SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Dermazin® 1% cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 10 mg of silver sulfadiazine.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream
white homogeneous cream

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Silver sulfadiazine is indicated particularly for:

- the treatment and prophylaxis of burn infections in burned patients.
- the treatment and prevention of infections in pressure sores, varicose ulcers, abrasions, minor trauma wounds, incisions and other clean wounds, and on donor free skin graft sites.

4.2 Posology and method of administration

An appropriate treatment regimen is promptly instituted after evaluating the depth of the burn wound. The burn wound is then cleansed and debrided and covered with Dermazin cream to a thickness of 2 to 4 mm. The cream is applied to sterile gauze which is placed over the burn. The cream may be also applied using a sterile spatula or a sterile gloved hand. The cream is usually applied to the burn area once daily, for more severe burns application of the cream can be repeated; however, the cream should be reapplied at least once in 24 hours. Prior to each cream reapplication, the burn wound must be cleaned off any previous cream remnants and wound exudates, which are copious after Dermazin application resembling pus in colour but actually aseptic, with water or an antiseptic agent. Dressings can be applied over the cream although it is not necessary.

<u>Renal/hepatic impairment</u>
Precaution is needed when Dermazin is used in patients with impaired hepatic and renal function sulfadiazine can be absorbed in significant quantities following prolonged treatment of extensive burns, and measurement of sulfadiazine levels may be indicated.

<u>Paediatric population</u>
The recommended dosage of the cream for infants older than 2 months and children does not differentiate between pediatric and adult population. The method of application in children is the same as in adults.

For treatment of infants less than two months see section 4.4.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings and special precautions for use

Life-threatening cutaneous reactions Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of 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, 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 sulfadiazine, sulfadiazine must not be re-started in this patient at any time.

Since sulfonamides may cause kernicterus, sulfadiazine silver should not be used in late pregnancy, in premature infants or infants younger than 2 months unless the expected benefit outweighs the potential risk.

Caution should be exercised when treating patients with hypersensitivity to sulfonamides, kidney failure and damage to liver parenchyma.

If signs for leukopenia are observed or if the patient is hypersensitive to sulfonamides, a white blood cell count is recommended.

Mainly under the influence of sunlight a gray discoloration of the skin may occur.
Patients with glucose-6-phosphate dehydrogenase deficiency, or in whom it is suspected, should be carefully monitored.

Important information about some of excipients of Dermazin
The cream contains methylparahydroxybenzoate and propylparahydroxybenzoate which may cause allergic reaction (possibly delayed). Dermazin contains arachis oil (peanut oil). If you are allergic to peanut or soya, do not use this medicinal product. It contains also propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Since silver can inactivate enzymatic products for wound debriding, concomitant use is not recommended.

For large burns where serum levels of silver sulfadiazine approach therapeutic levels, it should be noted that the effect of systemically administered drugs may change.

4.6 Pregnancy and breastfeeding

Pregnancy
There are insufficient data on the use of silver sulfadiazine in human pregnancy to assess the potential damage. Silver is absorbed to a small extent. Possible effects of silver sulfadiazine on the fetus have not been studied. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. There is a risk of hyperbilirubinemia and kernicterus in the newborn in case of systemic use of sulfonamides just before delivery, because sulfonamides displace bilirubin from the binding sites on albumin in the blood.

Given the limited experience and the above risks sulfadiazine silver should only be used with caution in pregnant women or women who want to conceive.

Breastfeeding
It is not known whether sulfadiazine silver is excreted into breast milk. The excretion of sulfadiazine silver in milk has not been studied in animals. However, sulfonamides are excreted in small quantities in breast milk. In premature neonates and infants with glucose-6-phosphate dehydrogenase deficiency an increased risk of hyperbilirubinemia and kernicterus must be taken into account. Otherwise it is possible to breast-feed during treatment with sulfadiazine silver.

4.7 Effects on ability to drive and use machines

There are no studies on the effect on the ability to drive or operate machines.

4.8 Undesirable effects

The following frequencies form the basis for the evaluation of side effects:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000),
Not known (cannot be estimated from the available data)
The following side effects have been reported in clinical trials:

Blood and lymphatic system disorders
Uncommon: Leukopenia

The following adverse reactions have been reported during post-marketing use, and in the scientific literature.

Blood and lymphatic system disorders:
Not known: Increased serum osmolality

Immune system disorders:
Not known: Hypersensitivity

Skin and subcutaneous tissue disorders:
Very rare: Severe cutaneous adverse reactions (SCARs): Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported (see section 4.4).
Not known: Allergic skin reactions such as rash, pruritus, contact dermatitis. Gray discoloration of the skin under the influence of sunlight.

General disorders and administration site conditions:
Unknown: Burning sensation or pain

Systemic absorption of silver sulfadiazine can very rarely cause side effects associated with systemic sulfonamide therapy.

4.9 Overdose

Elevated serum silver levels may occur after prolonged use of high doses of silver sulfadiazine, which normalize after discontinuation of treatment.

Symptoms in case of overdose are similar to the side effects of sulfadiazine silver.

Treatment consists of discontinuation of all silver-containing products and the standard measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Chemotherapeutics for topical use, sulphonamides
ATC code: D06BA01

Mechanism of action
Dermazin is a topical chemotherapeutic agent for the prevention and treatment of infections. Silver sulfadiazine disintegrates in the burn wound thereby causing a slow and sustained release of silver ions. These ions bind to bacterial desoxyribonucleic acid thus inhibiting the growth and multiplication of bacterial cells without damaging the cells of the skin and subcutaneous tissue. Silver sulfadiazine has a very broad antibacterial spectrum of activity including virtually all microorganisms likely to cause the infection of burn wounds and other skin wounds.
In vitro minimum inhibitory concentration (MIC) of silver sulfadiazine for some important germs:

MICROORGANISM	MIC (mcg/mL)
Pseudomonas aeruginosa	50 or less
Pseudomonas maltophilia	50 or less
Enterobacter	100 or less
E. cloacae	50 or less
Klebsiella	100 or less
E. coli	50 or less
Serratia	100 or less
Proteus	50 or less
Morganella morganii	50 or less
Providencia	50 or less
Citrobacter	50 or less
Acinetobacter	100 or less
Corynebacterium diphteriae	50 or less
Staphylococcus	100 or less
Streptococcus pyogenes	50 or less
Enterococcus spp	100 or less
Clostridium perfrigens	100 or less
Candida albicans	100 or less
Herpes	10
Dermatophytes	100
Herella	6.25
Aspergillus fumigatus	100
Aspergilus flavus	100
Mucor pussilus	50
Rhizopus nigricans	10

Dermazin penetrates into the necrotic tissue and exudates. This effect is particularly important because the systemic antibiotics are not effective against the bacterial flora of the avascular burn necrosis.

5.2 Pharmacokinetic properties

Silver sulfadiazine may be absorbed especially when it is applied in a large amount, over prolonged periods of time over extensive skin areas. Serum sulfonamide levels are proportional to the extent of burn areas and the amount of cream applied.
Following application of 500 to 1000 g silver sulfadiazine 1% (5 to 10 g of silver sulfadiazine) to the burn areas of the patients, the serum sulfadiazine levels of 2 to 5 mg/l and the urine levels of 50 to 1000 mg/l were reported.
Argyria due to increased systemic absorption of silver is minimal.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction, carcinogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Arachis oil hydrogenated
Cetyl alcohol,
Methyl parahydroxybenzoate,
Propylene glycol,
Propyl parahydroxybenzoate,
Polysorbate 60,
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
Do not use the medicinal product after the expiry date.

6.4 Special precautions for storage

Keep the medicinal product out of reach of children.
Store at a temperature up to 25°C.

6.5 Nature and contents of container

One box contains an aluminium tube with 50 g of cream and a package insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Lek d.d., Verovškova 57, Ljubljana, Slovenia

8. MANUFACTURER

Salutas Pharma GmbH, Osterweddingen, Germany

9. GENERAL CLASSIFICATION FOR SUPPLY

Available on prescription only.

10. DATE OF REVISION OF THE TEXT

May 2014