PACKAGE INSERT TEMPLATE FOR SILVER SULFADIAZINE CREAM

Brand or Product Name
[Product name] Cream 1% w/w

Name and Strength of Active Substance(s)
Silver sulfadiazine …..1 % w/w

Product Description
[Visual description of the appearance of the product (eg colour, viscosity etc)
eg White, smooth glossy cream with a characteristic odour

Pharmacodynamics
Silver sulfadiazine exerts its antibacterial effects by binding to cell membranes and, to a lesser extent, the bacterial cell wall, rather than by interacting with cellular DNA. When silver sulfadiazine comes into contact with skin, sulfadiazine is slowly released which is then absorbed to various extents. This reaction is dependent on the presence of chlorides and other anions in the exudate and is greater during eschar separation than in the early post-burn period when renal function may be altered. The free silver may react with both the sulfhydryl groups of bacterial enzymes and DNA, combining its bactericidal action with the bacteriostatic action of the sulfonamide against many organisms, particularly Pseudomonas aeruginosa .
The antibacterial effects of silver sulfadiazine are not inhibited by para-aminobenzoic acid or other metabolites frequently found in wounds. Silver sulfadiazine is a broad-spectrum antibacterial agent demonstrating bactericidal activity against many gram-positive and gram-negative organisms, including Pseudomonas aeruginosa, Escherichia coli, Proteus spp, staphylococcus, streptococcus, and yeasts

Pharmacokinetics
Absorption
- Although silver is not appreciably absorbed systemically, sulfadiazine may be absorbed into the blood especially when the drug is applied to large areas and/or over prolonged periods of time.
- Serum sulfonamide levels are proportional to the extent of burned areas and to the amount of cream applied. During prolonged treatment of wounds involving extensive areas of the body, pediatric serum sulfonamide levels may approach adult therapeutic levels (8 to 12 milligrams/deciliter). Sulfadiazine concentrations as high as 9.1 mg/dl within 24 hours of topical application were reported in the serum of severely burned patients receiving silver sulfadiazine. If renal function is sufficiently impaired, accumulation of sulfadiazine may occur particularly if the patient is dehydrated. In severely burned patients and in children, it is recommended that serum sulfa concentration be monitored.

Distribution
Other distribution sites: Liver

Elimination
- Excreted unchanged in the urine

- Urine sulfonamide levels proportional to the extent of burned areas and to the amount of cream applied. If renal function becomes sufficiently impaired, accumulation may occur, particularly if the patient is dehydrated
- Elimination half-life is 10 hours ; Half-life increases to 22 hours in anuric patients

Indication
For the prophylaxis and treatment of infection in burn wounds

Recommended Dosage:
Silver sulfadiazine 1% cream should be applied with a sterile, gloved hand to the burn surface once or twice daily to a thickness of approximately 1/16th inch (1.5mm), and continued until satisfactory healing occurs until the burn site is ready for grafting. Silver sulfadiazine should be applied more frequently to burn areas which might allow easier removal of the cream by movement of the patient. Dressings can be applied over the cream but this is usually not necessary

Renal Failure: No specific dosage adjustment of silver sulfadiazine is necessary. Although silver is not readily absorbed, sulfadiazine can be absorbed in significant quantities following prolonged treatment of extensive burns, and measurement of sulfadiazine levels may be indicated in patients with impaired renal function

Hepatic Insufficiency: No specific dosage adjustment of silver sulfadiazine is necessary. However, large amounts of sulfadiazine may be absorbed following prolonged treatment of extensive burns, and serum sulfonamide levels should be monitored during prolonged use of the drug in patients with impaired hepatic function
Safety and effectiveness not established in children

Mode of Administration
Topical

Contraindications
- hypersensitivity to silver or sulfonamide products
- pregnancy (approaching term)
- preterm infants or newborns under 2 months

Warnings and Precautions
- Caution of use is required in individuals known to have Glucose-6-phosphate dehydrogenase deficiency; hemolysis may occur
- Hepatic or renal impairment; accumulation may occur; discontinuation may be necessary
- blood dyscrasias (eg, agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia) may occur
- CNS reactions may occur
- Cross-sensitivity with other sulfonamides may occur; if allergic reactions occur, consider potential hazards of continuing therapy
- Cutaneous reactions, life-threatening (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis [TEN], exfoliative dermatitis), may occur
- Fungal proliferation, in or below the eschar, may occur
- Gastrointestinal reactions may occur
- Hepatitis or hepatocellular necrosis may occur
- Toxic nephrosis may occur

[Specific package insert requirement]

Discontinue treatment with this drug immediately if skin rash or any sign of adverse reaction occurs.

Fatalities associated with the administration of sulphonamides and trimethoprim, either alone or in combination, have occurred due to severe reactions, including Steven-Johnson syndrome, toxic epidermal necrolysis and other reactions. The drug should be discontinued at the first appearance of skin rash or any sign of adverse reaction.

Urinalyses may be required prior to and periodically during treatment to detect crystalluria and/or urinary calculi formation in patients on long-term or high-dose therapy and in patients with impaired renal function.

If allergic reactions or hepatic or renal function impairment with decreased elimination occurs, discontinuation of therapy with the medication should be considered.

*For external use only.

*Contact with the eyes should be avoided. In case of accidental contact with the eyes, rinse the eyes thoroughly with running water

Effects on the ability to drive and use machines
Unlikely to impair a patient's ability to drive or use machinery

Interactions with Other Medicaments
Concurrent application of papain and silver salt-containing formulations such as silver sulfadiazine may result in the inactivation of the enzymatic debriding action of papain

Statement on Usage During Pregnancy and Lactation
Pregnancy
There are no data on the use of silver sulfadiazine in pregnant women. Kernicterus in the infant is possible if significant amounts of maternally applied silver sulfadiazine cream are absorbed. Silver sulfadiazine should only be used during pregnancy if the maternal condition justifies the potential risks to the fetus. However, use in pregnant women approaching term or at term is contraindicated. Although silver is not appreciably absorbed systemically, sulfadiazine may be absorbed into the blood especially when the drug is applied to large areas or over prolonged periods of time

Lactation
It is not known whether silver sulfadiazine is excreted in breast milk. However, sulfonamides in general are excreted in breast milk and are associated with an increase in the possibility of kernicterus. The possibility of infant adverse effects from exposure to the drug in milk remains unknown. Due to the potential for serious adverse events, the manufacturer recommends to either discontinue nursing or discontinue the drug, considering the importance of the drug to the mother.

Adverse Effects / Undesirable Effects
Dermatologic: Local reactions such as burning, pruritus, rash, skin irritation, skin necrosis, erythema multiforme and skin discoloration may occur.

Hematologic: Disorder of hematopoietic structure (rare), Leukopenia (rare)

Renal: Interstitial nephritis

Overdose and Treatment
Management of over dosage is usually symptomatic and supportive.

Storage Conditions
[eg Store below…. °C]

Dosage Forms and Packaging Available
[Packaging type & pack size]

Name and Address of Manufacturer
[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder
[Name & full address of marketing authorization holder]

Date of Revision of Package Insert
[day/month/year]