Efemoline®

Composition
Active substances: Fluorometholone, tetryzoline hydrochloride
Excipients: Hypromellose; benzalkonium chloride as preservative, vehicle excipients

Pharmaceutical form and quantity of active substance per unit
Eye drops (suspension): 1 mg fluorometholone per ml, 0.25 mg tetryzoline hydrochloride per ml

Indications / Potential uses
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 (incl. anterior uveitis, episcleritis and scleritis).
Post-operative conditions following surgery for strabismus, cataract or glaucoma; in combination with antimicrobial therapy.

Dosage and Administration
Adults
1 drop, instilled into the conjunctival sac 2–3 times daily.
In adults, the dosage can be increased to 1 drop per hour for the first 24–48 hours. Caution is required in patients with reactive hyperaemia.

Children
No relevant studies have been performed. Efemoline should not be used in children under 6 years of age due to the risk of systemic adverse effects.

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.
- Efemoline eye drops are contraindicated in patients with dry eye, particularly those with keratoconjunctivitis sicca (Sjögren's syndrome).
- Efemoline must not be used in children under 6 years of age.

Warnings and Precautions
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 2–3 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 Efemoline. Hypersensitivity reactions to components of Efemoline 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
Patients with eye inflammation should not wear contact lenses.

Interactions
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.

Pregnancy and Lactation
Animal studies with corticosteroids have provided evidence of adverse effects on the fetus, and no controlled studies have been performed in humans. The medicinal product should therefore not be used during pregnancy unless clearly necessary.
Women who are breastfeeding are also advised not to use Efemoline.

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.

Adverse effects
Eye disorders
The following effects have been reported in conjunction with long-term topical steroid treatment:
- Increase in intraocular pressure (regular monitoring of intraocular pressure is essential).
- Posterior subcapsular cataract.
- Promotion of secondary fungal infection in eye tissue.
- Corneal melt.
- Perforation of the eyeball.

Tetryzoline may cause conjunctival irritation, mucosal dryness and, in rare cases, mydriasis.
A mild burning sensation may briefly occur after application. Reactive hyperaemia (rebound effect) may occur in conjunction with prolonged use of the product. In rare cases, there may be allergic reactions such as punctate keratitis, periocular dermatitis or eczema of the free margins of the eyelids.
In general, the following adverse effects may occur in conjunction with topical steroid treatment:
- Secondary infections, elevated susceptibility to infection (in particular mycosis, herpes simplex).
- Delayed wound healing.
- Mydriasis and, in very rare cases, ptosis.
- Trophic corneal damage (possible after only 1 week of treatment).
- Rarely, exophthalmus.

General disorders
Despite the low doses used in topical application, it is not possible – particularly in children and in geriatric patients – to rule out the adverse systemic sympathomimetic effects of vasoconstrictors: palpitations, arrhythmia, anginal symptoms, hypertension, occipital headache, pallor, central excitation, tremor, sweating.

Overdose
When the product is used as directed, there is almost no likelihood of an overdose. 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 oral 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.

Properties and Actions
ATC code: S01GA52
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. It exerts less of an immunosuppressive effect than does dexamethasone. Fluorometholone has less of an effect on intraocular pressure than other corticosteroids because it is degraded more rapidly in tissues.
The alpha-sympathomimetic agent tetryzoline brings about rapid local vasoconstriction, which alleviates conjunctival swelling, hyperaemia and irritation.
Efemoline contains hypromellose, a viscosity-enhancing excipient that prolongs retention time on the eye.

Pharmacokinetics
Fluorometholone
Peak concentrations of active substance were measured in the cornea and aqueous humour 30 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.

Tetryzoline
Tetryzoline 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 tetryzoline hydrochloride has its onset 30 seconds to 1 minute after application, and lasts for 1–4 hours.

Preclinical data
Fluorometholone
Generally, corticosteroids do not pose any risks unless there has been prolonged overdosage. Application of fluorometholone eye drops in rabbits three times a day for one month, at concentrations of 0.1%, 0.05% or 0.01%, did not cause any persistent local changes in the eyes.

Tetryzoline
Tetryzoline can be considered moderately to slightly toxic, having an acute oral LD50 of 420 mg/kg in mice and 785 mg/kg in rats and an intravenous LD50 of 40 mg/kg and 35 mg/kg, respectively, in these species.
No eye irritation was seen following repeated administration in rabbits. A sensitization test using a modified Draize method showed no contact allergenic potential. The minimum lethal intranasal dose for a 2 year old child is reported to be 5 mg tetryzoline. Oral ingestion of 4 mg led to severe symptoms in a 16 month old boy.
Nasal application of tetryzoline at doses higher than about 1 mg may be toxic in infants.

Other information
Shelf-life
When stored unopened, Efemoline eye drops may be used until the expiry date (= EXP) printed on the pack and on the dropper bottle.

Special precautions for storage
Store at room temperature.

Instructions for use and handling
Shake the dropper bottle prior to use. Close immediately after use. Do not touch the dropper tip. After opening, do not use for more than 1 month.

Pack sizes
Country specific pack sizes

Manufacturer
See folding box

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November 2006

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5 March 2007

® = registered trademark

Novartis Pharma AG, Basle, Switzerland

This is a medicament
– A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
– Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
– The doctor and the pharmacist are experts in medicine, its benefits and risks.
– Do not by yourself interrupt the period of treatment prescribed for you.
– Do not repeat the same prescription without consulting your doctor.

Keep medicaments out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

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