SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxybutynin Hydrochloride Tablets 2.5mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxybutynin hydrochloride 2.5mg

Excipient(s) with known effect: Contains 76.50 mg Lactose monohydrate per tablet.

Sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, i.e. is essentially 'sodium-free'.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

Blue, biconvex, uncoated capsule-shaped tablets, marked OB scoreline 2.5 on one side and plain on the reverse

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults: Urinary incontinence, urgency and frequency in unstable bladder conditions due to idiopathic detrusor instability (motor urge incontinence) or neurogenic bladder disorders (detrusor hyperreflexia) in conditions such as multiple sclerosis and spinabifida.

Paediatric population
Oxybutynin hydrochloride is indicated in children over 5 years of age 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

The dosage should be adapted individually. Unless otherwise specified, the following recommendations apply:

Adults
The usual initial dose is 2.5mg three times a day. This dose may be increased to a maximum dose of 5mg four times a day to obtain a clinical response provided that the side effects are well-tolerated.

Elderly (including frail elderly)
A lower dose is recommended because the elimination half-life is increased in the elderly. A dose of 2.5mg twice a day is likely to be adequate, particularly if the patient is frail. This dose may be increased if necessary to 5mg twice a day provided that the side effects are well tolerated.

Children (under 5 years of age)
Not recommended

Children (over 5 years of age)
Neurogenic bladder instability: The usual dose is 2.5mg twice a day. 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	2.5 mg three times daily
9-12 years	5 mg 2 times daily
Over 12 years	5 mg three times daily

Nocturnal enuresis: The usual dose is 2.5mg twice a day. This dose may be increased, if necessary, to 5mg two or three times daily provided that the side effects are well-tolerated. The last dose should be given before bedtime.

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

Oxybutynin hydrochloride tablets are contraindicated in patients with:

- hypersensitivity to oxybutynin hydrochloride or any of the excipients listed in section 6.1.
- myasthenia gravis
- narrow-angle glaucoma or shallow anterior chamber.
- pollakiuria or nycturia due to cardiac or renal insufficiency.
- gastrointestinal obstruction including pyloric stenosis, paralytic ileus and intestinal atony.

- ileostomy, colostomy, toxic megacolon, severe ulcerative colitis.
- bladder flow obstruction where urinary retention may be precipitated.
- porphyria
- frequent urination at night caused by heart or kidney disease
- hiatus hernia with reflux oesophagitis

4.4 Special warnings and precautions for use

Oxybutynin hydrochloride tablets 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), severe gastrointestinal motility disorders, 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 should be used with caution in patients with gastrointestinal obstructive disorders, intestinal atony and ulcerative colitis.

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

Anticholinergic central nervous system (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.

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.

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

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

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.

4.5 Interaction with other medicinal products and other forms of interaction

Enhanced effect with other anticholinergics

Care should be taken if other anticholinergic agents are administered together with oxybutynin, as potentiation of anticholinergic effects may 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 anti-Parkinsonian 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 CYP3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure (e.g. ketoconazole, itraconazole, erythromycin). Oxybutynin may antagonise 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).

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

Mutual Effect Mitigation
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).

Other interactions
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 from 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 / foetal development, parturition or postnatal development (see section 5.3).The potential risk for humans is unknown. Oxybutynin should not be used in pregnancy unless clearly necessary.

Breast-feeding:
Oxybutynin in small amount is excreted in breast milk during lactation. Oxybutynin should not be used during breast-feeding.

Fertility:
There are no data regarding effects on human fertility. Studies in animals have shown impaired fertility in females.

4.7 Effects on ability to drive and use machines

Oxybutynin hydrochloride tablets can cause drowsiness or blurred vision and patients should be cautioned regarding activities requiring mental alertness such as driving, operating machinery or performing hazardous work.

4.8 Undesirable effects

In clinical trials involving more than 3000 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.

Classification of expected frequencies:
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); not known (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".

	Very Common	**Common**	**Uncommon**	**Rare**	**Not Known**
Infections and infestations					urinary tract infection
Immune System Disorders					hypersensitivity
Psychiatric disorders		confusional state		Restlessness*, disorientation, concentration difficulties, excitation.	Agitation anxiety, hallucinations, nightmares*, paranoia, agitation,

	Very Common	Common	Uncommon	Rare	Not Known
					cognitive disorders in elderly, symptoms of depression, dependence to oxybutynin (in patients with history of drug or substance abuse)
Nervous System Disorders	somnolence, fatigue, headache, dizziness		drowsiness		Cognitive disorders*, convulsions*, disorientation
Eye disorders		decreased tear production /Dry eyes	light hypersensitivity		Narrow angle closure glaucoma*, mydriasis, ocular hypertension, blurred vision
Cardiac disorders		palpitation			cardiac arrhythmias, tachycardia
Vascular disorders	flushing which may be more marked in children				
Gastrointestinal Disorders	dry mouth, nausea, constipation	diarrhoea, vomiting, dyspepsia	anorexia, dysphagia, abdominal discomfort/pain, decreased appetite		gastroesophageal reflux disease, pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other drugs that decrease intestinal motility)
Skin and subcutaneous tissue disorders	dry skin/ decreased sweating			phototoxicity	angioedema, rash, urticaria, hypohidrosis,

	Very Common	Common	Uncommon	Rare	Not Known
Renal and urinary disorders		Urinary retention			difficulty in micturition
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 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

The symptoms of over dosage with oxybutynin progress from an intensification of the usual side effects of CNS disturbances (from restlessness confusion, hallucinations including psychotic behaviour, ataxia, bewilderment, nervousness), circulatory changes (hot feeling, flushing, fall in blood pressure, light-headedness, circulatory failure, arrhythmia, tachycardia, facial redness.), respiratory failure, paralysis and coma.

Measures to be taken are:
1. Immediate gastric lavage and administration of actual charcoal
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 5mg.
Children: 30 micrograms/kg of physostigmine by slow intravenous administration. Repeat 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 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: Urinary antispasmodics, ATC code: G04BD04

Oxybutynin has a direct antispasmodic effect on the smooth muscle of the bladder detrusor.

Oxybutynin also inhibits the effects of acetylcholine on smooth muscle by blocking muscarinic receptors. Pharmacological models have established differences in affinity for subtypes of muscarinic receptors.

The pharmacodynamic properties of oxybutynin result in relaxation of the bladder detrusor muscle. Patients with unstable bladder experience increased bladder volume and a decreased incidence of spontaneous contractions of the detrusor muscle.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, oxybutynin is rapidly absorbed from the gastrointestinal tract (t_{max} 0.5-1.4hours). Studies have established a C_{max} after a 5-10mg dose in young healthy patients of 8-12ng/ml. Larger inter-individual variations in plasma concentrations are seen. Oxybutynin is subject to extensive first pass metabolism, resulting in an absolute systemic availability of 6.2%.

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 undergoes extensive hepatic metabolism, with less than 0.02% of the administered dose excreted unchanged in the urine. Less than 0.1% of the administered dose is excreted as the metabolite N-desethyloxybutynin.

Oxybutynin is 83-85% plasma albumin bound.

Oxybutynin is eliminated biexponentially. Mean elimination half-life is 2 hours. Repeated administration results in little accumulation.

Elderly
Bioavailability is higher in elderly patients; AUC is 2-4-fold higher after repeated administration and half-life 3-5 times longer.

5.3 Preclinical safety data

Oxybutynin hydrochloride has been shown to have low acute toxicity when administered orally to either mice, rats or dogs. In a repeat dosing experiment of 6 months duration in rats, daily oral doses of 63mg/kg or more were associated with decreases in food consumption and body weight gain and with minor pathological changes in the liver and kidneys. At daily oral doses of 6mg/kg administered for 6 months, dogs exhibited transient anorexia, tremors and

nervousness but these effects were not associated with microscopic signs of tissue damage.

There is no evidence from preclinical studies to suggest either mutagenic or carcinogenic activity for oxybutynin.

Reproduction tests indicate no adverse effects on fertility or reproductive performance in rats given daily oral doses of 15mg/kg. Oxybutynin hydrochloride was not teratogenic in rats and rabbits at oral dose levels (20mg/kg/day in rats and 48mg/kg/day in rabbits) which did not cause significant maternal toxicity. At maternally toxic doses of oxybutynin (100mg/kg/day), increased incidence of extra thoracolumbar ribs in rat foetuses, as well as mortality of neonates, was observed. At oral daily dose levels up to

20mg/kg in rats, oxybutynin hydrochloride had no adverse effects on gestation or on the birth and development of offspring up to weaning.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate
Microcrystalline Cellulose
Calcium Stearate
Indigo Carmine (Aluminium Lake) E132

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C in a dry place. Protect from light.

6.5 Nature and contents of container

Polypropylene tablet container with tamper-evident polyethylene cap
Pack sizes: 20, 30, 50, 60, 84, 90, 100, 250, 500

PVC (250µm ± 5µm)/aluminium foil (25µm) blister packs
Pack sizes: 20, 30, 50, 56, 60, 84, 90, 100

Not all pack sizes may be marketed.

6.6 Instructions for use and handling <and disposal>

No specific instructions for use/handling

7 MARKETING AUTHORISATION HOLDER

Strides Pharma UK Ltd.
Unit 4, The Metro Centre,
Dwight Road, Watford, WD18 9SS
United Kingdom,

8. MARKETING AUTHORISATION NUMBER(S)

PL 13606/0070

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/03/2006

10 DATE OF REVISION OF THE TEXT

21/04/2026