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4 Questions and answers on sodium laurilsulfate in the  
5 context of the revision of the guideline on 'Excipients in  
6 the label and package leaflet of medicinal products for  
7 human use' (CPMP/463/00 Rev.1)  
8 Draft

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# 14 Questions and answers on sodium laurilsulfate in the 15 context of the revision of the guideline on 'Excipients in 16 the label and package leaflet of medicinal products for 17 human use' (CPMP/463/00 Rev.1)

## 18 **1. Background**

19 Following the European Commission decision to revise the Annex of the guideline on 'Excipients in the  
20 label and package leaflet of medicinal products for human use' (CPMP/463/00 Rev. 1) [1], a  
21 multidisciplinary group of experts involving SWP (lead), QWP, PDCO, PRAC (ex PVWP), CMD(h), VWP,  
22 BWP and BPWP was created in 2011.

23 The objective of this group is to update the labelling of selected excipients listed in the Annex of the  
24 above mentioned EC guideline, as well as to add new excipients to the list, based on a review of their  
25 safety. The main safety aspects to be addressed were summarised in a concept paper published in  
26 March 2012 [2].

27 Draft questions and answers (Q&A) documents on excipients are progressively released for public  
28 consultation. They include proposals for new or updated information for the label and package leaflet.  
29 The corresponding background report supporting the review is published for information only.

30 When one or several Q&As have been finalised, the new information in the package leaflet will be  
31 included in a revised annex of the guideline.

32 For more information see the [Excipients labelling webpage](#) on the EMA website.

## 33 **2. What is sodium laurilsulfate and why is it used as an** 34 **excipient?**

35 Sodium laurilsulfate (SLS), also known as sodium dodecyl sulfate, sodium lauryl sulfate or E487, is an  
36 organic compound with the formula  $\text{CH}_3(\text{CH}_2)_{11}\text{OSO}_3\text{Na}$ . SLS occurs as white or cream to pale yellow-  
37 coloured crystals, flakes, or powder having a smooth feel, a soapy, bitter taste, and a faint odour of  
38 fatty substances. The salt exhibits a neutral to alkaline pH (7.0–9.5 for a 1%  $\text{w/v}$  aqueous solution)  
39 depending upon its chemical purity.

40 In medicinal products, SLS has a number of functional uses as an emulsifying agent, modified-release  
41 agent, penetration enhancer, solubilising agent, tablet and capsule lubricant. It is not recommended  
42 for the parenteral route of administration. Authorised medical products contain SLS ranging from  
43 0.15% (e.g. creams) to 25% (medicated shampoos).

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

47 A related surfactant, Sodium Laureth Sulfate is more widely used as a detergent and surfactant in  
48 personal care products. It differs from SLS due to the presence of ethoxyl groups  $[(\text{OCH}_2\text{CH}_2)_n]$  in the  
49 backbone where  $n=3$  or more, which is thought to give it extra foaming activity. Sodium Laureth  
50 Sulfate is not the subject of this review.

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

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

### 55 **3. Which medicinal products contain sodium laurilsulfate?**

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

### 63 **4. What are the safety concerns?**

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

67 A large number of publications attest to the skin damaging properties of SLS applied on its own;  
68 however, case studies on formulated products are rare. The skin effects are more pronounced in  
69 patients with eczematous conditions [5]. When used in cleaning products designed to be washed off  
70 quickly, such as shampoos and soap, SLS rarely displays any adverse events.

71 A safety review by the MHRA in 2013 on emollients containing SLS (0.9%) in topical medicinal  
72 products concluded that such products may cause local skin reactions, such as stinging, burning,  
73 itching, and redness, when used as a leave-on emollient, particularly in children with atopic  
74 eczema [6]. Reactions were likely be exacerbated by the presence of excipients with known effects on  
75 the skin such as benzoic acid/benzoates, bronopol, cetostearyl alcohol, chlorocresol,  
76 parahydroxybenzoates and lanolin commonly found in topical preparations where SLS is also present.

77 The skin irritating property of SLS is made use of in the cosmetics industry to deliberately induce a  
78 skin a reaction as a comparative test reagent (positive control) in the development of semi-solid  
79 topical consumer products e.g. moisturisers, anti-ageing creams [7].

### 80 **5. What are the reasons for updating the information in the** 81 **package leaflet?**

82 There is currently no EU regulatory guideline or recommendation in place relating to the acceptable  
83 levels of SLS in medicinal products.

84 Skin sensitivity to SLS varies according to the concentration of SLS, contact time, patient population  
85 and experimental approaches. Furthermore, attempts to elucidate the skin irritation threshold in  
86 humans is found to be dependent upon the site of the application, the vehicle in which SLS is dissolved,  
87 the method of application, duration and frequency of application, the duration of the study, the  
88 presence of other skin-irritating excipients and whether the application is under occlusion [8].

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

93 **6. Proposal for new information in the package leaflet**

Name	Route of Administration	Threshold*	Information for the Package Leaflet	Comments
<b>Sodium laurilsulfate or E487</b>	Cutaneous	Zero	<p>This product contains sodium laurilsulfate x% w/w.</p> <p>Sodium laurilsulfate may cause local skin reactions (such as stinging or burning sensation) in particular if you have sensitive skin.</p> <p>May increase local reactions caused by other medicines when applied to the skin in the same area.</p>	<p>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).</p> <p>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).</p> <p>Patient populations with decreased skin barrier functions such as in atopic dermatitis are more sensitive to the irritant properties of SLS.</p> <p>Application of SLS can potentiate skin irritation caused by other medicines applied to the same area.</p>

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95 Note:

96 \* The threshold is a value, equal to or above which it is necessary to provide the information stated for the package leaflet. This threshold is not a highest acceptable limit. A  
 97 threshold of 'zero' means that it is necessary to state the information in all cases where the excipient is present in the medicinal product [1].

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