



New Zealand Data Sheet

APO-OXYBUTYNIN

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

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 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. 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.

Indications

Oxybutynin chloride is primarily indicated 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 complicating ulcerative colitis
- myasthenia gravis
- narrow angle glaucoma
- paralytic ileus
- partial or complete obstruction of the gastrointestinal tract
- severe colitis

Warnings and Precautions

Diarrhoea may be an early symptom of incomplete intestinal obstruction especially in patients with ileostomy or colostomy, and in this instance treatment with oxybutynin chloride would be inappropriate and possibly harmful.

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.

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 oesphagitis, since this condition may be aggravated by anticholinergic medicines.

Oxybutynin chloride may invoke photosensitivity in some individuals.

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

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

Cardiovascular:

Palpitations, tachycardia, vasodilation, chest pains, syncope

Dermatological:

Decreased sweating, rash, urticaria, flushing

Gastrointestinal / genitourinary:

Constipation, decreased gastrointestinal motility, dry mouth, nausea, anorexia, metallic taste, urinary hesitance and retention

Nervous System:

Asthenia, dizziness, drowsiness, hallucinations, insomnia, restlessness.

Ophthalmic:

Amblyopia, cycloplegia, decreased lacrimation, mydriasis

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.

Oxybutynin chloride may also enhance the effects of alcohol.

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

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 0.5 to 2 mg repeated as necessary but not exceeding 5 mg. Fever responds to symptomatic treatment e.g. alcohol sponging and ice packs. Excitement may be treated with sodium thiopental 2% solution given slowly intravenously or chloral hydrate 100-200mL of a 2% solution by rectal infusion. Tachycardia may be treated with propranolol and urinary retention with catheterisation. 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.

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.

Name and Address

APOTEX NZ Ltd
32 Hillside Road
Glenfield
Private Bag 102995
North Shore Mail Centre
Auckland
Tel: (09) 444 2073
Fax: (09) 444 2951

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