Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxybutynin Hydrochloride Tablets 2.5 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxybutynin hydrochloride 2.5 mg per tablet

For excipients see 6.1

3 PHARMACEUTICAL FORM

Tablet

Blue, biconvex, uncoated capsule shaped tablets, marked OB scored breakline 2.5 on one side and G on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Urinary incontinence, urgency and frequency in unstable bladder conditions. This may be due to idiopathic detrusor instability or due to neurogenic bladder disorders.

4.2 Posology and method of adminstration

General

Oxybutynin tablets are for oral use and may be taken with a glass of water on an empty stomach. The tablets may also be taken during meals or with some milk if gastric irritation occurs.

Adults

The initial dose is 2.5mg three times daily which if necessary may be titrated to the lowest effective dosage to obtain a satisfactory clinical response. The usual dose is 5mg two or three times a day with the maximum dosage of 5mg four times a day.

Elderly

In the elderly the elimination half life may be increased, hence the initial dose is 2.5mg twice daily which if necessary may be titrated to the lowest effective dosage to obtain a satisfactory clinical response. A usual dose of 10mg in two divided doses is likely to be sufficient, particularly if the patient is frail.

Children (older than 5 years of age)

Starting with 2.5mg twice a day, the dosage should be individually titrated to the lowest effective dosage to obtain a satisfactory clinical response. The recommended dose is 0.3 - 0.4 mg/kg body weight per day, the maximum dose adapted for body-weight is stated in the following table:

Age	Dosage
5 - 9 years	2.5mg 3 times daily
9 - 12 years	5mg 2 times daily
12 years and older	5mg 3 times daily

Children (under 5 years of age)

Use is not recommended.

4.3 Contraindications

Hypersensitivity to Oxybutynin or any of the excipients in the tablet.

Patients with bowel obstruction and in patients with significant urinary obstruction, including patients in whom this is due to prostatic hypertrophy, as urinary retention may be precipitated.

Patients with toxic megacolon, severe ulcerative colitis, intestinal atony, myasthenia gravis or narrow-angle glaucoma, tachyarrhythmia, cerebral sclerosis, and hiatus hernia with reflux oesophagitis.

Patients with urinary frequency or nocturia due to cardiac or renal insufficiency.

4.4 Special warnings and special precautions for use

Treatment with oxybutynin should be reviewed after a period of 4 - 6 weeks as a normal bladder habit may be re-established in some patients.

Oxybutynin hydrochloride tablets should not be used to treat stress or effort urinary incontinence.

Oxybutynin hydrochloride tablets should be used with caution in the frail elderly and children, who may be more sensitive to the effects of oxybutynin, and in patients with autonomic neuropathy, hiatus hernia or other serious gastro-intestinal disease and hepatic or renal disease.

Following administration of oxybutynin hydrochloride tablets symptoms of hyperthyroidism, coronary artery disease, congestive cardiac failure, cardiac arrhythmias, tachycardias and prostatic hypertrophy may be aggravated.

Because Oxybutynin may decrease sweating, treated patients may be at risk of over-heating in situations of increased environmental temperature or fever.

Prolonged use may contribute to the development of caries, periodontal disease, oral candidiasis and discomfort due to decrease in salivary flow.

If urinary tract infection is present, an appropriate antibacterial therapy should be started.

Chronic use may result in the development of dental caries, periodontal disease, thrush and oral discomfort as a consequence of reduced or inhibited salivation.

Patients should seek advice immediately if they are aware of a sudden loss of visual acuity.

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 e.g., antihistamines, tricyclic antidepressants, L-dopa and anticholinergic drugs used in Parkinson’s disease, atropine, disopyramide, and clozapine as potentiation of anticholinergic effects may occur. Concomitant use can also lead to confusion in the elderly.

Oxybutynin may antagonise the gastrointestinal effects of metoclopramide and domperidone.

Sublingual nitrates may fail to dissolve under the tongue owing to dry mouth, resulting in reduced therapeutic effect.

4.6 Pregnancy and lactation

There are no adequate data from the use of Oxybutynin in 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 during pregnancy unless clearly necessary.

Oxybutynin has been found in breast milk in animals and therefore it should not be used in breast feeding mothers.

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

Psychiatric Disorders
Cognitive effects (confusion, anxiety, paranoia, hallucinations) have been reported in elderly patients.
Anorexia
Restlessness

Nervous system disorders
Headache
Dizziness
Drowsiness

Eye disorders
Mydriasis
Blurred vision
Intraocular hypertension and induction of glaucoma (narrow-angle glaucoma)

Cardiac disorders
Tachycardia
Cardiac arrhythmias

Vascular disorders
Facial flushing (more marked in children than in adults)

Gastrointestinal, thoracic and mediastinal disorders
Dry mouth
Constipation
Nausea
Abdominal discomfort
Diarrhoea

Skin and subcutaneous tissue disorders
Dry skin
Rarely allergic skin reactions have occurred.

Renal and urinary disorders
Problems with micturition

Urinary retention

Reproductive system and breast disorders
Impotence

Dose reduction may reduce the incidence of some of the side effects.

4.9 Overdose

Symptoms of overdose 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.

In the event of overdose the following steps should be taken:

i) Immediate gastric lavage.

ii) Slow i.v. injection of 1.0 to 2.0mg of physostigmine, repeated as necessary up to a total of 5mg. The dose of physostigmine recommended in children is 30µg/kg by slow intravenous injection, repeated if necessary to a maximum total of 2mg.

Fever is to be treated with ice packs or tepid sponging.

For pronounced restlessness or excitement, diazepam 10mg may be given by intravenous injection.

For tachycardia an intravenous injection of propranolol may be given.

Catheterisation can be used to manage urinary retention.

Mechanical ventilation is required if paralysis of the respiratory muscles occurs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 to 1.4 hours).

Studies have established a Cmax after a 5-10mg dose in young healthy patients of 8-12ng/ml. Large 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, desethyloxybutynin, is pharmacologically active. Several other metabolites are produced, including phenylcyclohexyglycolic acid, but are inactive.

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.

Chronic toxicity was associated with decreases in food consumption and body weight gain, tremors and nervousness and minor pathological changes in the liver and kidneys did occur in one species.

Preclinical studies did not suggest mutagenicity, carcinogenicity, or adverse effects on fertility or reproductive performance. No adverse effects on gestation or on the birth and development of offspring up to weaning were observed.

Teratogenicity was not seen at oral-dose levels (rats - 20 mg/kg/day, rabbits- 48 mg/kg/day) which did not cause significant maternal toxicity; but at maternally toxic doses of oxybutynin (100mg/kg/day), increased incidence of extra thoracolumbar ribs in rat foetuses and mortality of neonates was observed.

Pre-clinical data reveal no special hazard for humans based on conventional studies of general toxicity, genotoxicity and carcinogenicity beyond the information included in other sections of the SPC.

Embryofetal studies in pregnant rats showed malformed hearts. Higher dosages additionally were associated with extra thoracolumbar ribs and increased neonatal mortality. Reproductive toxicity occurred only with concurrent general maternal toxicity. In the absence of exposure data, the relevance of these observations cannot be assessed.

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

Do not store above 25°C. Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Polypropylene tablet container with tamper-evident polyethylene cap.
Polyvinylchloride (PVC)/aluminium foil blister packs.

Not all pack sizes may be marketed.
Pack sizes: 20, 30, 50, 56, 60, 84, 90, 100, 250 and 500 – polypropylene
Pack sizes: 20, 30, 50, 56, 60, 84, 90 and 100 – blisters

6.6 Instructions for use and handling

No special requirements

7 MARKETING AUTHORISATION HOLDER

Generics (UK) Limited
12, Station Close
Potters Bar
Hertfordshire
EN6 1TL
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 405/33/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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