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Questions and answers on sodium laurilsulfate used as an excipient in medicinal products for human use

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This document should be read in the context of the revision of the Annex of the European Commission guideline 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017) [2].

* Deletion of the E number. Please see the corrected Annex for further details.

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1. What is sodium laurilsulfate and why is it used as an excipient?

Sodium laurilsulfate (SLS), also known as sodium dodecyl sulfate or sodium lauryl sulfate, is an organic compound with the formula $CH_3(CH_2)_{11}OSO_3Na$. SLS occurs as white or cream to pale yellow-coloured crystals, flakes, or powder having a smooth feel, a soapy, bitter taste, and a faint odour of fatty substances. The salt exhibits a neutral to alkaline pH (7.0–9.5 for a 1% $^{w}/_{v}$ aqueous solution) depending upon its chemical purity.

In medicinal products, SLS has a number of functional uses as an emulsifying agent, modified-release agent, penetration enhancer, solubilising agent, tablet and capsule lubricant. It is not recommended for the parenteral route of administration. Authorised medical products contain SLS ranging from 0.15% (e.g. creams) to 25% (medicated shampoos).

Being derived from inexpensive coconut and palm oils, SLS is a common component of many domestic cleaning products such as handsoaps, washing-up liquid etc. Sodium coco-sulfate is essentially the same compound, but made from less purified coconut oil.

A related surfactant, Sodium Laureth Sulfate is more widely used as a detergent and surfactant in personal care products. It differs from SLS due to the presence of ethoxyl groups $[(OCH_2CH_2)_n]$ in the backbone where n=3 or more, which is thought to give it extra foaming activity. Sodium Laureth Sulfate is not the subject of this review.

The cosmetic sector not only avoids the use of SLS in their products due to its skin-irritating properties but actually uses it as a test reagent in human volunteers to deliberately induce skin reactions in the testing of new cosmetic formulations

SLS is not a permitted food additive in the European Union.

2. Which medicinal products contain sodium laurilsulfate?

SLS is used in a wide variety of dosage forms dosage forms, for example as a wetting agent in oral liquids and toothpastes and as an emulsifying agent in topical dosage forms such as creams, ointments and medicated shampoos. The vast majority of dosage forms using SLS as an excipient are tablets and capsules where it is used as a lubricant and/or releasing agent. As there are no reported adverse reactions to SLS when used as excipient in tablets and capsules, the scope of the safety assessment is limited to medicinal products applied to the skin or the scalp, such as creams, ointments, gels and shampoos, which contain SLS.

3. What are the safety concerns?

Reported adverse reactions to SLS in pharmaceutical formulations are skin irritation following topical application [3, 4]. The skin irritancy is thought to be due its surfactant properties, producing disruption of cell membranes and conformational changes of proteins.

A large number of publications attest to the skin damaging properties of SLS applied on its own; however, case studies on formulated products are rare. The skin effects are more pronounced in patients with eczematous conditions [1]. When used in cleaning products designed to be washed off quickly, such as shampoos and soap, SLS rarely displays any adverse events.

A safety review by the MHRA in 2013 on emollients containing SLS (0.9%) in topical medicinal products concluded that such products may cause local skin reactions, such as stinging, burning,

itching, and redness, when used as a leave-on emollient, particularly in children with atopic eczema [7]. Reactions were likely be exacerbated by the presence of excipients with known effects on the skin such as benzoic acid/benzoates, bronopol, cetostearyl alcohol, chlorocresol, parahydroxybenzoates and lanolin commonly found in topical preparations where SLS is also present.

The skin irritating property of SLS is made use of in the cosmetics industry to deliberately induce a skin a reaction as a comparative test reagent (positive control) in the development of semi-solid topical consumer products e.g. moisturisers, anti-ageing creams [9].

4. What are the reasons for updating the information in the package leaflet?

SLS is not included in the Annex to the guideline on 'Excipients in the label and package leaflet of medicinal products for human use' (CPMP/463/00 Rev. 1) dated 2003 [5]. There is currently no EU regulatory guideline or recommendation in place relating to the acceptable levels of SLS in medicinal products.

Skin sensitivity to SLS varies according to the concentration of SLS, contact time, patient population and experimental approaches. Furthermore, attempts to elucidate the skin irritation threshold in humans is found to be dependent upon the site of the application, the vehicle in which SLS is dissolved, the method of application, duration and frequency of application, the duration of the study, the presence of other skin-irritating excipients and whether the application is under occlusion [6].

Recommending a threshold for SLS in topical products is difficult to establish given the range of confounding factors. However, it is a known skin irritant and is used as a positive (irritant) control in the cosmetic industry. It is, therefore, proposed to have a threshold of 0% for SLS in topical medicinal products for all age groups.

5. New information for the package leaflet

Name	Route of Administration	Threshold	Information for the Package Leaflet	Comments
Sodium laurilsulfate	Cutaneous	Zero	This medicine contains x mg sodium laurilsulfate in each <dosage unit><unit volume> <which is equivalent to x mg/<weight><volume>>. Sodium laurilsulfate may cause local skin reactions (such as stinging or burning sensation) or increase skin reactions caused by other products when applied on the same area.	The thickness of the skin varies considerably according to the body site and with age and can be an important factor in the sensitivity to sodium laurilsulfate (SLS). Sensitivity to SLS will also vary according the type of formulation (and effects of other excipients), the concentration of SLS, contact time and patient population (children, hydration level, skin color and disease). Patient populations with decreased skin barrier functions such as in atopic dermatitis are more sensitive to the irritant properties of SLS.

Further scientific background is available in the report entitled ‘Sodium laurilsulfate used as an excipient’ [8].

References

1. Agner, T., 'Susceptibility of atopic dermatitis patients to irritant dermatitis caused by sodium lauryl sulphate', Acta Derm Venereol, Vol. 71, 1991, p. 296–300.
2. Annex of the European Commission guideline 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017).
3. Annual Review of Cosmetic Ingredient Safety Assessments–2002/2003, Int J Toxicol., Vol. 24 (Suppl. I), 1 January 2005, p. 1–102.
4. Eubanks, S.W., Patterson, J.W, 'Dermatitis from sodium lauryl sulfate in hydrocortisone cream', Contact Dermatitis, Vol. 11, 1984, p. 250–251.
5. Guideline on excipients in the label and package leaflet of medicinal products for human use' (CPMP/463/00 Rev.1). July 2003.
6. Lee, C.H., Maibach, H.I., 'The sodium lauryl sulfate model: an overview', Contact Dermatitis, Vol. 33, 1995, p. 1–7.
7. MHRA, Aqueous cream: may cause skin irritation, particularly in children with eczema, possibly due to sodium lauryl sulfate content, 2013, available at: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON254804 (accessed 16 October 2014)
8. Sodium laurilsulfate used as an excipient (EMA/CHMP/606830/2014).
9. Tupker, R.A., et al, 'Guidelines on sodium lauryl sulfate exposure tests. A report from the Standardisation Group of the European Society of Contact Dermatitis', Contact Dermatitis, Vol. 36, 1997, p. 53–69.