PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr FLAMAZINE™

Silver Sulfadiazine

Cream, 1% w/w, Topical

Mfg Standard

Topical Antibacterial Agent

Smith & Nephew Inc.

2280 Argentia Road

Mississauga, Ontario

L5N 6H8 Canada

Date of Initial Authorization:
DEC 31, 1974

Date of Revision:
NOV 2, 2022

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RECENT MAJOR LABEL CHANGES

3 Serious Warnings and Precautions Box	11/2022
7 Warnings and Precautions, General	11/2022
7 Warnings and Precautions, Skin	11/2022

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Sections or subsections that are not applicable at the time of authorization are not listed .

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

FLAMAZINE (Silver Sulfadiazine Cream 1% w/w) is indicated for:

- the treatment of leg ulcers, burns, skin grafts, incisions and other clean lesions, abrasions, minor cuts and wounds;
- the treatment and prophylaxis of infection in serious burn victims.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of FLAMAZINE and other antibacterial drugs, FLAMAZINE should be used only to treat infections that are proven or strongly suspected to be cause by susceptible bacteria.

1.1 Pediatrics

Pediatrics (neonates): FLAMAZINE is contraindicated in premature infants or newborn infants during the first months of life (see 2 CONTRAINDICATIONS).

Pediatrics (> 2 months to 18 years): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics: There is no known evidence to suggest that use in the geriatric population is associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

- FLAMAZINE is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- FLAMAZINE is contraindicated in pregnant females at term, in premature infants, or in newborn infants during the first months of life as sulfonamide therapy is known to increase the possibility of kernicterus.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- Potentially life-threatening skin rashes (Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN)) have been reported with the use of silver sulfadiazine (see 7 WARNINGS AND PRECAUTIONS).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

For extensively burned patients or patients suspected of excessive absorption see 5 OVERDOSAGE.

4.2 Recommended Dose and Dosage Adjustment

Adults and children >2 months: Apply FLAMAZINE cream over all the affected areas to a depth of 3 - 5 mm. FLAMAZINE cream should be re-applied at least every 24 hours or more frequently if exudate levels are high.

Health Canada has not authorized an indication for pediatric use (See 1 INDICATIONS, Pediatrics). FLAMAZINE is contraindicated in premature infants or newborn infants during the first months of life (see 2 CONTRAINDICATIONS).

FLAMAZINE should be used with caution in patients with hepatic or renal impairment as both may reduce the elimination of absorbed sulfadiazine.

4.4 Administration

- Burns

  The burn wounds should be cleaned and FLAMAZINE cream applied over all the affected areas to a depth of 3 - 5 mm. One technique is to apply the cream with a sterile gloved hand and/or sterile spatula. Where necessary, the cream should be re-applied to any area from which it has been removed by patient activity. FLAMAZINE cream should be re-applied at least every 24 hours or more frequently if exudate levels are high.

- Hand burns and finger injuries

  One recommended method is to apply FLAMAZINE cream to the burn and the whole hand is then enclosed in a clear plastic bag or glove, which is then closed at the wrist. The patient should be encouraged to move the hand and fingers. The dressing should be changed every three days or when an excessive amount of exudate has accumulated in the bag.

- Leg ulcers

  One acceptable method involves filling the cavity of the ulcer with FLAMAZINE cream to a depth of at least 3-5 mm. Care should be taken to prevent the spread of the cream onto non-ulcerated areas. The cream should be followed by an absorbent pad or gauze dressing, with further application of pressure bandaging as appropriate for the ulcer. The dressing should be changed every 2 or 3 days, with cleaning and debriding being performed before application of FLAMAZINE cream. It is not recommended that FLAMAZINE cream be used in leg ulcers that are very exudative.

A container of FLAMAZINE cream should be reserved for use for a specific patient.

4.5 Missed Dose

If a single dose is missed, the patient should apply FLAMAZINE when he/she remembers and dosing should continue as usual for the next application, and the usual amount should be applied.

5 OVERDOSAGE

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 impairment.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Topical	Cream, 1% w/w	Cetyl Alcohol, Distilled Water, Glyceryl Stearate, Liquid Paraffin, Polysorbate 60, Polysorbate 80, Propylene Glycol

FLAMAZINE is a white cream containing 1% w/w silver sulfadiazine and is available in the following containers: 500g jars; 20g and 50g tubes. FLAMAZINE should be stored at 8°C to 25°C. Store FLAMAZINE in the original container to protect from light. To ensure sterility, 500g jars should be discarded 24 hours after opening and tubes of FLAMAZINE 7 days after opening.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

When treatment with silver sulfadiazine cream involves prolonged administration and/or large burned surfaces, considerable amount of silver sulfadiazine is absorbed. Serum concentration of sulfadiazine may approach adult therapeutic levels (8-12 mg %).

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

Patients treated with FLAMAZINE should not smoke or go near open flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc.) that has been in contact with FLAMAZINE burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

Hematologic

Silver sulfadiazine cream should be used with caution on patients with a history of glucose-6-phosphate dehydrogenase deficiency as hemolysis may occur.

Leukopenia has been reported following the use of silver sulfadiazine, especially on patients with large area burns. This may be a drug-related effect, and often occurs 2 to 3 days after treatment has commenced. It is usually self-limiting and therapy with FLAMAZINE cream does not normally need to be discontinued, as the WBC count usually returns to the normal range in a few days. WBC counts should be closely monitored.

Hepatic/Biliary/Pancreatic

Silver sulfadiazine cream should be used with caution in patients with hepatic impairment as the elimination of absorbed sulfadiazine may be reduced.

Renal

Silver sulfadiazine cream should be used with caution in patients with renal impairment as the

elimination of absorbed sulfadiazine may be reduced.

Sensitivity/Resistance

Sensitization to topically applied silver sulfadiazine is rarely predicted or proven by patch testing. Caution should be exercised in the use of FLAMAZINE cream in individuals who have previously shown sensitization reactions to sulfonamides.

Development of Drug Resistant Bacteria

Prescribing FLAMAZINE in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks development of resistant organisms.

Potential for Microbial Overgrowth

The use of FLAMAZINE may promote the selection on non-susceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

Skin

Potentially life-threatening skin rashes (Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN)) have been reported with the use of silver sulfadiazine, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs to look for include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These are often accompanied by flu-like symptoms and may progress to widespread blistering or peeling of the skin. The highest risk for occurrence of serious skin reactions is within the first few weeks of treatment. If your patient has developed Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of silver sulfadiazine, the patient must not be re-started on silver sulfadiazine at any time.

7.1 Special Populations

7.1.1 Pregnant Women

FLAMAZINE cream is contraindicated when the patient is near term. (See 2 CONTRAINDICATIONS). The safe use of FLAMAZINE has not been established in pregnancy. FLAMAZINE cream should only be used in badly burned pregnant women if the benefit to the patient outweighs the risk to the foetus.

7.1.2 Breast-feeding

The safe use of FLAMAZINE has not been established in lactation. The sulfonamide concentration in breast milk is 15-35% of that in the serum. Since all sulfonamides increase the possibility of kernicterus, caution is required in nursing mothers.

7.1.3 Pediatrics

Pediatrics (< 2 months): FLAMAZINE is contraindicated in premature infants and in newborn infants less than 2 months of age (See 2 CONTRAINDICATIONS).

Pediatrics (> 2 months): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

There is no known evidence to suggest that use in the geriatric population is associated with differences in safety or effectiveness.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Blood & Lymphatic Tissue Disorders

Common: ≥1% and <10%	Leukopenia Leukopenia has been reported in up to 3-5% of patients treated with FLAMAZINE cream. This may be a drug-related effect, and often occurs within 48-72 hours after therapy has commenced. It is usually self-limiting and therapy with FLAMAZINE does not usually need to be discontinued, although the blood count must be carefully monitored to ensure that it returns to normal within a few days.

Skin & Subcutaneous Tissue Disorders

Common: ≥1% and <10%	Application site rash, including eczema and contact dermatitis, may occur in about 2% of patients. Other commonly reported adverse reactions during treatment with FLAMAZINE are application site burning, rash, and itching and pruritus.
Rare: ≥0.01% and <0.1%	Argyria There is evidence that in large area burn wounds and/or after prolonged application, systemic absorption of silver can occur causing clinical argyria.
Very rare: <0.01%	Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) Life-threatening skin reactions such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the use of sulfadiazine. When symptoms or signs of SJS or TEN (e.g. progressive skin rash, often with blisters or mucosal lesions), treatment should be discontinued.

Renal & Urinary Disorders

Very rare: <0.01%	Renal failure

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

There may be an interaction between silver sulfadiazine and any of the following: oral hypoglycemic agents and phenytoin, cimetidine, and enzymatic debriding agents.

9.4 Drug-Drug Interactions

In patients with large area burns where serum sulfadiazine levels may approach therapeutic levels, the action of oral hypoglycemic agents and Phenytoin may be potentiated and it is recommended that blood levels be monitored.

In patients with large area burns, it has been reported that co-administration of cimetidine may increase the incidence of leukopenia.

FLAMAZINE may inactivate enzymatic debriding agents; thus the concomitant use of these compounds may be inappropriate.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The mechanism of silver sulfadiazine's antibacterial action has not been fully elucidated. After exposure to the drug, structural changes in the bacterial cell membrane occur, including distortion and enlargement of the cell and a weakening of the cell wall membrane. This is accompanied by reduced viability in sensitive strains due to interference with macromolecular synthesis. The sulfadiazine moiety also provides a bacteriostatic action against sensitive organisms.

10.2 Pharmacodynamics

Silver sulfadiazine is released slowly from the cream and thus, rapid depletion of chloride and associated electrolyte disturbances are minimized. Silver sulfadiazine is not inhibited by PABA.

10.3 Pharmacokinetics

Absorption

There is very little penetration of the silver below the outer layers of the wound surface and in burned pigs, the absorption of silver was less than 1% of the applied dose, however 5 to 8% of the sulfadiazine was absorbed. In adults, up to 10% of the sulfadiazine may be absorbed. The sulfadiazine concentration in burn wound exudate, was 900-1000 mg/L 24 hours after application, which is approximately 20 times the MIC of sensitive bacteria (50 mg/L).

Distribution:

After a 500 to 1000 g application of 1% silver sulfadiazine, (corresponding to 5-10 g of silver sulfadiazine), to burn patients, serum levels of sulfadiazine were 2-5 mg/L. The largest amount of the absorbed silver is found in the liver.

Metabolism:

High concentrations of silver have been measured in the bile, which suggest a hepatobiliary excretion of the silver moiety. The sulfadiazine moiety is metabolised and excreted via the kidneys.

Elimination

In one study of 23 patients, mean silver serum levels were moderately higher than the normal range however the urinary excretion of silver, was markedly elevated (0.402 mg/24h). Six patients with 60% or greater B.S.A. burns had a mean peak excretion of 1.100 mg/24 hours (approximately 1,0000 times the normal level). None of the patients had silver toxicity. In adults, 60-85 % of the absorbed sulfadiazine is excreted in the urine. In children with 13 % body surface area burns, the urinary sulfadiazine concentration was 31.8 mg/L. After a 500 to 1000 g application of 1% silver sulfadiazine, to burn patients, urine levels were 60-1000 mg/L and the daily urinary excretion of sulfadiazine was 100-200 mg, corresponding to less than 5% of the applied amount of silver sulfadiazine.

Special Populations and Conditions

- **Hepatic Insufficiency** FLAMAZINE Cream should be used with caution in patients with hepatic impairment as the elimination of absorbed sulfadiazine may be reduced.
- **Renal Insufficiency** FLAMAZINE Cream should be used with caution in patients with renal impairment as the elimination of absorbed sulfadiazine may be reduced.

11 STORAGE, STABILITY AND DISPOSAL

FLAMAZINE should be stored at 8°C to 25°C. Store FLAMAZINE in the original container to protect from light. To ensure sterility, 500g jars should be discarded 24 hours after opening and tubes of FLAMAZINE 7 days after opening.

12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions for FLAMAZINE.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

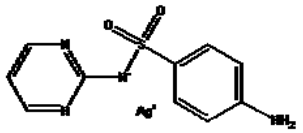
Drug Substance

Proper name: Silver sulfadiazine cream

Chemical name: Silver 2-(4-aminobenzenesulfonamido)-pyrimidine

Molecular formula and molecular mass: C10 H9 N4 O2 S Ag (molecular weight: 357.14)

Structural formula:



Physicochemical properties: Silver sulfadiazine is a light-stable white powder, very slightly soluble in water and most organic solvents, but readily soluble in nitric acid and concentrated ammonia solutions. The pH of the cream is between 3.5-6.0.

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

The minimum inhibitory concentration (MIC) as determined by the serial tube dilution of susceptible organisms is shown in Tables 1 & 2.

Table #1 - Minimum Inhibitory Concentration of Silver Sulphadiazine in mg/L

		At 24 hours		At 3 days	
ORGANISM	**STRAINS**	**Expt.1**	**Expt.2**	**Expt.1**	**Expt.2**
Pseudomonas aeruginosa	(SNR)	25	<6	100	100
Pseudomonas aeruginosa	6750 NCTC	25	12,5	100	12,5
Pseudomonas aeruginosa	USA 1*	>100	300	>100	>300
Pseudomonas aeruginosa	USA 4*	25	25	>100	>300
Pseudomonas aeruginosa	6741 NCTC	50	12,5	100	100
Pseudomonas aeruginosa	8203 NCTC	50	25	50	>100
Pseudomonas aeruginosa	661322 NCTC	50	37,5	>100	300
Aerobacter aerogenes	749 NCTC	25	>18,7	100	25
Escherichia coli	(SNR)	50	37,5	>100	150
Proteus vulgaris	(SNR)	25	37,5	>100	150
Staphylococcus aureus	(OxH)6571	50	50	100	100
Candida albicans	(SNT)	100	300	>100	>300
Aspergillus niger	(SNR)	25	18,7	>100	300

*These strains were isolated from burn patients treated with silver nitrate.

Table #2 - Susceptibility to Silver Sulphadiazine of 643 Isolates of 14 Bacterial Species

			Minimal Inhibitory Concentrations (cumulative percentage) mg/L Silver Sulphadiazine						
Micro-organism	**No. Tested**	**<0,78**	**1,56**	**3,13**	**6,25**	**12,5**	**25**	**50**	**100**
Pseudomonas aeruginosa	130	0,8	5,4	29,2	60,0	79,2	93,1	100	-
P. maltophilia	7	14,3	14,3	28,6	42,9	85,8	100	-	-
Klebsiella	54	7,4	11,1	14,8	31,5	61,1	74,1	98,2	100

Enterobacter (except *E. cloacae*)	50	0	8,0	10,0	20,0	44,0	66,0	96,0	100
E. cloacae	24	0	4,2	4,2	20,8	45,8	79,2	100	-
Escherichia coli	63	3,2	6,3	30,2	50,8	71,4	90.5	100	-
Proteus Mirabilis	53	24,5	50,9	73,6	88,7	96,2	96,2	100	-
P. morganii	10	10,0	30,0	40,0	80,0	80,0	90,0	100	-
Serratia	28	7,1	25,0	39,3	75,0	89,3	92,9	96,4	100
Citrobacter	10	20,0	20,0	40,0	60,0	60,0	80,0	100	-
Herellea	9	11,1	22,2	55,6	66,7	77,8	88,9	100	-
Staphylococcus aureus	101	3,0	6,0	16,9	27,8	37,7	76,3	99,1	100
S.epidermidis	51	3,9	7,8	29,4	51,0	74,5	86,3	100	-
Enteroccoccus (group D *Streptococcus*)	53	0	0	0	0	0	1,9	96,2	100

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

Acute Toxicity
The following LD50's were determined in mice, rats, guinea pigs, and rabbits.

SPECIES	ROUTE	LD_{50}
Mice (male)	I.P.	37,8 mg/kg
Rats (both sexes)	S.C.	> 2,150 mg/kg
Guinea pigs (both sexes)	S.C.	> 2,150 mg/kg
Rabbits (both sexes)	S.C.	> 2,150 mg/kg
Newborn rats	Oral	482 mg/kg
Adult rats (both sexes)	Oral	> 10,000 mg/kg

Subacute Studies
Ointments containing 1, 8 and 20% silver sulfadiazine were applied to the abraded and occluded skin of rabbits for six hours each day, seven days a week for three consecutive weeks. Additional groups of rabbits were treated with the ointment without silver sulfadiazine or received no treatment, and therefore served as procedural controls.

The same ointments were also applied to the intact and non-occluded skin of rabbits for six hours a day, seven days a week for thirteen consecutive weeks. An additional group of rabbits was treated with the ointment without silver sulfadiazine.

The ointment base alone and the ointments containing silver sulfadiazine elicited mild irritation of the

skin. The irritation produced by the silver sulfadiazine ointment was similar to or slightly less than the ointment alone.

Varying degrees of skin inflammation were observed histologically at week 13 in both ointment base and high concentration silver sulfadiazine ointment treated rabbits.

Urinary pH was lower at week 3 in the male rabbits treated with the high concentration of silver sulfadiazine and the ointment base alone.

There was a tendency to lowered RBC counts at 13 weeks in female rabbits treated with the high concentration of silver sulfadiazine.

Serum protein levels were elevated in some rabbits treated with the high concentration and with the ointment base alone.

In all other respects including food consumption, bodyweight change, ophthalmoscopy, urinalysis, blood chemistry, haematology, organ weights, macroscopic and microscopic pathology, the rabbits treated with silver sulfadiazine ointment remained comparable with the ointment base and "no treatment" control groups.

Skin Irritation Studies
The primary irritation potential of silver sulfadiazine cream was assessed using an occlusive patch test technique in rabbits. The primary irritation index was zero.

Eye Irritation Studies
Eye irritation studies in the rabbits revealed no behavioural indications of discomfort immediately after treatment. Four out of six animals had slightly red lids when observed after one hour, but this had completely disappeared by the time of the second observation at 24 hours. No other symptoms were observed.

Sensitivity Studies
The sensitizing potential of the silver sulfadiazine cream was assessed in guinea pigs using a standard technique. A positive control group was included in which the guinea pigs were challenged with the known sensitizer 2, 4-dinitrochlorobenzene. The animals were shown to be capable of sensitization by a positive response to the latter compound but did not react by sensitization to the silver sulfadiazine cream.

Carcinogenicity:
No carcinogenicity studies have been carried out.

Reproductive and Developmental Toxicology:

Teratological Studies
A study was conducted in rabbits using a control (placebo cream), 3% or 10% cream. 5 mL cream was applied to their shaved backs for four (4) hours each day, from day 6 through day 18 of gestation. There were no compound-related effects upon reproductive or fetal parameters observed in either the 3% or 10% groups. Variations between the silver sulfadiazine treated groups and the control groups were within the normal range of intergroup variations in studies of this type and were not significant.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

FLAMAZINE

Silver Sulfadiazine Cream

Read this carefully before you start taking **FLAMAZINE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **FLAMAZINE**.

Serious Warnings and Precautions

- Potentially life-threatening skin rashes (Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN)) have been reported with the use of silver sulfadiazine, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs to look for include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These potentially life-threatening skin rashes are often accompanied by flu-like symptoms. The rash may progress to widespread blistering or peeling of the skin. If you have developed Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of silver sulfadiazine, you must not be re-started on silver sulfadiazine at any time.

What is FLAMAZINE used for?

- Treatment of infections caused by bacteria which can be killed by FLAMAZINE:
    - Infection in serious burn victims.
    - Infection in leg ulcers, burns, skin grafts, incisions and other clean lesions, abrasions, minor cuts and wounds.

Antibacterial drugs like FLAMAZINE treat only bacterial infections. They do not treat viral infections.

How does FLAMAZINE work?

This medicine kills bacteria or stops their growth. This helps reduce or prevent infections. The time taken for the medicine to work will vary by wound type.

What are the ingredients in FLAMAZINE?

Medicinal ingredients: silver sulfadiazine

Non-medicinal ingredients: cetyl alcohol, distilled water, glyceryl stearate, liquid paraffin, polysorbate 60, polysorbate 80, propylene glycol

FLAMAZINE comes in the following dosage forms:

FLAMAZINE is a white cream containing 1% silver sulfadiazine. FLAMAZINE is available in 20g or 50g tube and 500g jar.

Do not use FLAMAZINE if:

- You are allergic to the medicinal ingredients in FLAMAZINE or any of its ingredients (see "What are the ingredients in FLAMAZINE").
- You are a pregnant female at term.
- Your child is a premature infant or is a newborn infant during the first months of life (< 2 months of age).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take FLAMAZINE. Talk about any health conditions or problems you may have, including if you:

- Have previously shown allergic reactions to sulfonamides.
- Have a history of glucose-6-phosphate dehydrogenase deficiency. Using sulfonamides like FLAMAZINE can lead to hemolysis (red blood cell breakdown).
- Have liver or kidney problems.
- Have previously had low white blood cell levels. Leukopenia (lowered white blood cell levels) has occurred after use of FLAMAZINE. Your doctor may order tests to monitor you white blood cell count while you are taking FLAMAZINE.
- Have developed Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of silver sulfadiazine
- Are pregnant or are planning to become pregnant. FLAMAZINE may cause harm to unborn children. Only use this medicine if your doctor thinks the benefit is greater than the risk to the foetus. Do not use this medicine if you are in the last month of your pregnancy.
- Are breast feeding or intend to breast feed. FLAMAZINE can pass into breast milk and cause harm to your baby. Talk to your doctor about how to feed your baby when you are on FLAMAZINE.

Other warnings you should know about:

- Do not use this medicine for longer than advised by your doctor. This may lead to increased chance of side effects.
- If you are using FLAMAZINE to treat large wounds, it is important to drink lots of liquids prevent dehydration and kidney damage
- FLAMAZINE may increase the time for dead tissue (eschar) to separate from the body. It may also change the appearance of burn wounds.
- If you are using FLAMAZINE you should not smoke or go near open flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc.) that has been in contact with FLAMAZINE burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with FLAMAZINE:

- Enzymatic debriding agents (remove dead tissue from wounds).
- Oral hypoglycemic agents (for treatment of type 2 diabetes)
- Phenytoin (prevents seizures).

- Cimetidine (used for heartburn and ulcers).

Your doctor may need to run blood tests if you are taking any of these medicines while taking FLAMAZINE.

How to take FLAMAZINE:

- For topical (body surface) use only. Do not get it in your eyes, nose, mouth, or vagina.
- Although you may feel better in early treatment, FLAMAZINE should be used exactly as directed.
- Misuse or overuse of FLAMAZINE could lead to growth of bacteria that will not be killed by FLAMAZINE (resistance). This means that FLAMAZINE may not work for you in the future.
- Do not share your medicine. Each jar or tube of FLAMAZINE should be used on one person only.

Usual dose:

Burns: Clean the wound. Apply a 3 - 5 mm layer of the cream to be burned area using a sterile (germ-free) glove and/or spatula. Reapply cream if it comes off or rubs away. Reapply cream at least every 24 hours or more frequently if wound fluid levels are high.

Hand burns and finger injuries: Clean the wound. Apply a 3 - 5 mm layer of the cream to be affected area using a sterile (germ-free) glove and/or spatula. Place whole hand in a clear plastic bag or glove and close at the wrist. Move your hands and fingers as regularly as possible. Change the dressing every 3 days or more regularly if wound fluid levels are high.

Leg ulcers: Fill ulcer wound with cream to a depth of at least 3 – 5 mm. Avoid non-ulcerated areas. Apply an absorbent pad or gauze dressing. Apply pressure bandaging over the pad/dressing as advised by your doctor. Change the dressing every 2 or 3 days. Cleaning and removal of dead tissue should be performed before each reapplication of FLAMAZINE. Do not apply FLAMAZINE to leg ulcers which have large amounts of wound fluid.

Overdose:

Overdose of sulfadiazine by mouth may lead to diarrhoea or a feeling of sickness.

If you think you, or a person you are caring for, have taken too much FLAMAZINE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to use FLAMAZINE, apply it as soon as you remember. If it is close to the time when you are due to apply your next dose, wait and apply your next scheduled dose and then continue as before. Do not apply extra FLAMAZINE to make up for missed doses.

What are possible side effects from using FLAMAZINE?

These are not all the possible side effects you may have when taking FLAMAZINE. If you experience any side effects not listed here, tell your healthcare professional.

Common side effects are local reactions such as burning, itching and skin rash (e.g. eczema or contact dermatitis.

Leukopenia (lowered white blood cells) has been reported in burns patients treated with FLAMAZINE. This often occurs within 48-72 hours after therapy has commenced. Your doctor may order blood tests to monitor your white blood cell level while you are taking FLAMAZINE.

In large area wounds and/or after prolonged application, systemic absorption of silver can occur causing clinical argyria (blue-grey discolouration of the skin).

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Life-threatening skin rashes (Steven-Johnsons Syndrome (SJS), toxic epidermal necrolysis (TEN)): reddish target-like spots or circular patches often with central blisters on the trunk, ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes), flu-like symptoms. The rash may progress to widespread blistering or peeling of the skin.			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 8°C and 25°C. Store FLAMAZINE in the original container to protect from light. To ensure sterility, 500g jars should be discarded 24 hours after opening and tubes of FLAMAZINE 7 days after opening. Keep out of reach and sight of children.

If you want more information about FLAMAZINE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.smith-nephew.com, or by calling 1-800-463-7439.

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