Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxybutynin hydrochloride 2.5 mg 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 incontinence as may occur in bladder overactivity 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

Posology
The dosage should be adapted individually. Unless otherwise specified, the following recommendations apply:
Adults: The initial starting dose is 2.5 mg three times daily. Thereafter, the lowest effective dose should be selected. The daily dose may vary between 5 mg two or three times daily (10 and 15 mg per day) and maximum dose is 5mg four times daily (maximum dose is 20 mg per day).
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 initial starting dose is 2.5 mg twice daily. Thereafter, 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

Method of administration
Oral use.

The tablets are swallowed with plenty of fluid (approx. 1 glass of water), also recommended because the tablets have an unpleasant taste

The duration of treatment is guided by the occurrence of symptoms.

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 or prostatic hypertrophy.
- Frequent urination at night caused by heart or kidney disease

4.4 Special warnings and precautions for use

Elderly people

- 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 hiatus hernia or other 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 must 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.

Nervous system

- 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.

Eye disorders

- Since oxybutynin can cause narrow-angle glaucoma, patients should be advised to contact a doctor immediately if they are aware of a sudden loss of visual acuity or ocular pain.

Infections

- In the event of a urinary tract infection during treatment with oxybutynin, appropriate antibacterial treatment must be initiated.

- 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.

Dependence

- When oxybutynin is used in high environmental temperatures, this can cause heat prostration due to decreased sweating.

Warning concerning excipients

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

Paediatric population

Children under 5 years old

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).

Children from 5 years and young people up to 18 years

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.

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken if other anticholinergic agents are administered together with Oxybutynin as potentiation of anticholinergic effects could occur. Concomitant treatment can also lead to confusion in the elderly.

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.

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 an oxybutynin (see section 4.7).

By reducing gastric motility, Oxybutynin may affect the absorption of other drugs.
Oxybutynin may also counteract the gastrointestinal effect if metoclopramide and domperidone.

Oxybutynin is metabolised by cytochrome P 450 via the isoenzyme CYP 3A4. Concomitant administration with a CYP 3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure (e.g. ketoconazole, itraconazole, erythromycin).

The ability to dissolve sublingual tablets under the tongue may be worsened due to dry mouth. Patients who take sublingual nitrates must therefore be advised to moisten their mouth with their tongue or with a little water before taking a sublingual tablet.

An interaction has been demonstrated between oxybutynin and itraconazole, which leads to a doubling of plasma oxybutynin levels but only a 10% increase in levels of the active metabolite. This appears to be of minor clinical significance.

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

Some undesirable effects (e.g. light-headedness, drowsiness and blurred vision) can impair the ability of the patient to concentrate and react and hence pose a risk in situations in which these abilities are of particular importance (e.g. driving a vehicle, using machines or carrying out dangerous activities)

4.8 Undesirable effects

In clinical trials involving more than 3,000 patients exposed to oxybutynin hydrochloride, side effects were caused mainly by anticholinergic effects of oxybutynin. 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, wherever possible: very common (≥ 1 / 10), common (≥ 1 / 100 and <1 / 10), uncommon (≥ 1 /1,000 and <1 / 100), rare (≥ 1 / 10,000 and <1 / 1,000), 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".

Bodysystems	**Very common**	**Common**	**Uncommon**	**Rare**	**unknown**
Infections and infestations					Urinary tract infection
Immune system disorders					hypersensitivity
Psychiatricdisorders		Confusion		Restlessness*, disorientation, concentration	Agitation anxiety hallucinations,

				difficulties, excitation.	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		angle closure glaucoma, mydriasis, ocular hypertension, blurred vision
Cardiac disorders		palpitation			tachycardia, cardiac arrhythmias
Vascular disorders	Facial flushing (which may be more marked in children)				
GastrointestinalDisorders	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 motility)
Skinandsubcutaneoustissue	Dry skin/ decreased sweating			phototoxicity ,	urticaria and angioedema, allergic reactions such as skin rash, hypohidrosis
Renalandurinary disorders		Urinary retention			
Reproductive systemandbreastdisorders				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

Website: www.hpra.ie

4.9 Overdose

Symptoms of Overdose of Oxybutynin may be manifested by an intensification of parasympatholytic effects in the central nervous system restlessness excitement confusion, hallucinations including psychotic behaviour, ataxia, bewilderment, nervousness. Changes in the circulatory system (e.g. hot feeling, drop in blood pressure, light-headedness, circulatory failure), arrhythmia, tachycardia, facial redness,respiratory failure, paralysis and coma.

Signs of anticholinergic intoxication (e.g. mydriasis, fever, red, hot skin and dry mucosa)

Therapy in severe overdose

1) Immediate gastric lavage and administration of actual charcoal.

2) In severe cases, administration by slow intravenous injection of physostigmine.

Adults: 0.5 -2.0 mg of i.v physostigmine if necessary the administration of physostigmine may be repeated several times up to daily dose of 5 mg.

Children: 30 µg physostigmine /kg body weight i.v. .(if necessary the administration of physostigmine can be repeated several times up to daily dose of 2mg.

Fever should be treated symptomatically.

In the event of marked nervous restlessness or excitement, diazepam 10mg may be injected intravenously .
Tachycardia may be treated intravenously with propranolol and Urinary retention may be relieved by bladder catheterisation.

If there is threatened paralysis of the respiratory musculature, artificial ventilation is required.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other urologicals, including antispasmodics, Urinary antispasmodics
ATC code: G04 BD04.
Oxybutynin is a synthetic tertiary amine, which 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 and is not affected by simultaneous food intake. First-passage effect is high and therefore less than 10% of the administered dose reaches the circulation unchanged. The maximum plasma concentrations reached within 1 – 1.5 hour and shows wide inter-individual variability.

Distribution
Oxybutynin is widely distributed in body tissues following systemic absorption. The volume of distribution is 100 – 200 L.

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

Elimination
Oxybutynin is eliminated rapidly; the half-life is 2 – 3 hours.
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 (se 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 30ºC. 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 pack in to carton along with leaflet in pack size 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 2012Date of last renewal: 21st March 2017

10 DATE OF REVISION OF THE TEXT

September 2023