SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NOVITROPAN 5 MG TABLETS

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

OXYBUTYNIN HYDROCHLORIDE 5 MG

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

3. PHARMACEUTICAL FORM

Tablets for oral administration.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Novitropan 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

Novitropan 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 nondrug therapy, when other treatment has failed.

4.2. Posology and method of administration

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

Novitropan is not recommended in children under 5 years of age due to the absence of data. Novitropan should be used in children 6 years of age and older due to potential swallowing difficulties and risk of choking in younger children.
For children under 6 years old, alternative treatments should be considered.

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.

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

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

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

4.5 Interaction with other medicinal products and other forms of interaction
Care should be taken if other anticholinergic agents are administered together with Novitropan, 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, Novitropan 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. Novitropan 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 Novitropan during breast feeding is therefore not recommended.

4.7 Effects on ability to drive and use machines

Novitropan 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 Disorders	Not known	hypersensitivity
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, pseudoobstruction in patients at risk (elderly or patients with constipation and treated with other 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

4.9 Overdose

Symptoms of intoxication

The symptoms of overdosage with Novitropan 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. Novitropan 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.

5.3 PHARMACEUTICAL FORM

Light blue biconvex tablet, with a score line on one side

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose, Maize Starch, Povidone, Calcium Carboxy methyl cellulose, Magnesium Stearate, FDC blue no. 2.

6.2 Incompatibilities
None known.

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage
Store at a temperature below 25°C.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

1155725985

Version 02/2025 according to the MOH guidelines.