Presentation
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.

Uses

Actions
Oxybutynin chloride is a tertiary amine anticholinergic agent which exerts an antimuscarinic action 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.

Pharmacokinetics
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 phenylcyclohexylglycolic acid and N-desethyl-oxybutynin being the two known metabolites in man. Phenylcyclohexylglycolic acid is pharmacologically inactive and is the major metabolite while N-desethyl-oxybutynin has similar pharmacological activity to oxybutynin chloride. Desethyl oxybutynin 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.
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.

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

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.

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.

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

Warnings and Precautions
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.

Please refer to Medsafe website (www.medsafe.govt.nz) for the most recent datasheet
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, 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.

**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.

**Use in Pregnancy and Lactation**

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.

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.

**Adverse Effects**

**Cardiac disorders:**
Palpitations, tachycardia, chest pains

**Vascular disorders:**
Flushing which may be more marked in children, syncope

**Skin and subcutaneous tissue disorders**
Dry skin, decreased sweating, rash, urticaria, angioedema

**Gastrointestinal-disorders:**
Constipation, decreased gastrointestinal motility, dry mouth, nausea, anorexia, metallic taste, diarrhoea, vomiting, dysphagia, gastrooesophageal reflux disease

**Renal and urinary disorders:**
Urinary retention, difficulty in micturition

**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.

Other:
Impotence, suppression of lactation, oedema, allergic reactions

Interactions
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.

Overdosage

Symptoms:
Overdosage 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:
Overdosage 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 catherisation.

Paralysis of the respiratory muscles may require artificial respiration.

Pharmaceutical Precautions
Tablets: Store below 30°C.
Syrup: Store between 15-25°C.
Protect from heat, light and moisture. Keep container tightly closed.
APO-OXYBUTYNIN

Oxybutynin chloride 5mg tablets and 5mg/5ml syrup

Medicine Classification
Prescription only medicine.

Package Quantities
APO-OXYBUTYNIN 5mg tablets:
Bottles of 100 and 500 tablets

APO-OXYBUTYNIN 5mg/5mL syrup:
Bottles containing 473mL syrup.

Further Information
Tablets contain lactose and FD&C Blue No. 1.

Syrup contains sucrose, sorbitol, methyl paraben, FD&C Green No. 3 and flavour.

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Please refer to Medsafe website (www.medsafe.govt.nz) for the most recent datasheet