**1.3.1.1 PACKAGE INSERT**

## SCHEDULING STATUS

S3

## PROPRIETARY NAME AND DOSAGE FORM

**DITROPAN®** Tablets

## COMPOSITION

Each tablet contains oxybutynin hydrochloride 5 mg.

*Excipients*

Indigo carmine aluminium lake (E132), microcrystalline cellulose, anhydrous lactose, calcium stearate.

Contains sugar (anhydrous lactose).

## PHARMACOLOGICAL CLASSIFICATION

A 5.4 Medicines affecting autonomic functions: cholinolytics (anticholinergics).

## PHARMACOLOGICAL ACTION

**Pharmacodynamic properties:**

Oxybutynin hydrochloride exerts a direct antispasmodic effect on smooth muscle and inhibits the muscarinic action of acetylcholine on smooth muscle.

In patients with uninhibited neurogenic and reflex neurogenic bladder, cystometric studies have demonstrated that oxybutynin hydrochloride increases bladder capacity, diminishes the frequency of uninhibited contractions of the detrusor muscle and delays the initial desire to void.

**Pharmacokinetic properties:**

Oxybutynin is poorly absorbed from the gastrointestinal tract. It is highly bound to plasma proteins, the peak plasma level in healthy young volunteers is reached between 0,5 and 1 hour after administration. The elimination phase is biexponential, with an elimination half-life of about 2-3 hours.

The elimination half-life is increased in the elderly, particularly if they are frail.

Oxybutynin and its metabolites are excreted in the feces and urine.

**INDICATIONS**

- DITROPAN tablets are indicated for the relief of symptoms associated with voiding in patients with uninhibited neurogenic and reflex neurogenic bladder, (i.e. urgency, frequency, urinary leakage, urge incontinence, dysuria).
- DITROPAN is indicated for spastic neurogenic bladder (and not hypotonic neurogenic bladder – see “CONTRAINDICATIONS”)
- Nocturnal enuresis.

**CONTRAINDICATIONS**

- hypersensitivity to oxybutynin or any component of DITROPAN
- narrow-angle glaucoma or shallow anterior chamber
- gastro-intestinal obstructive disorders, intestinal atony or paralytic ileus
- toxic megacolon
- severe ulcerative colitis
- myasthenia gravis
- patients with unstable cardio-vascular status in acute haemorrhage
- patients with bladder outflow obstruction where urinary retention may be precipitated, including prostate hypertrophy (see WARNINGS and SPECIALPRECAUTIONS)
- DITROPAN tablets are contraindicated in hypotonic neurogenic bladder
- DITROPAN tablets should not be given to pregnant women (see “HUMAN REPRODUCTION”)
- DITROPAN tablets are not recommended for children under 5 years of age
- DITROPAN tablets are contraindicated in patients with prostatic enlargement and should be used with caution in elderly men.

## WARNINGS AND SPECIAL PRECAUTIONS

DITROPAN tablets, when administered in the presence of high environmental temperature, can cause heat prostration (fever and heat stroke due to decreased sweating), especially in children. It should be used cautiously in patients with fever.

DITROPAN should be used with caution in the elderly, patients with Parkinson's disease and in children who are at greater risk of occurrence of side effects to DITROPAN, and in all patients with autonomic neuropathy, gastro-intestinal motility disorders, hepatic or renal impairment.

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

Administration of DITROPAN tablets to patients with ulcerative colitis may suppress intestinal motility producing a paralytic ileus and precipitate or aggravate "toxic megacolon", a serious complication of the disease.

DITROPAN tablets should be administered with caution to patients with hiatus hernia associated with reflux oesophagitis, since DITROPAN may aggravate this condition.

### Effects on ability to drive and use machines

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

### Lactose intolerance

DITROPAN contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## INTERACTIONS

- Care should be taken if other anticholinergic medicines are used together with DITROPAN, as a potentiation of anticholinergic effects may occur.
- Interactions have been reported with phenothiazines, butyrophenones, L-dopa, digitalis, tricyclic antidepressants, amantadine, atropine, scopolamine and the antihistamines. Care should be taken if oxybutynin is used concurrently with such medicines.
- By reducing gastric motility, DITROPAN may affect the absorption of other medicines.
- DITROPAN may antagonize the effect of prokinetic therapies.

## PREGNANCY AND LACTATION

**Pregnancy:**

The safety of DITROPAN administered to women who are or who may become pregnant has not been established. DITROPAN should not be used during pregnancy (see CONTRAINDICATIONS).

**Lactation:**

Breastfeeding while using DITROPAN is not recommended (see CONTRAINDICATIONS).

## DOSAGE AND DIRECTIONS FOR USE

Adults: The usual adult 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.

A dose of 5 mg twice daily should not be exceeded in elderly frail patients.

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

The use of DITROPAN in children under 5 years of age is not recommended.

Pre-treatment examination should include cystometry and other appropriate diagnostic procedures. Cystometry should be repeated at appropriate intervals to evaluate response to therapy. The appropriate antimicrobial therapy should be instituted in the presence of infection.

## SIDE EFFECTS

The following frequency rating has been used:

Very common: (>1/10); Common: (>1/100, <1/10); Uncommon: (>1/1000, <1/100); Rare: (>1/10 000, <1/1000); Very rare: (<1/10 000), including rare isolated cases.

The following side effects have been reported:

**Gastro-intestinal disorders:**

*Very common:* constipation, nausea, dry mouth

*Common:* diarrhoea, vomiting

*Uncommon:* abdominal discomfort, anorexia, dysphagia

**Psychiatric disorders:**

*Common:* confusional state

**Nervous system disorders:**

*Very common:* dizziness, headache, somnolence

**Eye disorders:**

*Very common:* blurred vision

*Common:* dry eyes

**Renal and urinary disorders:**

*Common:* Urinary retention.

**Skin and subcutaneous tissue disorders:**

*Very common:* dry skin

**Vascular disorders:**

*Common:* flushing.

**Post-marketing data:**

The frequencies of adverse effects found in post-marketing data are unknown.

**Gastro-intestinal disorders:**

gastroesophageal reflux, pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other drugs that decrease intestinal motility), thirst.

**Psychiatric disorders:**

agitation, anxiety, hallucinations, nightmares, paranoia, symptoms of depression, dependence to oxybutynin (in patients with history of drug or substance abuse).

**Nervous system disorders:**

cognitive disorders in elderly, convulsions, weakness, insomnia.

**Cardiac disorders:**

tachycardia, dysrhythmia.

**Eye disorders:**

angle closure glaucoma, intraocular hypertension, mydriasis, cycloplegia, photophobia.

**Skin and subcutaneous tissue disorders:**

angioedema, rash, urticaria, decreased sweating.

**Respiratory disorders:**

reduced bronchial secretion associated with the formation of mucus plugs may occur.

**Endocrine disorders:**

suppression of lactation.

**Reproductive system disorders:**

impotence.

**Injury, poisoning and procedural complications:**

heat stroke.

**Immune system disorders:**

hypersensitivity.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT**

**Signs and symptoms:**

The symptoms of overdosage with DITROPAN tablets progress from an intensification of the usual side effect of central nervous system disturbances (from restlessness, excitement and confusion) to psychotic behaviour, circulatory changes (flushing, fall in blood pressure, circulatory failure), respiratory failure, paralysis and coma. A rash may appear on the face and upper trunk.

**Management:**

Treatment is symptomatic and supportive.

1) Physostigmine may be used in cases with severe manifestations of overdose, and should not routinely be administered. Physostigmine by slow intravenous injection:
   Adults: 0,5 to 2,0 mg i.v. slowly, repeated if necessary, up to a maximum of 5 mg.
   Children: 30 µg/kg i.v. slowly, repeated if necessary, up to a maximum of 2 mg.

Fever should be treated symptomatically.

In pronounced restlessness or excitation, a benzodiazepine may be given by intravenous injection.

Tachycardia may be treated with intravenous beta-blockers and urinary retention managed by bladder catheterisation.

In the event of progression of curare-like effects of paralysis of the respiratory muscles, mechanical ventilation may be required.

## IDENTIFICATION

Light blue, round, biconvex, tablet with “OXB5” engraved on one side with scored line on reverse side.

## PRESENTATION

20 and 100 tablets packed in securitainers and blisters.

## STORAGE INSTRUCTIONS

Store at or below 25 °C.

Keep out of reach of children.

## REGISTRATION NUMBERS

L/5.4/104

## NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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## DATE OF PUBLICATION OF THE PACKAGE INSERT

Registration date: 18 October 1979

Approved (revised) by the Authority: **13 September 2018**