DESCRIPTION

SSD (1% Silver Sulfadiazine) Cream and SSD AF (1% Silver Sulfadiazine) Cream are topical antibacterial preparations which have as their active antimicrobial ingredient silver sulfadiazine. The active moiety is contained within an opaque, white, water miscible cream base.

Each 1000 grams of SSD/SSD AF Cream contains 10 grams of silver sulfadiazine

Inactive Ingredients: cetyl alcohol (SSD Cream only), isopropyl myristate, polyoxyl 40 stearate, propylene glycol, purified water, stearyl alcohol, sodium hydroxide, sorbitan monooleate, white petrolatum; with 0.3% methyl paraben, as a preservative.

Silver sulfadiazine has an empirical formula of \( \text{C}_{10}\text{H}_9\text{AgN}_4\text{O}_2\text{S} \), molecular weight of 357.14 and structural formula as shown:

![Structural formula of silver sulfadiazine](image)

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 1% Concentration of Silver Sulfadiazine

<table>
<thead>
<tr>
<th>Genus and Species</th>
<th>50 ( \mu \text{g/mL} )</th>
<th>100 ( \mu \text{g/mL} )</th>
</tr>
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<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>130/130</td>
<td>130/130</td>
</tr>
<tr>
<td>Pseudomonas maltophilia</td>
<td>7/7</td>
<td>7/7</td>
</tr>
<tr>
<td>Enterobacter species</td>
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<td>50/50</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
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<td>24/24</td>
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<tr>
<td>Klebsiella species</td>
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<td>54/54</td>
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<tr>
<td>Escherichia coli</td>
<td>63/63</td>
<td>63/63</td>
</tr>
<tr>
<td>Serratia species</td>
<td>27/28</td>
<td>28/28</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>53/53</td>
<td>53/53</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>10/10</td>
<td>10/10</td>
</tr>
</tbody>
</table>
Silver sulfadiazine is not a carbonic anhydrase inhibitor and may be useful in situations where such agents are contraindicated.

**INDICATIONS AND USAGE**

Silver Sulfadiazine 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**

Silver Sulfadiazine 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, Silver Sulfadiazine 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 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 Silver Sulfadiazine 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 drug decreases, accumulation may occur and discontinuation of Silver Sulfadiazine Cream should be weighed against the therapeutic benefit being achieved.

In considering the use of topical proteolytic enzymes in conjunction with Silver Sulfadiazine 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 and Mutagenesis and 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 Silver Sulfadiazine Cream
revealed no evidence of carcinogenicity.

**Pregnancy: 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 Silver Sulfadiazine 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 Silver Sulfadiazine 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 possibility 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 leukopenia have been reported in patients receiving silver sulfadiazine
therapy. Leukopenia 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 leukopenia
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, including agranulocytosis, aplastic anemia,
thrombocytopenia, leucopenia and hemolytic anemia, dermatologic and and allergic reactions, including
Stevens-Johnson syndrome and exfoliative dermatitis, gastrointestinal reactions, hepatitis and
hepatocellular necrosis, CNS reactions, and toxic nephrosis.
DOSAGE AND ADMINISTRATION

FOR TOPICAL USE ONLY - NOT FOR OPHTHALMIC USE:

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; and Silver Sulfadiazine Cream is applied under sterile conditions. The burn areas should be covered with Silver Sulfadiazine Cream at all times. The cream should be applied once to twice daily to a thickness of approximately 1/16 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 Silver Sulfadiazine 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

SSD™ (1% Silver Sulfadiazine) Cream: white to off-white cream.

| 50 gram jar | 400 gram jar | 25 gram tube | 50 gram tube | 85 gram tube |

SSD AF™ (1% Silver Sulfadiazine) Cream: white to off-white cream.

| 50 gram jar | 400 gram jar |

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

SSD is a trademark of Dr. Reddy's Laboratories Louisiana, LLC

Manufactured for
Par Pharmaceutical Companies, Inc.
Spring Valley, NY 10977

Manufactured by
Dr. Reddy's Laboratories Louisiana, LLC
Shreveport, LA 71106

Repacked by
H.J. Harkins Company, Inc.
Nipomo, CA 93444

Aug 2011

PRINCIPAL DISPLAY PANEL – 50 GRAM TUBE
**SILVER SULFADIAZINE**
silver sulfadiazine cream

### Product Information

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### Active Ingredient/Active Moiety

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### Inactive Ingredients

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<td>WATER (UNII: 059QF0K00R)</td>
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### Packaging

Take as directed by your Doctor or See insert for usual dosage information
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**Labeler** - H.J. Harkins Company, Inc. (147681894)

**Registrant** - Dr. Reddy's Laboratories Inc. DBA Dr. Reddy's Laboratories Louisiana, LLC (830397282)

### Establishment

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Revised: 11/2011

H.J. Harkins Company, Inc.