Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxybutynin hydrochloride 2.5 mg/5 ml oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml solution contains 2.5mg oxybutynin hydrochloride.

Excipients with known effect: Each 5ml of solution contains 896mg sorbitol (E420) and 6.0mg methyl parahydroxybenzoate (E218) and 15.5mg propylene glycol (E1520).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

Clear, colourless solution with raspberry odour.

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).

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 dose is 5mg (10ml) two or three times a day. This may be increased to a maximum of 5mg (10ml) four times a day to obtain a clinical response provided that the side effects are tolerated.

Elderly (including frail elderly):
The elimination half-life is increased in the elderly. Therefore, a dose of 2.5mg (5ml) twice a day, particularly if the patient is frail, is likely to be adequate. This dose may be titrated upwards to 5mg (10ml) twice a day to obtain a clinical response provided that the side effects are tolerated.

Children (under 5 years of age):
Not recommended.

Children (over 5 years of age):

Neurogenic bladder instability:
The usual dose is 2.5mg (5ml) twice a day. This dose may be titrated upwards to 5mg (10ml) two or three times a day to obtain a clinical response provided that the side effects are tolerated.

Nocturnal enuresis:

The usual dose is 2.5mg (5ml) twice a day. This dose may be titrated upwards to 5mg (10ml) two or three times a day to obtain a clinical response provided that the side effects are tolerated. The last dose should be given before bedtime.

Method of administration
For oral administration.
Measure the prescribed dose with the 2.5-5ml double ended spoon provided in the pack.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Oxybutynin should be used with caution in the frail elderly and in 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), hepatic or renal impairment and 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 hyperthyroidism, congestive heart failure, coronary heart disease, cardiac arrhythmias, 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 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 esophagitis.

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

Paediatric population
Oxybutynin hydrochloride is not recommended for use in children below age 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 adverse reactions.

Excipient Warnings
This product contains:
Methyl parahydroxybenzoate (E218): This may cause allergic reactions (possibly delayed).
Liquid sorbitol (non-crystallising) (E420): This medicinal product contains 896mg sorbitol in each 5ml dose which is equivalent to 179.2mg/ml. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.
Sodium: This medicinal product contains less than 1 mmol sodium (23mg) per 5ml dose, that is to say essentially 'sodium-free'.

Propylene glycol (E1520): This medicinal product contains 15.5mg propylene glycol in each 5ml dose which is equivalent to 3.1mg/ml.

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 a potentiation of anticholinergic effects could 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 P450 isoenzyme CYP 3A4. Concomitant administration with a CYP3A4 inhibitor can inhibit oxybutynin metabolism and increase oxybutynin exposure.
Oxybutynin may antagonise 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 hydrochloride in pregnant women. Animal studies are insufficient with respect to effects on pregnancy, embryonic/foetal development, parturition or postnatal development. 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 the mother's milk. Use of oxybutynin during breast feeding is therefore not recommended.

4.7 Effects on ability to drive and use machines

As Oxybutynin hydrochloride oral solution may produce drowsiness or blurred vision, the patient 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

Adverse effects have been listed under headings of body systems and their frequencies as follows, where possible: very common (≥ 1 / 10), common (≥ 1 / 100 to <1 / 10), uncommon (≥ 1 /1000 to <1 / 100), rare (≥ 1 / 10, 000 to <1 / 1000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Table 1: Adverse effects and their frequencies:

Body systems	**Very common** (1/10)	**Common** (1/100 to <1/10)	**Uncommon** (≥ 1 /1000 to <1 / 100)	**Not known**
Infections and infestations	-	-	-	urinary tract infection
Gastrointestinal disorders	constipation, nausea, dry mouth	diarrhoea, vomiting	abdominal discomfort, anorexia, decreased appetite, dysphagia	gastroesophageal reflux disease
Psychiatric disorders	-	confusional state	-	agitation, anxiety, hallucinations, nightmares, paranoia, cognitive disorders in

				elderly
Nervous system disorders	dizziness, headache, somnolence	-	-	cognitive disorders, convulsions
Cardiac disorders	-	-	-	tachycardia, arrhythmia, palpitation
Injury, poisoning and procedural complications	-	-	-	heat stroke
Eye disorders	-	dry eyes	-	Angle closure glaucoma, mydriasis, ocular hypertension, vision blurred
Renal and urinary disorders	-	urinary retention	-	-
Vascular disorders	-	flushing	-	-
Skin and subcutaneous tissue disorders	dry skin	-	-	angioedema, rash, urticaria, hypohidrosis
Immune system disorders	-	-	-	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 Website: www.hpra.ie.

4.9 Overdose

The symptoms of overdose with oxybutynin progress from an intensification of the usual side effects of CNS disturbances (from restlessness and excitement to psychotic behaviour), circulation 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 2.0mg of physostigmine by slow intravenous administration. Repeat after 5 minutes, if necessary up to a maximum total dose of 5mg.

Children: 30micrograms/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 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: anticholinergic as well as antispasmodic, ATC Code: G04B D04
Oxybutynin has both direct antispasmodic action on the smooth muscle of the bladder detrusor muscle as well as an 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 increases bladder capacity and reduces the incidence of spontaneous contractions of the detrusor muscle.

5.2 Pharmacokinetic properties

Absorption
Oxybutynin is rapidly absorbed from the gastrointestinal tract following oral administration with maximum plasma concentrations reached in less than 1 hour. First-passage effect is high and less than 10% of the administered dose reaches the circulation unchanged.

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 5mg oxybutynin hydrochloride.

Metabolism
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.

Excretion
Oxybutynin is extensively metabolised in the liver, see above, with less than 0.1% of the administered dose excreted unchanged in the urine. Also, less than 0.1% of the administered dose is excreted as the metabolite N-desethyloxybutynin.

Elderly
Bioavailability is higher in elderly patients; AUC is 2-4-fold higher after repeated administration and half-life 3-5 times longer (see section 4.2).

5.3 Preclinical safety data

No data of therapeutic relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate (E330)
Sodium citrate (E331)
Liquid sorbitol (non-crystallising) (E420)
Glycerol (E422)
Methyl parahydroxybenzoate (E218)
Raspberry flavour (containing propylene glycol (E1520))
Purified water

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.
Discard 30 days after first opening. Store in the original packaging after first opening.

6.4 Special precautions for storage

Do not store above 25°C.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Bottle: Ph. Eur Type III Amber glass.
Closure: Tamper evident, child resistant, plastic (Polypropylene/ Polyethylene) cap with EPE liner.
Pack size: 100ml and 150ml.
Not all pack sizes may be marketed.
Dosing device: Double ended white polypropylene plastic spoon with 2.5ml and 5ml measuring ends.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Syri Pharma Limited t/a Thame Laboratories
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1 WML
1 Windmill Lane
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8 MARKETING AUTHORISATION NUMBER

PA22697/014/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th March 2015
Date of last renewal: 1st March 2020

10 DATE OF REVISION OF THE TEXT

July 2023