Silver sulfadiazine cream: disproportionate adverse effects

Due to *silver sulfadiazine*'s lack of demonstrated efficacy as well as its disproportionate adverse effects, the French Health Products Agency (ANSM) has recommended restricting its indications to second-degree or more serious burns. However, even in these situations, proof of its value is lacking.

In France, the antibacterial agent *silver sulfadiazine* has been marketed in the form of a cream since the 1970s for use as an antiseptic for infected wounds, burns and "skin conditions due to primary bacterial infection or those with susceptibility to secondary infection" (1).

Serious adverse effects of sulphonamides even when applied to the skin. In these situations, *silver sulfadiazine* has no demonstrated clinical value compared to a range of other options. Furthermore, when used to prevent infection of burns, its application seems to slow healing and increase pain (2,3).

Silver sulfadiazine carries a risk of the serious systemic adverse effects common to sulphonamides, particularly when applied to damaged skin, a large surface area, or under an occlusive dressing; they include haematological, renal and cutaneous disorders. Altered consciousness and peripheral neuropathy have also been reported, linked to absorption of silver through the skin (1-4).

Towards restricted use in France. In late 2017, the Committee of the French Health Products Agency (ANSM) responsible for reassessment of drugs proposed amending the summary of product characteristics (SPC) and the information leaflet, adding a contraindication to use in children less than 2 years of age as well as mention of the following serious adverse effects: bullous reactions akin to Stevens-Johnson syndrome and toxic epidermal necrolysis, cytopenia (leukopenia, neutropenia and agranulocytosis) and renal failure (5).

The committee also proposed restricting the indications listed in the SPC to the "*prevention and treatment of infections arising during treatment of second degree or more serious burns*". This was based solely on "*established practice*" without proof of efficacy.

As of 27 February 2018, neither the SPC nor the information leaflet had been modified.

The ANSM did not include the cream based on *silver sulfadiazine* combined with *cerous nitrate* (Flammacérium®) in this assessment (1,5). It carries the same risks as *silver sulfadiazine* alone and has not been shown to be more effective (6).

In practice Antiseptics are for the most part poorly evaluated and often are part of care practices in which the healing of wounds and burns cannot be clearly attributed to any particular component of treatment. Among the antibiotics, *silver sulfadiazine* is notable for carrying a risk of well-documented serious adverse effects. In the absence of evaluated treatment strategies specifically showing a favourable harm-benefit balance for *silver sulfadiazine* in certain situations, it has only a marginal place in treatment, as a last resort. For the treatment and prevention of infections, there are several other options that are less dangerous or more effective than *silver sulfadiazine,* including frequent cleaning with soap and water, a variety of skin antiseptics, such as *chlorhexidine,* and various antibiotics for topical or systemic administration.

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6- "Cerous nitrate". In: "Martindale The Complete Drug Reference" The Pharmaceutical Press, London. www.medicinescomplete.com accessed 24 February 2018: 45 pages.

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