Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

COSOPT 20mg/ml + 5mg/ml eye drops, solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 22.26 mg of dorzolamide hydrochloride corresponding to 20 mg dorzolamide and 6.83 mg of timolol maleate corresponding to 5 mg timolol.

Excipients: Benzalkonium chloride

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, Solution

Product imported from Italy:
Clear, colourless to nearly colourless, slightly viscous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Indicated in the treatment of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or pseudoexfoliative glaucoma when topical beta-blocker monotherapy is not sufficient.

4.2 Posology and method of administration

The dose is one drop of COSOPT in the [conjunctival sac of the] affected eye(s) two times daily.

If another topical ophthalmic agent is being used, COSOPT and the other agent should be administered at least ten minutes apart.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.

Please see section 6.6 Instructions for use/handling.

Efficacy in paediatric patients has not been established.

Safety in paediatric patients below the age of 2 years has not been established. (For information regarding safety in paediatric patients 2 and <6 years of age, see section 5.1).

4.3 Contraindications

COSOPT is contraindicated in patients with:

- reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease
- sinus bradycardia, sick sinus syndrome sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker. Overt cardiac failure, cardiogenic shock

• severe renal impairment (CrCl < 30 ml/min) or hyperchloremic acidosis
• hypersensitivity to the active substance (substances), or to any of the excipients.
The above are based on the components and are not unique to the combination.

4.4 Special warnings and precautions for use

Like other topically applied ophthalmic agents Timolol is absorbed systemically. Due to beta adrenergic component, Timolol the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see 4.2.

Cardiovascular/Respiratory Reactions

As with other topically-applied ophthalmic agents, this drug may be absorbed systemically. The timolol component is a beta-blocker. Therefore, the same types of adverse reactions found with systemic administration of beta-blockers may occur with topical administration, including worsening of Prinzmetal angina, worsening of severe peripheral and central circulatory disorders, and hypotension.

Because of the timolol maleate component, cardiac failure should be adequately controlled before beginning therapy with COSOPT. In patients with a history of severe cardiac disease, signs of cardiac failure should be watched for and pulse rates should be checked.

Respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma and rarely death in association with cardiac failure, have been reported following administration of timolol maleate.

Cardiac disorders

In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.

Due to its negative effect on conduction time, betablockers should only be given with caution to patients with first degree heart block.

Vascular disorders

Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud’s disease or Raynaud’s syndrome) should be treated with caution.

Respiratory disorders

Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers.

Cosopt should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.

Hypoglycaemia/diabetes

Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia.

Beta-blockers may also mask the signs of hyperthyroidism.

Corneal diseases

Ophthalmic β-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

Other beta-blocking agents

The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when Timolol is given to the patients already receiving a systemic beta-blocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).

Anaphylactic reactions

While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.

Choroidal detachment

Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.

Surgical anaesthesia

β-blocking ophthalmological preparations may block systemic β-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving Timolol.

Hepatic Impairment

COSOPT has not been studied in patients with hepatic impairment and therefore should be used with caution in such patients.

Immunology and Hypersensitivity

As with other topically-applied ophthalmic agents, this drug may be absorbed systemically. The dorzolamide component is a sulfonamide. Therefore the same types of adverse reactions found with systemic administration of sulfonamides may occur with topical administration. If signs of serious reactions or hypersensitivity occur, discontinue use of this preparation.

Local ocular adverse effects, similar to those observed with dorzolamide hydrochloride eye drops, have been seen with COSOPT. If such reactions occur, discontinuation of COSOPT should be considered.

While taking β-blockers, patients with a history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to accidental, diagnostic, or therapeutic repeated challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

Concomitant Therapy

The following concomitant medication is not recommended:
- dorzolamide and oral carbonic anhydrase inhibitors
- topical beta-adrenergic blocking agents

Withdrawal of Therapy

As with systemic beta-blockers, if discontinuation of ophthalmic timolol is needed in patients with coronary heart disease, therapy should be withdrawn gradually.

Additional Effects of Beta-Blockade

Therapy with beta-blockers may mask certain symptoms of hypoglycemia in patients with diabetes mellitus or hypoglycemia.

Therapy with beta-blockers may mask certain symptoms of hyperthyroidism. Abrupt withdrawal of beta-blocker therapy may precipitate a worsening of symptoms.

Therapy with beta-blockers may aggravate symptoms of myasthenia gravis.

Additional Effects of Carbonic Anhydrase Inhibition

Therapy with oral carbonic anhydrase inhibitors has been associated with urolithiasis as a result of acid-base disturbances, especially in patients with a prior history of renal calculi. Although no acid-base disturbances have been observed with COSOPT, urolithiasis has been reported infrequently. Because COSOPT contains a topical carbonic anhydrase inhibitor that is absorbed systemically, patients with a prior history of renal calculi may be at increased risk of urolithiasis while using COSOPT.

Other

The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. COSOPT has not been studied in patients with acute angle-closure glaucoma.

Corneal oedema and irreversible corneal decompensation have been reported in patients with pre-existing chronic corneal defects and/or a history of intraocular surgery while using dorzolamide. Topical dorzolamide should be used with caution in such patients.

Choroidal detachment concomitant with ocular hypotony have been reported after filtration procedures with administration of aqueous suppressant therapies.

As with the use of other antiglaucoma drugs, diminished responsiveness to ophthalmic timolol maleate after prolonged therapy has been reported in some patients. However, in clinical studies in which 164 patients have been followed for at least three years, no significant difference in mean intraocular pressure has been observed after initial stabilization.

Contact Lens Use

COSOPT contains the preservative benzalkonium chloride, which may cause eye irritation. Remove contact lenses prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

Paediatric Use

See section 5.1.

4.5 Interaction with other medicinal products and other forms of interaction

No Specific drug interaction studies have been performed with Timolol.

In clinical studies, COSOPT was used concomitantly with the following systemic medications without evidence of adverse interactions: ACE-inhibitors, calcium channel blockers, diuretics, non-steroidal anti-inflammatory drugs including aspirin, and hormones (e.g., estrogen, insulin, thyroxine).

There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics, guanethidine.

Potentiated systemic beta-blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) and timolol.

Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.

The dorzolamide component of COSOPT is a carbonic anhydrase inhibitor and although administered topically, is absorbed systemically. In clinical studies, dorzolamide hydrochloride ophthalmic solution was not associated with acid-base disturbances. However, these disturbances have been reported with oral carbonic anhydrase inhibitors and have in some instances, resulted in drug interactions (e.g., toxicity associated with high-dose salicylate therapy). Therefore, the potential for such drug interactions should be considered in patients receiving COSOPT.

Although COSOPT alone has little or no effect on pupil size, mydriasis resulting from concomitant use of ophthalmic timolol maleate and epinephrine has been reported occasionally.

Beta-blockers may increase the hypoglycemic effect of antidiabetic agents.

Oral β-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine.

4.6 Fertility, pregnancy and lactation

Use During Pregnancy

There are no adequate data for the use of Timololin pregnant women. Timolol should not be used during pregnancy unless clearly necessary. To reduce the systemic absorption, see 4.2.

Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when betablockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If COSOPT is administered until delivery, the neonate should be carefully monitored during the first days of life.

Use During Lactation

Beta-blockers are excreted in breast milk. However, at therapeutic doses of Timolol in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant. To reduce the systemic absorption, see 4.2.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Possible side effects such as blurred vision may affect some patients' ability to drive and/or operate machinery.

4.8 Undesirable effects

Like other topically applied ophthalmic drugs, Timolol is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic betablocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.

In clinical studies no adverse experiences specific to COSOPT have been observed; adverse experiences have been limited to those that were reported previously with dorzolamide hydrochloride and/or timolol maleate. In general, common adverse experiences were mild and did not cause discontinuation.

During clinical studies, 1035 patients were treated with COSOPT. Approximately 2.4% of all patients discontinued therapy with COSOPT because of local ocular adverse reactions, approximately 1.2% of all patients discontinued because of local adverse reactions suggestive of allergy or hypersensitivity (such as lid inflammation and conjunctivitis).

The following adverse reactions have been reported with COSOPT or one of its components either during clinical trials or during post-marketing experience:

[Very Common: >1/10), Common: >1/100, <1/10), Uncommon: >1/1000, <1/100), and Rare: >1/10,000, <1/1000)]

Musculoskeletal and connective tissue disorders:

Timolol maleate ophthalmic solution:

Rare: systemic lupus erythematosus

Nervous system and psychiatric disorders:

Dorzolamide hydrochloride ophthalmic solution:

Common: headache

Rare: dizziness, paresthesia

Timolol maleate ophthalmic solution:

Common: headache

Uncommon: dizziness, depression

Rare: insomnia, nightmares, memory loss, paresthesia, increase in signs and symptoms of myasthenia gravis, decreased libido, cerebrovascular accident

Eye disorders:

COSOPT:

Very Common: burning and stinging

Common: conjunctival injection, blurred vision, corneal erosion, ocular itching, tearing

Dorzolamide hydrochloride ophthalmic solution:

Common: eyelid inflammation, eyelid irritation

Uncommon: iridocyclitis

Rare: irritation including redness, pain, eyelid crusting, transient myopia (which resolved upon discontinuation of therapy), corneal oedema, ocular hypotony, choroidal detachment (following filtration surgery)

Timolol maleate ophthalmic solution:

Common: signs and symptoms of ocular irritation including blepharitis, keratitis, decreased corneal sensitivity, and dry eyes

Uncommon: visual disturbances including refractive changes (due to withdrawal of miotic therapy in some cases)

Rare: ptosis, diplopia, choroidal detachment (following filtration surgery)

Ear and labyrinth disorders:

Timolol maleate ophthalmic solution:

Rare: tinnitus

Cardiac and vascular disorders:

Timolol maleate ophthalmic solution:

Uncommon: bradycardia, syncope

Rare: hypotension, chest pain, palpitation, edema, arrhythmia, congestive heart failure, heart block, cardiac arrest, cerebral ischemia, claudication, Raynaud's phenomenon, cold hands and feet

Respiratory, thoracic, and mediastinal disorders:

COSOPT:

Common: sinusitis

Rare: shortness of breath, respiratory failure, rhinitis

Dorzolamide hydrochloride ophthalmic solution:

Rare: epistaxis

Timolol maleate ophthalmic solution:

Uncommon: dyspnea

Rare: bronchospasm (predominantly in patients with pre-existing bronchospastic disease), cough

Gastrointestinal disorders:

COSOPT:

Very Common: taste perversion

Dorzolamide hydrochloride ophthalmic solution:

Common: nausea

Rare: throat irritation, dry mouth

Timolol maleate ophthalmic solution:

Uncommon: nausea, dyspepsia

Rare: diarrhea, dry mouth

Skin and subcutaneous tissue disorders:

COSOPT:

Rare: contact dermatitis

Dorzolamide hydrochloride ophthalmic solution:

Rare: rash

Timolol maleate ophthalmic solution:

Rare: alopecia, psoriasiform rash or exacerbation of psoriasis

Renal disorders:

COSOPT:

Uncommon: urolithiasis

Reproductive system and breast disorders:

Timolol maleate ophthalmic solution:

Rare: Peyronie's disease

General disorders and administration site disorders:

COSOPT:

Rare: signs and symptoms of systemic allergic reactions, including angioedema, urticaria, pruritus, rash, anaphylaxis, rarely bronchospasm

Dorzolamide hydrochloride ophthalmic solution:

Common: asthenia/fatigue

Timolol maleate ophthalmic solution:

Uncommon: asthenia/fatigue

These adverse reactions were also observed with COSOPT during post-marketing experience.

Laboratory Findings

COSOPT was not associated with clinically meaningful electrolyte disturbances in clinical studies.

Additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with COSOPT:

Immune system disorders:

Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus,anaphylactic reaction.

Metabolism and nutrition disorders:

Hypoglycaemia.

Psychiatric disorders:

Insomnia, depression, nightmares, memory loss.

Nervous system disorders:

Syncope, cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, dizziness, paraesthesia, and headache.

Eye disorders:

Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), blepharitis, keratitis, blurred vision and choroidal detachment following filtration surgery (see 4.4 Special warnings and special precautions for use). decreased corneal sensitivity, dry
eyes, corneal erosion ptosis, diplopia.

Cardiac disorders:

Bradycardia, chest pain, palpitations, oedema, arrhythmia, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure.

Vascular disorders:

Hypotension, Raynaud's phenomenon, cold hands and feet.

Respiratory, thoracic, and mediastinal disorders:

Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnoea, cough.

Gastrointestinal disorders:

Dysgeusia, nausea, dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.

Skin and subcutaneous tissue disorders:

Alopecia, psoriasiform rash or exacerbation of psoriasis, skin rash.

Musculoskeletal and connective tissue disorders:

Myalgia.

Reproductive system and breast disorders:

Sexual dysfunction, decreased libido.

General disorders and administration site conditions:

Asthenia/fatigue.

4.9 Overdose

No data are available in humans in regard to overdose by accidental or deliberate ingestion of COSOPT.

Symptoms
There have been reports of inadvertent overdoses with timolol maleate ophthalmic solution resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest. The most common signs and symptoms to be expected with overdoses of dorzolamide are electrolyte imbalance, development of an acidotic state, and possibly central nervous system effects.

Only limited information is available with regard to human overdose by accidental or deliberate ingestion of dorzolamide hydrochloride. With oral ingestion, somnolence has been reported. With topical application the following have been reported: nausea, dizziness, headache, fatigue, abnormal dreams, and dysphagia.

Treatment
Treatment should be symptomatic and supportive. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored. Studies have shown that timolol does not dialyze readily.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiglaucoma preparations and miotics, Beta blocking agents, Timolol, combinations, ATC code: S01ED51

Mechanism of Action

COSOPT is comprised of two components: dorzolamide hydrochloride and timolol maleate. Each of these two components decreases elevated intraocular pressure by reducing aqueous humor secretion, but does so by a different mechanism of action.

Dorzolamide hydrochloride is a potent inhibitor of human carbonic anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. Timolol maleate is a nonselective beta-adrenergic receptor blocking agent. The precise mechanism of action of timolol maleate in lowering intraocular pressure is not clearly established at this time, although a fluorescein study and tonography studies indicate that the predominant action may be related to reduced aqueous formation. However, in some studies a slight increase in outflow facility was also observed.
The combined effect of these two agents results in additional intraocular pressure reduction (IOP) compared to either component administered alone.

Following topical administration, COSOPT reduces elevated intraocular pressure, whether or not associated with glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. COSOPT reduces intraocular pressure without the common side effects of miotics such as night blindness, accommodative spasm and pupillary constriction.

Pharmacodynamic effects

Clinical Effects
Clinical studies of up to 15 months duration were conducted to compare the IOP-lowering effect of COSOPT b.i.d. (dosed morning and bedtime) to individually- and concomitantly-administered 0.5% timolol and 2.0% dorzolamide in patients with glaucoma or ocular hypertension for whom concomitant therapy was considered appropriate in the trials. This included both untreated patients and patients inadequately controlled with timolol monotherapy. The majority of patients were treated with topical beta-blocker monotherapy prior to study enrollment. In an analysis of the combined studies, the IOP-lowering effect of COSOPT b.i.d. was greater than

that of monotherapy with either 2% dorzolamide t.i.d. or 0.5% timolol b.i.d. The IOP-lowering effect of COSOPT b.i.d. was equivalent to that of concomitant therapy with dorzolamide b.i.d. and timolol b.i.d. The IOP-lowering effect of COSOPT b.i.d. was demonstrated when measured at various time points throughout the day and this effect was maintained during long-term administration.

Paediatric use

A 3 month controlled study, with the primary objective of documenting the safety of 2% dorzolamide hydrochloride ophthalmic solution in children under the age of 6 years has been conducted. In this study, 30 patients under 6 and greater than or equal to 2 years of age whose IOP was not adequately controlled with monotherapy by dorzolamide or timolol received COSOPT in an open label phase. Efficacy in those patients has not been established. In this small group of patients, twice daily administration of COSOPT was generally well tolerated with 19 patients completing the treatment period and 11 patients discontinuing for surgery, a change in medication, or other reasons.

5.2 Pharmacokinetic properties

Dorzolamide Hydrochloride

Unlike oral carbonic anhydrase inhibitors, topical administration of dorzolamide hydrochloride allows for the active substance to exert its effects directly in the eye at substantially lower doses and therefore with less systemic exposure. In clinical trials, this resulted in a reduction in IOP without the acid-base disturbances or alterations in electrolytes characteristic of oral carbonic anhydrase inhibitors.

When topically applied, dorzolamide reaches the systemic circulation. To assess the potential for systemic carbonic anhydrase inhibition following topical administration, active substance and metabolite concentrations in red blood cells (RBCs) and plasma and carbonic anhydrase inhibition in RBCs were measured. Dorzolamide accumulates in RBCs during chronic dosing as a result of selective binding to CA-II while extremely low concentrations of free active substance in plasma are maintained. The parent active substance forms a single N-desethyl metabolite that inhibits CA-II less potently than the parent active substance but also inhibits a less active isoenzyme (CA-I). The metabolite also accumulates in RBCs where it binds primarily to CA-I. Dorzolamide binds moderately to plasma proteins (approximately 33%). Dorzolamide is primarily excreted unchanged in the urine; the metabolite is also excreted in urine. After dosing ends, dorzolamide washes out of RBCs nonlinearly, resulting in a rapid decline of active substance concentration initially, followed by a slower elimination phase with a half-life of about four months.

When dorzolamide was given orally to simulate the maximum systemic exposure after long term topical ocular administration, steady state was reached within 13 weeks. At steady state, there was virtually no free active substance or metabolite in plasma; CA inhibition in RBCs was less than that anticipated to be necessary for a pharmacological effect on renal function or respiration. Similar pharmacokinetic results were observed after chronic, topical administration of dorzolamide hydrochloride. However, some elderly patients with renal impairment (estimated CrCl 30-60 ml/min) had higher metabolite concentrations in RBCs, but no meaningful differences in carbonic anhydrase inhibition and no clinically significant systemic side effects were directly attributable to this finding.

Timolol Maleate

In a study of plasma active substance concentration in six subjects, the systemic exposure to timolol was determined following twice daily topical administration of timolol maleate ophthalmic solution 0.5%. The mean peak plasma concentration following morning dosing was 0.46 ng/ml and following afternoon dosing was 0.35 ng/ml.

5.3 Preclinical safety data

The ocular and systemic safety profile of the individual components is well established.

Dorzolamide
In rabbits given maternotoxic doses of dorzolamide associated with metabolic acidosis, malformations of the vertebral bodies were observed.

Timolol
Animal studies have not shown teratogenic effect.

Furthermore, no adverse ocular effects were seen in animals treated topically with dorzolamide hydrochloride and timolol maleate ophthalmic solution or with concomitantly-administered dorzolamide hydrochloride and timolol maleate. *In vitro* and *in vivo* studies with each of the components did not reveal a mutagenic potential. Therefore, no significant risk for human safety is expected with therapeutic doses of COSOPT.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hyetellose
Mannitol
Sodium citrate
Sodium hydroxide
Benzalkonium chloride
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

COSOPT should be used no longer than 28 days after first opening the container.

6.4 Special precautions for storage

Keep the bottle in the outer carton, in order to protect from light.

6.5 Nature and contents of container

Tamper-evident bottle with dropper.
1 x 5ml bottle in an overlabelled outer carton.

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 PARALLEL PRODUCT AUTHORISATION HOLDER

G & A Licensing Ltd
Ballymurray
Co. Roscommon
Ireland

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1447/40/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31st March 2010

10 DATE OF REVISION OF THE TEXT

May 2012