New Zealand Data Sheet

APO-OXYBUTYNIN

1. APO-OXYBUTYNIN (5mg tablets and 5mg/5ml syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxybutynin hydrochloride 5mg
Oxybutynin hydrochloride 5mg/5ml

Excipient with known effect

Apo-Oxybutynin tablets contain lactose and the colourant FD&C Blue No.1 (Brilliant Blue FCF, C.I. 42090, E133).

Apo-Oxybutynin syrup contains sucrose, sorbitol, the colourant FD&C Green No.3 (Fast green FCF, C.I. 42053, E143) and an artificial berry flavour.

Apo-Oxybutynin tablets and syrup contain no gluten.
Apo-Oxybutynin syrup contains no lactose.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

APO-OXYBUTYNIN 5mg tablets are round, blue, biconvex tablets. 8mm in diameter, identified APO over 5 on one side, other side plain. Each tablet contains 5mg oxybutynin chloride and typically weighs 175 mg.

APO-OXYBUTYNIN 5mg/5mL syrup is a clear, green coloured, slightly viscous syrup with a berry odour and flavour. Each 5mL of syrup contains 5mg oxybutynin chloride.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxybutynin chloride is indicated in adults and children over 5 years of age for the management of urgency and incontinence that characterise neurogenic bladder disorders and idiopathic detrusor instability.

4.2 Dose and method of administration

Pre-treatment examination should include cystometry and other appropriate diagnostic procedures. Cystometry should be repeated at appropriate intervals to evaluate response to therapy. Appropriate antimicrobial therapy should be instituted in the presence of infection.

Dose

Adults

The usual dosage is 5mg taken 2 to 3 times daily. The maximum recommended dose is 5mg taken 4 times daily.

Elderly patients

Initially treatment should be 2.5mg taken 2 times daily, and increased as necessary.

Children over 5 years

The usual dosage is 5mg taken twice daily. The maximum recommended dose is 5mg taken 3 times daily.

APO-OXYBUTYNIN is not recommended for children under 5 years.

Method of administration

APO-OXYBUTYNIN is intended to be administered orally.

Maximum tolerated Daily Dose

The maximum daily dose is 20mg.

4.3 Contraindications

- Patients with unstable cardiovascular status in acute haemorrhage
- Hypersensitivity to any component of the preparation
- Intestinal atony of the elderly or debilitated patient
- Megacolon and toxic megacolon
- Myasthenia gravis
- Narrow angle glaucoma
- Paralytic ileus
- Partial or complete obstruction of the gastrointestinal tract
- Patients with severe colitis patients with bladder outflow obstruction where urinary retention may be precipitated

4.4 Special warnings and precautions for use

Oxybutynin chloride should be cautiously prescribed to patients presenting ulcerative colitis, since intestinal motility may be suppressed to the point of producing a paralytic ileus and promote or aggravate toxic megacolon - a serious complication.

Oxybutynin chloride should be used with caution in the elderly and in patients with autonomic neuropathy, hepatic or renal disease. Elderly patients are at higher risk of oxybutynin induced cognitive impairment.

Oxybutynin chloride should not be taken by patients exposed to high environmental temperatures, since heat stroke and fever may result from decreased sweating.

Oxybutynin chloride should be cautiously prescribed to patients presenting hiatus hernia associated with reflux oesophagitis, or who are currently taking medicines (such as bisphosphonates) that can cause or exacerbate oesophagitis, since this condition may be aggravated by anticholinergic medicines.

Oxybutynin chloride may invoke photosensitivity in some individuals.

Oxybutynin chloride may aggravate the symptoms of hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, tachycardia, hypertension, and prostatic hypertrophy.

Anticholinergic CNS effects (e.g. hallucinations, agitation, confusion, and somnolence) have been reported; monitoring is recommended especially in the first few months after initiating therapy or increasing the dose. Therapy should be discontinued or the dose reduced if these effects develop.

Since oxybutynin can cause narrow-angle glaucoma, patients should be advised to contact a physician immediately if they are aware of a sudden loss of visual acuity or ocular pain.

Oxybutynin may reduce salivary secretions which could result in dental caries, parodontosis or oral candidiasis.

4.5 Interaction with other medicines and other forms of interaction

Oxybutynin chloride may enhance the effects of other anticholinergic medicines e.g. atropine, hyoscine, ipratropium bromide, propantheline bromide, benzhexol hydrochloride, dicyclomine hydrochloride, clozapine.

Alcohol may enhance the drowsiness caused by oxybutynin.

Caution must be taken when treating patients already receiving phenothiazines, amantidine, butyrophenones, levodopa, digoxin, MAOIs and tricyclic antidepressants.

By reducing gastric motility, oxybutynin may affect the absorption of other medicines.

Concomitant use with cholinesterase inhibitors may result in reduced cholinesterase inhibitor efficacy.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category B1.

Oxybutynin chloride should not be prescribed to pregnant patients or patients planning pregnancy unless in the opinion of the medical practitioner, the probable benefits outweigh the potential risks to the foetus.

Breast-feeding

Oxybutynin chloride may be excreted in breast milk, and may also restrict the mammary secretion of breast milk. In consideration of potential risks to the infant, oxybutynin chloride should not be administered to women who are breastfeeding.

Fertility

No information available

4.7 Effects on ability to drive and use machines

Oxybutynin chloride may produce drowsiness and blurred vision. Patients should be cautioned that engagement in potentially hazardous activities requiring mental alertness such as operating machinery or driving a motor vehicle may be inappropriate while taking this medicine.

4.8 Undesirable effects

Nervous system disorders

Asthenia, dizziness, drowsiness, insomnia, restlessness, headache, cognitive disorders, convulsions, disorientation.

Psychiatric disorders

Confusional state, agitation, anxiety, hallucinations, nightmares, paranoia, symptoms of depression, dependence (in patients with a history of drug or substance abuse).

Eye disorders

Amblyopia, cycloplegia, decreased lacrimation, dry eyes, mydriasis, angle closure glaucoma, ocular hypertension.

Cardiac disorders

Palpitations, tachycardia, chest pains

Vascular disorders

Flushing which may be more marked in children, syncope

Gastrointestinal disorders

Constipation, decreased gastrointestinal motility, dry mouth, nausea, anorexia, metallic taste, diarrhoea, vomiting, dysphagia, gastro-oesophageal reflux disease.

Skin and subcutaneous tissue disorders

Dry skin, decreased sweating, rash, urticaria, angioedema.

Renal and urinary disorder

Urinary retention, difficulty in micturition

Reproductive system and breast disorders

Impotence and suppression of lactation

Miscellaneous

Oedema and allergic reactions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare

professional are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Symptoms

Over dosage with oxybutynin chloride progress from initial restlessness and excitement to psychotic behaviour, peripheral vasodilation and hypotension progressing to circulatory failure, respiratory failure, paralysis and coma.

Treatment

Over dosage should be immediately treated by gastric lavage, and intravenous administration of physostigmine.

Adults:

0.5 to 2mg physostigmine by slow intravenous administration. Repeat after 5 minutes if necessary but not exceeding 5 mg.

Children:

30 micrograms/kg of physostigmine by slow intravenous administration. Repeat after 5 minutes if necessary up to a maximum dose of 2mg.

Fever responds to symptomatic treatment e.g. alcohol sponging and ice packs.

Excitement may be treated with diazepam 10mg by intravenous injection.

Tachycardia may be treated with propranolol and urinary retention with catheterisation.

Paralysis of the respiratory muscles may require artificial respiration.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: urinary frequency and incontinence
ATC code: G04BD04

Mechanism of Action

Oxybutynin chloride is a tertiary amine anticholinergic agent which exerts an antimuscarinic as well as a direct antispasmodic action on smooth muscle.

Oxybutynin chloride also possesses useful analgesic and local anaesthetic properties. Oxybutynin possesses one fifth of the anticholinergic activity of atropine, but has four to ten times the antispasmodic activity when tested on rabbit detrusor muscle.

Oxybutynin chloride has no effect at skeletal neuromuscular junctions or autonomic ganglia.

In patients with uninhibited neurogenic and reflex neurogenic bladder conditions, cystometric studies have demonstrated that oxybutynin chloride increases bladder capacity, diminishes the frequency of uninhibited contractions of the detrusor muscle and delays the initial desire to void. Oxybutynin chloride thus decreases urgency and the frequency of both incontinent episodes and voluntary urination. These effects are more consistently improved in patients with uninhibited neurogenic bladder. The onset of action is approximately one hour after an oral dose and its duration is 6-10 hours.

5.2 Pharmacokinetic properties

Oxybutynin chloride is rapidly absorbed from all parts of the gastrointestinal tract except the stomach, and peak plasma levels are attained within one hour of oral administration. The absolute bioavailability of orally administered oxybutynin chloride is about 6%. Oxybutynin distributes readily in the body compartments and there is no evidence of accumulation from multiple dosing.

Oxybutynin chloride undergoes significant first pass metabolism. Very little unchanged medicine or metabolites are detected in the urine suggesting the importance of biliary excretion. Glucuronide conjugation, de-ethylation, ester hydrolysis, and hydroxylation at the 3' and 4' sites on the cyclohexyl ring have been identified as possible metabolic pathways with phenylcyclohexyl glycolic acid and N-desethyloxybutynin being the two known metabolites in man. Phenylcyclohexyl glycolic acid is pharmacologically inactive and is the major metabolite while N-desethyloxybutynin has similar pharmacological activity to oxybutynin chloride. Desethyloxybutynin and oxybutynin N-oxide are the metabolites found in rats. No metabolite activity is known for either of these metabolites and oxybutynin N-oxide is unstable. Oxybutynin N-oxide does not appear to be present in man. Oxybutynin chloride does not appear to have enzyme-inducing properties.

Oxybutynin is eliminated from the plasma with a half-life of less than 2 hours.

Studies have shown oxybutynin chloride to be rapidly absorbed in the elderly with maximal plasma levels being reached in less than one hour. Plasma levels then decreased biexponentially with an elimination half-life of about 2.5 hours.

After repeated administration there was a tendency towards an increase in AUC and elimination half-life. Because it is primarily metabolised in the liver its use in hepatic impairment should be carefully monitored.

5.3 Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Apo-Oxybutynin 5mg tablets contains the following excipients:

- FD&C Blue No.1 (Brilliant Blue FCF, C.I. 42090, E133)
- Lactose monohydrate

- Magnesium Stearate
- Microcrystalline cellulose.

Apo-Oxybutynin 5mg/5ml syrup contains the following excipients:
- FD&C Green No.3 (Fast green FCF, C.I. 42053, E143)
- Artificial Berry Flavour
- Citric acid monohydrate
- Glycerol (Glycerine)
- Purified water
- Sodium citrate dehydrate
- Sorbitol
- Sucrose
- Methyl paraben (Methyl hydroxybenzoate)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Apo-Oxybutynin 5mg tablet has a shelf life of 24 months from the date of manufacture
Apo-Oxybutynin 5mg/5ml syrup has a shelf life of 36 months from the date of manufacture

6.4 Special Precautions

Store Apo-Oxybutynin 5mg tablets at or below 30°C.
Store Apo-Oxybutynin 5mg/5ml syrup between 15-25°C.
Protect from heat, light and moisture. Keep the container tightly closed.

6.5 Nature and contents of container

APO-OXYBUTYNIN 5mg: HDPE bottles of 100 or 500 tablets
APO-OXYBUTYNIN 5mg/5ml: Plastic amber PET round bottle with a child-resistant cap in pack size of 473ml.
Not all pack sizes maybe marketed.

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Apotex NZ Ltd.
32 Hillside Road
Glenfield

AUCKLAND 0627
Telephone: (09) 444 2073
Fax: (09) 444 2951
E-mail: NZcustomerservice@apotex.com

9. DATE OF FIRST APPROVAL

Apo-Oxybutynin 5mg tablets: 09 April 1998
Apo-Oxybutynin syrup 5mg/5ml: 29 July 1999

10. DATE OF REVISION OF THE TEXT

19 March 2018

Summary Table of Changes

Section changed	Summary of new information
Whole data sheet	Reformatted as per Medsafe new data sheet