SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxybutynin Hydrochloride Tablets 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The tablets contain 5mg of oxybutynin hydrochloride.

Excipient with known effect: Lactose Monohydrate 118.9mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet

Light blue circular, flat bevelled edge tablets with a diameter of approximately 7.5 mm, marked 'OXB 5' on one side with a breakline on the reverse. The tablets can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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

Posology

Adults: The usual dose is 5mg two or three times a day. This may be increased up to a maximum of 5mg four times a day to obtain a clinical response, provided that the side effects are tolerated. It is usually wise to institute treatment slowly to minimise the anticholinergic side effects especially that of a dry mouth.

Elderly (including frail 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 5 years of age and over:

Neurogenic bladder instability: The usual dose is 2.5mg twice a day. This dose may be titrated upwards to 5mg two or three times a day to obtain a clinical response provided the side effects are well tolerated.

Nocturnal enuresis: The usual dose is 2.5 mg twice a day. This dose may be titrated upwards to 5mg two or three times a day to obtain a clinical response provided the side effects are tolerated. The last dose should be given before bedtime.

Children under 5 years of age: Not recommended.

Method of administration

The tablets are for oral administration. The tablets should be swallowed with plenty of water or other fluid.

4.3 Contraindications

- Hypersensitivity to oxybutynin or any of the excipients listed in section 6.1
- Patients with bladder outflow obstruction where urinary retention may be precipitated
- Gastro-intestinal obstructive disorders, intestinal atony or paralytic ileus
- Toxic megacolon
- Severe ulcerative colitis
- Myasthenia gravis
- Narrow-angle glaucoma or shallow anterior chamber

4.4 Special warnings and precautions for use

Oxybutynin 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 gastro-intestinal motility disorders, hepatic or renal impairment.

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 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 the 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.

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 overactivity).

In children over 5 years of age, oxybutynin should be used with caution as they may be more sensitive to the effects of the product, particularly the CNS and psychiatric adverse reactions.

Lactose

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

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken if other anticholinergic agents are used together with oxybutynin, as a potentiation of anticholinergic effects may 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 CYP3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure.

Oxybutynin, as an antichlolinergic agent, may antagonize the effect of prokinetic therapies.

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 from the use of oxybutynin in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal 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. Use of oxybutynin during breast feeding is therefore not recommended.

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

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); very rare (<1/10,000), not known (cannot be estimated from the available data).

- Infections and infestations

Not known: urinary tract infection

- Gastrointestinal disorders

Very common: constipation, nausea, dry mouth

Common: diarrhoea, vomiting

Uncommon: abdominal discomfort, anorexia, decreased appetite, dysphagia

Not known: gastroesophageal reflux disease, pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other medicinal products that decrease intestinal motility)

- Psychiatric disorders

Common: confusional state

Not known: 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

Very common: dizziness, headache, somnolence

Not known: cognitive disorders, convulsions, drowsiness, disorientation

- Cardiac disorders

Common: Palpitation

Not known: tachycardia, arrhythmia

- Injury, poisoning and procedural complications

Not known: heat stroke

- Eye disorders

Very common: vision blurred

Common: dry eyes

Not known: Angle closure glaucoma, mydriasis, ocular hypertension

- Renal and urinary disorders

Common: urinary retention

Not known: difficulty in micturition

- Vascular disorders

Common: flushing which may be more marked in children

- Skin and subcutaneous tissue disorders

Very common: dry skin

Not known: angioedema, rash, urticaria, hypohidrosis, photosensitivity

- Immune system disorders

Not known: hypersensitivity

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 the 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

Symptoms

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.

Management

Measures to be taken are:

1) immediate gastric lavage
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 5 mg.

Children: 30micrograms/kg of physostigmine by slow intravenous administration. Repeat after 5 minutes, if necessary, up to a maximum total dose of 2 mg.

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

In pronounced restlessness or excitation, diazepam 10 mg may be given by intravenous injection, tachycardia may be treated with intravenous propranolol and urinary retention managed by bladder catheterisation.

In the event of progression of curare-like effects to paralysis of the respiratory muscles, mechanical ventilation will be required.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals, Drugs for urinary frequency and incontinence

ATC code: G04 BD04

Oxybutynin hydrochloride has 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 hydrochloride increases bladder capacity and reduces the incidence of spontaneous contraction of the detrusor muscle.

5.2 Pharmacokinetic properties

Following oral administration, oxybutynin hydrochloride undergoes extensive first-pass metabolism in the liver. This shows considerable inter-subject variability, with maximum plasma concentrations differing by as much as four- or five-fold amongst individuals. However, this does not significantly affect the pharmacological actions of oxybutynin hydrochloride as much of the oral dose (approximately 90%) is metabolised to desethyloxybutynin. This is the major metabolite which is pharmacologically active with similar potency and efficacy to the parent compound.

Oxybutynin hydrochloride is rapidly and well absorbed from the gastro-intestinal tract. In the bioequivalence study peak plasma concentrations for oxybutynin were reached in 0.5 to 1.25 hours with a mean of 0.7 hours. Peak plasma concentrations for desethyloxybutynin were reached in 0.5 to 1.5 hours with a mean of 0.9 hours. Mean elimination half-life for oxybutynin and desethyloxybutynin were 1.4 hours and 2.1 hours respectively.

In man oxybutynin hydrochloride is 83-85% bound to plasma albumin. It is distributed throughout most of the body, with high concentrations in the stomach, intestines and liver, but only very small amounts are found in the central nervous

system. It is estimated that only 0.01% of the dose will enter the cerebrospinal fluid. In rats the concentrations achieved in breast milk and in the foetus are approximately 50-60% of those found in the maternal blood. Distribution of the drug in the foetus is similar to that in the mother.

The elimination of oxybutynin hydrochloride is rapid with a short plasma elimination half-life so that repeated administration of oxybutynin hydrochloride results in little accumulation. Very little oxybutynin hydrochloride is excreted unchanged in the urine - more is excreted in the faeces (approximately 23% compared with 8%).

5.3 Preclinical safety data

There was no evidence of genotoxic or carcinogenic potential. High doses of oxybutynin increased the incidence of extra thoracolumbar ribs in rat foetuses as well as mortality of neonates. However, these effects on the reproductive processes occurred only at doses associated with maternal toxicity (100mg/kg/day).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crospovidone

Microcrystalline cellulose

Lactose monohydrate

Magnesium stearate

Indigo carmine aluminium lake (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Three years

Do not use after the ‘Use Before’ date given on the pack.

6.4 Special precautions for storage

Store below 25ºC in a dry place.

6.5 Nature and contents of container

The tablets are available in Aluminium / µPVC/PVdC strips in boxes of 20, 28, 30, 56, 60, 84 and 120. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 19611/0027

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07/08/2023