SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
Oxybutynin Hydrochloride Tablets 5mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Oxybutynin hydrochloride 5mg
For excipients, see 6.1

3. PHARMACEUTICAL FORM
Tablet
Blue, round, biconvex, uncoated tablets, marked OB scoreline 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.

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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

Adults
The usual initial dose is 5mg two or 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. This dose may be increased, if necessary, to 5mg two or three times daily provided that the side effects are well-tolerated.

**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.

### 4.3 Contraindications

Oxybutynin hydrochloride tablets are contraindicated in patients with:

- Hypersensitivity to oxybutynin or any of the excipients.
- Myasthenia Gravis
- Narrow-angle glaucoma or shallow anterior chamber.
- Gastrointestinal obstruction including paralytic ileus and intestinal atony.
- Toxic megacolon, severe ulcerative colitis.
- Patients with bladder flow obstruction where urinary retention may be precipitated.
- Porphyria

### 4.4 Special warnings and precautions for use

Oxybutynin hydrochloride tablets should be used with caution in elderly patients (especially if frail) and in children who may be more susceptible to adverse effects.

Caution is also recommended in patients with autonomic neuropathy, hepatic or renal impairment and severe gastrointestinal motility disorders (see also section 4.3).

Oxybutynin may aggravate the symptoms of hyperthyroidism, congestive cardiac failure, coronary heart disease, cardiac arrhythmias, tachycardia, hypertension and prostatic hypertrophy.

When oxybutynin is used in patients with fever or in high environmental temperatures, it can cause heat prostration, or heat stroke, due to decreased sweating.

Special care should be taken in patients with hiatus hernia associated with reflex oesophagitis, as anticholinergic drugs can aggravate this condition.

Oxybutynin may lead to decreased salivary secretions, which could result in dental caries or oral infections particularly candidiasis.

Patients with rare hereditary problems of galactose intolerance, the LAPP lactase deficiency or glucose-galactose malabsorption should not take this medicine.
As oxybutynin may trigger angle-closure glaucoma, visual acuity and intraocular pressure should be monitored periodically during therapy. Patients should be advised to seek medical advice immediately if they are aware of a sudden loss of visual acuity.

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.

Paediatric population:
Oxybutynin hydrochloride is not recommended for use in children below 5 years due to insufficient data on safety and efficacy.

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

The concomitant use of oxybutynin with other anticholinergic medicinal products or drugs with anticholinergic activity, such as phenothiazines, clozapine, digoxin, amantadine, butyrophenones, levodopa, antihistamines, tricyclic antidepressants and MAOIs, may increase the frequency or severity of dry mouth, constipation and drowsiness.

Anticholinergic agents may potentiate alter the absorption of some concomitantly administered drugs due to anticholinergic effects on gastrointestinal motility. They may also antagonise the gastrointestinal prokinetic effects of metoclopramide and domperidone.

Itraconazole and ketoconazole may inhibit oxybutynin metabolism via cytochrome p450 3A4 inhibition. The clinical relevance of this interaction is unknown.

If patients experience a dry mouth whilst taking oxybutynin tablets, sublingually administered drugs, such as glyceryl trinitrate, may fail to dissolve under the tongue and therefore have a reduced effect.

Patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin.

4.6 Pregnancy and lactation

Pregnancy:
There are no adequate data from the use of oxybutynin pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown. Oxybutynin should not be used in pregnancy unless clearly necessary.

Lactation:
Oxybutynin is excreted in breast milk. Oxybutynin should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines
Oxybutynin hydrochloride tablets can cause drowsiness or blurred vision and patients should be cautioned as to potential effects on the ability to drive, operate machinery or perform hazardous work.

4.8 Undesirable effects

The table below reflects the data obtained with Oxybutynin hydrochloride tablets in clinical trials and from post marketing experience. In clinical trials with Oxybutynin hydrochloride tablets (n=1006), adverse events were associated mainly with the anticholinergic actions of oxybutynin. Adverse events were generally dose related. As with other oxybutynin formulations, dry mouth was the most frequently reported adverse reaction.

<table>
<thead>
<tr>
<th></th>
<th>Very Common ≥ 1/10</th>
<th>Common ≥ 1/100 to &lt;1/10</th>
<th>Uncommon ≥ 1/1000 to &lt;1/1000</th>
<th>Rare &lt;1/1000</th>
<th>Not Known*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>urinary tract infection, cystitis, pharyngitis, nasopharyngitis, upper respiratory tract infection, bronchitis, sinusitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Blood and Lymphatic system disorders</td>
<td></td>
<td></td>
<td>leukopenia, thrombocytopenia</td>
<td></td>
<td></td>
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<tr>
<td>Immune System Disorders</td>
<td></td>
<td></td>
<td>hypersensitivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolism &amp; Nutrition Disorders</td>
<td>anorexia, dehydration, hyperglycaemia</td>
<td></td>
<td></td>
<td>appetite increased</td>
<td></td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>insomnia, depression, nervousness, confusional state</td>
<td>anxiety, abnormal dreams</td>
<td></td>
<td>hallucinations, night terror, psychotic disorder, agitation, Dependence to oxybutynin (in patients with history of drug or substance abuse)</td>
<td></td>
</tr>
</tbody>
</table>

*Not Known* may represent an occurrence rate of less than 1/10,000.
<table>
<thead>
<tr>
<th><strong>Nervous System Disorders</strong></th>
<th>somnolence, headache, dizziness, dysgeusia</th>
<th>paraesthesia, vertigo</th>
<th>hypertonia, tremor, tinnitus</th>
<th>convulsions, disorientation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye disorders</strong></td>
<td>vision blurred, dry eye, keratoconjunctivitis sicca</td>
<td>conjunctivitis</td>
<td>diplopia, glaucoma, photophobia</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac disorders</strong></td>
<td>palpitations</td>
<td></td>
<td>atrial arrhythmia, bradycardia, bundle branch block, nodal arrhythmia, supraventricular extrasystoles</td>
<td>arrhythmia tachycardia, heat stroke</td>
</tr>
<tr>
<td><strong>Vascular disorders</strong></td>
<td>hypertension</td>
<td>vasodilatation, migraine</td>
<td>hypotension, phlebitis, ecchymosis</td>
<td>flushing</td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
<td>nasal dryness, mucosal dryness, cough, pharyngo-laryngeal pain, dry throat</td>
<td>rhinitis, hoarseness, epistaxis, dyspnoea</td>
<td>laryngitis, laryngeal oedema, respiratory disorder, sputum increased</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td>dry mouth</td>
<td>constipation, diarrhoea, nausea, dyspepsia, abdominal pain, flatulence, gastroesophageal reflux disease, loose stools, vomiting</td>
<td>dysphagia, mouth ulceration, abdominal distension, glossitis, stomatitis</td>
<td>faecal abnormality, oesophageal stenosis acquired, gastritis, gastroenteritis viral, hernia, rectal disorder, gastric atony, tongue disorder, tongue oedema, Pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other drugs that decrease intestinal motility)</td>
</tr>
<tr>
<td><strong>Skin and subcutaneous tissue disorders</strong></td>
<td>dry skin, pruritus</td>
<td>acne, urticaria, face oedema, alopecia, eczema, nail disorder, skin discolouration, anhidrosis</td>
<td>hair disorder, rash maculo-papular, granuloma, sweating increased, photosensitivity reaction</td>
<td>rash</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td>pain in extremity, back pain, arthralgia</td>
<td>muscle cramps, myalgia</td>
<td>arthritis</td>
<td></td>
</tr>
<tr>
<td><strong>Renal and urinary disorders</strong></td>
<td>micturition disorder, residual urine</td>
<td>urinary frequency, urinary tract</td>
<td>urinary incontinence, urine abnormal, impotence, erectile dysfunction</td>
<td></td>
</tr>
</tbody>
</table>
volume, urinary retention, dysuria, urinary hesitation

disorder, haematuria, nocturia, pyuria, micturition urgency

urogenital disorder

Reproductive system and breast disorders

breast pain, vaginitis

vulvovaginal disorder, uterine cervical disorder, genital discharge

General disorders and administration site conditions

asthenia, oedema peripheral, fatigue, chest pain

pain, thirst, oedema

rigor, pyrexia, influenza like illness, malaise, pelvic pain

Investigations

blood pressure increased

electrocardiogram abnormal, blood urea increased, blood creatinine increased

blood alkaline phosphatase increased, blood lactase dehydrogenase increased, blood aspartate, aminotransferase increased, blood alanine aminotransferase increased

Injury, poisoning and procedural complications

fall

*Cannot be estimated from the available clinical data.

Other Undesirable effects

In addition, cyclopegia, mydriasis and suppression of lactation have been reported with the use of other oxybutynin hydrochloride

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.

4.9 Overdose

Symptoms of overdosage progress from an intensification of the possible side effects of CNS disturbances (from restlessness to excitement to psychotic behaviour), circulatory changes (flushing, drop in blood pressure, circulatory failure etc), respiratory failure, paralysis and coma.

If the patient presents within one hour of an overdose, gastric lavage may be used in adults or activated charcoal may be given to adults or children. Supportive therapy should be given as
required. Convulsions should be treated with intravenous diazepam and delirium with oral diazepam. Hypoxia and acidosis should be corrected. Mechanical ventilation is required if paralysis of respiratory muscles occurs.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Urinary antispasmodics G04B D04

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

Following oral administration, oxybutynin is rapidly absorbed from the gastrointestinal tract ($t_{max}$ 0.5-1.4 hours).

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%.

The major metabolite produced is desethyloxybutynin. Several other metabolites are produced, including phenylcyclohexylglycolic acid.

Urinary excretion has been established as less than 0.02% of an administered dose.

Oxybutynin is 83-85% plasma albumin bound.

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

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

None known

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 (20µm) blister packs
Pack sizes: 20, 30, 50, 56, 60, 84, 90, 100

Not all pack sizes may be marketed

6.6 Special precautions for disposal

No specific instructions for use/handling

7. MARKETING AUTHORISATION HOLDER

Strides Shasun (UK) Ltd
Unit 4 Metro Centre
Tolpits Lane
Watford
Hertfordshire
WD18 9SS
Trading as: Co-pharma

8. MARKETING AUTHORISATION NUMBER(S)
PL 13606/0071

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

3 June 1998 / 21 March 2006

10. DATE OF REVISION OF THE TEXT

18.05.2016