NEW ZEALAND DATA SHEET

1. OXYBUTYNIN 5 mg tablets

Oxybutynin 5 mg tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxybutynin hydrochloride 5 mg

Excipient with known effect:
Lactose monohydrate: 106.5 mg in each tablet

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Tablets

White, round tablets, scored on both sides and marked “OBC5” on one side.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxybutynin hydrochloride 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.

Oxybutynin is not recommended for children under 5 years.

Method of administration

Oxybutynin is intended to be administered orally.

Maximum tolerated Daily Dose

The maximum daily dose is 20mg.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1.
- Angle-closure glaucoma or any other condition associated with decreased aqueous outflow (e.g. narrow anterior chamber angles)
- Obstructive uropathy (e.g. prostatic hypertrophy or urethrostenosis)
- Obstruction of the gastro-intestinal tract, ileus, inflammatory colonic ulcers
- Intestinal atony
- Severe dilatation of the colon (toxic megacolon)
- Myasthenia gravis

Use in children

Oxybutynin is not intended for use in children under 5 years of age.

4.4 Special warnings and precautions for use

Anticholinergics should be used with caution in elderly patients due to the risk of cognitive impairment.

Caution should be exercised in the frail elderly patients and children because these may show a more sensitive response to oxybutynin. Elderly patients and children, therefore, may require lower dosages.

Caution should be exercised in patients with autonomic neuropathy (such as those with Parkinson's disease), hiatus hernia with gastrooesophageal reflux disease or any other severe motility disorder of the gastro-intestinal tract.

Anticholinergic medicines should be used with caution in patients who have hiatus hernia/gastro-oesophageal reflux and/or who are concurrently taking medicines (such as bisphosphonates) that can cause or exacerbate oesophagitis.

Gastrointestinal disorders:
Anticholinergic medicines may decrease gastrointestinal motility and should be used with caution in patients with gastrointestinal obstructive disorders, intestinal atony and ulcerative colitis.

Caution should also be exercised in patients with hepatic and/or renal impairment, especially in those with severe impairment, as no pharmacokinetic data are available on these patient groups. Dosage reduction may be necessary.

Oxybutynin hydrochloride may exacerbate the symptoms of hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, tachycardia, hypertension, cognitive disorders and symptoms of prostatic hypertrophy.

Anticholinergic CNS effects (e.g. hallucinations, agitation, confusion, somnolence) have been reported; monitoring recommended especially in first few months after initiating therapy or increasing the dose; consider discontinuing therapy or reducing the dose if anticholinergic CNS effects develop.

Caution should be exercised in patients with fever or when oxybutynin hydrochloride is administered in the presence of high environmental temperature because decreased sweating (a side effect of oxybutynin hydrochloride) may result in heat stroke.

Oxybutynin may result in the development of dental caries, periodontal disease, thrush and discomfort as a consequence of reduction or inhibition of salivation.

Urogenital tract infection occurring during oxybutynin therapy requires institution of appropriate antibacterial therapy.

As oxybutynin may trigger angle-closure glaucoma, visual acuity and intraocular pressure should be monitored periodically during therapy. Patients should be advised to seek advice immediately if they are aware of a sudden loss of visual acuity or ocular pain.

Oxybutynin hydrochloride tablets should not be used to treat stress or stress urinary incontinence.

Caution should be exercised in patients with frequency of micturition or nocturia due to cardiac or renal insufficiency.

In patients with Parkinson disease and/or pre-existing cognitive impairment, oxybutynin may trigger neuropsychiatric side effects.

Oxybutynin 5 mg tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

<u>Paediatric population</u>

Oxybutynin hydrochloride is not recommended for use in children below age 5 years due to insufficient data on safety and efficacy.

There is limited evidence supporting the use of oxybutynin in children with monosymptomatic nocturnal enuresis (not related to detrusor overactivity).

In children over 5 years of age, oxybutynin hydrochloride should be used with caution as they may be more sensitive to the effects of the product, particularly the CNS and psychiatric adverse reactions.

4.5 Interaction with other medicines and other forms of interaction

Care should be taken if other anticholinergic agents are used together with oxybutynin, as a potentiation of anticholinergic effects may occur. The anticholinergic activity of oxybutynin is increased by concurrent use of other anticholinergics or medicines with anticholinergic activity, such as:

- amantadine and other antiparkinsonian medicines (e.g. biperiden, levodopa), antihistamines, antipsychotics (e.g. phenothiazines, butyrophenones, clozapine)
- quinidine
- digitalis
- tricyclic antidepressants
- atropine and related compounds like atropinic antispasmodics
- dipyridamole

By reducing gastro-intestinal motility, oxybutynin may alter the absorption of other medicines.

As oxybutynin is metabolised by cytochrome P 450 isoenzyme CYP 3A4, interactions with medicines that inhibit this isoenzyme cannot be ruled out. Concomitant administration with a CYP 3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure. This should be borne in mind when using azole antifungals (e.g. ketoconazole) or macrolide antibiotics (e.g. erythromycin) concurrently with oxybutynin. Itraconazole has been demonstrated to inhibit oxybutynin metabolism. This led to the doubling of the oxybutynin plasma levels, but only to a 10 % increase for the active metabolite. Because the metabolite is responsible for about 90 % of the antimuscarinic activity, the changes appear to be of minor clinical significance.

The effects of prokinetics (e.g. cisapride, metoclopramide, domperidone) on gastro-intestinal motility may be decreased by the concomitant treatment with oxybutynin.

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

Patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin (see Section 4.7).

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no clinical practice experience with use of oxybutynin in pregnant women. Animal studies during the reproduction process revealed toxic effects on the offspring (see Section 5.3).

The potential risk for humans is unknown. Therefore, oxybutynin must not be used in the first trimester of pregnancy and should be used in the second and third trimesters only if clearly needed.

Breastfeeding

As oxybutynin is excreted in breast milk, it must not be used during lactation.

Fertility

No information is available on oxybutynin's effect on fertility.

4.7 Effects on ability to drive and use machines

Even when used as directed, this medicine may alter reaction times (may cause drowsiness) and visual acuity (may cause blurred vision) to such an extent that the ability to actively participate in road traffic, operate machines, perform hazardous work or work without a firm support is impaired, especially at the start of therapy, when increasing the dose, switching medications or using alcohol at the same time.

4.8 Undesirable effects

The side-effects of oxybutynin are mainly due to its anticholinergic activity. Dose reduction may reduce the incidence of these side-effects.

Side effects	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Very rare (< 1/10,000)	Not known (cannot be estimated from the available data)
Infections and infestations						urinary tract infection
Immune system disorders						hypersensitivity
Psychiatric disorders		confusional state	Disorientation, passivity	concentration and behavioural disorders		agitation, anxiety, hallucinations, nightmares, paranoia, cognitive disorders in older people, symptoms of depression, dependence (in patients with history of medicine or substance abuse)
Nervous system disorders	dizziness, headache, somnolence	vertigo	fatigue		convulsions	cognitive disorder
Eye disorders		blurred vision, mydriasis, dry eyes	light sensitivity		glaucoma	ocular hypertension
Cardiac disorders			tachycardia	palpitation, arrhythmia		
Vascular disorders		flushing				

Side effects	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Very rare (< 1/10,000)	Not known (cannot be estimated from the available data)
Gastrointestinal disorders	constipation, nausea, dry mouth	diarrhoea, vomiting, abdominal discomfort, dyspepsia	anorexia, dysphagia	heartburn		gastroesophageal reflux disease, pseudo-obstruction in patients at risk (older people or patients with constipation and treated with other medicines that decrease intestinal motility)
Skin and subcutaneous tissue disorders	dry skin	skin redness			angiooedema, allergic skin reactions (erythema, urticaria), photosensitivity	hypohidrosis,
Renal and urinary disorders		problems with micturition, urinary retention			impotence	
General disorders and administration site conditions					heat stroke	

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

4.9 Overdose

Symptoms

Overdosage with oxybutynin is characterised by increased anticholinergic (side) effects. Patients may experience symptoms of (exaggerated) responses of the central nervous system (e.g. ataxia, confusion, nervous restlessness, excitement, hallucinations to the point of psychotic behaviour) and circulatory system (e.g. flushing, fall in blood pressure, circulatory failure, tachycardia and dizziness), as well as dilatation of the pupils (mydriasis), fever, hot, red skin, dry mucous membranes, respiratory failure, paralysis and coma.

Management

In the event of overdose, and if possible, immediate gastric lavage should be performed and activated charcoal to prevent absorption should be given.

Adult dosage:

Give 0.5-2 mg of physostigmine by slow intravenous administration. Repeat after 5 minutes if necessary up to a maximum total dose of 5 mg.

Paediatric dosage:

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

Diazepam 10 mg i.v. may be injected in case of pronounced nervous restlessness or agitation. Tachycardia can be treated with intravenous propranolol, and urinary retention can be managed by catheterisation of the urinary bladder. Should the muscle relaxant effect progress to respiratory paralysis, mechanical ventilation is indicated.

Fever should be treated symptomatically.

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

ATC code
G04B D04

Pharmacotherapeutic group
Anticholinergic and spasmolytic

Oxybutynin hydrochloride (4-diethylamino-2-butynyl-2-phenyl-2-cyclohexylglycolate hydrochloride) - a synthetic tertiary amine - is an anticholinergic agent with additional antispasmodic activity on bladder smooth muscle. Oxybutynin exhibits about one fifth of the anticholinergic activity of atropine on the rabbit detrusor muscle. Oxybutynin increases bladder capacity, reduces the frequency of

uninhibited contractions of the detrusor muscle and delays the initial desire to void. Oxybutynin thus relieves the symptoms of bladder instability (urinary incontinence).

This medicine has been given a provisional consent under Section 23 of the Act to address an urgent shortage in the market with the following condition: the medicine may only be marketed or distributed when no other oxybutynin hydrochloride tablet medicine with consent under section 20 of the Medicines Act 1981 is available in the New Zealand market, or to meet PHARMAC supply obligations.

5.2 Pharmacokinetic properties

Oxybutynin is absorbed rapidly, attaining peak plasma concentrations after 30-90 minutes. Large inter-individual variations in plasma concentrations are seen. Concurrent ingestion of food, especially of a meal rich in fat, delays oxybutynin absorption, but increases overall bioavailability.

The duration of action of oxybutynin hydrochloride is 6-10 hours. Oxybutynin is subject to extensive first pass metabolism. Oxybutynin hydrochloride is metabolised via cytochrome P 3A4. Differences in individual predisposition may result in significant interindividual variations in oxybutynin metabolism.

The bioavailability of oral oxybutynin hydrochloride is 2-11 %. Main metabolites are inactive metabolite 2,2-phenylcyclohexylglycolic acid and active metabolite N-desethyloxybutynin, which has similar pharmacological activity to oxybutynin.

Oxybutynin elimination is biphasic. N-Desethyloxybutynin elimination is monophasic. Mean elimination half-life is 2 hours. In elderly patients, especially the frail elderly, the bioavailability (2-4 times higher AUC after multiple dosing) and half-life (3-5 hours) are increased. Urinary excretion has been established as less than 0.02 % of an administered dose. Oxybutynin is 83-85 % plasma albumin bound.

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans based on conventional studies of general toxicity, genotoxicity and carcinogenicity beyond the information included in other sections of the Data Sheet.

Embryofoetal studies in pregnant rats showed malformed hearts. Higher dosages additionally were associated with extra thoracolumbar ribs and increased neonatal mortality. Reproductive toxicity occurred only with concurrent general maternal toxicity. In the absence of exposure data, the relevance of these observations cannot be assessed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, lactose monohydrate, magnesium stearate, talc.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25°C. Store in the original package.

6.5 Nature and contents of container

PVC/aluminium foil blister strip

Pack size: 100 tablets

6.6 Special precautions for disposal

No special requirements.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

Alchemy Health Limited
120 Ngapuhi Road
Remuera
Auckland 1050
NEW ZEALAND

Medical enquiries: 0508 ALCHEMY (0508 252436)

9. DATE OF FIRST APPROVAL

6 July 2023

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6 July 2023