

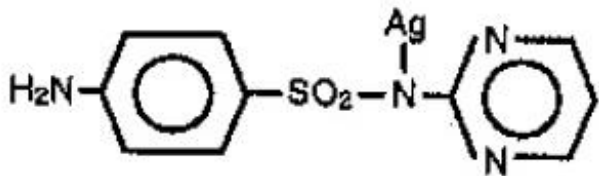
THERMAZENE- silver sulfadiazine cream
COVIDIEN INC.

KENDALL
THERMAZENE*
(Silver Sulfadiazine) Cream, 1%

DESCRIPTION

Thermazene (silver sulfadiazine) Cream, 1% is a soft, water dispersible cream containing silver sulfadiazine in micronized form for topical application. Each gram of Thermazene contains 10mg of micronized silver sulfadiazine.

This active agent has the following structural formula:



Thermazene contains 1% w/w silver sulfadiazine. The vehicle in which the active ingredient is dispersed consists of water, stearyl alcohol NF, white petrolatum USP, polyoxyl 40 stearate NF, propylene glycol USP, isopropyl myristate NF, and sorbitan monooleate NF with 0.3% methylparaben NF as a preservative.

CLINICAL PHARMACOLOGY

Silver sulfadiazine has broad antimicrobial activity. It is bactericidal for many gram-negative and gram-positive bacteria as well as being effective against yeast. Results from in vitro testing are listed below.

Sufficient data have been obtained to demonstrate that silver sulfadiazine will inhibit bacteria that are resistant to other antimicrobial agents and that the compound is superior to sulfadiazine.

Studies utilizing radioactive micronized silver sulfadiazine, electron microscopy, and biochemical techniques have revealed that the mechanism of action of silver sulfadiazine on bacteria differs from silver nitrate and sodium sulfadiazine. Silver sulfadiazine acts only on the cell wall to produce its bactericidal effect.

Results of in Vitro Testing With Silver Sulfadiazine Cream, 1% Concentration of Silver Sulfadiazine Number of Sensitive Strains / Total Number of Strains Tested

Genus and Species	50 µg/mL	100 µg/mL
<i>Pseudomonas aeruginosa</i>	130/130	130/130
<i>Xanthomonas (Pseudomonas) maltophilia</i>	7/7	7/7
<i>Enterobacter species</i>	48/50	50/50
<i>Enterobacter cloacae</i>	24/24	24/24
<i>Klebsiella species</i>	53/54	54/54

Escherichia coli	63/63	63/63
Serratia species	27/28	28/28
Proteus mirabilis	53/53	53/53
Morganella morganii	10/10	10/10
Providencia rettgeri	2/2	2/2
Proteus vulgaris	2/2	2/2
Providencia species	1/1	1/1
Citrobacter species	10/10	10/10
Acinetobacter calcoaceticus	10/11	11/11
Stahylococcus aureus	100/101	101/101
Staphylococcus epidermidis	51/51	51/51
B-Hemolytic streptococcus	4/4	4/4
Enterococcus species	52/53	53/53
Corynebacterium diphtheriae	2/2	2/2
Clostridium perfringens	0/2	2/2
Candida albicans	43/50	50/50

Silver sulfadiazine is not a carbonic anhydrase inhibitor and may be useful in situations where such agents are contraindicated.

INDICATIONS AND USAGE

Thermazene Cream is a topical antimicrobial drug indicated as an adjunct for the prevention and treatment of wound sepsis in patients with second and third degree burns.

CONTRAINDICATIONS

Thermazene Cream is contraindicated in patients who are hypersensitive to silver sulfadiazine or any of the other ingredients in the preparation.

Because sulfonamide therapy is known to increase the possibility of kernicterus, Thermazene Cream should not be used on pregnant women approaching or at term, on premature infants, or on newborn infants during the first 2 months of life.

WARNINGS

There is a potential cross-sensitivity between silver sulfadiazine and other sulfonamides. If allergic reactions attributable to treatment with silver sulfadiazine occur, continuation of therapy must be weighed against the potential hazards of the particular allergic reaction.

Fungal proliferation in and below the eschar may occur. However, the incidence of clinically reported fungal superinfection is low.

The use of Thermazene Cream in some cases of glucose-6-phosphate dehydrogenase-deficient individuals may be hazardous, as hemolysis may occur.

PRECAUTIONS

General. If hepatic and renal functions become impaired and elimination of the drug decreases accumulation may occur. Discontinuation of Thermazene Cream should be weighed against the therapeutic benefit being achieved.

In considering the use of topical proteolytic enzymes in conjunction with Thermazene Cream, the

possibility should be noted that silver may inactivate such enzymes.

Laboratory Tests. In the treatment of burn wounds involving extensive areas of the body, the serum sulfa concentrations may approach adult therapeutic levels (8 to 12mg %). Therefore, in these patients it would be advisable to monitor serum sulfa concentrations. Renal function should be carefully monitored and the urine should be checked for sulfa crystals.

Absorption of the propylene glycol vehicle has been reported to affect serum osmolality, which may affect the interpretation of laboratory tests.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term dermal toxicity studies of 24 months duration in rats and 18 months in mice with concentrations of silver sulfadiazine three to ten times the concentration in Thermazene (Silver Sulfadiazine) Cream, 1% revealed no evidence of carcinogenicity.

Pregnancy: Teratogenic Effects:

Pregnancy Category B. A reproductive study has been performed in rabbits at doses up to three to ten times the concentration of silver sulfadiazine in Thermazene Cream and has revealed no evidence of harm to the fetus due to silver sulfadiazine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly justified, especially in pregnant women approaching or at term. (See CONTRAINDICATIONS).

Nursing Mothers. It is not known whether Thermazene Cream is excreted in human milk. However, sulfonamides are known to be excreted in human milk and all sulfonamides derivatives are known to increase the possibility of kernicterus. Because of the potential for serious adverse reactions in nursing infants from sulfonamides, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use. Safety and effectiveness in children have not been established. (See CONTRAINDICATIONS)

ADVERSE REACTIONS

Several cases of transient leucopenia have been reported in patients receiving silver sulfadiazine therapy. Leucopenia associated with silver sulfadiazine administration is primarily characterized by decreased neutrophil count. Maximal white blood cell depression occurs within two to four days of initiation of therapy. Rebound to normal leukocyte levels follows onset within two to three days. Recovery is not influenced by continuation of silver sulfadiazine therapy. The incidence of leucopenia in various reports averages about 20%. A higher incidence has been seen in patients treated concurrently with cimetidine.

Other infrequently occurring events include skin necrosis, erythema multiforme, skin discoloration, burning sensation, rashes, and interstitial nephritis.

Reduction in bacterial growth after application of topical antibacterial agents has been reported to permit spontaneous healing of deep partial thickness burns by preventing conversion of the partial thickness to full thickness by sepsis. However, reduction in bacterial colonization has caused delayed separation, in some cases necessitating escharotomy in order to prevent contracture.

Absorption of silver sulfadiazine varies depending upon the percent of body surface area and the extent of the tissue damage. Although few have been reported, it is possible that any adverse reaction associated with sulfonamides may occur. Some of the reactions which have been associated with sulfonamides are as follows: blood dyscrasias, agranulocytosis, aplastic anemia, thrombocytopenia, leucopenia, hemolytic anemia, dermatologic reactions, allergic reactions, Stevens-Johnson syndrome,

exfoliative dermatitis, gastrointestinal reactions, hepatitis, hepatocellular necrosis, CNS reactions, and toxic nephrosis.

DOSAGE AND ADMINISTRATION

Prompt institution of appropriate regimens for care of the burned patient is of prime importance and includes the control of shock and pain. The burn wounds are then cleansed and debrided; Thermazene Cream is then applied under sterile conditions. The burn areas should be covered with Thermazene Cream at all times. The cream should be applied once to twice daily to a thickness of approximately one sixteenth of an inch. Whenever necessary, the cream should be reapplied to any areas from which it has been removed due to patient activity. Administration may be accomplished in minimal time because dressings are not required. However, if individual patient requirements make dressings necessary, they may be used.

Reapply immediately after hydrotherapy. Treatment with Thermazene Cream should be continued until satisfactory healing has occurred or until the burn site is ready for grafting. The drug should not be withdrawn from the therapeutic regimen while there remains the possibility of infection except if a significant adverse reaction occurs.

HOW SUPPLIED

Reorder No. 8884-	NDC No.	Size	No. in Case
472609	8880-9505-02	20g tube	24
473888	8880-9505-85	85g tube	12
473000	8880-9505-05	50g jar	6
473250	8880-9505-50	50g tube	36
473400	8880-9505-40	400g jar	6
473800	8880-9505-10	1000g jar	6

Store at controlled room temperature 15° - 30°C (59° - 86°F)

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MANSFIELD, MA 02048

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Reorder

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KENDALL

THERMAZENE*

(Silver Sulfadiazine) Cream, 1%

NET WT. 35oz (1000g)

For Topical Use Only

NDC 8880-9505-10

Reorder
888473800

KENDALL
THERMAZENE
(Silver Sulfadiazine) Cream, 1%

NET WT. 35oz (1000g)

For Topical Use Only

NDC 8880-9505-10

Silver Sulfadiazine (microsized) 1% in a Hydrophilic (water dispersible) base consisting of Water, Stearyl Alcohol NF, White Petrolatum USP, Polyoxyl 40 Stearate NF, Propylene Glycol USP, Isopropyl Myristate NF, Sorbitan Monooleate NF, with 0.3% Methylparaben NF as a preservative.

DOSAGE AND ADMINISTRATION: See insert provided with this package.

CAUTION: Federal law prohibits dispensing without prescription.

WARNING: KEEP OUT OF REACH OF CHILDREN. STORE AT ROOM

TEMPERATURE 15°-30°C (59°-86°F).

SEE BOTTOM OF JAR FOR BATCH NUMBER AND EXPIRATION DATE.

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THERMAZENE

silver sulfadiazine cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:8880-9505
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
SILVER SULFADIAZINE (UNII: W46JY43EJR) (SULFADIAZINE - UNII:0N7609K889)	SILVER SULFADIAZINE	10 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
WATER (UNII: 059QF0KO0R)	
STEARYL ALCOHOL (UNII: 2KR8914H1Y)	
PETROLATUM (UNII: 4T6H12BN9U)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
ISOPROPYL MYRISTATE (UNII: 0RE8K4LNJS)	
SORBITAN MONOOLEATE (UNII: 06XEA2VD56)	
METHYLPARABEN (UNII: A218C7H9T)	
POLYOXYL 40 STEARATE (UNII: 13A4J4NH9I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:8880-9505-02	24 in 1 CASE		
1		20 g in 1 TUBE		
2	NDC:8880-9505-50	36 in 1 CASE		
2		50 g in 1 TUBE		

3	NDC:8880-9505-85	12 in 1 CASE		
3		85 g in 1 TUBE		
4	NDC:8880-9505-05	6 in 1 CASE		
4		50 g in 1 JAR		
5	NDC:8880-9505-40	6 in 1 CASE		
5		400 g in 1 JAR		
6	NDC:8880-9505-10	6 in 1 CASE		
6		1000 g in 1 JAR		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA018810	08/20/2012	

Labeler - COVIDIEN INC. (805770828)

Revised: 8/2012

COVIDIEN INC.