

Summary of Product Characteristics

Silverol Cream

Dermal cream

1. NAME OF THE MEDICINAL PRODUCT

Silverol Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition

Active Ingredient

Silver Sulfadiazine 1%

Excipients with known effect:

Propylene glycol, cetostearyl alcohol.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dermal cream.

White to slightly grey-white or pinkish-white.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Antimicrobial preparation for local treatment of burns, infected pressure sores and leg ulcers.

4.2 Posology and method of administration

Silverol should be applied in a layer approximately 3-5 mm thick with a sterile, gloved hand or spatula, to completely cover the burn area. Ordinarily, blisters are not opened, but loose tissue is generally removed prior to application.

After application of Silverol, the wound should either be left exposed or covered with a fine mesh gauze and an elastic mesh bandage.

The exposure method is preferable in some patients (such as children) and for certain parts of the body (face, genitalia, etc.). When the wound is exposed, Silverol should be reapplied at about 12-hour intervals, or more frequently if the medication is rubbed off on the bedding. When dressings are used, they should be changed daily or on alternate days. Use of dressings serves to press the medication firmly against the wound, helps keep the area moist, reduces evaporative water loss and prevents drying/caking of the medication.

Silverol dressings can usually be left in place for about 48 hours during the first 2 weeks post burn. Subsequently, necrotic tissue undergoes proteolytic decomposition, producing considerable exudate which dilutes the drug and necessitates more frequent dressing changes. When feasible, patients should be bathed daily as an aid in debridement. A whirlpool bath is particularly helpful, but patients may be bathed in bed or in a shower.

With Silverol treatment, there will generally be an absence of infection, and examination of the wound will reveal soft pliable eschars. These will separate gradually, leaving a clear granulating surface. In partial-thickness burns, the regenerating epithelium often appears in about 2 weeks, and burns initially classified as full-thickness injuries often heal within 5 weeks without grafting.

In leg ulcers, Silverol should be applied followed by an absorbent gauze dressing and a support bandage, e.g. 10 cm elastic bandage. Care should be taken not to spread Silverol on to non-ulcerated skin, and it should not be used on every wet ulcer. The dressing should be changed at least 3 times a week, and de-sloughing and cleansing should be carried out at the same time.

Any Silverol remaining at the end of treatment should be discarded.

Treatment with Silverol 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 the possibility of infection remains, unless a significant side effect occurs.

4.3 Contraindications

As sulfonamides are known to cause kernicterus, Silverol Cream should not be used at, or near term of pregnancy, on premature infants or on newborn infants during the first months of life.

Silverol cream is also contraindicated in patients known to be hypersensitive to silver sulphadiazine or to other components of the preparation such as cetostearyl alcohol or propylene glycol.

4.4 Special warnings and precautions for use

Life-threatening cutaneous reactions (Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)) have been reported with the use of silver sulfadiazine. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. The highest risk for occurrence of SJS or TEN is within the first weeks of treatment.

If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesions) are present, silver sulfadiazine treatment should be discontinued.

The best results in managing SJS and TEN come from early diagnosis and immediate discontinuation of any suspect drug. Early withdrawal is associated with a better prognosis.

If the patient has developed SJS or TEN with the use of silver sulfadiazine, silver sulfadiazine must not be re-started in this patient at any time.

Silverol cream should be used with caution in the presence of significant hepatic or renal impairment.

Caution of use is required in patients known to be sensitive to systemic sulphonamides and in individuals known to have glucose-6-phosphate dehydrogenase deficiency.

Use of Silverol cream may delay separation of burn eschar and may alter the appearance of the burn wounds.

Important information on excipients

This medicine contains 7 grams of propylene glycol (E 1520) in 100 grams of cream. Propylene glycol may cause skin irritation. Do not use this medicine in babies less than 4 weeks old with open wounds or large areas of broken or damaged skin (such as burns) without talking to your doctor or pharmacist.

This medicine contains cetostearyl alcohol, which may cause local skin reaction (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

As silver may inactivate enzymatic debriding agents, their concomitant use may be inappropriate.

In large-area burns where serum sulfadiazine levels may approach therapeutic levels, it should be noted that the effects of systematically administered medicines may be altered. This can especially apply to oral-hypoglycaemic agents and to phenytoin. In the case of these medicines, it is recommended that blood levels should be monitored as their effect can be potentiated.

4.6 Fertility, pregnancy and breastfeeding

For Silverol Cream no clinical data on exposed pregnancies are available, although animal studies have not shown any hazard.

Since all sulphonamides increase the risk of kernicterus, Silverol Cream should not be used in pregnant females at term and caution is required in nursing mothers.

Systemically absorbed sulphadiazine can be excreted in breast milk although at concentrations 15-35% of those found in serum.

4.7 Effects on ability to drive and use machines

Silverol Cream has no effects on the ability to drive and use machines.

4.8 Undesirable effects

Adverse drug reactions were identified for silver sulfadiazine from clinical trials and post-marketing environment. They are listed by class and frequency. Frequencies are defined as follows:

<u>Very common</u>	<u>(≥1/10)</u>
<u>Common</u>	<u>(≥1/100 to < 1/10)</u>
<u>Uncommon</u>	<u>(≥1/1 000 to < 1/100)</u>
<u>Rare</u>	<u>(≥1/10 000 to <1/1 000)</u>
<u>Very rare</u>	<u>(<1/10 000)</u>
<u>Not known</u>	<u>(cannot be estimated from the available data)</u>

Blood and lymphatic system disorders

Common: Leucopenia

Leukopenia has been reported in 3-5% of burns patients treated with Silverol Cream. This may be a drug related effect, and often manifests itself 2-3 days after treatment has commenced. It is usually self-limiting and therapy with Silverol Cream cream does not usually need to be discontinued, although the blood count must be monitored to ensure that it returns to normal within a few days.

General disorders & administration site conditions

Common: Application site burning

Renal and Urinary Disorders

Very rare: renal failure

Skin & Subcutaneous Tissues Disorders

Common: Pruritis, Application site rash (including eczema and contact dermatitis).

Rare: Argyria

Very rare: Severe cutaneous adverse reactions (SCARs), Steves-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) (see section 4.4).

There is evidence that in large area wounds and/or after prolonged application, systemic absorption of silver can occur causing clinical argyria.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

<https://sideeffects.health.gov.il>

4.9 Overdose

Not likely to occur with normal usage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: silver sulfadiazine, ATC code: D06BA01

Silver Sulfadiazine has bacteriostatic and bactericidal properties. This combination provides a wide spectrum of antimicrobial activity.

5.2 Pharmacokinetic properties

The sulfadiazine readily diffuses across wounds and enters the general circulation. The degree of uptake will significantly depend upon the nature of the wound and the dosing regime. Sulfadiazine is excreted in the urine.

5.3 Preclinical safety data

None stated.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mineral oil (paraffin liquid), propylene glycol, cetostearyl alcohol, glycerol monostearate, glyceryl monostearate self emulsifying, polysorbate 60, polysorbate 80, methylparaben (methyl parahydroxybenzoate), purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a dark place below 25°C.

The medicine can be used for up to 12 months after first opening but not after the expiry date.

The contents of one tube are for the treatment of one person.

6.5 Nature and contents of container

Tubes containing 50 gram cream.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 License Holder and Manufacturer

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8 Registration Number

020.56.20515

The leaflet was revised in November 2023 according to Ministry of Health guidelines.