Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ditropan 2.5mg/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 2.5mg oxybutynin hydrochloride.

Excipients: Each 5ml contains 1.265g sucrose, 1.925g sorbitol (E420) and 2.85mg sodium methyl-*p*-hydroxybenzoate (E219)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral Solution
A clear colourless viscous oral solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an anticholinergic agent, also with a direct relaxant effect on smooth muscle, oxybutynin inhibits bladder muscle contractions and spasm. For use in 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

Adults: The usual dose is 5mg (10ml) two or three times a day. This may be increased to a maximum of 5mg 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 (5ml) 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: the usual dose is 2.5mg (5ml) 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 (5ml) 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.

Following initial control, it may be possible to introduce a reduced maintenance dose.

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 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 prostastic enlargement.

4.4 Special warnings and precautions for use

Due to the presence of sorbitol and sucrose in this product, patients with rare hereditary problems of fructose intolerance should not take this medicine.

Due to the presence of sucrose in this product, patients with glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Sodium methyl-p-hydroxybenzoate may cause allergic reactions (possibly delayed), and exceptionally, bronchospasm.

Oxybutynin should be used with caution in the frail elderly who may be more sensitive to the effects of the product and in patients with autonomic neuropathy, hepatic or renal impairment, gastrointestinal pathology including severe gastrointestinal motility disorders.

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

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.

Chronic use may result in an increase in dental caries, as a consequence of reduced or inhibited salivation. Regular dental check-ups are therefore advisable during long-term treatment.

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, 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.

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken if other anticholinergic agents are administered together with Ditropan as potentiation of anticholinergic effects could occur.

Occasional cases of interaction between anticholinergics and phenothiazines, amantadine, butyrophenones, L-dopa, digitalis and tricyclic antidepressants have been reported and care should be taken if Ditropan is administered concurrently with such drugs.

By reducing gastric motility, oxybutynin may affect the absorption of other drugs.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no evidence as to the safety of Ditropan in human pregnancy nor is there evidence from animal work that is totally free from hazard. Avoid in pregnancy unless there is no safer alternative.

Lactation
Small amounts of oxybutynin have been found in mother's milk of lactating animals. Breast feeding while using oxybutynin is therefore not recommended.

4.7 Effects on ability to drive and use machines

The product may cause drowsiness or blurred vision. Patients should not drive or operate machinery unless it has been shown not to affect physical or mental ability.

4.8 Undesirable effects

Gastro-intestinal disorders
Nausea, diarrhoea, constipation, dry mouth, abdominal discomfort, anorexia, vomiting, gastroesophageal reflux.

CNS and psychiatric disorders
Agitation, headache, dizziness, drowsiness, cognitive disorders (disorientation, anxiety, paranoia), hallucinations, nightmares, convulsions.

Cardiovascular disorders
Tachycardia, cardiac arrhythmia.

Vision disorders
Blurred vision, mydriasis, intraocular hypertension, onset of narrow-angle glaucoma, dry eyes.

Renal and urinary disorders
Urinary retention, difficulty in micturition.

Skin and appendages
Facial flushing which may be more marked in children, dry skin, allergic reactions such as rash, urticaria, angioedema, photosensitivity.

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

Children: 30 μg/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

Oxybutynin hydrochloride has both direct antispasmodic action on the smooth muscle of the bladder detrusor 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. 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

Citric Acid monohydrate
Sodium Citrate dihydrate
Sucrose
Sorbitol liquid (non-crystallising) (E420)
Glycerol (E422)
Sodium Methyl-*p*-Hydroxybenzoate (E219)
Purified Water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Unopened: 2.5 years.
Once opened: Discard any remaining solution 28 days after first opening the bottle.

6.4 Special precautions for storage

Store below 25°C. Store in the original container in order to protect from light.

6.5 Nature and contents of container

30ml (sample size) and 150ml type III amber glass bottle with a polypropylene child-proof cap containing PVDC/PE liner.

Not all pack sizes may be marketed.

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

PA 540/146/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th January 1994

Date of last renewal: 1st March 2008

10 DATE OF REVISION OF THE TEXT

April 2012