ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 16
E-mail: mail@emea.eu.int http://www.emea.eu.int

1. NAME OF THE MEDICINAL PRODUCT

OPATANOL 1 mg/ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains 1mg olopatadine (as hydrochloride).

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution.

The solution is clear and colourless.

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.

Use in children and adolescents
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 eyedrops (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 olopatadine or to any of the excipients.

4.4 Special warnings and special 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 clinical interaction studies were performed with OPATANOL.

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 approximately 950 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 5.0% of patients can be expected to experience undesirable effects; however, only 1.4% of these patients discontinued from the clinical studies due to undesirable effects related to OPATANOL. No serious ophthalmic or systemic undesirable effects related to OPATANOL were reported in clinical studies. The most frequently reported treatment-related undesirable effect was ocular discomfort at an incidence of 0.9%.

The following undesirable effects, which were determined to be definitely, probably or possibly related to treatment, were reported during the clinical studies with OPATANOL. The incidence of all undesirable effects was uncommon (0.1-1%).

Ocular Effects
Uncommon:

- Ocular discomfort
- Ocular pruritus
- Ocular hyperaemia
- Ocular discharge
- Keratitis
- Dry eye
- Lid oedema
- Foreign body sensation
- Photophobia

Systemic Effects
Uncommon:

- Body as a whole:
  - headache
  - asthenia
- Nervous:
  - dizziness
- Respiratory system:
  - dry nose

The following additional undesirable effects have been very rarely (<0.01%) reported from post marketing experiences with OPATANOL. They are generally accepted as related to the use of antiallergic/antihistaminic agents: blurred vision, dry mouth, rhinitis, and erythema.

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

Preclinical data revealed 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

None known.

6.3 Shelf-life

3 years.

Discard four weeks after first opening.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and content of container

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

The following pack sizes are available: cartons containing 1 x 5 ml and 3 x 5 ml bottles. Not all pack sizes may be marketed.

6.6 Instructions for use and handling

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 NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

ANNEX II

A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

SA Alcon-Couvreur NV
Rijksweg 14
B-2870, Puurs
Belgium

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

- **OTHER CONDITIONS**

The holder of this marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING

BOX OF 1 BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

OPATANOL 1 mg/ml eye drops, solution
Olopatadine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml of solution contains 1mg 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; 5 ml

5. METHOD AND ROUTE(S) 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:

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.
Boundary Way
Pentagon Park
Hemel Hempstead
Herts., HP2 7UD
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. MANUFACTURER'S BATCH NUMBER

Batch No.: xxxxx

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING

BOX OF 3 BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

OPATANOL 1 mg/ml eye drops, solution
Olopatadine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml of solution contains 1mg 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; 3 x 5 ml

5. METHOD AND ROUTE(S) 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 (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.
Boundary Way
Pentagon Park
Hemel Hempstead
Herts., HP2 7UD
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. MANUFACTURER'S BATCH NUMBER

Batch No.: xxxxx

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

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

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.
Discard four weeks after first opening.
Opened:

3. EXPIRY DATE

Exp: xx/xxxx

4. BATCH NUMBER

Batch No.: xxxxx

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 ml

B. PACKAGE LEAFLET

PACKAGE LEAFLET

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

Read all of this leaflet carefully before you start using this medicine.

This medicine has been prescribed for you personally. You should not pass it on to other people. It may harm them even if they have the same symptoms as you.

Keep this leaflet. You may need to read it again. If you still have questions after reading it, please ask your doctor or your pharmacist.

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

Other ingredients: 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.

The marketing authorisation holder for OPATANOL is Alcon Laboratories (UK) Ltd., Boundary Way, Hemel Hempstead, Herts., HP2 7UD, United Kingdom.

The manufacturer of OPATANOL is SA Alcon-Couvreur NV, Rijksweg 14, B-2870 Puurs, Belgium.

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.

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

2. BEFORE YOU USE OPATANOL

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

Ask your doctor for advice.

Take special care using OPATANOL...

- **Do not use OPATANOL in children under the age of 3 years.**
- **If you are breast feeding. Do not use OPATANOL,** it may get into your milk.

- **If you wear 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.

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

Driving or 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 your vision is clear.

OPATANOL and other medicines

Tell your doctor or pharmacist if you are taking (or have recently taken) any other medicines. Don't forget to mention any other medicines that you have bought yourself without prescription.

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

3. HOW TO USE OPATANOL

How much to use

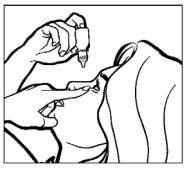
One drop in the eye or eyes, twice a day – morning and evening.
Use this much unless your doctor tells you to do differently. Only use OPATANOL in both eyes if your doctor told you to. Use it for as long as your doctor told you to.

Only use OPATANOL as an eye drop.

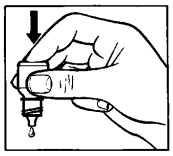
TURN THE PAGE FOR MORE ADVICE

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 get too much in your eyes, 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.

Don’t forget to tell your doctor or pharmacist about any other medicines you are taking or have recently taken-including any you have bought yourself.

4. POSSIBLE SIDE EFFECTS

A small number of people who use OPATANOL may get side effects. These can be unpleasant, but most of them disappear quickly.

The most frequent side effect is discomfort in the eye such as burning and stinging.
Other possible effects in the eye are itching, redness, discharge, inflammation of the surface of the eye, dryness, swollen eye lids, feeling like there is something in the eye, dislike of bright lights.
Possible effects in the body are headache, tiredness, dizziness and dryness in the nose.
All of these effects have been reported by less than 1 in 100 people.

You can usually continue using the drops, unless the effects are serious. If you're worried, talk to a doctor or pharmacist.

If you notice any other side effects, apart from these, tell your doctor or pharmacist.

5. STORING OPATANOL

You must throw away the bottle four weeks after you first opened it, to guard against infections. Write down the date you opened it in the space on each bottle label and box and in the spaces below. For a pack containing a single bottle, write only one date.

Opened (1st bottle):
Opened (2nd bottle):
Opened (3rd bottle):

Keep the drops in a safe place where children can’t see or reach them.

Do not use the drops after the expiry date (marked ‘Exp’) on the bottle and the box.

If you have any other questions about your medicines you should ask your doctor or pharmacist.

This leaflet was last approved in xxxxxx

FURTHER INFORMATION

For any information about these drops, please contact your local Alcon office.

België/Belgique/Belgien
SA Alcon-Couvreur NV
Rijksweg 14
B-2870 Puurs
☎ + 32 (0)3 890 27 11

Danmark
Alcon Danmark A/S
Rødovre Parkvej 25
DK-2610 Rødovre
☎ +45 3636 3434

Deutschland
Alcon Pharma GmbH
Blankreutestrasse 1
D-79108 Freiburg
☎ + 49 (0)761 1304-0

Ελλάδα
Άλκον Λαμπράτορις Ελλάς ΑΕΒΕ
Κηφισίας 18
GR-151 25 Μαρούσι
☎ + 30 210 68 00 811

España
Alcon Cusí, S.A.
C/Camil Fabra, 58
E-08320 El Masnou-Barcelona
☎ + 34 93 497 7000

France
Laboratoires Alcon
Immeuble "Les Colonnades"
4, Rue Henri Sainte-Claire Deville
F-92563 Rueil-Malmaison Cedex
☎ + 33 (0)1 47 10 47 10

Ireland
Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Herts., HP2 7UD
UK
☎ + 44 1442 34 1234

Luxembourg/Luxemburg
SA Alcon-Couvreur NV
Rijksweg 14
B-2870 Puurs
Belgique/Belgien
☎ + 32 3 890 27 11

Nederland
Alcon Nederland BV
Avelingen-West 5
NL-4202 MS Gorinchem
☎ + 31 (0) 183 654321

Norge
Alcon Norge AS
Eyvind Lyches v 10, Postboks.22
N-1300 Sandvika
☎ + 47 67 81 79 00

Österreich
Alcon Ophthalmika GmbH
Mariahilferstr. 121b
A-1060 Wien
☎ + 43 (0)1 596 69 70

Portugal
Alcon Portugal
Produtos e Equipamentos Oftalmológicos, Lda.
Quinta da Fonte, Edifício D. Sancho I – Piso 3
Rua dos Malhões, nº 4
P-2780-730 Paço D'Arcos
☎ + 351 214 40 03 30

Suomi/Finland
Alcon Finland Oy
PL 13
FIN-01641 Vantaa
☎ + 358 (0)9 8520 2260

Sverige
Alcon Sverige AB
Box 12233
S-102 26 Stockholm
☎ + 46 (0)8 634 40 00

Ísland
K. Pétursson ehf.
Ljárskógar 15
IS-109 Reykjavik
☎ +354 567 3730

Italia
Alcon Italia S.p.A.
Viale Giulio Richard, 1/B
I-20143 Milano
☎ + 39 02 81803.1

United Kingdom
Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Herts., HP2 7UD
UK
☎ + 44 (0)1442 34 1234