NOVARTIS

Efemoline®

Other Ophthalmics

DESCRIPTION AND COMPOSITION

Pharmaceutical form

Eye drop, suspension

Active substances

Fluorometholone 1mg/ ml, tetryzoline hydrochloride 0.25mg/ ml eye drops. Certain dosage strengths and dosage forms may not be available in all countries.

Active moieties

Fluorometholone
Tetryzoline

Excipients

Benzalkonium chloride, Aluminium hydroxide gel, Boric acid, Borax, Sodium chloride, Disodium edetate, hypromellose and water for injection.
Pharmaceutical formulations may vary between countries.

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.

DOSAGE AND ADMINISTRATION

One drop of Efemoline solution 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

Instill 1 drop of Efemoline solution 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.

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 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 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

Efemoline contains benzalkonium chloride as a preservative. Benzalkonium chloride may cause eye irritation and is known to discolour soft contact lenses. Therefore, Efemoline 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.

Driving and using 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 DRUG REACTIONS

Adverse drug reactions from spontaneous reports (frequency not known)

The following adverse drug reactions have been derived from post-marketing experience with Efemoline 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

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.

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 Efemoline 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 NON-CLINICAL SAFETY DATA).
Efemoline 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 Efemoline.

Fertility

There is no information about the effects of Efemoline on human fertility.

OVERDOSAGE

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.

CLINICAL PHARMACOLOGY

Pharmacodynamics (PD)

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 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 (PK)

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.

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 to 4 hours.

CLINICAL STUDIES

No recent clinical trial was conducted with Efemoline.

NON-CLINICAL 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 tetryzoline 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 tetryzoline has not been adequately studied. In view of the low quantities of fluorometholone and tetryzoline in Efemoline eye drop, 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 tetryzoline, 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.

STORAGE

See folding box.
Efemoline should not be used after the date marked “EXP” on the pack.
Efemoline must be kept out of the reach and sight of children.

INSTRUCTIONS FOR USE AND HANDLING

Shake bottle before use.
Close immediately after use. Do not touch the dropper tip. After opening, do not use for more than 1 month.

Manufacturer:

See folding box.

International Package Leaflet

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Novartis Pharma AG, Basel, Switzerland