ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

OPATANOL 1 mg/ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains 1 mg olopatadine (as hydrochloride).

Excipients: Benzalkonium chloride 0.1 mg/ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops).

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of ocular signs and symptoms of seasonal allergic conjunctivitis.

4.2 Posology and method of administration

The dose is one drop of OPATANOL in the conjunctival sac of the affected eye(s) twice daily (8 hourly). Treatment may be maintained for up to four months, if considered necessary.

To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas, or other surfaces with the dropper tip of the bottle. Keep the bottle tightly closed when not in use.

In case of concomitant therapy with other topical ocular medicines, an interval of five to ten minutes should be allowed between successive applications.

Use in elderly
No dosage adjustment in elderly patients is necessary.

Paediatric patients
OPATANOL may be used in paediatric patients (three years of age and older) at the same dose as in adults.

Use in hepatic and renal impairment
Olopatadine in the form of eye drops (OPATANOL) has not been studied in patients with renal or hepatic disease. However, no dosage adjustment is expected to be necessary in hepatic or renal impairment (see section 5.2).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

OPATANOL is an antiallergic/antihistaminic agent and, although administered topically, is absorbed systemically. If signs of serious reactions or hypersensitivity occur, discontinue the use of this treatment.

Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Since OPATANOL contains benzalkonium chloride, close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

Contact lenses
Patients should be instructed to wait 10-15 minutes after instillation of OPATANOL before inserting contact lenses. OPATANOL should not be administered while wearing contact lenses.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

In vitro studies have shown that olopatadine did not inhibit metabolic reactions which involve cytochrome P-450 isozymes 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4. These results indicate that olopatadine is unlikely to result in metabolic interactions with other concomitantly administered active substances.

4.6 Pregnancy and lactation

Pregnancy
For olopatadine, no clinical data on exposed pregnancies are available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).

Caution should be exercised when prescribing to pregnant women.

Breast-feeding mothers
OPATANOL is not recommended for breast-feeding mothers.

Olopatadine has been detected in the milk of nursing rats following oral administration. Studies in animals have shown reduced growth of nursing pups of dams receiving systemic doses of olopatadine well in excess of the maximum level recommended for human ocular use. It is not known whether topical administration to humans could result in sufficient systemic absorption to produce detectable quantities in human breast milk.

4.7 Effects on ability to drive and use machines

As with any eye drop, temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

In clinical studies involving 1680 patients, OPATANOL was administered one to four times daily in both eyes for up to four months as monotherapy or adjunctive therapy to loratadine 10 mg. Approximately 4.5% of patients can be expected to experience undesirable effects associated with the use of OPATANOL; however, only 1.6% of patients discontinued from the clinical studies due to these undesirable effects. No serious ophthalmic or systemic undesirable effects related to OPATANOL were reported in clinical studies. The most frequent treatment-related undesirable effect was eye pain, reported at an overall incidence of 0.7%.

The following undesirable effects were assessed to be treatment-related and are classified according to the following convention: very common (≥1/10), common (>1/100 to <1/10), uncommon (>1/1,000 to ≤1/100), rare (>1/10,000 to ≤1/1000), or very rare (≤1/10,000). Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Infections and infestations
Uncommon: rhinitis

Nervous system disorders
Common: headache, dysgeusia
Uncommon: dizziness, hypoaesthesia

Eye disorders
Common: eye pain, eye irritation, dry eye, abnormal sensation in eyes
Uncommon: corneal erosion, corneal epithelium defect, corneal epithelium disorder, punctate keratitis, keratitis, corneal staining, eye discharge, photophobia, vision blurred, visual acuity reduced, blepharospasm, ocular discomfort, eye pruritus, conjunctival follicles, conjunctival disorder, foreign body sensation in eyes, lacrimation increased, eyelids pruritus, erythema of eyelid, eyelid oedema, eyelid disorder, conjunctival hyperaemia, ocular hyperaemia

Respiratory, thoracic, and mediastinal disorders
Common: nasal dryness

Skin and subcutaneous tissue disorders
Uncommon: dermatitis contact, skin burning sensation, dry skin

General disorders and administration site conditions
Common: fatigue

Not known (cannot be estimated from the available data):
Adverse reactions identified from post-marketing experience that have not been reported previously in clinical trials with OPATANOL include those detailed below. Unlike data from clinical trials, due to the nature of post-marketing surveillance, the frequency at which these events occur is not known and cannot be estimated based upon the available data.

Ocular: corneal oedema, conjunctivitis, eye oedema, eye swelling, mydriasis, visual disturbance, eyelid margin crusting
Systemic: hypersensitivity, dyspnea, somnolence, swelling face, dermatitis, erythema, nausea, vomiting, sinusitis, asthenia, malaise

4.9 Overdose

No data are available in humans regarding overdose by accidental or deliberate ingestion. Olopatadine has a low order of acute toxicity in animals. Accidental ingestion of the entire contents of a bottle of OPATANOL would deliver a maximum systemic exposure of 5 mg olopatadine. This exposure would result in a final dose of 0.5 mg/kg in a 10 kg infant, assuming 100% absorption.

Prolongation of the QTc interval in dogs was observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. A 5 mg oral dose was administered twice-daily for 2.5 days to 102 young and elderly male and female healthy volunteers with no significant prolongation of QTc interval compared to placebo. The range of peak steady-state olopatadine plasma concentrations (35 to 127 ng/ml) seen in this study represents at least a 70-fold safety margin for topical olopatadine with respect to effects on cardiac repolarisation.

In the case of overdose, appropriate monitoring and management of the patient should be implemented.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: ophthalmologicals; decongestant and antiallergics; other antiallergics.

ATC code: S01GX 09

Olopatadine is a potent selective antiallergic/antihistaminic agent that exerts its effects through multiple distinct mechanisms of action. It antagonises histamine (the primary mediator of allergic response in humans) and prevents histamine induced inflammatory cytokine production by human conjunctival epithelial cells. Data from *in vitro* studies suggest that it may act on human conjunctival mast cells to inhibit the release of pro-inflammatory mediators. In patients with patent nasolacrimal ducts, topical ocular administration of OPATANOL was suggested to reduce the nasal signs and symptoms that frequently accompany seasonal allergic conjunctivitis. It does not produce a clinically significant change in pupil diameter.

5.2 Pharmacokinetic properties

Olopatadine is absorbed systemically, as are other topically administered medicinal products. However, systemic absorption of topically applied olopatadine is minimal with plasma concentrations ranging from below the assay quantitation limit (<0.5 ng/ml) up to 1.3 ng/ml. These concentrations are 50-to 200-fold lower than those following well tolerated oral doses. From oral pharmacokinetic studies, the half-life of olopatadine in plasma was approximately eight to 12 hours, and elimination was predominantly through renal excretion. Approximately 60-70% of the dose was recovered in the urine as active substance. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

Since olopatadine is excreted in urine primarily as unchanged active substance, impairment of renal function alters the pharmacokinetics of olopatadine with peak plasma concentrations 2.3-fold greater in patients with severe renal impairment (mean creatinine clearance of 13.0 ml/min) compared to healthy adults. Following a 10 mg oral dose in patients undergoing haemodialysis (with no urinary output), plasma olopatadine concentrations were significantly lower on the haemodialysis day than on the non-haemodialysis day suggesting olopatadine can be removed by haemodialysis.

Studies comparing the pharmacokinetics of 10 mg oral doses of olopatadine in young (mean age 21 years) and elderly (mean age 74 years) showed no significant differences in the plasma concentrations (AUC), protein binding or urinary excretion of unchanged parent drug and metabolites.

A renal impairment study after oral dosing of olopatadine has been performed in patients with severe renal impairment. The results indicate that a somewhat higher plasma concentration can be expected with OPATANOL in this population. Since plasma concentrations following topical ocular dosing of olopatadine are 50-to 200-fold lower than after well-tolerated oral doses, dose adjustment is not expected to be necessary in the elderly or in the renally impaired population. Liver metabolism is a minor route of elimination. Dose adjustment is not expected to be necessary with hepatic impairment.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride,
sodium chloride,
disodium phosphate dodecahydrate (E339),
hydrochloric acid (E507) and/or sodium hydroxide (E524) (to adjust pH),
purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

3 years.

Discard four weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and content of container

5 ml opaque low density polyethylene bottles with polypropylene screw caps (DROP-TAINER).

Cartons containing 1 or 3 bottles. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Herts., HP2 7UD
United Kingdom

8. MARKETING AUTHORISATION NUMBERS

EU/1/02/217/001-002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th May 2002
Date of last renewal: 22nd May 2007

10. DATE OF REVISION OF THE TEXT

ANNEX II

A. MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE

Names and addresses of the manufacturer(s) responsible for batch release

S.A. Alcon-Couvreur N.V.,
Rijksweg 14,
B-2870 Puurs,
Belgium.

or

Alcon Cusí, S.A.,
Camil Fabra 58,
08320 El Masnou,
Barcelona,
Spain.

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOX OF 1 BOTTLE + BOX OF 3 BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

OPATANOL 1 mg/ml eye drops, solution
Olopatadine

2. STATEMENT OF ACTIVE SUBSTANCE

1 ml of solution contains 1 mg olopatadine (as hydrochloride).

3. LIST OF EXCIPIENTS

Benzalkonium chloride, sodium chloride, disodium phosphate dodecahydrate, hydrochloric acid/sodium hydroxide (to adjust pH) and purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution;
1 x 5 ml
3 x 5 ml

5. METHOD AND ROUTE OF ADMINISTRATION

Ocular use. Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Exp: xx/xxxx
Discard four weeks after first opening.
Opened:
Opened (1):
Opened (2):
Opened (3):

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Herts., HP2 7UD
United Kingdom

12. MARKETING AUTHORISATION NUMBERS

EU/1/02/217/001 1 x 5 ml
EU/1/02/217/002 3 x 5 ml

13. BATCH NUMBER

Lot: xxxxx

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Opatanol

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

OPATANOL 1 mg/ml eye drops.
Olopatadine. Ocular use.

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

Exp: xx/xxxx
Discard four weeks after first opening.
Opened:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 ml

6 OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

OPATANOL 1 mg/ml eye drops, solution.
Olopatadine.

Read all of this leaflet carefully before you start using this medicine.
Keep this leaflet. You may need to read it again. If you have any further questions , ask your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if their symptoms are the same as yours.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

1. WHAT OPATANOL DOES

OPATANOL is used for the treatment of signs and symptoms of seasonal allergic conjunctivitis.

Allergic conjunctivitis. Some materials (allergens) like pollens, house dust or animal fur may cause allergic reactions resulting in itching, redness as well as swelling of the surface of your eye.

OPATANOL is a medicine for treatment of allergic conditions of the eye. It works by reducing the intensity of the allergic reaction.

2. BEFORE YOU USE OPATANOL

Do not use OPATANOL
- **If you are allergic** (hypersensitive) to olopatadine or any of the other ingredients of OPATANOL.

Ask your doctor for advice.

Take special care with OPATANOL...
- **Do not use OPATANOL in children under the age of 3 years.**

Using other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

If you are using other eye drops at the same time as OPATANOL, follow the advice at the end of section 3.

Pregnant women
If you are pregnant, or might get pregnant, talk to your doctor before you use OPATANOL.

Breast feeding women
If you are breast feeding. Do not use OPATANOL, it may get into your milk.

Ask your doctor for advice before taking any medicine

Driving and using machines
You may find that your vision is blurred for a time just after you use OPATANOL. Do not drive or use machines until this has worn off.

Important information about some of the ingredients of OPATANOL
If you wear soft contact lenses. Do not use the drops while your contact lenses are in your eyes. Wait 10-15 minutes after using the eye drops before putting your lenses back into your eyes. A preservative in OPATANOL (benzalkonium chloride) can affect soft lenses.

3. HOW TO USE OPATANOL

Always use OPATANOL exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is…

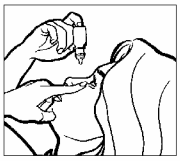
one drop in the eye or eyes, twice a day – morning and evening.
Use this much unless your doctor tells you to do differently. Only use OPATANOL in both eyes if your doctor told you to. Use it for as long as your doctor told you to.

Only use OPATANOL as an eye drop.

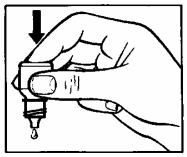
TURN THE PAGE FOR MORE ADVICE

Now turn over>

3. HOW TO USE OPATANOL (*continued)*



1



2

How much to use
< see side 1

- Get the OPATANOL bottle and a mirror.
- Wash your hands.
- Take the bottle and twist off the cap.
- Hold the bottle, pointing down, between your thumb and middle finger.
- Tilt your head back. Pull down your eyelid with a clean finger, until there is a 'pocket' between the eyelid and your eye. The drop will go in here (picture 1).
- Bring the bottle tip close to the eye. Use the mirror if it helps.
- **Don't touch your eye or eyelid, surrounding areas or other surfaces with the dropper.** It could infect the drops left in the bottle.
- **Gently press on the base** of the bottle to release one drop of OPATANOL at a time.
- **Don't squeeze the bottle,** it is designed so that just a gentle press on the bottom is needed (picture 2).
- If you use drops in both eyes, repeat the steps for your other eye.
- Put the bottle cap back on firmly immediately after use.
- Use up one bottle before opening the next bottle.

If a drop misses your eye, try again.

If you use more OPATANOL than you should rinse it all out with warm water. Don't put in any more drops until it's time for your next regular dose.

If you forget to use OPATANOL, use a single drop as soon as you remember, and then go back to your regular routine. **Do not** use a double dose to make up for the one missed.

If you are using other eye drops, wait at least five to ten minutes between putting in OPATANOL and the other drops.

If you have any further questions on the use of this product, ask your doctor or pharmacist

4. POSSIBLE SIDE EFFECTS

Like all medicines, OPATANOL can cause side effects, although not everybody gets them.

Common side effects
These may affect up to 10 in every 100 people

Effects in the eye: eye pain or swelling, eye irritation, dry eye, abnormal eye sensation

Effects in the body: headache, fatigue, dry nose, bad taste

Uncommon side effects
These may affect up to 1 in every 100 people

Effects in the eye: blurred, reduced, or abnormal vision, corneal disorder, inflammation or infection of the conjunctiva, eye discharge, eye allergy, sensitivity to light, increased tear production, itchy eye, redness of the eye, eyelid abnormality, itching, redness, swelling, or crusting of the eyelid.

Effects in the body: abnormal or decreased sensation, dizziness, runny nose, dry skin, skin inflammation, redness, and itching.

Additional side effects that have been reported include:

Effects in the eye: change in pupil size

Effects in the body: shortness of breath, increased allergic symptoms, facial swelling, drowsiness, generalized weakness, nausea, vomiting, sinus infection

You can usually carry on taking the drops, unless the effects are serious.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE OPATANOL

Keep out of the reach and sight of children.

Do not use OPATANOL after the expiry date which is stated on the bottle and the boxafter 'Exp'. The expiry date refers to the last day of the month.

This medicine does not require any special storage conditions.

You must throw away the bottle four weeks after you first opened it, to prevent infections, and use a new bottle. Write down the date you opened it in the space on each bottle label and box

Medicines should be disposed of via waste water or household waste. Ask your pharmacist how to dispose of medicines no longer required. This will help protect the environment.

6 FURTHER INFORMATION

What OPATANOL CONTAINS

The active substance is olopatadine 1 mg/ml (as hydrochloride).

The other ingredients are: benzalkonium chloride, sodium chloride, disodium phosphate dodecahydrate (E339), and purified water. Tiny amounts of hydrochloric acid (E507) and/or sodium hydroxide (E524) are sometimes added to keep acidity levels (pH levels) normal.

What OPATANOL looks like and the contents of the pack

OPATANOL is a clear liquid (a solution) supplied in a pack containing either one 5 ml plastic bottle or three 5 ml bottles with screw caps. Not all pack sizes may be marketed.

The marketing authorisation holder	Manufacturer	Manufacturer
Alcon Laboratories (UK) Ltd Pentagon Park Boundary Way Hemel Hempstead Herts HP2 7UD United Kingdom	S.A. Alcon –Couvreur N.V. Rijksweg 14 B-2870 Puurs Belgium	Alcon Cusí. S.A. Camil Fabra 58 08320 El Masnou Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last approved on XXXXX