CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74511

DRAFT FINAL PRINTED LABELING

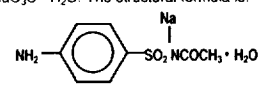
SULSTER™
SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10%/0.23% (prednisolone phosphate)

DESCRIPTION: Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution is a sterile corticosteroid and antibacterial topical combination which has the following composition:

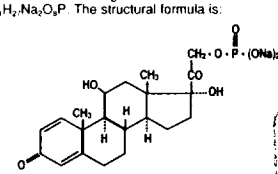
Each mL contains:

Active: Sulfacetamide Sodium (present as the monohydrate) 100 mg (10%), Prednisolone Sodium Phosphate 2.5 mg (equivalent to prednisolone phosphate 2.3 mg) (0.23%).
Preservative: Thimerosal 0.1 mg (0.01%).
Inactive: Boric Acid, Edetate Disodium, Poloxamer 407, Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH to 6.5-7.5), Purified Water USP.

The chemical name for sulfacetamide sodium is *N*-sulfanilylacetamide monosodium salt monohydrate. The molecular weight is 254.24 and the molecular formula is $C_8H_9N_2NaO_3S \cdot H_2O$. The structural formula is:



The chemical name for prednisolone sodium phosphate is 11β, 17,21-trihydroxypregna-1,4-diene-3,20-dione, 21-(disodium phosphate). The molecular weight is 484.40 and the molecular formula is $C_{21}H_{27}Na_2O_8P$. The structural formula is:



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 antibacterial drug may be used when this inhibition is considered to be clinically significant in a particular case.

When a decision to administer both a corticosteroid and an antibacterial 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, plus assured compatibility of ingredients when both types of drugs are in the same formulation and, particularly, that the correct amount of drug is delivered and retained.

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

Microbiology: Sulfacetamide exerts a bacteriostatic effect against susceptible bacteria by restricting the synthesis of folic acid required for growth through competition with p-aminobenzoic acid.

Some strains of bacteria may be resistant to sulfacetamide or resistant strains may emerge *in vivo*.

The anti-infective component in SULSTER™ is included to provide action against specific organisms susceptible to it. Sulfacetamide sodium is active *in vitro* against susceptible strains of the following microorganisms: *Escherichia coli, Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus* (viridans group), *Haemophilus influenzae, Klebsiella* species and *Enterobacter* species. This product does not provide adequate coverage against: *Neisseria* species, *Pseudomonas* species, *Serratia marcescens* (see **INDICATIONS AND USAGE**).

INDICATIONS AND USAGE: SULSTER™ 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 corticosteroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of corticosteroid use in certain infective conjunctivitides is accepted to obtain 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 antibacterial drug in this product is active against the following common bacterial eye pathogens: *Escherichia coli, Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus* (viridans group), *Haemophilus influenzae, Klebsiella* species, and *Enterobacter* species.

The product does not provide adequate coverage against: *Neisseria* species, *Pseudomonas* species, and *Serratia marcescens*.

A significant percentage of staphylococcal isolates are completely resistant to sulfa drugs.

CONTRAINDICATIONS: SULSTER™ 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 ocular structures. This product is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation, to other sulfonamides and to other corticosteroids. See **WARNINGS**. (Hypersensitivity to the antimicrobial component occurs at a higher rate than for other components(s).)

WARNINGS: NOT FOR INJECTION INTO THE EYE. Prolonged use of corticosteroids may result in ocular hypertension/glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation.

Acute anterior uveitis may occur in susceptible individuals.

Prolonged use of SULSTER™ (Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution) may suppress the host response and thus increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforation has been reported to occur with the use of topical corticosteroids. In acute purulent conditions of the eye, corticosteroids may mask infection or enhance existing infection.

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. Corticosteroids should be used with caution in the presence of glaucoma.

A significant percentage of staphylococcal isolates are completely resistant to sulfonamides.

The use of steroids after cataract surgery may delay healing and increase the incidence of filtering blebs.

The use of ocular corticosteroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Employment of corticosteroid medication in the treatment of herpes simplex requires great caution.

Topical corticosteroids are not effective in mustard gas keratitis and Sjögren's keratoconjunctivitis.

Fatalities have occurred, although rarely, due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias. Sensitizations may recur when a sulfonamide is readministered, irrespective of the route of administration. If signs of hypersensitivity or other serious reactions occur, discontinue use of this preparation. Cross-sensitivity among corticosteroids has been demonstrated (see **ADVERSE REACTIONS**).

Do not administer this product to patients who are sensitive/allergic to thimerosal or any other mercury-containing ingredient.

PRECAUTIONS: General: The initial prescription and renewal of the medication order beyond 20 mL of SULSTER™ (Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution) should be made by a physician only after examination of the patient with the aid of magnification, such as slit-lamp biomicroscopy and, where appropriate, fluorescein staining. If signs and symp-

toms fail to improve after two days, the patient should be re-evaluated.

The possibility of fungal infections of the cornea should be considered after prolonged corticosteroid dosing. Use with caution in patients with severe dry eye. Fungal cultures should be taken when appropriate.

The p-aminobenzoic acid present in purulent exudates competes with sulfonamides and can reduce their effectiveness.

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. (see **WARNINGS**.)

This product is sterile when packaged. To prevent contamination, care should be taken to avoid touching the dropper tip to eyelids or to any other surface. The use of this dropper bottle by more than one person may spread infection. Keep bottle tightly closed when not in use. Protect from light. Sulfonamide solutions darken on prolonged standing and exposure to heat and light. Do not use if solution has darkened. Yellowing does not affect activity. Keep out of the reach of children.

Laboratory Tests: Eyelid cultures and tests to determine the susceptibility of organisms to sulfacetamide may be indicated if signs and symptoms persist or recur in spite of the recommended course of treatment with SULSTER™ (Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution).

Drug Interactions: SULSTER™ is incompatible with silver preparations. Local anesthetics related to p-aminobenzoic acid may antagonize the action of the sulfonamides.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Prednisolone has been reported to be noncarcinogenic. Long-term animal studies for carcinogenic potential have not been performed with sulfacetamide.

Mutagenic studies with prednisolone have been negative. Studies on reproduction and fertility have not been performed with sulfacetamide. A long-term chronic toxicity study in dogs showed that high oral doses of prednisolone prevented estrus. A decrease in fertility was seen in male and female rats that were mated following oral dosing with another glucocorticosteroid.

Pregnancy: ***Teratogenic Effects:*** **Pregnancy Category C:** Animal reproduction studies have not been conducted with sulfacetamide sodium. Prednisolone has been shown to be teratogenic in rabbits, hamsters, and mice. In mice, prednisolone has been shown to be teratogenic when given in doses 1 to 10 times the human ocular dose. Dexamethasone, hydrocortisone and prednisolone were ocularly 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 dosed with corticosteroids.

Kernicterus may be precipitated in infants by sulfonamides being given systemically during the third trimester of pregnancy. It is not known whether sulfacetamide sodium can cause fetal harm when administered to a pregnant woman or whether it can affect reproductive capacity.

SULSTER™ 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 other untoward effects. Systemically administered sulfonamides are capable of producing kernicterus in infants of lactating women. Because of the potential for serious adverse reactions in nursing infants from SULSTER™ (Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution) a decision should be made whether to discontinue nursing or to discontinue the medication taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of six have not been established.

ADVERSE REACTIONS: Adverse reactions have occurred with corticosteroid/antibacterial combination drugs which can be attributed to the corticosteroid component, the antibacterial component, or the combination. The exact incidence is not known.

Reactions occurring most often from the presence of the antibacterial ingredient are allergic sensitizations. Fatalities have occurred, although rarely, due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias (see **WARNINGS**).

Sulfacetamide sodium may cause local irritation.

The reactions due to the corticosteroid 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.

Although systemic effects are extremely uncommon, there have been rare occurrences of systemic hypercorticoidism after use of topical steroids.

Corticosteroid-containing preparations can also cause acute anterior uveitis or perforation of the globe. Mydriasis, loss of accommodation and ptosis have occasionally been reported following local use of corticosteroids.

Secondary Infection: The development of secondary infection has occurred after use of combinations containing corticosteroids and antibacterials. Fungal and viral infections of the cornea are particularly prone to develop coincidentally with long-term applications of corticosteroid. The possibility of fungal invasion must be considered in any persistent corneal ulceration where corticosteroid treatment has been used.

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

DOSAGE AND ADMINISTRATION: Instill two drops of SULSTER™ topically in the eye(s) every four hours.

Not more than 20 mL should be prescribed initially.

The dosing of SULSTER™ may be reduced, but care should be taken not to discontinue therapy prematurely. In chronic conditions, withdrawal of treatment should be carried out by gradually decreasing the frequency of application.

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

HOW SUPPLIED: SULSTER™ (Sulfacetamide Sodium and Prednisolone Sodium Phosphate Ophthalmic Solution, 10%/0.23% [prednisolone phosphate]) is supplied as a sterile solution in plastic dropper bottles in two sizes:

5 mL — NDC 17478-116-10

10 mL — NDC 17478-116-11

Storage: To be dispensed only in original, unopened container. Store at controlled room temperature 15°-30°C (59°-86°F). Keep from freezing. PROTECT FROM LIGHT.

Sulfonamide solutions darken on prolonged standing and exposure to heat and light. Do not use if solution has darkened. Yellowing does not affect activity.

WARNING — KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

CAUTION: Federal (USA) law prohibits dispensing without prescription.

Akorn

Akorn, Inc.
Abita Springs, LA 70420

FOR TOPICAL OPHTHALMIC USE ONLY.
Usual Dosage: See package insert.
Storage: Store at controlled room temperature 15°-30°C (59°-86°F).
Keep tightly closed. Protect from light. Keep from freezing. Do not use if solution has darkened. Yellowing does not affect activity. Caution: Federal (USA) law prohibits dispensing without prescription. Note: Bottle filled to 1/2 capacity for proper drop control.
Akorn, Inc., Abita Springs, LA 70420
SPAEL rev. 3/96

NDC 17478-116-10 Akorn

[redacted]

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10% / 0.23% (prednisolone phosphate)

5 mL Sterile

Each mL contains:
Active: Sulfacetamide Sodium (present as the monohydrate) 100 mg (10%), Prednisolone Sodium Phosphate 2.5 mg equivalent to prednisolone phosphate 2.3 mg (0.23%).
Preservatives: Thimerosal 0.1 mg (0.01%).
Inactive: Boric Acid, Edetate Disodium, Poloxamer 407, Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH to 6.5-7.5), Purified Water USP.

WARNING-KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

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FOR TOPICAL OPHTHALMIC USE ONLY.
Usual Dosage: See package insert. **Storage:** Store at controlled room temperature 15°-30°C (59°-86°F). Keep tightly closed. Protect from light. Keep from freezing. Do not use if solution has darkened. Yellowing does not affect activity. Caution: Federal (USA) law prohibits dispensing without prescription. **Note:** Bottle filled to 2/3 capacity for proper drop control.

Akorn, Inc., Abita Springs, LA 70420
SPAGL rev. 2/96

NDC 17478-116-11 Akorn

[redacted]

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10% / 0.23% (prednisolone phosphate)

10 mL Sterile

Each mL contains:
Active: Sulfacetamide Sodium (present as the monohydrate) 100 mg (10%), Prednisolone Sodium Phosphate 2.5 mg (equivalent to prednisolone phosphate 2.3 mg) (0.23%).
Preservatives: Thimerosal 0.1 mg (0.01%).
Inactive: Boric Acid, Edetate Disodium, Poloxamer 407, Hydrochloric Acid and/or Sodium Hydroxide (to adjust pH to 6.5-7.5), Purified Water USP.
WARNING-KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

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SULSTER™
SULFACETAMIDE
SODIUM AND PREDNISOLONE
SODIUM PHOSPHATE
OPHTHALMIC SOLUTION,
10% /0.23% (prednisolone
phosphate) Sterile

5 mL

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FOR TOPICAL OPHTHALMIC USE ONLY.

Usual Dosage: See package insert.

WARNING-KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Storage: Store at controlled room temperature 15°-30°C (59°-86°F). Keep tightly closed. Protect from light. Keep from freezing. Do not use if solution has darkened. Yellowing does not affect activity.

DO NOT USE IF IMPRINTED SEAL IS BROKEN OR MISSING

NDC 17478-116-10

5 mL

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10% /0.23% (prednisolone phosphate) Sterile

Caution: Federal (USA) law prohibits dispensing without prescription.

Akorn

Each mL contains:
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Akorn, Inc.
Abita Springs, LA 70420

SPAEC rev. 2/96

NDC 17478-116-10

5 mL

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10% /0.23% (prednisolone phosphate) Sterile

Caution: Federal (USA) law prohibits dispensing without prescription.

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Akorn

Lot No.

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Exp. Date

FOR TOPICAL OPHTHALMIC USE ONLY.

Usual Dosage: See package insert.

WARNING-KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Storage: Store at controlled room temperature 15°-30°C (59°-86°F). Keep tightly closed. Protect from light. Keep from freezing. Do not use if solution has darkened. Yellowing does not affect activity.

DO NOT USE IF IMPRINTED SEAL IS BROKEN OR MISSING

NDC 17478-116-11

10 mL

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10%/0.23% (prednisolone phosphate) Sterile

Caution: Federal (USA) law prohibits dispensing without prescription.

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Each mL contains:
Active: Sulfacetamide Sodium (present as the monohydrate) 100 mg (10%), Prednisolone Sodium Phosphate 2.5 mg (equivalent to prednisolone phosphate 2.3 mg) (0.23%).
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Note: Bottle filled to 2/3 capacity for proper drop control.

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Akorn, Inc.
Abita Springs, LA 70420

SPAGC rev. 2/96

NDC 17478-116-11

10 mL

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10%/0.23% (prednisolone phosphate) Sterile

Caution: Federal (USA) law prohibits dispensing without prescription.

Akorn

APPROVED

JUL 30 1996

10 mL

SULSTER™

SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE OPHTHALMIC SOLUTION, 10%/0.23% (prednisolone phosphate) Sterile

NOSCO

Lot No.

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Exp. Date

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