SODIUM CROMOGLICATE 2% W/V EYE DROPS
PL 15872/0010

UKPAR

TABLE OF CONTENTS

SODIUM CROMOGLICATE 2% W/V EYE DROPS
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LAY SUMMARY

The MHRA granted FDC International Ltd a Marketing Authorisation (licence) for the medicinal product Sodium Cromoglicate 2% w/v Eye Drops (PL 15872/0010). This is a prescription only medicine (POM) for the treatment of red, watery, itchy eyes caused by allergies such as hayfever, house dust mites and pet hairs.

Sodium Cromoglicate 2% w/v Eye Drops contain the active ingredient sodium cromoglicate which is an anti-inflammatory/anti-allergy agent.

The test product was considered to be equivalent to the reference product Opticrom Aqueous Eye Drops (Fisons plc, trading as Rhône Poulenc Rorer) based on the data submitted.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of using Sodium Cromoglicate 2% w/v Eye Drops outweigh the risks, hence a Marketing Authorisation has been granted.

SODIUM CROMOGLICATE 2% W/V EYE DROPS
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SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation for the medicinal product Sodium Cromoglicate 2% w/v Eye Drops to FDC International Ltd on 16 May 2007. This is a prescription only medicine.

The application was submitted as an abridged application according to Article 10.1 of Directive 2001/83/EC as amended, claiming to be a generic product of Opticrom Aqueous Eye Drops (Fisons plc, trading as Rhône Poulenc Rorer). The reference product has been authorised in the UK since December 1985 and so the 10-year period of data exclusivity has expired.

The product contains the active ingredient sodium cromoglicate and is indicated for the prevention and treatment of acute, seasonal and perennial allergic conjunctivitis.

Sodium cromoglicate is a mast cell stabilizer. It is used to inhibit the degranulation of sensitised mast cells which usually occurs after exposure to allergens and thereby prevents the release of allergic mediators such as histamine.

PHARMACEUTICAL ASSESSMENT

COMPOSITION

The product is formulated as an eye drop solution containing 2.0% w/v of the active pharmaceutical ingredient sodium cromoglicate. The excipients present are benzalkonium chloride, disodium edetate, sodium chloride, polysorbate 80 and water for injection.

Sodium Cromoglicate 2% w/v Eye Drops are presented in an LDPE bottle with a polystyrene spiked cap closure in a pack size of 13.5 ml.

DRUG SUBSTANCE

Sodium Cromoglicate

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate specification based on the European Pharmacopoeia monograph is provided for sodium cromoglicate.

Analytical methods have been validated and are satisfactory for ensuring compliance with the relevant specifications.

Batch analysis data are provided for three batches and comply with the proposed specification.

Sodium cromoglicate is stored in appropriate packaging.

Stability data have been generated supporting a suitable retest period when stored in the proposed packaging protected from light.

DRUG PRODUCT

Other ingredients

All excipients used in the manufacture of the eye drop solution are routinely tested for compliance with current relevant international standards.

Satisfactory certificates of analysis have been provided for all excipients.

No excipients used contain material of animal or human origin.

Manufacture

A full description and a detailed flow-chart of the manufacturing method including in-process control steps has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out and the results are satisfactory.

Finished product specification
The proposed finished product specification is acceptable and the analytical methods used have been suitably validated. Batch analysis data have demonstrated compliance with the proposed release specification. Suitable reference standards were used.

Container Closure System
Satisfactory specifications and certificates of analysis have been provided for the packaging components. The manufacturing process ensures that filling is performed under aseptic conditions and that the LDPE bottles are hermetically sealed under aseptic conditions as well.

Stability
Finished product stability data support the proposed shelf-life of 2 years unopened and 1 month opened with storage conditions "Do not store above 30°C. Protect from direct sunlight. To avoid contamination do not touch dropper tip to any surface."

Bioequivalence/bioavailability
A bioequivalence study was not required for this application.

SPC, PIL and Labels
The SPC, PIL and labels are pharmaceutically acceptable.

The marketing authorisation holder has provided a commitment to update the marketing authorisation with a patient information leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 01 July 2008.

CONCLUSION

The proposed product has been shown to be a generic product of the reference product and has met the requirements with respect to qualitative and quantitative content of the active substance. It is recommended that a Marketing Authorisation should be granted for this application.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

INTRODUCTION AND BACKGROUND

This is a generic abridged application for an eye drop solution containing 2.0% w/v sodium cromoglycate.

The application is submitted under the provisions of Directive 2001/83/EC Article 10.1, claiming that Sodium Cromoglicate 2% w/v Eye Dops is a generic product of Opticrom Aqueous Eye Drops (Fisons plc, trading as Rhône Poulenc Rorer) which was authorised in the UK in December 1985.

Sodium cromoglicate is a well established mast cell stabilizer for use in the indications sought.

INDICATIONS

The following indications have been approved:

> The prevention and treatment of acute, seasonal and perennial allergic conjunctivitis.

DOSE AND DOSE SCHEDULE

The proposed dose and dose schedule for these products to be used for the above indications is one or two drops into each eye, up to four times a day and is consistent with that for the reference product.

CLINICAL PHARMACOLOGY

No new data were submitted. Sodium cromoglicate inhibits the degranulation of sensitised mast cells which normally occurs after exposure to allergens and thereby prevents the release of allergic mediators such as histamine. It is poorly absorbed from the eye (approximately 0.03% in healthy volunteers) due to its lipid insolubility. Orally, it is poorly absorbed from the gastrointestinal tract with a reported bioavailability of 1%.

Bioequivalence data are not relevant for a topical product of this type.

CLINICAL EFFICACY

No new data are submitted. The site of action is very superficial in the conjunctiva and efficacy does not depend on ocular penetration. In principle, as the product is an aqueous solution, formal efficacy data are not required as the formulation does not differ in any important respect from the reference product, either qualitatively or quantitatively.

CLINICAL SAFETY

No formal safety data are presented in this application and none are required. The safety profile of sodium cromoglicate is well known.

CLINICAL EXPERT REPORT

The clinical expert report has been written by an appropriately qualified medical doctor. It is an adequate summary of the clinical data provided in the dossier.

SPC, PIL and LABELS

The SPC, PIL and labels are acceptable.

CONCLUSIONS

The clinical efficacy and safety of sodium cromoglicate is well known from its extensive use in clinical practice. No new data were submitted and this is acceptable. Bioequivalence data are not required for a formulation of this type. A Marketing Authorisation should be granted for this application.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Sodium Cromoglicate 2% w/v Eye Drops are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

A bioequivalence study was not required for this product due to the type of formulation. The applicant has demonstrated that Sodium Cromoglicate 2% w/v Eye Drops is a generic product of Opticrom Aqueous Eye Drops (Fisons plc, trading as Rhône Poulenc Rorer).

No new or unexpected safety concerns arose from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The data submitted support the claim that the applicant's product and the reference product are interchangeable. The risk benefit is, therefore, considered to be positive.

SODIUM CROMOGLICATE 2% W/V EYE DROPS
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STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 03 January 2002.

2 Following standard checks and communication with the applicant, the MHRA considered the application valid on 12 February 2002.

3 Following assessment of the application, the MHRA requested further information relating to the quality dossier on 26 March 2002, 14 February 2003, 20 February 2003, 23 July 2003, 16 December 2003, 28 September 2006, 07 November 2006 and 30 November 2006 and further information relating to the clinical dossier on 26 March 2002.

4 The applicant responded to the MHRA's requests, providing further information on 19 December 2002, 17 November 2006 and 12 December 2006 for the quality sections, and again on 19 December 2002 for the clinical sections.

5 The application was determined on 16 May 2007.

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STEPS TAKEN AFTER AUTHORISATION – SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sodium Cromoglicate 2% w/v Eye Drops

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Cromoglicate 2% w/v

3 PHARMACEUTICAL FORM

Eye drops, solution.

A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The prevention and treatment of acute, seasonal and perennial allergic conjunctivitis.

4.2 Posology and method of administration

Adults, Elderly & Children : One or two drops into each eye up to four times a day.

4.3 Contraindications

Patients with known hypersensitivity to any of the ingredients.

4.4 Special warnings and precautions for use

This formulation of Sodium Cromoglicate Eye Drops contains benzalkonium chloride as a preservative. Benzalkonium chloride may be deposited in soft contact lenses. Hence, Sodium Cromoglicate Eye Drops should not be used while wearing these lenses. The lenses should be removed before instillation of the drops and not reinserted earlier than 15 minutes after use.

Patients should also be instructed that ocular solutions, if handled improperly can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions. Patients should also be advised that if they develop any intercurrent ocular condition (e.g. trauma, ocular surgery or infection), they should immediately seek their physician's advice concerning the continued use of present multi-dose container. There have been reports of bacterial keratitis associated with the use of topical ophthalmic products.

4.5 Interaction with other medicinal products and other forms of interaction

None known

4.6 Pregnancy and lactation

There are no adequeate and well-controlled studies of Sodium Cromoglicate eye drops in pregnant women. Therefore, use during pregnancy is not recommended unless the benefit outweighs the potential risk.

It is not known whether Sodium Cromoglicate is excreted in human milk. Therefore caution should be exercised when the eye drops are administered to nursing mothers.

4.7 Effects on ability to drive and use machines

Transient stinging or blurring of vision may occur on instillation of the drops.

Do not drive or use machinery until normal vision is restored.

4.8 Undesirable effects

Transient stinging and burning on instillation of the drops. Rarely, other symptoms of local irritation.

4.9 Overdose

Medical observation is recommended in cases of overdosage.

Sodium cromoglicate is poorly absorbed both from the eye and from the gastrointestinal tract.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Sodium cromoglicate inhibits the degranulation of sensitised mast cells which normally occurs after exposure to allergens and thereby prevents the release of allergic mediators such as histamine.

5.2 Pharmacokinetic properties

Sodium cromoglicate is poorly absorbed from the eye (approximately 0.03% in healthy volunteers) due to its lipid insolubility. Orally, it is poorly absorbed from the gastrointestinal tract with a reported bioavailability of 1%. Systemically, sodium cromoglicate is excreted unchanged in the bile and urine.

Trace amounts have been detected in the aqueous humour of rabbit eyes up to 24 hours after administration.

5.3 Preclinical safety data

Pre-clinical safety data does not add anything of further significance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride

Disodium edetate

Sodium chloride

Polysorbate 80

Water for injection

6.2 Incompatibilities

Benzalkonium chloride may be deposited in and is known to discolour soft contact lenses. These lenses should therefore be removed before instillation of the eye drops and not reinserted earlier than 15 minutes after use.

6.3 Shelf life

Unopened: 24 months

Opened: 1 month

6.4 Special precautions for storage

Do not store above 30°C. Protect from direct sunlight.

To avoid contamination do not touch dropper tip to any surface

6.5 Nature and contents of container

The container is a bottle of low density polyethylene (LDPE) with a polystyrene spiked cap closure which contains 13.5ml of Sodium Cromoglicate 2% w/v Eye Drops solution.

6.6 Special precautions for disposal

No special instructions.

7 MARKETING AUTHORISATION HOLDER

FDC International Ltd

10 The Tanneries, East St,

Titchfield, Hants. PO14 4AR

8 MARKETING AUTHORISATION NUMBER(S)

PL 15872/0010

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/05/2007

10 DATE OF REVISION OF THE TEXT

16/05/2007

PATIENT INFORMATION LEAFLET

SODIUM CROMOGLICATE 2% W/V EYE DROPS

Please read this leaflet carefully before you start using this medicine

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

What do Sodium Cromoglicate Eye Drops contain?

The active ingredient is Sodium Cromoglicate 2% w/v.
The eye drops also contain benzalkonium chloride (as preservative), sodium chloride, disodium edetate, polysorbate 80 and water for injections.

Product Licence Holder: FDC International Ltd, 10 The Tanneries, East Street, Titchfield, Fareham. Hants PO14 4AR, UK

Manufacturer: FDC International Ltd, 10 The Tanneries, East Street, Titchfield, Fareham. Hants PO14 4AR, UK

What are Sodium Cromoglicate Eye Drops and what are they used for?

Sodium Cromoglicate Eye Drops are a sterile, preserved, aqueous solution used as eye drops.
The active ingredient Sodium Cromoglicate belongs to a group of medicines called anti-inflammatory/anti-allergy agents.
Each bottle contains 5 ml, 10ml or 13.5ml of Sodium Cromoglicate Eye Drops.
Sodium Cromoglicate Eye Drops are used to treat red, watery, itchy eyes caused by allergies such as hayfever, house dust mites and pet hairs.

Before You Use Sodium Cromoglicate Eye Drops

You must be sure that your irritated eyes are due to an allergy. Allergies normally affect both eyes and the nose and do not impair sight except by making your eyes water. If only one eye is affected, you do not have a runny nose or if your sight is impaired, you should see your doctor before using these drops.

- DO NOT use Sodium Cromoglicate Eye Drops if you have previously had a bad reaction to any of the ingredients which are listed at the beginning of this leaflet
- Talk to your doctor before using this medicine, if you are pregnant or thinking about becoming pregnant; also if you are breast feeding.
- DO NOT wear contact lenses during instillation of the drug. They should not be inserted until at least 15 minutes after instillation of Sodium Cromoglicate Eye Drops. Benzalkonium Chloride is known to discolour soft contact lenses
- Avoid driving motor vehicles or operating machines if your vision becomes blurred immediately after using the drops.

How to use Sodium Cromoglicate Eye Drops.

Put one or two drops into each eye up to four times each day, unless your doctor tells you otherwise. If you miss a dose, use it as soon as possible, then continue as before..

- First wash your hands.
- These drops are supplied as a sealed bottle with a spiked cap. When using a bottle for the first time, screw the cap down tightly in order to pierce the tip of the bottle.
- Pull the lower eyelid gently downwards with one hand.
- Bend your head backwards.
- With the other hand hold the bottle upside down above your eye.
- Gently squeeze the bottle and instill one or two drops.
- Repeat for the other eye, if necessary

Avoid touching the eye (or any other surface) with the tip of the bottle.

If your symptoms do not improve within 2 days, or if you need to use these drops for more than 3 months, you should consult your doctor.

Possible Side Effects

Some people find that their eyes sting or their sight is blurred immediately after using the drops. These effects should wear off after a short time. If you suffer from severe stinging or if it lasts for a long time, speak to your doctor or pharmacist.

If you have any unusual symptoms or feelings, see your doctor as soon as possible.

You should avoid driving motor vehicles or operating machines if your vision becomes blurred when you use the drops.

Storing Sodium Cromoglicate Eye Drops

Do not store above 30°C.
Protect from direct sunlight.
Discard within 28 days of opening
Do not use after the date indicated on the pack with "EXP".

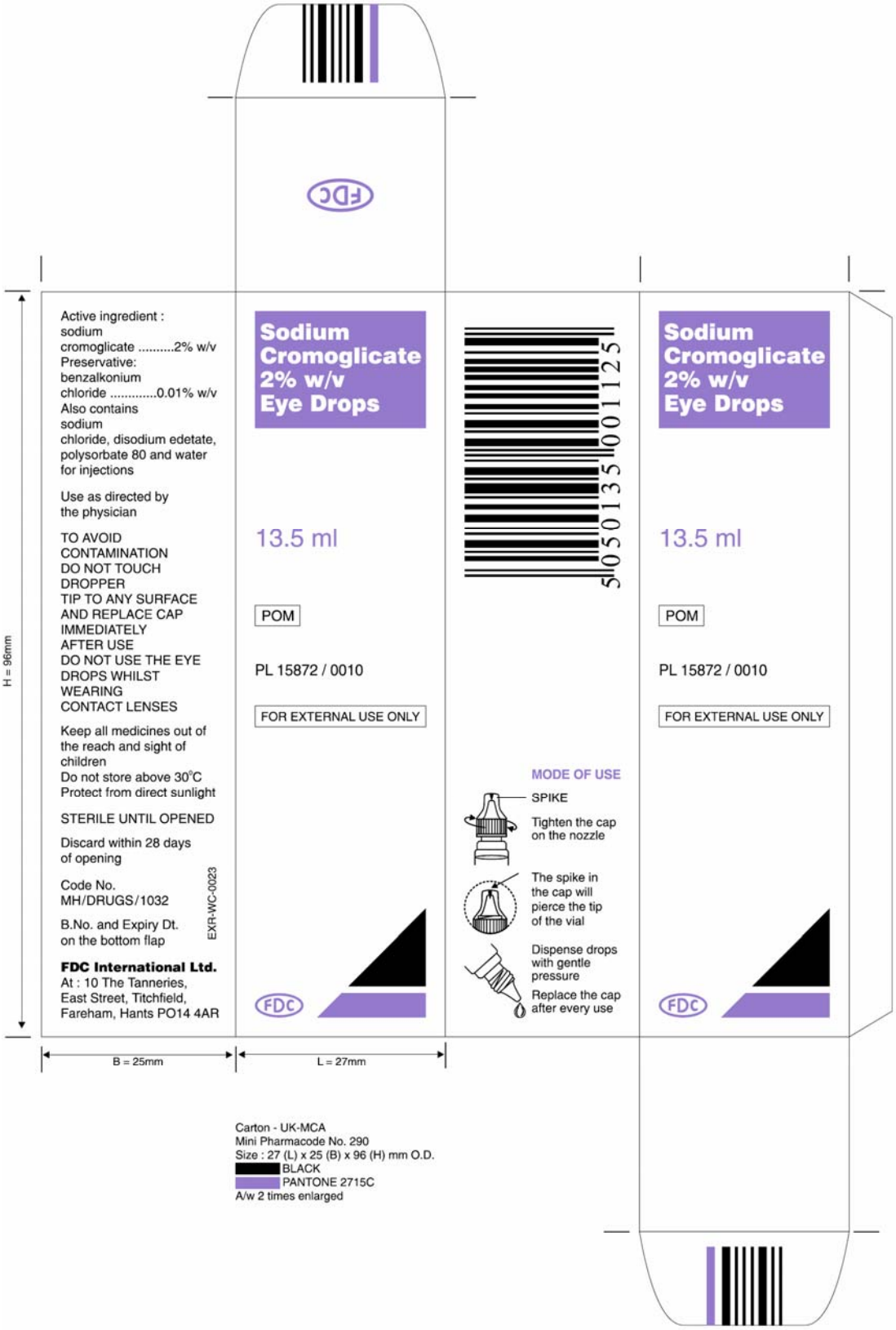
Close the bottle immediately after use.
Be careful not to touch the tip of the bottle on your eye or on any other surface.
Ocular solutions, if handled wrongly, can become contaminated by common bacteria and cause eye infections. If you do develop any other eye condition whilst using this product, see your doctor immediately.

Medicines should always be stored safely out of the reach and sight of children.

Date of preparation of this leaflet: March 2007

EXR-WI-0018

LABELLING


Active ingredient :
sodium
cromoglicate .....2% w/v
Preservative:
benzalkonium
chloride .....0.01% w/v
Also contains
sodium
chloride, disodium edetate,
polysorbate 80 and water
for injections
Use as directed by
the physician
TO AVOID
CONTAMINATION
DO NOT TOUCH
DROPPER
TIP TO ANY SURFACE
AND REPLACE CAP
IMMEDIATELY
AFTER USE
DO NOT USE THE EYE
DROPS WHILST
WEARING
CONTACT LENSES
Keep all medicines out of
the reach and sight of
children
Do not store above 30°C
Protect from direct sunlight
STERILE UNTIL OPENED
Discard within 28 days
of opening
Code No.
MH/DRUGS/1032
B.No. and Expiry Dt.
on the bottom flap
EXR-WC-0023
FDC International Ltd.
At : 10 The Tanneries,
East Street, Titchfield,
Fareham, Hants PO14 4AR
H = 96mm
B = 25mm
L = 27mm
Sodium
Cromoglicate
2% w/v
Eye Drops
13.5 ml
POM
PL 15872 / 0010
FOR EXTERNAL USE ONLY
5 050135 001125
MODE OF USE
SPIKE
Tighten the cap
on the nozzle
The spike in
the cap will
pierce the tip
of the vial
Dispense drops
with gentle
pressure
Replace the cap
after every use
Sodium
Cromoglicate
2% w/v
Eye Drops
13.5 ml
POM
PL 15872 / 0010
FOR EXTERNAL USE ONLY
Carton - UK-MCA
Mini Pharmacode No. 290
Size : 27 (L) x 25 (B) x 96 (H) mm O.D.
BLACK
PANTONE 2715C
A/w 2 times enlarged

13.5 ml

Code No.
MH/DRUGS/1032

B. No.

Expiry Dt.

Sodium Cromoglicate 2% w/v Eye Drops

POM

PL 15872 / 0010

EXR-WL-0019

Preservative benzalkonium chloride .....0.01% w/v

Use as directed by the physician

Keep all medicines out of the reach and sight of children

Do not store above 30°C

Protect from direct sunlight

STERILE UNTIL OPENED

Discard within 28 days of opening

FOR EXTERNAL USE ONLY

FDC International Ltd.
At : 10 The Tanneries,
East Street, Titchfield,
Fareham, Hants PO14 4AR

FDC