesics e.g. pethidine; phenothiazines, tricyclic antidepressants or other psychoactive agents.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Effects on fertility

There is no information available on the possible effects of propantheline bromide on human fertility.

### Use in pregnancy

Safe use of PRO-BANTHINE in pregnancy has not been established. Therefore, the use of this medicine in women of child-bearing potential requires that the benefits be weighed against its possible hazards to mother and foetus.

### Use in lactation

Information regarding the secretion of propantheline bromide in breast milk is limited to uncontrolled data derived from marketing experience. Such experience does not suggest that significant quantities of propantheline bromide are secreted in breast milk, since propantheline bromide is incompletely absorbed from the gastrointestinal tract and has poor lipid solubility. Because many agents are excreted in human milk, caution should be exercised when propantheline bromide is administered to a breast-feeding woman. Suppression of lactation may occur with anticholinergic agents.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

PRO-BANTHINE may produce drowsiness or blurred vision. Patients should be cautioned regarding operating machinery or motor vehicles during treatment with this medicine.

## 4.8 UNDESIRABLE EFFECTS

The adverse effects of propantheline bromide are usually dose-related and are usually reversible when the therapy is discontinued. The following adverse effects have been reported:

**Cardiovascular**
Palpitations, tachycardia.

**Neurological**
Insomnia, drowsiness, dizziness, nervousness, headache, mental confusion, weakness.

**Dermatological and Hypersensitivity Reactions**
Anaphylaxis, urticaria, rashes, allergic dermatitis.

**Gastrointestinal**
Bloatedness, nausea, vomiting, constipation.

**Genitourinary**
Urinary hesitancy and retention, impotence.

**Respiratory**
Reduced bronchial secretions.

**Ophthalmic**
Blurred vision, mydriasis, cycloplegia, increased ocular tension.

**Other Effects**
Xerostomia (dry mouth), decreased salivary secretions, decreased sweating (anhidrosis), heat stroke, flushing, dryness of the skin, thirst, difficulty in swallowing and talking, loss of the sense of taste, suppression of lactation.

### Reporting suspected adverse effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://nzphvc.otago.ac.nz/reporting/.

## 4.9 OVERDOSE

**Symptoms:**

The symptoms of overdosage with propantheline bromide progress from an intensification of the usual side effects (from nausea and vomiting) to CNS disturbances (from restlessness and excitement to psychotic behaviour), hyperthermia, circulatory changes, (flushing, fall in blood pressure, circulatory failure), respiratory failure, paralysis and coma. With overdosage, a curare- like action may occur i.e. neuromuscular blockade leading to muscular weakness and possible paralysis. Additionally, a rash may appear on the face or the upper trunk of the body. At high doses, propantheline bromide has some ganglion-blocking activity; therefore postural hypotension and impotency may occur.

**Treatment:**

Treatment of overdosage of propantheline bromide consists of symptomatic and supportive therapy. An aqueous slurry of activated charcoal may be administered to decrease medicine adsorption. For the reversal of severe overdosage symptoms, an intravenous injection of

physostigmine 0.5 to 2mg is administered, and repeated as necessary up to a total of 5mg. Fever may be treated symptomatically (alcohol sponging, ice packs).

Excitement of a degree which demands attention may be managed with sodium thiopentone 2% solution given slowly intravenously or diazepam, 5 to 10mg intravenously or 10mg intramuscularly. In the event of progression of the curare-like effect to paralysis of the respiratory muscles, artificial respiration should be instituted and maintained until effective respiratory action returns. Adequate hydration is also required.

For advice on the management of overdose, contact the National Poisons Centre on 0800 POISON (0800764766).

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

### Mechanism of action

PRO-BANTHINE is an anticholinergic agent which inhibits neural impulses at the effector sites of the parasympathetic nervous system and at the ganglia of the sympathetic and parasympathetic nervous system with peripheral effects similar to atropine. PRO-BANTHINE does not readily cross the blood brain barrier thus avoiding the central effects seen with atropine. PRO-BANTHINE reduces gastric acid secretion and inhibits gastrointestinal motility and has spasmolytic properties. Other secretions including pancreatic juice, sweat and saliva are reduced.

### Clinical trials

No Data Available

## 5.2 PHARMACOKINETIC PROPERTIES

After oral administration to man, propantheline bromide is extensively metabolized primarily by hydrolysis to the inactive materials xanthene-9- carboxylic acid and (2-hydroxyethyl) diisopropylmethylammonium bromide, approximately half of which occurs in the gastrointestinal tract prior to its absorption. Food appears to substantially decrease the extent of absorption following oral administration. After a single 15mg oral dose of carbon-14 labelled medicine given to a healthy man, 390ng/ml peak plasma concentration of total -$^{14}$C material is attained at 6 hours.

Single oral doses of 15, 30, 45, 60, 75, 90mg of PRO-BANTHINE tablets were administered to each of 6 subjects and were rapidly absorbed. The absorption half-life of propantheline bromide was 8-30 minutes, and half-life of elimination between 1.3 and 2.1 hours.

Average peak plasma concentrations of propantheline after the 15, 30, 45, 60, 75 and 90mg doses were 6, 29, 81, 62, 148 and 146ng/ml respectively, and were attained within 3 hours of oral dosing. Similarly the average amount of unmetabolized propantheline excreted in the urine was 0.70, 1.08, 1.59, 1.85, 2.42 and 3.06ng/ml respectively.

Unmetabolized medicine represents only a small proportion of the total -$^{14}$C materials. The plasma half-life of the total -$^{14}$C material is about 9 hours and approximately 70 per cent of the dose is excreted in the urine, mostly as metabolites. The urinary excretion of the intact propantheline is about 5 per cent after oral administration and about 20 per cent after intravenous administration.

The distribution of propantheline bromide in the body has not been determined. It appears that it does not readily penetrate the CNS and eye, due to complete ionisation and poor lipid solubility.

### 5.3 PRECLINICAL SAFETY DATA

#### Genotoxicity

Animal studies to determine the mutagenic potential of propantheline bromide have not been established.

#### Carcinogenicity

Animal studies to determine the carcinogenic potential of propantheline bromide have not been established.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 LIST OF EXCIPIENTS

PRO-BANTHINE 15mg tablets contain the following excipients: Lactose monohydrate, talc- purified, starch-maize, magnesium stearate, and OPADRY II complete film coating system 85G63218 ORANGE.

Refer to Section 2 - Qualitative and quantitative composition.

### 6.2 INCOMPATIBILITIES

Not applicable.

### 6.3 SHELF LIFE

24 months from date of manufacture

### 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Stored at or below 25°C

### 6.5 NATURE AND CONTENTS OF CONTAINER

PRO-BANTHINE 15mg in bottles of 100 and 500*.

* Not all presentations are actively marketed.

### 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Any unused medicine or waste material should be disposed of in accordance with local requirements.

Keep this medication out of the reach of children.

## 7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Medicine.

## 8 SPONSOR

Exclusive New Zealand distributors:

Pharmacy Retailing (NZ) Ltd trading as Healthcare Logistics

58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand

Tel: +64 9 918 5100

## 9 DATE OF FIRST APPROVAL

4th April 2013

## 10 DATE OF REVISION OF THE TEXT

13 May 2019

**SUMMARY TABLE OF CHANGES**

| Section Changed | Summary of new information |
|---|---|
| All | Reformatted |
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