1. NAME OF THE MEDICINAL PRODUCT

MELOTEARS EYE DROPS

(Hypromellose Ophthalmic Solution USP 0.3%)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative Declaration:

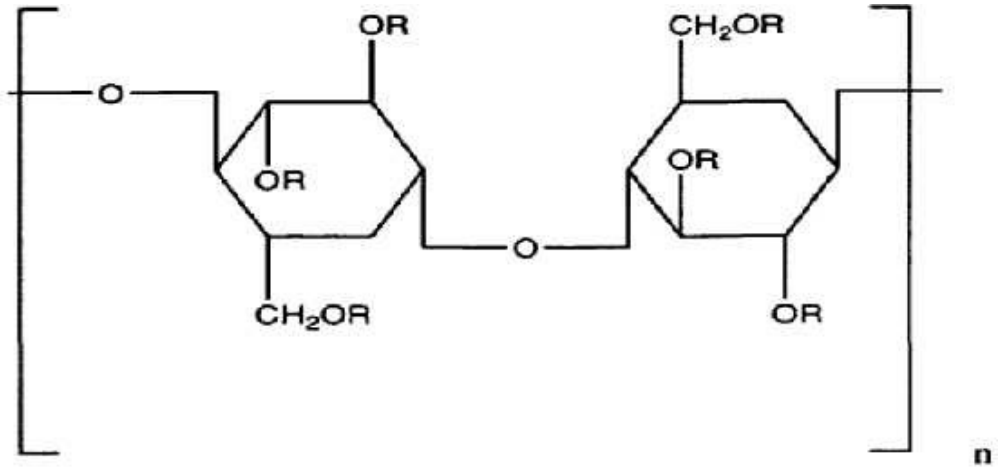
Hypromellose Ophthalmic Solution USP 0.3%

❖ **Hydroxypropyl Methylcellulose (Hypromellose)**

Chemical Name:
2-[6-[4,5-bis(2-hydroxypropoxy)-2-(2-hydroxypropoxymethyl)-6-methoxyoxan-3-yl]oxy-4,5-dimethoxy-2-(methoxymethyl)oxan-3-yl]oxy-6-(hydroxymethyl)-5-methoxyoxane-3,4-diol
Molecular Weight: - 1261.45 g/mol

Molecular Formula: - $C_{56}H_{108}O_{30}$

Structure:-



Pharmaceutical Form Visual description of the appearance of product:
Clear Colourless Solution, Free from any type of visible particles.

Quantitative Declaration:
Composition:

Hypromellose	USP	0.3% w/v
Benzalkonium Chloride Solution (As preservative)	NF	0.02% w/v
Sterile Aqueous Base		Qs

3. PHARMACEUTICAL FORM

Eye Drops

Description: Clear Colourless Solution, Free from any type of visible particles

4. Clinical particulars

4.1 Therapeutic indications

INDICATIONS AND USAGE

Hypromellose is used as artificial tears to prevent damage to the cornea in patients with keratoconjunctivitis sicca accompanying rheumatoid arthritis, xerophthalmias or keratitis or during gonioscopy procedures. It is also used to moisten hard contact lenses and to lubricate artificial eyes.

Hypromellose provides immediate relief of dry eye conditions (including dry eye conditions associated with the use of VDUs and TVs, infrequent blinking, certain medical treatments, atmospheric pollution and drying atmospheres e.g. air-conditioning, central heating, wind and sun).

4.2 Posology and method of administration

DOSAGE AND ADMINISTRATION

The recommended dosage for adults, children and elderly is one or two drops topically instilled into the eye three times daily as needed, or as directed by a physician.

Method of administration: For ocular use only.

4.3 Contraindications

Hypersensitivity to the active substance, Hypromellose or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Warnings and Precautions

May cause transient mild stinging or temporary blurred vision. If irritation persists or worsens, or headache, eye pain, vision changes or continued redness occur, patients should discontinue use and consult a physician or pharmacist (see section 4.8).

In order to preserve the sterility, the dropper should not be allowed to touch any part of the eye or any other surface. (Label warning: Do not touch any part of the eye with the dropper).

This formulation of Hypromellose eye drops contains 0.1mg/ml benzalkonium chloride as preservative which may be deposited in soft contact lenses. Hence, Hypromellose 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.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Fertility, Pregnancy and Lactation

USE IN SPECIFIC POPULATIONS

Fertility

Studies have not been performed to evaluate the effect of topical ocular administration of hypromellose on fertility. Hypromellose is a pharmacologically inert compound and it would not be expected to have any effect on fertility.

Pregnancy

There are no or limited amount of data from the use of ophthalmic hypromellose in pregnant women. Systemic exposure to hypromellose following topical ocular administration is negligible and the product has no pharmacological properties.

Lactation

It is unknown whether topical hypromellose/metabolites are excreted in human milk. No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding women to hypromellose is negligible. In addition to this, hypromellose is pharmacologically inert.

4.7 Effects on ability to drive and use machines

May cause transient blurring of vision on instillation. Do not drive or operate hazardous machinery unless vision is clear.

4.8 Undesirable effects

The following adverse reactions have been reported following administration of Hypromellose.

Frequency cannot be estimated from the available data:

Eye disorder:

• transient mild stinging or vision blurred,

• eye pain,

• foreign body sensation in eyes,

• eye irritation,

• ocular hyperaemia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow card scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Due to the characteristics of this preparation, no toxic effects are to be expected with an ocular overdose of this product, nor in the event of accidental ingestion of the contents of one bottle.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacodynamics

Hypromellose
Pharmacotherapeutic group: Lubricant / Tear Substitute
ATC code: S01KA02

Pharmacodynamic properties:
Hydroxypropyl cellulose (cellulose, 2-hydroxypropyl ether) is a derivative of cellulose with both water solubility and organic solubility. Hydroxypropyl cellulose acts to stabilize and thicken the precorneal tear film and prolong the tear film breakup time which is usually accelerated in patients with dry eye states. Hydroxypropyl cellulose also acts to lubricate and protect the eye. Hydroxypropyl cellulose usually reduces the signs and symptoms resulting from moderate to severe dry eye syndromes, such as conjunctival hyperemia, corneal and conjunctival staining with rose bengal, exudation, itching, burning, foreign body sensation, smarting, photophobia, dryness and blurred or cloudy vision. Progressive visual deterioration which occurs in some patients may be retarded, halted, or sometimes reversed.

Mechanism of action:
Hydroxypropyl cellulose is a derivative of cellulose that is soluble in both water and organic solvents. It is particularly good at trapping water and producing a film that serves as a barrier to water loss. Hydroxypropyl cellulose possesses good surface activity but does not gel as it forms open helical coils. In general Hydroxypropyl cellulose is a water-soluble thickener, emulsifier and film-former often used in tablet coating.

Application:
HPMC is used primarily in construction materials like tile adhesives and renders where it is used as a rheology modifier and water retention agent. Agricultural Research Service scientists are investigating using the plant-derived HPMC as a substitute for gluten in making all-oat and other grain breads. Gluten, which is present in wheat, rye, and barley is absent (or present only in trace quantities) in oat and other grains. Like gluten, HPMC can trap air bubbles formed by the yeast in bread dough, causing the bread to rise. Hypromellose solutions were patented as a semisynthetic substitute for tear-film. Its molecular structure is predicated upon a base celluloid compound that is highly water-soluble. Post-application, celluloid attributes of good water solubility reportedly aid in visual clarity. When applied, a Hypromellose solution acts to swell and absorb water, thereby expanding the thickness of the tear-film. Hypromellose augmentation therefore results in

extended lubricant time presence on the cornea, which theoretically results in decreased eye irritation, especially in dry climates, home, or work environments. On a molecular level, this polymer contains beta-linked D-glucose units that remain metabolically intact for days to weeks. On a manufacturing note, since Hypromellose is a vegetarian substitute for gelatin, it is slightly more expensive to produce due to semisynthetic manufacturing processes. Aside from its widespread commercial and retail availability over the counter in a variety of products, Hypromellose 2% solution has been documented to be used during surgery to aid in corneal protection and during orbital surgery. In addition to its use in ophthalmic liquids, Hypromellose has been used as an excipient in oral tablet and capsule formulations, where, depending on the grade, it functions as controlled release agent to delay the release of a medicinal compound into the digestive tract. It is also used as a binder and as a component of tablet coatings.

5.2 Pharmacokinetics Properties
Pharmacokinetics

Not applicable to topical (ophthalmic) preparations.

Hypromellose is an inert substance. It has no pharmacological activity and not absorbed systemically. Hence, the pharmacokinetic properties have not been studied.

5.3 Preclinical safety data

Clinical Studies
Hypromellose is an inert substance and is not expected to be absorbed systemically. Hence, although no systemic toxicity studies have been conducted it is not expected to demonstrate any systemic toxicity or to have any effect on reproductive processes.

Similarly no specific local ocular toxicity or irritation studies have been conducted; however no adverse effects are anticipated. Indeed, hypromellose ophthalmic solution is used as a control in some ophthalmic drugs studies because of the acknowledged low level of toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

MATERIAL NAME	SPECS.
BENZALKONIUM CHLORIDE SOLUTION (50%)	NF
BORAX	NF
BORIC ACID	NF
SODIUM CHLORIDE	NF
POTASSIUM CHLORIDE	NF
HYDROCHLORIC ACID	NF
SODIUM HYDROXIDE PELLETS	NF
PURIFIED WATER	BP/IH

6.2 Shelf life
24 months

6.3 Special precautions for storage

Store below 30° C.
Do not freeze.

Protect from light.

Keep out of the reach of children.

Prescription only Medicine.

6.4 Nature and contents of container

The liquid is filled in a multi dose container, and contain Benzalkonium Chloride Solution, Borax, Boric Acid, Sodium Chloride, Potassium Chloride, Hydrochloric Acid, and Sodium Hydroxide Pellets for pH adjustment.
Solution is filled in 10 ml Opaque sterile plastic bottle (LDPE).

6.5 Special precaution for disposal of a used medicinal product or waste materials derived such medicinal product and other handling of the product

No special requirements

7.0 Name and complete address (es) of the Applicant & manufacturer(s) of the FPP

Applicant

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