Clean amended proposed professional information for SILBECOR

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

SILBECOR 10 mg/g cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains 10 mg silver sulfadiazine.

Excipients with known effect:

Preservatives:

Methyl hydroxybenzoate 0,15 % *m/m*.

Propyl hydroxybenzoate 0,05 % *m/m*.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream.

Odourless, white homogenous cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SILBECOR is a topical antibacterial medicine for the prevention and treatment of infections in wounds, burns, leg ulcers and pressure sores.

4.2 Posology and method of administration

SILBECOR should be applied daily in a layer approximately 3 – 5 mm thick with a sterile gloved

hand or spatula. The wound may be dressed or left open. One container of SILBECOR should be reserved for one patient and any remaining cream should be discarded on completion of treatment.

4.3 Contraindications

- Hypersensitivity to silver sulfadiazine, sulphonamides or any of the excipients of SILBECOR (see section 6.1).
- SILBECOR contains arachis oil (peanut oil). Patients allergic to peanuts or soya must not use SILBECOR.
- Sulphonamide therapy is known to increase the possibility of kernicterus. SILBECOR should therefore not be used in pregnant women, premature infants or in infants during the first months of life (see section 4.6).
- Lactation (see section 4.6).
- SILBECOR should not be used if hepatic or renal function becomes impaired.
- Porphyria.

4.4 Special warnings and precautions for use

FOR EXTERNAL USE ONLY.

Patients sensitive to sulphonamides, furosemide, thiazide diuretics, sulphonylureas or carbonic anhydrase inhibitors may be sensitive to SILBECOR.

Local reactions have been reported in patients treated with silver sulfadiazine, as contained in SILBECOR. The separation of the eschar may be delayed, and fungal invasion of the wound may occur.

Caution is advised in patients known to have glucose-6-phosphate dehydrogenase deficiency. The use of SILBECOR in glucose-6-phosphate dehydrogenase deficient patients may cause haemolysis.

Leucopenia has been reported (see section 4.8). In burn patients, this usually manifests in 2 – 3 days after treatment has commenced, but it is not thought to be associated with the treatment used and probably reflects the condition of the burned patient. It is usually self-limiting and therapy with SILBECOR does not usually need to be discontinued, although the blood count should be monitored to ensure that it returns to normal within a few days (see section 4.5).
Appreciable amounts of sulfadiazine may be absorbed to produce systemic side effects, when SILBECOR is applied to a large area and when the lesion(s) is/are deep.
Systemic absorption of silver, resulting in argyria, with discolouration of the skin and sensorimotor neuropathy, can occur when SILBECOR is applied to large area wounds or over prolonged periods (see section 4.8).

In patients with extensive burns, serum sulphonamide concentrations and renal function should be monitored, and urine examined for sulphonamide crystals. The risk of crystallisation in the urine may be reduced with the administration of fluids to maintain high urine output. Adequate fluid intake and normalisation of acid base balance is important (see section 4.8).

Local skin sensitivity to SILBECOR may occur, especially when exposed to sunlight.
Treatment should be discontinued if a rash appears because of the danger of a severe allergic reaction (Stevens-Johnson syndrome) (see section 4.8).

Sulfadiazine may displace serum bound bilirubin resulting in jaundice and kernicterus in premature neonates (see section 4.3).
Elderly patients and patients with acquired immunodeficiency syndrome (AIDS) may be particularly prone to the adverse reactions.

Effects on laboratory tests

In the treatment of burn wounds involving extensive areas of the body, the serum sulphonamide

derivative concentrations may approach adult therapeutic levels (8 mg % to 12 mg %). Therefore, in these patients it would be advisable to monitor serum sulphonamide concentrations. Renal function should be carefully monitored, and the urine should be checked for sulphonamide crystals. Absorption of the propylene glycol vehicle has been reported to affect serum osmolality, which may affect the interpretation of laboratory tests.

Excipients:

SILBECOR contains cetyl alcohol which may cause local skin reactions (e.g. contact dermatitis) and 100 mg/g propylene glycol which may cause skin irritation.

4.5 Interaction with other medicines and other forms of interaction

In large area burns where serum sulfadiazine levels approach therapeutic levels, it should be noted that the effects of systemically administered medicines may be altered.

SILBECOR may potentiate the effects of the following medicines and consequently their blood levels have to be monitored:

- Oral hypoglycaemic medicines.
- Oral anticoagulants.
- Methotrexate.
- Phenytoin.

High doses of SILBECOR can have a hypoglycaemic effect; the antidiabetic effect of the sulphonylurea medicines may be enhanced by SILBECOR.

The silver content of SILBECOR may inactivate enzymatic debriding medicines and their concomitant use may be inappropriate.

Concurrent use with cimetidine may increase the incidence of leucopenia (see section 4.4 and 4.8).

4.6 Fertility, pregnancy and lactation

SILBECOR is contraindicated during pregnancy and lactation (see section 4.3).

4.7 Effects on ability to drive and use machines

SILBECOR is not likely to affect the ability to drive a vehicle or operate machinery. However, patients should ensure they know how SILBECOR affects them before driving a vehicle, operating machinery or do anything else requiring their attention.

4.8 Undesirable effects

Blood and lymphatic system disorders

These effects are thought to be hypersensitivity effects:

Frequent: leucopenia (see section 4.4).

Less frequent:

- Agranulocytosis.
- Aplastic anaemia.
- Thrombocytopenia.
- Hypoprothrombinaemia.
- Eosinophilia.

Endocrine disorders

Frequent: hypoglycaemia.

Frequency unknown: hypothyroidism.

Nervous system disorders

Frequency unknown: aseptic meningitis, ataxia, benign intracranial hypertension, convulsions, dizziness, drowsiness, fatigue, headache, insomnia, mental depression, peripheral or optic neuropathies, psychoses, vertigo.

Gastrointestinal disorders

Frequent: nausea, vomiting, anorexia, diarrhoea.

Hepato-biliary disorders

Frequency unknown: jaundice, kernicterus in premature neonates.

Skin and subcutaneous tissue disorders

Frequent: application site rash (including eczema and contact dermatitis), photosensitive reactions, exfoliative dermatitis, dermatitis, erythema nodosum, pruritis.

Less frequent: argyria.

Frequency unknown: toxic epidermal necrolysis, Stevens-Johnson syndrome, systemic lupus erythematosus.

Renal and urinary disorders

Frequent: nephrotoxic reactions (including interstitial nephritis and tubular necrosis), lumbar pain, haematuria, oliguria and anuria may also occur due to crystallisation in the urine.

Less frequent: renal failure.

General disorders and administration site conditions

Frequent: fever, application site burning.

Less frequent: local pain and irritation, fungal invasion of wound, anaphylaxis.

Frequency unknown: generalised hypersensitivity effects include:

- Syndrome resembling serum sickness.
- Liver necrosis.
- Hepatomegaly, jaundice and myocarditis.
- Pancreatitis.
- Pulmonary eosinophilia.

- Fibrosing alveolitis.
- Vasculitis including polyarthritis nodosa.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **Adverse Drug Reactions Reporting Form**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

In overdose, side effects may be precipitated and/or be of increased severity (see section 4.8). Treatment is symptomatic and supportive. In extensively burned patients or in patients suspected of showing symptoms of excessive absorption, it is important to optimally maintain fluid balance, not only to prevent dehydration but also to avoid the possibility of renal failure.

If renal function is normal, fluids should be administered to maintain high urine output and assist in the rapid elimination of the medicine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A14.2 Wound dressing.

Pharmacotherapeutic group: Antibiotics and chemotherapeutics for dermatological use, sulphonamides.

ATC code: D06BA01.

Silver sulfadiazine is a sulphonamide and inhibits the growth *in-vitro* of pathogenic bacteria and fungi. Not all strains of a particular organism may be susceptible. Silver is released slowly from the preparation in concentrations that are selectively toxic to micro-organisms. Silver sulfadiazine acts

on the cell membrane and cell wall. Unlike sulfadiazine or other sulphonamides, the antibacterial action of the silver salt of sulfadiazine does not appear to depend on inhibition of folic acid synthesis. Its action is not antagonised by p-aminobenzoic acid. Bacteria may develop resistance to silver sulfadiazine.

5.2 Pharmacokinetic properties

Sulfadiazine is slowly released by silver sulfadiazine when in contact with wound exudates. Up to 10 % of the sulfadiazine may be absorbed. Blood concentrations of 10 to 20 micrograms/mL have been reported although higher concentrations may be achieved when extensive areas of the body are treated. There is a possibility that some silver may also be absorbed.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Arachis oil (hydrogenated)

Cetyl alcohol

Methyl paraben

Propyl hydroxy benzoate (propyl paraben)

Polysorbate 60

Propylene glycol

Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

6.5 Nature and contents of container

SILBECOR will be packed in either of the following packaging material:

1. 250 g plastic jar

   Black blow moulded HDPE jar with black polypropylene cap.

2. 500 g plastic jar

   Black blow moulded HDPE jar with black polypropylene cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park

400 16th Road, Randjespark, Midrand, 1685

South Africa

8. REGISTRATION NUMBER

29/14.2/0338

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 29 August 1995

10. DATE OF REVISION OF THE TEXT

01 December 2021

Signed: