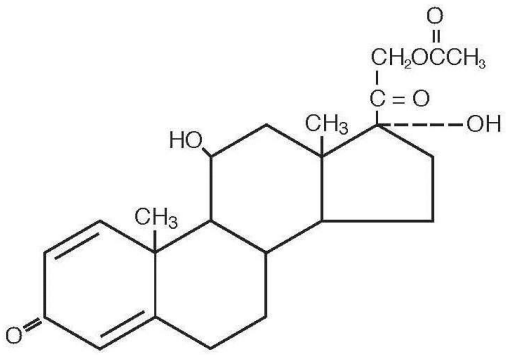
PRED-G®
(gentamicin and prednisolone acetate ophthalmic suspension, USP) 0.3%/1%
sterile

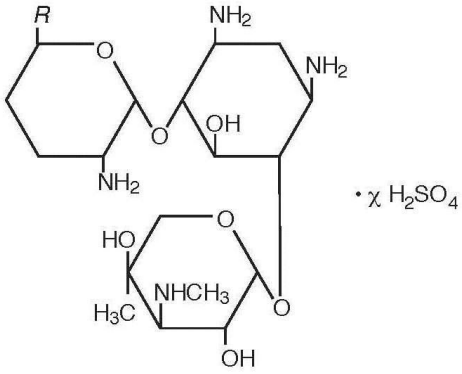
DESCRIPTION

PRED-G® sterile ophthalmic suspension is a topical anti-inflammatory/anti-infective combination product for ophthalmic use.

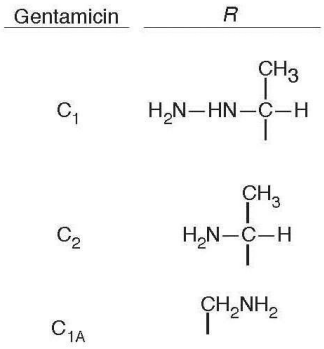
Structural Formulae:



prednisolone acetate



gentamicin sulfate



Chemical Names: Prednisolone acetate: 11ß,17,21-Trihydroxypregna-1,4-diene-3,20-dione 21-acetate.

Gentamicin sulfate is the sulfate salt of gentamicin C_1, gentamicin C_2, and gentamicin C_{1A} which are produced by the growth of *Micromonospora purpurea*.

Contains: Actives: Gentamicin sulfate equivalent to 0.3% gentamicin base; prednisolone acetate (microfine suspension) 1%. **Preservative:** Benzalkonium chloride 0.005%. **Inactives:** edetate disodium; hypromellose; polyvinyl alcohol 1.4%; polysorbate 80; purified water; sodium chloride; and sodium citrate, dihydrate. May contain sodium hydroxide and/or hydrochloric acid to adjust pH (5.4 to 6.6).

PRED-G® suspension is formulated with a pH from 5.4 to 6.6 and its osmolality ranges from 260 to 340 mOsm/kg.

CLINICAL PHARMACOLOGY

Corticosteroids suppress the inflammatory response to a variety of agents and they probably delay or slow healing. Since corticosteroids may inhibit the body's defense mechanism against infection, a concomitant antimicrobial drug may be used when this inhibition is considered to be clinically significant in a particular case.

The anti-infective component in **PRED-G®** is included to provide action against specific organisms susceptible to it. Gentamicin sulfate is active *in vitro* against susceptible strains of the following microorganisms: *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae, Enterobacter aerogenes, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Neisseria gonorrhoeae, Pseudomonas aeruginosa*, and *Serratia marcescens.*

When a decision to administer both a corticosteroid and an antimicrobial is made, the administration of such drugs in combination has the advantage of greater patient compliance and convenience, with the added assurance that the appropriate dosage of both drugs is administered. When both types of drugs are in the same formulation, compatibility of ingredients is assured and the correct volume of drug is delivered and retained.

The relative potency of corticosteroids depends on the molecular structure, concentration, and release from the vehicle.

INDICATIONS AND USAGE

PRED-G® suspension is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation, or thermal burns or penetration of foreign bodies.

The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

The particular anti-infective drug in this product is active against the following common bacterial eye pathogens: *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae, Enterobacter aerogenes, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Neisseria gonorrhoeae, Pseudomonas aeruginosa*, and *Serratia marcescens*.

CONTRAINDICATIONS

PRED-G® suspension is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of the ocular structures.

PRED-G® suspension is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation or to other corticosteroids.

WARNINGS

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections.

Various ocular diseases and long-term use of topical corticosteroids have been known to cause corneal and scleral thinning. Use of topical corticosteroids in the presence of thin corneal or scleral tissue may lead to perforation.

Acute purulent infections of the eye may be masked or enhanced by the presence of corticosteroid medication.

If this product is used for 10 days or longer, intraocular pressure should be routinely monitored even though it may be difficult in children and uncooperative patients. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be checked frequently.

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution; frequent slit lamp microscopy is recommended.

PRED-G® sterile ophthalmic suspension is not for injection. It should never be injected subconjunctivally, nor should it be directly introduced into the anterior chamber of the eye.

PRECAUTIONS

General
Ocular irritation and punctate keratitis have been associated with the use of **PRED-G®** suspension. The initial prescription and renewal of the medication order beyond 20 milliliters should be made by a physician only after examination of the patient's intraocular pressure, examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

As fungal infections of the cornea are particularly prone to develop coincidentally with long-term corticosteroid applications, fungal invasion should be suspected in any persistent corneal ulceration where a corticosteroid has been used or is in use. Fungal cultures should be taken when appropriate.

Information for Patients
If inflammation or pain persists longer than 48 hours or becomes aggravated, the patient should be advised to discontinue use of the medication and consult a physician.

This product is sterile when packaged. To prevent contamination, care should be taken to avoid touching the bottle tip to eyelids or to any other surface. The use of this bottle by more than one person may spread infection. Store at 15°-25°C (59°-77°F). Protect from freezing and from heat of 40°C (104°F) and above. Keep out of the reach of children. Shake well before using.

Carcinogenesis, Mutagenesis, Impairment of Fertility
There are no published carcinogenicity or impairment of fertility studies on gentamicin. Aminoglycoside antibiotics have been found to be non-mutagenic.

There are no published mutagenicity or impairment of fertility studies on prednisolone. Prednisolone has been reported to be non-carcinogenic.

Pregnancy
Gentamicin has been shown to depress body weight, kidney weight, and median glomerular counts in newborn rats when administered systemically to pregnant rats in daily doses approximately 500 times the maximum recommended ophthalmic human dose. There are no adequate and well-controlled studies in pregnant women. Gentamicin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Prednisolone has been shown to be teratogenic in mice when given in doses 1-10 times the human ocular dose. Dexamethasone, hydrocortisone and prednisolone were applied to both eyes of pregnant mice five times per day on days 10 through 13 of gestation. A significant increase in the incidence of cleft palate was observed in the fetuses of the treated mice. There are no adequate well-controlled studies in pregnant women. **PRED-G®** suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause untoward effects. Because of the potential for serious adverse reactions in nursing infants from **PRED-G®** suspension, a decision should be made whether to discontinue nursing while the drug is being administered or to discontinue the medication.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, the anti-infective component, or the combination. Exact incidence figures are not available since no denominator of treated patients is available.

Reactions reported with **PRED-G®** include eye burning, eye stinging, eye irritation, ocular hyperemia, eye pain, eye discharge, lacrimation increased, eye edema, visual impairment, blurry vision, foreign body sensation in eyes, and dysgeusia. Hypersensitivity including signs and symptoms related to ocular allergy (e.g. conjunctivitis), angioedema (e.g. tongue edema) and allergic skin reactions (e.g. rash and contact allergy) has also been reported. Superficial punctate keratitis has been reported occasionally with onset occurring typically after several days of use.

Reactions occurring most often from the presence of the anti-infective ingredient are allergic sensitizations. The reactions due to the steroid component in decreasing order of frequency are: elevation of intraocular pressure (IOP) with possible development of glaucoma, and infrequent optic nerve damage; posterior subcapsular cataract formation; and delayed wound healing.

Secondary Infection
The development of secondary ocular infection has occurred after use of combinations containing steroids and antimicrobials. Fungal and viral infections of the cornea are particularly prone to develop coincidentally with long-term applications of steroids. The possibility of fungal invasion should be considered in any persistent corneal ulceration where steroid treatment has been used (see WARNINGS).

Secondary bacterial ocular infection following suppression of host responses also occurs.

DOSAGE AND ADMINISTRATION

Instill one drop into the conjunctival sac two to four times daily. During the initial 24 to 48 hours, the dosing frequency may be increased, if necessary, up to 1 drop every hour. Care should be taken not to discontinue therapy prematurely.

If signs and symptoms fail to improve after two days, the patient should be re-evaluated (see PRECAUTIONS).

Not more than 20 milliliters should be prescribed initially, and the prescription should not be refilled without further evaluation as outlined in PRECAUTIONS above.

HOW SUPPLIED

PRED-G® (gentamicin and prednisolone acetate ophthalmic suspension, USP) 0.3%/1% is supplied sterile in white LDPE plastic bottles with droppers with white high impact polystyrene (HIPS) caps as follows:

5 mL in 10 mL bottle – NDC 0023-0106-05

Storage: Store at 15°-25°C (59°-77°F). Avoid excessive heat, 40°C (104°F) and above. Protect from freezing. Shake well before using.

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