Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pro-banthine 15 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Propantheline Bromide Ph.Eur. 15 mg
Excipients: also includes lactose monohydrate 31mg per tablet, and sucrose 26.74mg per tablet
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Coated Tablets (Tablets)
Pink coloured, biconvex, sugar coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adjunctive in GI disorders characterised by smooth muscle spasm.
Hyperhidrosis.
Adult enuresis.

4.2 Posology and method of administration

Adults
The recommended initial starting dose is one tablet before each meal, and two tablets at bedtime. Subsequently, dosage should be adjusted according to the patient's individual response and tolerance. Doses up to 120mg may be required in some patients.

Elderly
Elderly patients may be more susceptible to antimuscarinic side effects; glaucoma and urinary retention may occur. Consideration should be given to the presence of other disease and concomitant drug therapy (see contraindications, warnings etc).

Children
Safety and efficacy of Pro-Banthine in children have not been established.

Caution
Food has been reported to reduce the bioavailability of Pro-Banthine. Tablets should be taken at least one hour before meals.

Route of administration
Oral.

4.3 Contraindications

Pro-Banthine is contraindicated in patients with obstructive diseases of the gastrointestinal or urinary tract, pyloric stenosis, paralytic ileus, intestinal atony, severe ulcerative colitis or toxic megacolon, hiatus hernia associated with reflux oesophagitis, unstable cardiovascular adjustment in acute haemorrhage, myasthenia gravis, prostatic enlargement and in patients who are hypersensitive to propantheline bromide.

Pro-Banthine should not be given to patients with closed-angle glaucoma or those with shallow anterior chamber, since it may raise intra-ocular pressure.

4.4 Special warnings and precautions for use

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.

Patients with severe heart disease in whom an increase in heart rate is undesirable should be observed closely if Pro-Banthine is administered.

Patients with ulcerative colitis should be treated with caution, since Pro-Banthine may suppress intestinal mobility to the point of producing paralytic ileus, thus precipitating or aggravating toxic megacolon.

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

Pro-Banthine may induce fever and heat stroke in patients in a high environmental temperature due to decreased sweating.

Pro-Banthine should be used with caution in patients with Down’s syndrome.

Pro-Banthine should also be used with caution in gastrointestinal reflux disease, acute myocardial infarction, cardiac insufficiency and pyrexia.

Pro-Banthine tablets contain sucrose and lactose monohydrate therefore patients with rare hereditary problems of fructose or galactose intolerance, the glucose-galacatose malabsorption, sucrase-isomaltase insufficiency or the Lapp lactase deficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Since antimuscarinics tend to delay gastric emptying they may alter the absorption of other medication given concomitantly.

Analgesics: increased risk of antimuscarinic side effects when antimuscarinics are given with nefopam. The absorption of paracetamol has been reported to be reduced and retarded.

Anti-arrhythmics: increased risk of antimuscarinic side effects with disopyramide.

Antidepressants: increased risk of antimuscarinic side effects when antimuscarinics are given with MAOIs or tricyclics or tricyclic-related antidepressants.

Antifungals: antimuscarinics reduce absorption of ketoconazole.

Antihistamines: increased risk of antimuscarinic side effects when antimuscarinics are given with antihistamines.

Anti-infectives: the absorption of nitrofurantoin has been reported to be enhanced.

Antimuscarinics: excessive muscarinic blockade may occur if Pro-Banthine is given concomitantly with belladonna alkaloids, synthetic and semi-synthetic antimuscarinic agents or other drugs with antimuscarinic activity.

Antipsychotics: antimuscarinics possibly reduce effects of haloperidol; increased risk of antimuscarinic side effects when antimuscarinics are given with clozapine; antimuscarinics reduce plasma concentration of phenothiazines, but risk of antimuscarinic side effects is increased.

Digoxin: concurrent use of Pro-Banthine with slow-dissolving tablets of digoxin may cause increased serum digoxin levels.

Domperidone: antimuscarinics antagonise effects of domperidone on gastrointestinal activity.

Dopaminergics: increased risk of antimuscarinic side effects when antimuscarinics are given with amantadine; antimuscarinics possibly reduce absorption of levodopa.

Memantine: effects of antimuscarinics possibly enhanced by memantine.

Metoclopramide: antimuscarinics antagonise effects of metoclopramide on gastrointestinal activity.

Nitrates: antimuscarinics possibly reduce effects of sublingual tablets of nitrates (failure to dissolve under tongue owing to dry mouth).

Parasympathomimetics: antimuscarinics antagonise effects of parasympathomimetics.

4.6 Fertility, pregnancy and lactation

Animal reproduction and teratology studies have not been performed. Cohort data on parasympatholytics indicate a possible association with minor malformations. In view of this, Pro-Banthine should not be administered in pregnancy unless considered essential.

It is unknown whether propantheline bromide is excreted in human breast milk. No animal studies have been conducted. In view of this, Pro-Banthine should not be administered during breast-feeding unless considered essential. Suppression of lactation may occur with parasympatholytics.

4.7 Effects on ability to drive and use machines

Pro-Banthine may produce drowsiness or blurred vision. Patients should not drive or operate machinery if affected this way.

4.8 Undesirable effects

Side effects of antimuscarinics include dryness of the mouth with difficulty in swallowing and thirst, dilatation of the pupils with loss of accommodation and sensitivity to light, increased intra-ocular pressure, flushing, dryness of the skin, decreased sweating, heat stroke, bradycardia followed by tachycardia, palpitations and arrhythmias, urinary hesitancy and retention, constipation, reduced bronchial secretions, occasional confusion in the elderly, occasional nausea and vomiting, and occasional dizziness.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product 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 via
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail.medsafety@hpra.ie.

4.9 Overdose

Intensification of the usual side effects may occur. In severe intoxication disturbances of the central nervous system may occur resulting in convulsion, coma, circulatory failure, respiratory depression, delirium, hallucinations and restlessness. Toxic doses of propantheline bromide may produce non-depolarising neuromuscular blocking effects with paralysis of voluntary muscle.

In the event of overdosage, empty the stomach and give activated charcoal. Excitement may be controlled by diazepam. Supportive treatment may require oxygen, assisted ventilation and the administration of fluids. In severe cases (convulsions, hyperpyrexia, respiratory depression) the use of intravenous physostigmine (0.5mg to 2mg) should be considered. Since it has a brief duration of action of about 1 to 2 hours, it may be necessary to repeat injections up to a total dose of 5mg.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pro-Banthine inhibits parasympathetic activity by blocking the action of the neurohormone, acetylcholine, on the neuroeffector cell. This blocking action of Pro-Banthine is instrumental in reducing gastric acid secretion and gastrointestinal motor activity.

5.2 Pharmacokinetic properties

Propantheline bromide is extensively metabolised in man. Some enzymic hydrolysis of the drug may occur in the gastrointestinal tract prior to its absorption.

Studies in healthy men demonstrated that peak plasma levels of unchanged drug were reached within 2 hours of a single, oral dose of propantheline bromide. Following single oral dosing the plasma elimination half-life was about 2 to 3 hours and some 1% to 10% of propantheline bromide was excreted in urine as unchanged drug.

In healthy men studies have shown onset of antimuscarinic effects within 1 hour of oral administration. Effects persisted for up to 6 hours after oral dosing.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Talc
Light liquid paraffin
Magnesium stearate

<u>Coating</u>

Sucrose
Cosmetic red oxide (E172)
Cosmetic ochre No. 1624 (E172)
Calcium carbonate
Saccharin sodium
Titanium dioxide (E171)
Talc
Carnauba wax
Magnesium carbonate
Castor oil virgin

6.2 Incompatibilities

Not applicable

6.3 Shelf life

HDPE bottles: 18 months
Blister packs: 18 months

6.4 Special precautions for storage

Do not store above 25°C.
Store in original container in order to protect from light.

6.5 Nature and contents of container

HDPE bottles and foil/PVC-PVdC strips of the appropriate size to accommodate 100, 112, 1000, and 5000 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Archimedes Pharma UK Limited
Galabank Business Park
Galashiels TD1 1QH
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0757/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25 February 1992

Date of last renewal: 25 February 2007

10 DATE OF REVISION OF THE TEXT

May 2015