

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxybutynin Hydrochloride 2.5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2.5 mg tablet contains 2.5mg Oxybutynin hydrochloride
Excipient(s) with known effect: Contains 53.25 mg Lactose monohydrate per tablet.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets

White to off white, odourless, 5mm round biconvex, uncoated tablets with inscription "BS" on one side and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adults

Treatment of frequency, urgency or urge in continence as may occur in bladder over activity whether due to neurogenic bladder disorders (detrusor hyperreflexia) or idiopathic detrusor overactivity.

Paediatric population

Oxybutynin hydrochloride is indicated for children over 5 years for:

- Urinary incontinence, urgency and frequency in overactive bladder conditions caused by idiopathic overactive bladder or neurogenic bladder dysfunction (detrusor over activity).
- Nocturnal enuresis associated with detrusor over activity, in conjunction with non-drug therapy , when other treatment not been successful.

4.2 Posology and method of administration

Dosage and administration:

Adults: The dosage should be determined individually, with an initial dose of 2.5 mg three times daily. Thereafter, the lowest effective dose should be selected. The daily dose may vary between 10 and 15 mg per day (maximum dose is 20 mg per day) divided into 2-3 (max. 4) doses.

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

Children (under 5 years of age): The safety and efficacy of oxybutynin hydrochloride in children below 5 years of age has not been established. No data are available.

Children (over 5 years of age): The dosage should be determined individually, with an initial dose of 2.5 mg twice daily. There after, the lowest effective dose should be selected. The maximum dose, which is related to body weight (0,3 - 0,4 mg / kg / day), is expressed in the following table:

Age	Dosage
5-9 years	2.5mg three times daily
9-12 years	5mg 2 times daily
Over 12 years	5mg three times daily

The tablets can be taken on an empty stomach.

The tablet should be swallowed whole, with appropriate amount of water.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Myasthenia gravis.
- Narrow-angle glaucoma or shallow anterior chamber.
- Functional or organic gastrointestinal obstruction including pyloric stenosis, paralytic ileus
intestinal atony
- Patients with ileostomy, colostomy, toxic megacolon, severe ulcerative colitis.
- Patients with bladder outflow obstruction where urinary retention may be precipitated.
- Frequent urination at night caused by heart or kidney disease

4.4 Special warnings and precautions for use

- Oxybutynin hydrochloride should be used with caution in the frail elderly and children who may be more sensitive to the effects of the product and in patients with autonomic neuropathy (such as those with Parkinson's disease), hepatic or renal impairment and severe gastro-intestinal motility disorders (also see section 4.3).

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

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

- Oxybutynin hydrochloride may aggravate tachycardia (and thus hyperthyroidism, congestive heart failure, cardiac arrhythmia, coronary heart disease, 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.
- Since oxybutynin 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 may reduce salivary secretions which could result in dental caries, parodontosis or oral candidiasis. Regular dental check-ups are therefore advisable during long-term treatment.
- 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 oxybutynin is used in high environmental temperatures, this can cause heat prostration due to decreased sweating.

Paediatric population

The use of oxybutynin in children under 5 years of age is not recommended; it has not been established whether oxybutynin can be safely used in this age group.

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

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.

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

4.5 Interaction with other medicinal products and other forms of interactions

Care should be taken if other anticholinergic agents are administered together with Oxybutynin 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, Oxybutynin may affect the absorption of other drugs. Oxybutynin is metabolised by cytochrome P 450 isoenzyme CYP 3A4. Concomitant administration with a CYP 3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure (e.g. ketoconazole, itraconazole, erythromycin).

Oxybutynin, as an anticholinergic agent, may antagonize the effect of prokinetic therapies (e.g. metoclopramide and domperidone). 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 on the use of oxybutynin in pregnant women. Studies in animals have shown minor reproductive toxicity (see section 5.3). Animal studies are insufficient with respect to effects on pregnancy, embryonic / fetal development, parturition or postnatal development (see section 5.3). The potential risk for humans is unknown. Oxybutynin 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. Breast feeding while using Oxybutynin is therefore not recommended

Fertility

There are no data regarding effects on human fertility. Studies in animals have shown impaired fertility in females (see section 5.3).

4.7 Effects on ability to drive and use machines

Oxybutynin 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 drug.

4.8 Undesirable effects

Inclinical trials involving more than 3000 patients exposed to oxybutynin hydrochloride, side effects were caused mainly by oxybutynin hydrochloride anticholinergic effects. Dry mouth was the most commonly reported side effect.

Frequency of adverse reactions is based on safety data from clinical studies with oxybutynin hydrochloride 2.5 mg and 5 mg, and the experience gained after the drug has been marketed.

Responses have been ranked under headings of body systems and their frequencies as follows, where possible: very common ($\geq 1 / 10$), common ($\geq 1 / 100$ and $< 1 / 10$), uncommon ($\geq 1 / 1000$ and $< 1 / 100$), rare ($\geq 1 / 10\ 000$ and $< 1 / 1000$), very rare ($< 1 / 10.000$), unknown (cannot be estimated from the available data).

The following adverse events (marked with an asterisk *), which has not been observed in clinical trials but reported after the drug has been marketed, has been ranked in the frequency of rare/unknown.

Body systems	Very common	Common	Uncommon	Rare	unknown
Infections and infestations					Urinary tract infection
Immune system disorders					Hypersensitivity
Psychiatric disorders		Confusional state		Restlessness disorientation, concentration difficulties.	Excitation/agitation anxiety* hallucinations, nightmares*, paranoia, Cognitive disorders in elderly, symptoms of depression, dependence (in patients with history of drug or substance abuse)

Nervous system disorders	Dizziness, headache, somnolence/ fatigue		Drowsiness		Convulsions*, cognitive dysfunction*
Eye disorders	Decreased tear production /dry eyes		Light hypersensitivity		Narrow angle closure glaucoma*, mydriasis, ocular hypertension, blurred vision
Cardiac disorders					Tachycardia, cardiac arrhythmias
Vascular disorders	Facial flushing (which may be more marked in children)				
Gastrointestinal Disorders	Constipation nausea dry mouth	Dyspepsia diarrhea vomiting	Abdominal discomfort / pain, anorexia decreased appetite, dysphagia		Gastroesophageal reflux disease, pseudo-obstruction in patients at risk(elderly or patients with constipation and treated with other medicinal products that decrease intestinal mobility)
Skin and subcutaneous tissue	Dry skin/ decreased sweating			Phototoxicity	Urticaria and angioedema, allergic reactions such as rash, hypohidrosis
Renal and urinary disorders	Urinary retention				
Reproductive system and breast disorders				Erectile dysfunction	
Injury, poisoning and procedural complications					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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

The symptoms of overdosage with Oxybutynin progress from an intensification of the usual adverse 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.

Measures to be taken are:

- 1) Immediate gastric lavage.
- 2) Physostigmine by slow intravenous injection.

Adults: 0.5 to 2.0 mg physostigmine i.v. slowly, repeated after 5 minutes if necessary, up to a maximum total dose of 5mg.

Children: 30 micrograms/kg physostigmine i.v. slowly, repeated after 5 minutes if necessary, up to a maximum total dose of 2mg.

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

In pronounced restlessness or excitation, diazepam 10mg may be given by intravenous injection, tachycardia may be treated by intravenous injection of propranolol and urinary retention can be managed by 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: Other urologicals, including antispasmodics, Urinary antispasmodics

ATC code: G04 BD04.

Oxybutynin has both direct antispasmodic action on the smooth muscle of the bladder detrusor muscle as well as 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. Oxybutynin 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 following oral administration with maximum plasma concentrations reached in less than 1 hour. First-passage effect is high and less than 10% of the administered dose reaches the circulation unchanged.

Distribution

Oxybutynin is widely distributed in body tissues following systemic absorption. The volume of distribution was estimated to be 193 L after intravenous administration of 5 mg oxybutynin hydrochloride.

Biotransformation

Oxybutynin is extensively metabolised by the liver, primarily by the cytochrome P450 enzyme system, particularly CYP 3A4 found mostly in the liver and gut wall. Metabolites include phenylcyclohexylglycolic acid, which is pharmacologically inactive, and N-desethyloxybutynin, which is pharmacologically active.

Elimination

Oxybutynin is extensively metabolised in the liver, see above, with less than 0.1% of the administered dose excreted unchanged in the urine. Also, less than 0.1% of the administered dose is excreted as the metabolite N-desethyloxybutynin.

Elderly

Bioavailability is higher in elderly patients; AUC is 2-4-fold higher after repeated administration and half-life 3-5 times longer (see section 4.2).

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans based on studies for acute toxicology, repeat dose toxicity, genotoxicity, carcinogenic potential and local toxicity. At a concentration of 0.4 mg/kg/day oxybutynin administered subcutaneously, the occurrence of organ anomalies is significantly increased, but is observed only in the presence of maternal toxicity. However, in the absence of understanding the association between maternal toxicity and developmental effect, the relevance to human safety cannot be addressed. In the subcutaneous fertility study in rats, no

effects have been reported in males, while in females, fertility was impaired (no observed adverse effect level stated to be 5 mg/kg).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powdered cellulose
Lactose monohydrate
Talc
Magnesium stearate (E572)

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Oxybutynin Tablets 2.5mg are packed in PVC/PVdC-Alu blister/ Clear PVC –Plain Alu blister pack. The blisters are further packed into cartons along with leaflet in pack sizes of 6, 20, 21, 28, 30, 50, 56, 60, 84 and 100 tablets per pack.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Ltd.
Euro House
Euro Business Park
Little Island
Cork T45 K857

Ireland

8 MARKETING AUTHORISATION NUMBER

PA2315/038/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th May 2012

Date of last renewal: 21st March 2017

10 DATE OF REVISION OF THE TEXT

January 2019