ICH CTD
MODULE 1.3

1.3 PRODUCT INFORMATION

1.3.1 Summary of product characteristics (SmPC)

Provided in the following pages**.**

Product Name: AFM-T Ophthalmic Suspension

(Fluorometholone & Tetrahydrozoline HCl Ophthalmic Suspension, 0.1%/0.025% w/v)

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product:

1.1 Product Name: AFM-T Ophthalmic Suspension

1.2 Strength: Provided in quality and quantitative composition

1.3 Pharmaceutical Dosage Form: Eye Drops, Suspension

2. Quality and Quantitative Composition:

2.1 Qualitative Declaration

2.2 Quantitative Declaration

Name of the Ingredients	Specification	Quantity/100 ml	Overage	Function
Active Ingredients				
Fluorometholone (Sterile & Micronized)	USP	0.100 g	–	Corticosteroid
Tetrahydrozoline Hydrochloride	USP	0.025 g	–	Vasoconstrictor
Excipients				
Polyvinyl Alcohol	USP	1.400 g	–	Viscosity increasing agent
Sodium Chloride	BP	0.750 g	–	Tonicity adjusting agent
Disodium Edetate	BP	0.050 g	–	Chelating agent
Sodium Dihydrogen Phosphate Dihydrate	BP	0.200 g	–	Buffering agent
Tyloxapol	USP	0.300 g	–	Surfactant
Benzalkonium Chloride Solution	BP	0.010 ml	–	Antimicrobial preservative
Aminocaproic Acid	USP	0.100 g	–	
Sodium Hydroxide or Hydrochloric Acid	BP	qs to adjust pH at 5.80–7.50	–	pH adjustment agent
Water for Injections	BP	q.s to 100.00 ml	–	Solvent

3. Pharmaceutical Form:

Eye drops, suspension. An almost white suspension.

4. Clinical particulars

4.1 Therapeutic indications

- Acute, non-infectious allergic conjunctivitis and keratitis (especially when accompanied by severe swelling and intense injection).
- Non-infectious inflammation of the anterior segment of the eye (including anterior uveitis, episcleritis and scleritis).
- Post-operative conditions following surgery for strabismus, cataract or glaucoma; in combination with antimicrobial therapy.

4.2 Posology and method of administration

Instill one drop in the affected eye(s) 2–3 times daily. In adults, the dosage can be increased for the first 24-48 hours as directed by the physician.

Special populations

Pediatric population

Safety and efficacy have not been established in the pediatric age group.

Geriatric population

No information is available to suggest dosage adjustment in patients above 65 years of age.

Renal impairment/hepatic impairment

No studies have been performed in renally/hepatically impaired patients.

Method of administration

Shake well before use.

Instill 1 drop of AFM-T into the lower conjunctival sac of the affected eye(s), looking upwards and gently pulling the lower eyelid downwards.

The contents remain sterile until the original closure is broken. To avoid contamination do not touch any surface with the tip of the container. The tip of the container should also not come into contact with the eye as this may cause injury to the eye.

4.3 Contraindications

- Hypersensitivity to Fluorometholone, Tetryzoline, or any other component of the formulation.
- Infectious conjunctivitis or keratitis
- Corneal lesions and ulcerative processes particularly in patients with infections caused by viruses, bacteria or fungi (e.g. herpes simplex, vaccinia, untreated purulent infections, tuberculosis).
- Glaucoma
- Topical application of steroids may lead to perforation in diseases that cause parenchymal thinning of the cornea or sclera.
- AFM-T is contraindicated in patients with dry eye, particularly those with keratoconjunctivitis sicca (Sjögren's syndrome).
- AFM-T must not be used in children under 6 years of age.

4.4 Special warnings and precautions for use

A careful appraisal of the risk-benefit ratio must be undertaken before using the product in patients undergoing treatment with MAO inhibitors or other drugs that may increase blood pressure, in patients with severe cardiovascular disease (e.g. coronary heart disease, hypertension, phaeochromocytoma) or metabolic disorders (e.g. hyperthyroidism, diabetes), and in patients with a history of cataract or herpes simplex infection.

Use with caution in patients with rhinitis sicca. Reactive hyperaemia may occur following withdrawal of the product.

This medicinal product is not intended for long-term use. Monitoring–in particular of systemic adverse effects, intraocular pressure and secondary infections–is necessary if treatment is to last longer than 2 to 3 days.

The possibility of fungal infection must be considered if symptoms of chronic eye inflammation persist.

Eye infections may be masked, activated or exacerbated by AFM-T. Hypersensitivity reactions to components of AFM-T may be masked.

Corticosteroids may raise intraocular pressure in predisposed patients. Although this property is not very pronounced in fluorometholone, intraocular pressure should be carefully checked when there is prolonged use. Prolonged use entails the risk of lens opacity.

Note for contact lens wearers

AFM-T contains benzalkonium chloride as a preservative. Benzalkonium chloride may cause eye irritation and is known to discolour soft contact lenses. Therefore, AFM-T should not be administered while wearing lenses. The lenses should be removed before application of the drops and not reinserted earlier than 15 minutes after use. Patients with eye inflammation should not wear contact lenses.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions known to occur with systemic corticosteroids are of secondary importance in patients undergoing topical administration.

Concomitant administration of MAO inhibitors and tricyclic antidepressants may cause elevated blood pressure by potentiating the vasoconstrictor effect.

4.6 Women of Child-Bearing Potential, Pregnancy, Breast-Feeding and Fertility

Women of child-bearing potential
There is no special recommendation.

Pregnancy
There is insufficient experience in the use of AFM-T in pregnant women. Fluorometholone has been shown to be embryocytotoxic and teratogenic in rabbits following topical ophthalmic application at doses approximating the human ocular dose (see section 5.3 Pre-Clinical Safety Data). AFM-T should be used during pregnancy only if the expected benefit justifies the potential risk to the fetus.

Breast-feeding
It is unknown whether the active substances pass into breast milk. Women who are breastfeeding are advised not to use AFM-T.

Fertility
There is no information about the effects of AFM-T on human fertility.

4.7 Effects on ability to drive and use machines

Temporary blurring–or other impairment–of vision may adversely affect the patient's ability to drive or use machines. Patients should not carry out these activities until such disturbances have subsided.

4.8 Undesirable effects

Adverse drug reactions from spontaneous reports (frequency not known)

The following adverse drug reactions have been derived from postmarketing experience with AFM-T via spontaneous case reports. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known. Adverse drug reactions are listed according to system organ classes in MedDRA. Within each system organ class, ADRs are presented in order of decreasing seriousness.

Table 1 Adverse drug reactions from spontaneous reports (frequency not known)

Infections and infestations Infections
Nervous system disorders Headaches, Central nervous system stimulation, Tremor
Eye disorders Foreign body sensation, Burning/stinging upon instillation, Irritation , Intraocular pressure increased, Vision blurred, Eyelid Ptosis, Mydriasis, Iris atrophy, Conjunctivitis, Impaired healing, Corneal Thinning, conjunctival hyperaemia, Ocular/Hyperaemia, Angle closure Glaucoma, Cataract subcapsular, Ulcerative keratitis, Eye penetration, Exophthalmus.
Cardiac disorders Palpitations, Arrhythmia , Angina pectoris, Hypertension, Pallor
General disorders and administration site conditions Eye irritation, Hyperhidrosis
Immune system disorders Hypersensitivity

4.9 Overdose

When the product is used as directed, there is almost no likelihood of an overdose. No information on overdosage with fluorometholone is available. Overdosage with fluorometholone is unlikely to cause acute problems. The symptoms of acute overdosage with tetryzoline are CNS, cardiac and psychiatric disturbances, mydriasis, cyanosis and fever. CNS functions may be inhibited under certain circumstances.

The following measures are possible in case of accidental ingestion and the occurrence of symptoms of intoxication: administration of activated charcoal, gastric lavage, artificial ventilation with oxygen, use of phentolamine to lower blood pressure (5 mg in saline solution, given i.v.). Vasopressors are contraindicated. Antipyretic and anticonvulsive therapy can be administered as necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The anti-inflammatory effect of fluorometholone is over 40 times greater than that of hydrocortisone. Like all glucocorticoids, fluorometholone inhibits phospholipase A2, the first step in prostaglandin synthesis. In addition, it inhibits the chemotactic migration of neutrophils into the focus of inflammation. Unlike other topical ophthalmic glucocorticoids, fluorometholone has only a slight effect on intraocular pressure because it is degraded more rapidly in tissues. It exerts less of an immunosuppressive effect than does dexamethasone.

The alpha-sympathomimetic agent tetrahydrozoline hydrochloride brings about rapid local vasoconstriction, which alleviates conjunctival swelling, hyperaemia and irritation.

5.2 Pharmacokinetic properties

Fluorometholone

Peak concentrations of active substance were measured in the cornea and aqueous humour 30-60 minutes after a single application of eye drops containing 0.1% fluorometholone. The half-life of fluorometholone in the aqueous humour is reported to be 54 minutes.

Tetrahydrozoline hydrochloride

Tetrahydrozoline hydrochloride can be easily absorbed, even following topical application to the eye, so systemic effects may occur in the event of overdosage. The vasoconstrictor effect of tetrahydrozoline hydrochloride has its onset 30 seconds to 1 minute after application, and lasts for 1 to 4 hours.

5.3 Preclinical safety data

Repeated dose toxicity

Ocular administration of fluorometholone solutions three times a day for one month at concentrations of 0.01%, 0.05% or 0.1% did not cause untoward local effects in rabbits. No difference in local tolerability was observed when tetrahydrozoline hydrochloride 0.0025% or 0.025% was concurrently administered to the eye. Systemic effects typical for steroids were observed predominantly at high topical fluorometholone doses.

Mutagenicity and carcinogenicity

The genotoxic and carcinogenic potential of fluorometholone and tetrahydrozoline hydrochloride has not been adequately studied. In view of the low quantities of fluorometholone and tetrahydrozoline hydrochloride in AFM-T, the short treatment duration and the long-term clinical experience with these compounds, there are no concerns when the product is used as directed.

Reproductive toxicity

Reproductive and developmental toxicity studies have not been conducted with tetrahydrozoline hydrochloride, and no animal fertility study was performed with fluorometholone.

Fluorometholone has been shown to be embryocidal and teratogenic in rabbits following topical ophthalmic application at doses approximating the human ocular dose. Dose-related fetal loss and fetal abnormalities including cleft palate, deformed rib cage, anomalous limbs and neural abnormalities such as encephalocele, craniorachischisis, and spina bifida were observed.

6. Pharmaceutical particulars

6.1 List of excipients

- Polyvinyl Alcohol
- Sodium Chloride
- Disodium Edetate
- Sodium Dihydrogen Phosphate Dihydrate
- Tyloxapol
- Benzalkonium Chloride Solution
- Aminocaproic Acid
- Sodium Hydroxide or Hydrochloric Acid
- Water for Injections

6.2 Incompatibilities

None Known.

6.3 Shelf life

2 years from the date of manufacture..

6.4 Special precautions for storage

- Store below 30°C (86°F) and protect from light.
- Discard 30 days after opening.
- Keep out of the reach of children.

6.5 Nature and contents of container

LDPE dropper bottle sealed with LDPE tip and HDPE screw cap. Each box contains 1 labeled bottle containing 5 ml suspension with a folded package insert.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

Aristopharma Ltd.
7, Purana Paltan Line, Dhaka – 1000, Bangladesh

8. Marketing authorization number(s)

378–065–052

9. Date of first authorization of the authorization

Date of inclusion: 05/08/2020