SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ditropan tablets 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg oxybutynin hydrochloride as the active ingredient.

Excipients with known effect: lactose, sodium
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ditropan tablets 5mg are pale blue circular tablets with a 8.0 mm nominal diameter, with a centre breakline on one side, and marked OXB5 on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ditropan is indicated for the symptomatic treatment of urinary incontinence, urgency, and frequency in the unstable bladder, whether due to neurogenic bladder disorders (detrusor hyperreflexia) in conditions such as multiple sclerosis and spina bifida, or to idiopathic detrusor instability (motor urge incontinence).

Paediatric population
Ditropan is indicated in children of 5 years of age or older for:
- Urinary incontinence, urgency, and frequency in unstable bladder conditions due to idiopathic overactive bladder or neurogenic bladder disorders (detrusor overactivity).
- Nocturnal enuresis associated with detrusor overactivity, in conjunction with non-drug therapy, when other treatment has failed.

4.2 Posology and method of administration

Posology

The dosage should be determined individually.

Adults
The usual dose is 5 mg two or three times a day. This may be increased to a maximum of 5 mg four times a day (maximum dose 20 mg oxybutynin hydrochloride per day) to obtain a clinical response provided that the side effects are tolerated.

Elderly
The elimination half-life is increased in the elderly. Therefore, a dose of 2.5 mg twice a day, particularly if the patient is frail, is likely to be adequate. This dose may be increased to 5 mg two times a day to obtain a clinical response provided the side effects are well tolerated.

Paediatric population
Children (under 5 years of age)
Ditropan is not recommended in children under 5 years of age due to the absence of data.

Children (5 years of age or older)
Neurogenic bladder instability: the usual dose is 2.5 mg twice a day. This dose may be increased to 5 mg two or three times a day to obtain a clinical response provided the side effects are well tolerated. Nocturnal enuresis: the usual dose is 2.5 mg twice a day. This dose may be increased to 5 mg two or three times a day to obtain a clinical response provided the side effects are tolerated. The last dose should be given before bedtime.

Method of administration
For oral use.

The tablets taste unpleasant and should therefore be swallowed with a glass of water.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the other excipients listed in section 6.1
- Myasthenia gravis
- Narrow-angle glaucoma or shallow anterior chamber
- Gastrointestinal obstructive disorders including paralytic ileus, intestinal atony
- Toxic megacolon
- Severe ulcerative colitis
- Bladder outflow obstruction where urinary retention may be precipitated

4.4 Special warnings and precautions for use

- Ditropan should be used with caution in patients with Parkinson's disease who are at greater risk of occurrence of adverse reactions to the product and in patients with autonomic neuropathy (such as those with Parkinson's disease), severe gastro-intestinal motility disorders, hepatic, or renal impairment.
- Anticholinergic medicinal products may decrease gastrointestinal motility and should be used with caution in patients with gastrointestinal obstructive disorders, intestinal atony, and ulcerative colitis.
- Ditropan may aggravate cognitive disorders, symptoms of prostatic hypertrophy and tachycardia (thus be cautious in case of hyperthyroidism, congestive heart failure, cardiac arrhythmia, coronary heart disease, hypertension).

- Anticholinergic CNS effects (such as hallucinations, agitation, confusion, somnolence) have been reported. Monitoring recommended, particularly in first few months after initiating therapy or increasing the dose. If anticholinergic CNS effects develop, termination of treatment or dose reduction may be considered.
- 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.
- Ditropan may reduce salivary secretions which could result in dental caries, parodontosis or oral candidiasis.
- 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.
- When Ditropan is used in high environmental temperatures, this can cause heat prostration due to decreased sweating.

Elderly
Anticholinergic medicinal products should be used with caution in elderly patients due to the risk of cognitive impairment. They also have a higher risk of occurrence of adverse reactions to the product.

Paediatric population
The use of Ditropan in children under 5 years of age is not recommended. It has not been established whether Ditropan can be safely used in this age group.
There is limited evidence supporting the use of Ditropan in children with monosymptomatic nocturnal enuresis (not related to detrusor overactivity).

In children of 5 years of age or older, Ditropan 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.

Warnings on excipients
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken if other anticholinergic agents are administered together with Ditropan, as potentiation of anticholinergic effects could occur.

The anticholinergic activity of oxybutynin is increased by concurrent use of other anticholinergics or medicinal products with anticholinergic activity, such as amantadine and other anticholinergic antiparkinsonian medicinal products (e.g. biperiden, levodopa), antihistamines, antipsychotics (e.g. phenothiazines, butyrophenones, clozapine), quinidine, digitalis, tricyclic antidepressants, atropine and related compounds like atropinic antispasmodics and dipyridamole.

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

Oxybutynin is metabolised by cytochrome P 450 isoenzyme CYP 3A4. Concomitant administration with a CYP3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure.

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

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 are no adequate data from the use of oxybutynin in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition, or postnatal development (see section 5.3). The potential risk for humans is unknown. Ditropan should not be used during pregnancy unless clearly necessary.

Breast-feeding

- When oxybutynin is used during lactation, a small amount is excreted in mother's milk. Use of Ditropan during breast feeding is therefore not recommended.

4.7 Effects on ability to drive and use machines

Ditropan may cause drowsiness or blurred vision. Patients should be cautioned regarding activities requiring mental alertness such as driving, operating machinery, or performing hazardous work while taking this medicine.

4.8 Undesirable effects

Like all medicines, oxybutynin can cause undesirable effects, although not everybody gets them. The frequency of possible undesirable effects listed below are currently defined as:

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).

ADVERSE REACTIONS REPORTED		
System Organ Class	**Frequency**	**Adverse Reaction (MedDRA Terms)**
Infections and Infestations	Not known	urinary tract infection
Immune System	Not known	hypersensitivity

ADVERSE REACTIONS REPORTED		
System Organ Class	**Frequency**	**Adverse Reaction (MedDRA Terms)**
Disorders		
Psychiatric Disorders	Common	confusional state
	Not known	agitation, anxiety, cognitive disorders in elderly, hallucinations, nightmares, paranoia, symptoms of depression, dependence to oxybutynin (in patients with history of drug or substance abuse)
Nervous System Disorders	Very common	dizziness, headache, somnolence
	Not known	cognitive disorders, convulsions, drowsiness, disorientation
Eye Disorders	Very common	vision blurred
	Common	dry eyes
	Not known	angle closure glaucoma, increased intraocular pressure, mydriasis
Cardiac Disorders	Common	palpitation
	Not known	arrhythmia, tachycardia
Vascular Disorders	Common	flushing (which may be more marked in children)
Respiratory, thoracic, and mediastinal disorders	Not known	epistaxis
Gastrointestinal Disorders	Very common	constipation, dry mouth, nausea
	Common	diarrhoea, vomiting
	Uncommon	abdominal discomfort, anorexia, decreased appetite, dysphagia
	Not known	gastroesophageal reflux, pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other

ADVERSE REACTIONS REPORTED		
System Organ Class	**Frequency**	**Adverse Reaction (MedDRA Terms)**
		drugs that decrease intestinal motility)
Skin and Subcutaneous Tissue Disorders	Very common	dry skin
	Not known	angioedema, hypohidrosis, rash, urticaria, photosensitivity
Musculoskeletal and connective tissue disorders	Not known	Muscle disorders manifested as muscle weakness, myalgia and/ or muscle spasms
Renal and Urinary Disorders	Common	urinary retention
	Not known	difficulty in micturition
Injury, Poisoning and Procedural Complications	Not known	heat stroke

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

Management
Measures to be taken are:
1) immediate gastric lavage
2) physostigmine by slow intravenous injection
   - *Adults:* 0.5 to 2.0 mg of physostigmine by slow intravenous administration. Repeat after 5 minutes, if necessary up to a maximum total dose of 5 mg.

   - *Paediatric population:* 30 micrograms/kg of physostigmine by slow intravenous administration. Repeat after 5 minutes, if necessary up to a maximum total dose of 2 mg.

Fever should be treated symptomatically with tepid sponging or ice packs.

In pronounced restlessness or excitation, diazepam 10 mg may be given by intravenous injection, tachycardia may be treated by intravenous injection of propranolol and urinary retention can be managed by bladder catheterisation.

In the event of progression of the curare-like effect to the paralysis of the respiratory muscles, mechanical ventilation will be required.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: genito urinary system and sex hormones - urologicals – drugs for urinary frequency and incontinence, ATC code: G04BD04

Mechanism of action
Oxybutynin has both direct antispasmodic action on the smooth muscle of the bladder detrusor muscle as well as an anticholinergic action in blocking the muscarinic effects of acetylcholine on smooth muscle. These properties cause relaxation of the detrusor muscle of the bladder in patients with an unstable bladder. Ditropan increases bladder capacity and reduces the incidence of spontaneous contractions of the detrusor muscle.

5.2 Pharmacokinetic properties

Absorption
Oxybutynin is rapidly absorbed from the gastrointestinal tract, the peak plasma level is reached between 0.5 to 1 hour after administration.

Distribution
It is highly bound to plasma proteins.

Biotransformation
Oxybutynin undergoes extensive first-pass metabolism, particularly by the cytochrome P450 isoenzyme CYP3A4, and systemic oral bioavailability has been reported to be only 6%. N-desethyloxybutynin is an active metabolite.

Elimination
The half-life is biexponential, the first phase being about 40 minutes and the second about 2 – 3 hours. Oxybutynin and its metabolites are excreted in the faeces and urine. There is no evidence of accumulation. The elimination half-life may be increased in the elderly, particularly if they are frail.

3 PHARMACEUTICAL FORM

Tablets.

Ditropan tablets 5 mg are pale blue, circular, biconvex tablets with an 8.0 mm nominal diameter, with a centre break-line on one side and marked OXB5 on the reverse.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

lactose, cellulose, calcium stearate and indigo carmine (E132)

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

PVC/Aluminium blisters in cartons containing 6, 21 or 84 tablets.

Not all pack sizes may be marketed.

6.5 Nature and contents of container

PVC/Aluminium blisters in cartons containing 6, 21 or 84 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th December 2000

Date of latest renewal: 11th March 2005

7 MARKETING AUTHORISATION HOLDER

Neon Healthcare Ltd.
8 The Chase, John Tate Road,
Hertford,
SG13 7NN
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 45043/0036

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12th December 2000
Date of latest renewal: 11th March 2005

10 DATE OF REVISION OF THE TEXT

24/08/2023