AUSTRALIAN PRODUCT INFORMATION – DITROPAN (OXYBUTYNIN HYDROCHLORIDE)

1 NAME OF THE MEDICINE

oxybutynin hydrochloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains oxybutynin hydrochloride 5 mg.

Excipients with known effect:

Sugars as lactose

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Light blue, round, single scored uncoated tablet, blank on both sides.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Treatment of detrusor over-activity where conservative measures have failed.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults: The usual dose is one 5 mg tablet two to three times a day. The maximum recommended dose is one 5 mg tablet four times a day.

In the frail and elderly patient it is advisable to initiate treatment at a low dose and, if necessary to increase the dose carefully according to tolerance and response. Initial doses for geriatric patients of 2.5 mg twice daily have been reported in the literature.

Children over 5 years of age: The usual dose is one 5 mg tablet twice a day. The maximum recommended dose is one 5 mg tablet three times a day.

4.3 CONTRAINDICATIONS

Ditropan is contraindicated in patients with increased intraocular pressure associated with angle closure (glaucoma) or shallow anterior chamber since anticholinergic drugs may

aggravate this condition. It is also contraindicated in partial or complete obstruction of the gastrointestinal tract, paralytic ileus, intestinal atony of the elderly or debilitated patient, megacolon, toxic megacolon complicating ulcerative colitis, severe colitis, and myasthenia gravis. It is contraindicated in patients with obstructive uropathy and in patients with unstable cardiovascular status in acute haemorrhage.

Ditropan is contraindicated in patients who have demonstrated hypersensitivity to the product.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Avoid dosage in high environmental temperatures and excessive exercise in high temperatures since oxybutynin hydrochloride administered under these conditions can cause heat prostration (fever and heat stroke due to decreased sweating).

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

Anticholinergic CNS effects (such as hallucinations, agitation, confusion, sleep disturbance) have been reported. Monitoring is recommended, particularly during the first few months of treatment or after increasing the dose. If anticholinergic CNS effects develop, termination or dose reduction may be considered.

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

Oxybutynin may produce drowsiness or blurred vision. The patient should be cautioned regarding activities requiring mental alertness, such as operating a motor vehicle or other machinery or performing hazardous work while taking this drug.

Alcohol or other sedative drugs may enhance the drowsiness caused by Ditropan.

Pretreatment examinations should normally include cystometry, and other appropriate diagnostic procedures. Cystometry should be repeated at appropriate intervals to evaluate response to therapy. The appropriate antibiotic therapy should be instituted in the presence of infection.

Use with caution in patients with Parkinson’s disease as they are at greater risk of adverse reactions. Use with caution in patients with autonomic neuropathy. Administration of oxybutynin in large doses to patients with ulcerative colitis may suppress intestinal motility to the point of producing a paralytic ileus and precipitate or aggravate toxic megacolon, a serious complication of the disease.

Oxybutynin may aggravate cognitive disorders, symptoms of prostatic hypertrophy and tachycardia (thus be cautious in case of hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension).

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

Since Ditropan 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 dependence has been observed in patients with a history of substance or drug abuse.

Since Ditropan may reduce salivary secretions which could result in dental caries, periodontitis or oral candidiasis.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Use in hepatic impairment

Use with caution in patients with hepatic disease.

Use in renal impairment

Use with caution in patients with renal disease.

Use in the elderly

Oxybutynin should be used with caution and only where there is evidence of detrusor overactivity in the elderly.

Paediatric use

Ditropan should be used with caution in children as they may be more sensitive to the effects of the product. Oxybutynin should not be used in children with enuresis without definitive evidence of detrusor overactivity. As there is insufficient clinical data for children under age five, Ditropan is not recommended for this age group. The safety and efficacy of Ditropan administration have been demonstrated for children five years of age and older (see Section 4.2 Dose and method of administration).

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The anticholinergic effect of Ditropan is enhanced by its concomitant use with other agents with anticholinergic properties and care should be taken if Ditropan is used concurrently with such drugs. These include the phenothiazines, butyrophenones, L-dopa, digitalis, tricyclic antidepressants, amantadine, scopolamine and some of the antihistamines.

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

Oxybutynin, as an anticholinergic agent, may antagonise the effect of prokinetic therapies.

Oxybutynin is metabolised by cytochrome P450 isoenzyme CYP3A4. Concomitant administration with a CYP3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure.

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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Category B1

Animal studies showed no clear evidence of teratogenicity or other embryotoxic effects in rats and rabbits at oral doses up to 160 and 100mg/kg/day respectively. However, the incidence of abortion was slightly increased at the highest dose level in rabbits.

There are no adequate data from animal studies with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development.

Embryo/foetal studies in pregnant rats showed malformed hearts, and higher doses were associated with extra thoracolumbar ribs and increased neonatal toxicity. The relevance of these observations were difficult to access.

The safety of oxybutynin hydrochloride in women who are or who may become pregnant has not been established, it should be given only when the potential benefits outweigh the possible hazards.

Use in lactation

There is some evidence from animal studies that oxybutynin or its metabolites are excreted in milk. Ditropan is not recommended for administration to a nursing woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Oxybutynin may produce drowsiness or blurred vision. The patient should be cautioned regarding activities requiring mental alertness, such as operating a motor vehicle or other machinery or performing hazardous work while taking this drug.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Following administration of Ditropan, the symptoms that can be associated with the use of other anticholinergic drugs may occur.

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).

Musculoskeletal and Connective Tissue Disorders

Not known: Muscle disorders manifested as muscle weakness, myalgia and/ or muscle spasms

Respiratory, Thoracic, and Mediastinal Disorders

Not known: Epistaxis

Cardiac Disorders

Not known: palpitations, cardiac arrhythmia, tachycardia, vasodilation

Skin and Subcutaneous Tissue Disorders

Very common: dry skin

Common: flushing

Not known: angio-oedema, rash, urticaria, decreased sweating

Infections and Infestations

Not known: Urinary tract infection

Immune System Disorders

Not known: Hypersensitivity

Gastrointestinal Disorders

Very common: constipation, nausea, dry mouth

Common: diarrhoea, vomiting

Uncommon: abdominal discomfort, anorexia, dysphagia, decreased appetite

Not known: gastroesophageal reflux, pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other drugs that decrease intestinal motility), decreased gastrointestinal motility

Renal and Urinary Disorders

Common: Urinary hesitance and retention

Nervous System Disorders

Very common: dizziness, headache, drowsiness, confusion

Not known: cognitive disorders in elderly, convulsions, agitation, nightmares, anxiety, paranoia, symptoms of depression, hallucinations, asthenia, insomnia, restlessness, dependence to oxybutynin (in patients with history of drug or substance abuse)

Eye Disorders

Very common: blurred vision

Common: dry eyes

Not known: onset of narrow-angle glaucoma, mydriasis, intraocular hypertension

amblyopia, cycloplegia, decreased lacrimation

Injury, Poisoning and Procedural Complications

Not known: heat stroke

Other

Impotence, suppression of lactation

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms

The symptoms of overdosage progress from an intensification of the usual side effects of CNS disturbances (from restlessness and excitement to psychotic behaviour) and circulatory changes (flushing, fall in blood pressure, circulatory failure) to respiratory failure, paralysis and coma.

Treatment

Measures to be taken are immediate emptying of the stomach (emesis is contraindicated if patient is comatose, drowsy, convulsing or psychotic). Consider injection of physostigmine

to reverse symptoms of anticholinergic intoxication. Adult doses are 0.5 to 2 mg I.M. or I.V. repeated as necessary up to a total of 5 mg. I.V. administration should be at a slow, controlled rate of no more than 1 mg/minute. For children the dose of physostigmine is 0.02 mg/kg at no more than 0.5 mg/minute - not to exceed 2 mg. Elevated temperature may be treated symptomatically (alcohol sponging, ice packs).

Excessive excitement may require management, for example with sodium thiopental 2% solution given slowly via I.V or Diazepam 10 mg by I.V. Tachycardia may be treated with intravenous propranolol and urinary retention managed by bladder catheterisation. In the event of progression of the curare-like effect to paralysis of the respiratory muscles, artificial respiration is required.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Drugs for urinary frequency and incontinence, ATC code: G04BD04.

Mechanism of action

Oxybutynin hydrochloride exerts a direct antispasmodic effect on smooth muscle and inhibits the muscarinic action of acetylcholine on smooth muscle. Oxybutynin hydrochloride exhibits four to ten times the antispasmodic potency of atropine, but only one fifth of the anticholinergic activity of atropine on the rabbit detrusor muscle. No blocking effects occur at skeletal neuromuscular junctions or autonomic ganglia (antinicotinic effects).

Ditropan relaxes bladder smooth muscle. In patients with conditions characterised by involuntary bladder contractions, cystometric studies have demonstrated that Ditropan increases bladder (vesical) capacity, diminishes the frequency of uninhibited contractions of the detrusor muscle, and delays the initial desire to void. Ditropan thus decreases urgency and the frequency of both incontinent episodes and voluntary urination.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Oxybutynin hydrochloride is readily absorbed (peak plasma concentration in approx. 1 hour) and rapidly eliminated (plasma half life about 2 hours). Absolute bioavailability after oral dosing has been reported to be about 6%. Oxybutynin hydrochloride undergoes significant first pass metabolism. Very little unchanged drug or metabolites are detected in the urine suggesting the importance of biliary excretion.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Calcium stearate

Microcrystalline cellulose

Lactose

Brilliant blue FCF aluminium lake.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Protect from light.

Store below 25˚C.

6.5 NATURE AND CONTENTS OF CONTAINER

Bottles containing 30, 90 and 100◆ tablets.

◆Marketed pack

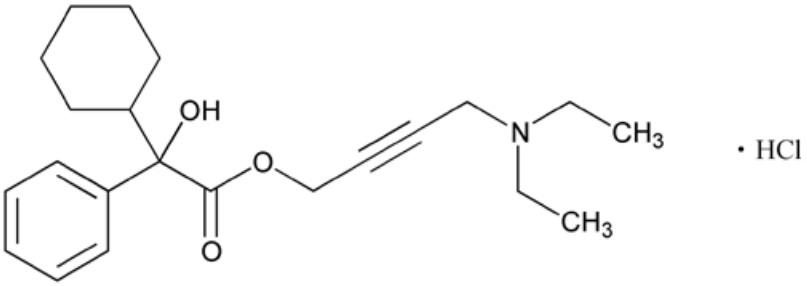
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Oxybutynin hydrochloride is 4-diethylamino-2-butynyl phenylcyclohexylglycolate hydrochloride. It is a white crystalline solid (MW 393.9), which is readily soluble in water and acids, but relatively insoluble in alkalis.

Chemical structure



CAS number

1508-65-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

sanofi-aventis australia pty ltd
12-24 Talavera Road
Macquarie Park NSW 2113
Australia
Toll Free Number (medical information): 1800 818 806
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

30 May 1994

10 DATE OF REVISION

22 July 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.4	Added new warnings to align with mandatory text from the company core data sheet.
4.5	Added new interactions to align with mandatory text from the company core data sheet.
4.8	Added new adverse effects for epistaxis and muscle disorders based on new safety signals. Added new adverse effects to align with mandatory text from the company core data sheet. Editorial changes.