Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ditropan 2.5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2.5mg oxybutynin hydrochloride as the active ingredient.

Also contains 76.53mg lactose, anhydrous

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
Pale blue oval bi-convex tablet, 8mm x 5.5mm, marked ‘OXB2.5’ on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Urinary incontinence, urgency and frequency in the 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). It is also useful in the control of vesical hyperactivity seen after surgery of the bladder or prostate or accompanying cystitis.

Peadiatric population

Oxybutnin 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

Dosage and administration:

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

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): Not recommended

Children (over 5 years of age): 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 that the side effects are well tolerated. Nocturnal enuresis: 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. The last dose should be given before bedtime.

4.3 Contraindications

Hypersensitivity to oxybutynin or any component.
Myasthenia gravis.
Narrow-angle glaucoma or shallow anterior chamber.
Due to the risk of provoking hyperpyrexia, this product should not be given to patients with pyrexia or where the ambient temperature is high.
Use in children under the age of five years.
Use in oesophageal dysfunction including hiatus hernia.
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 such as prostatic enlargement.

4.4 Special warnings and precautions for use

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

Oxybutynin should be used with caution in the frail elderly, patients with Parkinson's disease and children who are at greater risk of occurrence of adverse reactions to the product and in patients with autonomic neuropathy, 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 (see section 4.3).

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 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 doctor immediately if they are aware of a sudden loss of visual acuity or ocular pain.

Oxybutynin should not be given to patients with pyrexia (especially children).
When oxybutynin is used in high environmental temperatures, this can cause heat prostration due to decreased sweating.

Oxybutynin hydrochloride is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in animals and in vitro systems.

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.

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 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, Oxybutnin 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. It should not be given to children with pyrexia due to the possibility of heat prostration (see Section 4.3).

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, as anticholinergic agent, may antagonise the effect of prokinetic therapies.

Oxybutynin is metabolised by cytochrome P 450 isoenzyme CYP 3A4. Concomitant administration with a CYP3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure.

Concomitant use with cholinesterase inhibitors may result in reduced cholinesterase inhibitor efficacy.

Concomitant use with bisphosphonates may increase the risk of oesophagitis.

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.

Lactation:
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.

- Gastro-intestinal disorders

Very common: constipation, nausea, dry mouth.
Common: diarrhoea, vomiting.
Uncommon: abdominal discomfort, anorexia, decreased appetite, dysphagia
Not known: gastroesophageal reflux, pseudo-obstruction in patients at risk (elderly or patients with constipation and treated with other drugs that decrease intestinal motility)

- Psychiatric disorders

Common: confusional state.
Not known: agitation, anxiety, hallucinations, nightmares, paranoia, cognitive disorders in elderly, symptoms of depression, dependence to oxybutynin (in patients with a history of drug or substance abuse).

- Nervous system disorders

Very common: dizziness, headache, somnolence
Not known: cognitive disorders, convulsions.

- Cardiac disorders

Not known: tachycardia, arrhythmia.

- Injury, poisoning and procedural complications

Not known: heat stroke.

- Eye disorders

Common: dry eyes.
Not known: angle closure glaucoma, vision blurred, ocular hypertension, mydriasis.

- Renal and urinary disorders

Common: urinary retention.

- Vascular disorders:

Common: flushing.

- Skin and subcutaneous tissue disorders

Very common: dry skin.
Not known: angioedema, rash, urticaria, photosensitivity, hypohidrosis.

- 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

4.9 Overdose

The symptoms of overdosage with Ditropan progress from an intensification of the usual side 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.

Measures to be taken are:
1) Immediate gastric lavage.
2) Physostigmine by slow intravenous injection.

Adults: 0.5 to 2.0 mg physostigmine i.v. slowly, repeated after 5 minutes if necessary, up to a maximum total dose of 5mg.

Children: 30 micrograms/kg physostigmine i.v. slowly, repeated 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 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: G04 BD04.

Oxybutynin has both direct antispasmodic action on the smooth muscle of the bladder detrusor 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 Ditropan increases bladder capacity and reduces the incidence of spontaneous contractions of the detrusor muscle.

5.2 Pharmacokinetic properties

Pharmacokinetic reports show oxybutynin to be rapidly absorbed from the gastrointestinal tract following oral administration with maximum plasma concentrations reached in less than 1 hour subsequently falling biexponentially with a half-life of between 2 and 3 hours. Maximum effect can be seen within 3-4 hours with some effect still evident after 10 hours.

Repeated oral administration achieved steady state after eight days. Oxybutynin does not appear to accumulate in active elderly patients and the pharmacokinetics are similar to those in other adults. However, in frail elderly patients, C_{max} and AUC values are significantly increased. 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, the metabolites also appearing to have antimuscarinic properties. The main elimination route is via the kidneys with only 0.3-0.4% of unchanged drug appearing in the urine of the rat after 24 hours and 1% appearing in the urine of the dog after 48 hours. In rats and dogs therefore, oxybutynin appears to be almost completely metabolised.

5.3 Preclinical safety data

No data of therapeutic relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, anhydrous
Microcrystalline cellulose
Calcium stearate
Indigo Carmine Aluminium Lake (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Do not store above 30^{o}C.

6.5 Nature and contents of container

Packs containing 84 tablets in four uPVC and aluminium foil blister strips of 21 tablets each.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Ireland Ltd. T/A SANOFI
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0540/146/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24th August 1995

Date of last renewal: 28th February 2010

10 DATE OF REVISION OF THE TEXT

November 2016