Safeguarding public health

MHRA

Public Assessment Report

Hypromellose 0.3% Eye Drops BP without preservative (unit dose)

PL 11412/0001

Medicines and Healthcare products Regulatory Agency

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

UKPAR

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HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) has granted Moorfields Eye Hospital NHS Foundation Trust a Marketing Authorisation (licence) for the medicinal product Hypromellose 0.3% Eye Drops BP without preservative (unit dose) (PL 11412/0001). This is a pharmacy [P] medicine used for the relief of the symptoms of dry eye conditions. These drops are particularly useful in cases where it is not advisable for patients to expose their eyes to preservatives found in other eye drops.

The physical characteristics of hypromellose eye drops are similar to those of natural tears, providing lubrication to the surface of the eye.

The clinical data presented to the MHRA, before licensing, demonstrated that Hypromellose 0.3% Eye Drops BP without preservative (unit dose) is essentially similar or equivalent to the approved product, Hypromellose Eye drops, BP 0.3%, but with the preservative removed.

No new or unexpected safety concerns arose from this application and it was decided that the benefits of using Hypromellose 0.3% Eye Drops BP without preservative (unit dose) outweigh the risks, hence a Marketing Authorisation has been granted.

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Hypromellose 0.3% Eye Drops BP without preservative (unit dose) (PL 11412/0001) to Moorfields Eye Hospital NHS Foundation Trust on 31 May 2006. The product is a pharmacy medicine.

The application was submitted as an abridged application according to Article 10.1(a)(iii) of Directive 2001/83/EC, claiming essential similarity to Hypromellose Eye drops, BP 0.3% (PL 00109/0168), granted 25 July 1988.

Hypromellose 0.3% Eye Drops BP without preservative (unit dose) is for ocular lubrication in the relief of dry eye syndromes associated with deficient tear secretions or lubrication with rigid or gas permeable contact lenses. These drops are of particular value where preservatives are contra-indicated.

The physical characteristics of the product are similar to those of natural tears, providing lubrication to the ocular surface and maintaining corneal hydration in dry eye syndromes.

PHARMACEUTICAL ASSESSMENT

LICENCE NO:	**PL 11412/0001**
PROPRIETARY NAME:	**Hypromellose 0.3% Eye Drops BP without preservative (unit dose)**
ACTIVE(S):	**Hypromellose**
COMPANY NAME:	**Moorfields Eye Hospital NHS Foundation Trust**
E.C. ARTICLE:	**10.1(a)(iii), first paragraph**
LEGAL STATUS:	**P**

INTRODUCTION

This is an application for Hypromellose Eye Drops, single use unpreserved.

Essential similarity is claimed to Hypromellose Eye drops, BP 0.3% Roussel Laboratories Ltd, UK, licensed 25 July 1988, PL 00109/0168. It contains benzalkonium chloride (BZK) as a preservative.

This product has not been previously marketed. The formulation is that of the BPC Hypromellose Eye Drops, but with the benzalkonium chloride removed. Some patients with "decompensated corneas" (grafts, dystrophies, etc) require eye drops without preservatives, several of which have been shown to be potentially toxic to corneal cells.

BACKGROUND

Batch release is by Moorfields Eye Hospital NHS Foundation Trust, 34 Nile Street, London N17 7TP.

Moorfields has been making Hypromellose Eye Drops since 1968, using the BPC formula, which included benzalkonium chloride.

Preservative-free eye drops have been in use since 1982. From 1993 onwards it was formulated to include 0.02% EDTA. No formal clinical trials have been carried out with this product. The product to which this application relates does not contain EDTA.

COMPOSITION

Name of active substance(s)	**Reference/Monograph standard**
Hypromellose	Ph.Eur./BP
Name of excipient(s)	**Reference/Monograph standard**
Sodium chloride	Ph.Eur.
Potassium chloride	Ph.Eur.
Borax	Ph.Eur.
Boric acid	Ph.Eur.
Water for injections	Ph.Eur.

The containers are filled to contain 0.4ml of product.

METHOD OF PREPARATION

The compounding process is described and validation data provided.

CONTROL OF STARTING MATERIALS

No TSE issues arise.

ACTIVE SUBSTANCES

Hypromellose, BP.

The source of the active substance is named.

The BP Hypromellose Eye Drops monograph states that one of the following grades is used - Hypromellose 4000, Hypromellose 4500 or Hypromellose 5000.

A general method of manufacture for hypromellose is given. As the source of hypromellose is used in other current product licences, there are no concerns about this material.

Moorfields' analysis of 3 raw material batches used for the 3 product batches made at the manufacturing site are given.

OTHER INGREDIENTS

All excipients are of Ph.Eur. quality.

PACKAGING MATERIAL (IMMEDIATE PACKAGING)

Polyethylene is stated to comply with the Ph.Eur. monograph for polyethylene without additives for parenteral and ophthalmic use.

CONTROL TESTS ON THE FINISHED MEDICINAL PRODUCT

An acceptable finished product specification has been provided.

Batch data are presented.

STABILITY

Stability tests on active substances

No data supplied. Given the use of this source in other licensed products, this is not considered an issue.

Moisture gain is recognised, but the amount of drug used to formulate the product is corrected accordingly.

Stability tests on the finished medicinal product

Proposed storage conditions: Do not store above 25ºC.
Shelf life: 24 months, unopened.

The studies were carried out at 25ºC/60%RH for 36 months, 30ºC/60%RH for 12 months and 40ºC/75%RH for 6 months. These are acceptable.

Stability testing will be undertaken in accordance with the latest ICH guidelines at the new manufacturing facilities.

EXPERT REPORT

The pharmaceutical expert report is acceptable.

PRODUCT NAME & APPEARANCE

Acceptable.

SUMMARY OF PRODUCT CHARACTERISTICS, PATIENT INFORMATION LEAFLET & LABELLING

Satisfactory.

CONCLUSIONS

A marketing authorisation may be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required.

CLINICAL ASSESSMENT

LICENCE NO:	**PL 11412/0001**
PROPRIETARY NAME:	**Hypromellose 0.3% Eye Drops BP without preservative (unit dose)**
ACTIVE(S):	**Hypromellose**
COMPANY NAME:	**Moorfields Eye Hospital NHS Foundation Trust**
E.C. ARTICLE:	**10.1(a)(iii), first paragraph**
LEGAL STATUS:	**P**

INTRODUCTION

This is a national abridged standard application for a marketing authorisation for Hypromellose 0.3% Eye Drops without preservative (unit dose), PL 11412/0001. The applicant, Moorfields Eye Hospital NHS Foundation Trust, submitted this application under Article 10.1(a)(iii), first paragraph of Directive 2001/83/EC, as essentially similar to Hypromellose 0.3% Eye Drops BP, PL 00109/0168, licensed in the UK on 25 July 1988 with Roussel Laboratories Ltd as the marketing authorisation holder.

BACKGROUND

Hypromellose is widely used in ophthalmic preparations as a suspending and thickening agent to maintain the characteristics of natural tears.

INDICATIONS

Ocular lubrication for the relief of dry eye syndromes associated with deficient tear secretions or lubrication with rigid or gas permeable contact lenses. These drops are of particular value where preservatives are contra-indicated.

DOSE & DOSE SCHEDULE

Topical ophthalmic use

Adults, the elderly and children:

One drop as required to the lower conjunctival sac. Leave an interval of at least 5 minutes before the instillation of another ophthalmic medication.

TOXICOLOGY

No new toxicology data have been submitted or are required.

CLINICAL PHARMACOLOGY

Pharmacokinetics

Not applicable. Hypromellose is not systemically absorbed.

Pharmacodynamics

The physical characteristics of the product are similar to those of natural tears, providing lubrication to the ocular surface and maintaining corneal hydration in dry eye syndromes.

BIOEQUIVALENCE

Hypromellose is not systemically absorbed and the pharmacokinetic properties have not been studied. It is acceptable that a bioequivalence study has not been conducted.

EFFICACY

No new efficacy data have been submitted or are required.

SAFETY

No new safety data have been submitted or are required.

EXPERT REPORT

A clinical expert report has been submitted.

The expert provides a discussion of the relevant clinical aspects and considers the applicant's product to be safe and efficacious.

SUMMARY OF PRODUCT CHARACTERISTICS, PATIENT INFORMATION LEAFLET & LABELLING

These are satisfactory.

DISCUSSION

This is an abridged application for a marketing authorisation for Hypromellose 0.3% Eye Drops BP without preservative (unit dose), submitted as essentially similar to Hypromellose 0.3% Eye Drops (PL 00109/0168), licensed in the UK on 25 July 1988.

Hypromellose is widely used in ophthalmic preparations as a suspending and thickening agent to maintain the characteristics of natural tears.

The applicant's product is preservative free compared to the cross-referred product. A clinical expert report provides a discussion on the available data and concludes with a satisfactory risk/benefit ratio.

CONCLUSIONS

The efficacy and safety of Hypromellose 0.3% Eye Drops BP without preservative (unit dose) are satisfactory for the grant of a marketing authorisation.

OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Hypromellose 0.3% Eye Drops BP without preservative (unit dose) 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

The applicant's product is preservative free compared to the cross-referred product Hypromellose 0.3% Eye Drops BP (PL 00109/0168).

No new or unexpected safety concerns arise from this application.

The SPCs, PILs and labelling are satisfactory.

RISK-BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Hypromellose is widely used in ophthalmic preparations as a suspending and thickening agent to maintain the characteristics of natural tears. The risk-benefit assessment is therefore considered to be favourable.

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application for Hypromellose 0.3% Eye Drops BP without preservative (unit dose) on 1 April 2003.
2	The MHRA's assessment of the submitted quality data was completed on 4 July 2003.
3	Further information (quality) was requested from the company on 9 July 2003.
4	The MHRA's assessment of the submitted clinical data was completed on 1 August 2003.
5	Further information (clinical) was requested from the company on 4 August 2003.
6	The applicant's response to further information requests (quality and clinical) was received on 21 September 2004.
7	Further information was requested from the company on 7 July 2005.
8	The applicant responded to further information request in a letter dated 2 December 2005.
9	Additional information was requested in a letter dated 26 January 2006.
10	The applicant responded to additional information request in a letter dated 20 April 2006.
11	The MHRA completed its assessment of the application on 23 May 2006.
12	The application was determined on 31 May 2006.

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

Hypromellose 0.3% Eye Drops BP without preservative (unit dose)

Abbreviated name "HPRM 0.3%" appears on the unit dose container

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Hypromellose 4000, 0.3% w/v

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution

A clear colourless solution, free from particles.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Ocular lubrication for the relief of dry eye syndromes associated with deficient tear secretions or lubrication with rigid or gas permeable contact lenses. These drops are of particular value where preservatives are contra-indicated.

4.2. Posology and Method of Administration

Topical ophthalmic use

Adults, the elderly and children:
One drop into each affected eye as required. Avoid touching the eye with the container dropper. If the drop of medication is not retained for any reason, another drop should be instilled.

Leave an interval of at least 5 minutes before the instillation of another ophthalmic medication.

4.3. Contra-indications

Hypersensitivity to any of the ingredients.

4.4. Special Warnings and Precautions for Use

If irritation persists or worsens, or headache, eye pain, vision changes or continued redness occur, discontinue use and consult a physician.

4.5. Interactions with other Medicaments and other forms of Interaction

Hypromellose prolongs the contact time of topically applied drugs commonly used in ophthalmology.

4.6. Pregnancy and Lactation

There is insufficient evidence as to the safety of Hypromellose 0.3% eye drops in pregnancy and lactation. Caution should be exercised when administered to pregnant or nursing patients.

4.7. Effects on Ability to Drive and Use Machines

If changes to vision occur do not drive or operate machinery until vision is clear.

4.8. Undesirable Effects

Transient mild stinging and blurred vision may occur on instillation.

4.9. Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group (ATC code): Artificial tears (S01X A20).

The physical characteristics of the product are similar to those of natural tears, providing lubrication to the ocular surface and maintaining corneal hydration in dry eye syndromes.

5.2. Pharmacokinetic Properties

Hypromellose is not systemically absorbed through the cornea.

5.3. Preclinical Safety Data

There is no preclinical data of relevance to the prescriber.

6.1. List of Excipients

Sodium chloride, potassium chloride, borax, boric acid, water for injections.

6.2. Incompatibilities

None known.

6.3. Shelf Life

24 months unopened.

6.4. Special Precautions for Storage

Do not store above 25°C.

6.5. Nature and Contents of Container

Unit-dose container composed of polyethylene, containing 0.4ml of product. 30 single-dose containers per carton.

6.6. Instruction for Use/Handling

Discard after first use.

7. MARKETING AUTHORISATION HOLDER

Moorfields Eye Hospital NHS Foundation Trust
Trading as Moorfields Pharmaceuticals
34 Nile Street
London N1 7TP

8. MARKETING AUTHORISATION NUMBER

PL 11412/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31/05/2006

10 DATE OF REVISION OF THE TEXT

31/05/2006

Patient Information Leaflets

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

PATIENT INFORMATION LEAFLET

HYPROMELLOSE 0.3% EYE DROPS BP without preservative (unit dose) (HPRM 0.3%)

HPRM 0.3% is the abbreviation for the name of the drug and is used on the unit dose container because of the small size of the container.

Read all of this leaflet carefully because it contains important information for you.
This medicine is available with or without a prescription. It is used to help relieve the symptoms of a mild 'dry eye' condition.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms do not improve or get worse.

What is in your Hypromellose 0.3% Eye Drops BP without preservative?

- Each unit dose container holds 0.4ml of Hypromellose 0.3% Eye Drops BP and there are 30 single unit doses in each carton.
- The drug in the eye drops is Hypromellose 0.3%w/v (3mg/ml). Hypromellose is a thickening agent which helps the eye drops to stay in your eye longer.
- Other ingredients are Sodium Chloride, Potassium Chloride, Borax, Boric Acid, Water for Injections. Sodium Chloride, Potassium Chloride and Water are all present in natural tears. Borax and Boric Acid are used to adjust the acid/alkaline balance of the eye drops to the level found most comfortable by patients in clinical studies (pH value 8.4).

Who makes your Hypromellose 0.3% Eye Drops BP without preservative?

Marketing authorisation holder and Manufacturer:
Moorfields Eye Hospital NHS Foundation Trust
Trading as Moorfields Pharmaceuticals
34 Nile Street London N1 7TP

Why do you need to use Hypromellose 0.3% Eye Drops BP without preservative?

Hypromellose eye drops are part of a group of medicines known as artificial tears and are used for the relief of the symptoms of dry eye conditions associated with lack of natural tears. Such symptoms may include discomfort, a chronic gritty sensation, disturbance of vision and increased sensitivity to light. These eye drops can be used by wearers of rigid or gas permeable contact lenses. These eye drops are suitable for use by people who are sensitive to preservatives in other kinds of eye drops.

Before you use Hypromellose 0.3% Eye Drops BP without preservative

DO NOT USE HYPROMELLOSE 0.3% EYE DROPS BP without preservative IF YOU ARE ALLERGIC (SENSITIVE) TO ANY OF THE INGREDIENTS LISTED ABOVE.

PREGNANCY AND BREAST-FEEDING
Ask your doctor or pharmacist for advice if you are pregnant or breast-feeding.

USING OTHER MEDICINES
If you use more than one type of eye drop, wait 5 minutes before putting the next one in. This prevents the first drop from being washed away.

How to use Hypromellose 0.3% Eye Drops BP without preservative

Hypromellose 0.3% Eye Drops BP without preservative are for ocular use (use in the eye) and may be used as often as you feel necessary.

1. Read the instructions on the carton.
2. Wash your hands.
3. Break off one unit dose container from the strip.
4. Open the unit dose container by bending/twisting the tab. (fig 1)
5. Tilt your head backwards.
6. Gently pull down the lower lid to form a pocket. (fig 2)

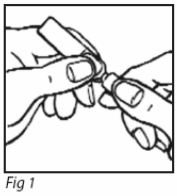

Fig 1

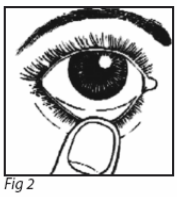

Fig 2

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

PL 11412/0001

7. With the unit dose in the other hand, put one drop inside the pocket by gently squeezing the container. Try not to touch anything with the tip. (fig 3)

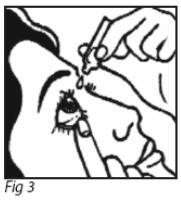

Fig 3

8. Close the eye for about 30 seconds and at the same time gently press a finger against the corner of the closed eye, nearest the nose. (fig 4)

9. Some drops may roll down your face. This is normal. The eye pocket holds less than one drop. Wipe away the excess with a clean tissue. If the drop of medication is not retained for any reason, another drop should be dropped into the eye pocket.

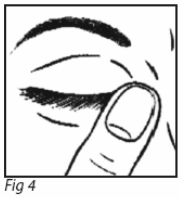

Fig 4

10. If you use more than one type of eye drop, wait 5 minutes before putting in the next one. This prevents the first drop from being washed away.

11. Repeat instructions 5-10 for the other eye if required.

12. Wash your hands.

Possible side effects from Hypromellose 0.3% Eye Drops BP without preservative

Hypromellose eye drops have been used safely for over 30 years. Sometimes they can cause minor side effects such as mild stinging or blurred vision, but these effects are usually minor and temporary. If you experience these effects you should not drive or operate machinery until your normal vision returns. If you have eye irritation that continues or worsens, changes in vision, your eyes become red, or you suffer from headache or pain in your eye, stop using these eye drops and speak to your doctor or pharmacist. If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Storing Hypromellose 0.3% Eye Drops BP without preservative

DO NOT STORE ABOVE 25°C.

USE ONCE AND DISCARD THE CONTAINER.

Use by date

DO NOT USE HYPROMELLOSE 0.3% EYE DROPS BP without preservative AFTER THE EXPIRY DATE MARKED ON THE CARTON AND THE UNIT DOSE CONTAINER. THE EYE DROPS DO NOT APPEAR ANY DIFFERENT EVEN AFTER THEY HAVE EXPIRED.

This leaflet was approved May 2006.

MOORFIELDS
PHARMACEUTICALS
Moorfields Pharmaceuticals
34 Nile Street London N1 7TP

Labels/Packaging

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

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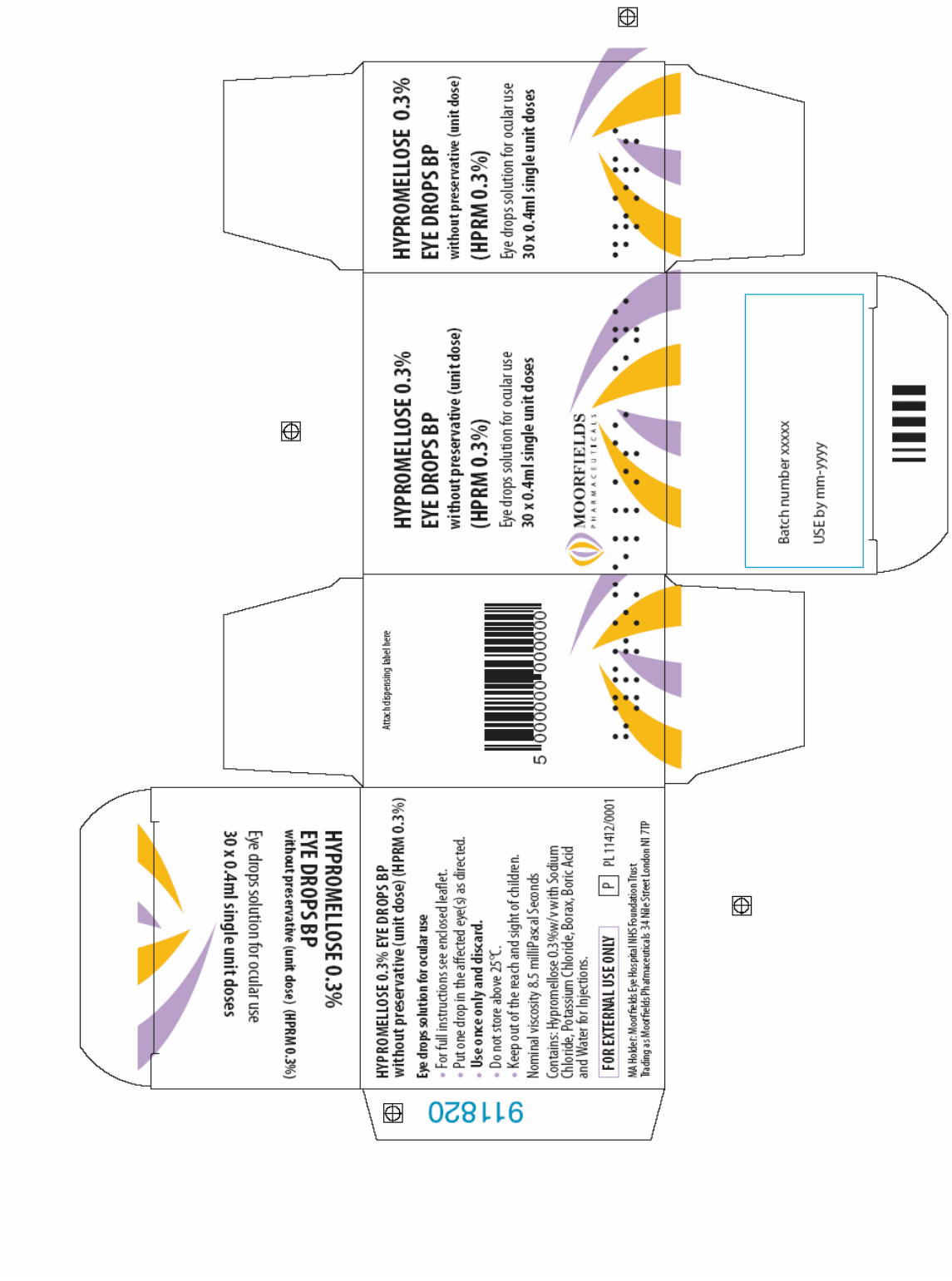

HYPROMELLOSE 0.3% EYE DROPS BP WITHOUT PRESERVATIVE (UNIT DOSE)

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Container label