Scientific Committee on Consumer Safety

SCCS

ADDENDUM

to the scientific Opinions on Climbazole (P64)

ref. SCCS/1506/13 and SCCS/1590/17

The SCCS adopted this document
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ACKNOWLEDGMENTS

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This Addendum to the Opinion is final and was not subject to a commenting period as requested by the mandating DG because the terms of reference requested a revision of the calculation on margin of safety only.

Keywords: SCCS, addendum, scientific opinion, Climbazole, preservative, P64, CAS 38083-17-9, EC 253-775-4, SCCS/1600/18, Regulation 1223/2009

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SCCS

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1. MANDATE FROM THE EUROPEAN COMMISSION

Background

The cosmetic ingredient Climbazole (CAS 38083-17-9), with the chemical name 1-(4-chlorophenoxy)-1-imidazol-1-yl-3,3-dimethyl-2-butanone, is currently regulated in the Cosmetics Regulation (EC) 1223/2009 as a preservative in Annex V, entry 32, up to a maximum authorized concentration of 0.5%.

Climbazole has been subject to different safety evaluations by the SCCP in 2005 (SCCP/0918/05[1]) and 2009 (SCCP/1204/08[2]) and by the SCCS in 2013 (SCCS/1506/13[3] and SCCS/1500/13[4]).

In October 2017 the SCCS adopted an addendum (SCCS/1590/17)5 to the opinion of Climbazole (P64) ref. SCCS/1506/13 that concludes:

The maximum concentrations of Climbazole considered as safe for human health under an aggregate exposure scenario are as follows:
2% as anti-dandruff agent in rinse-off shampoos and 0.2% as cosmetic preservative in leave – on formulations (face cream, hair lotion, foot care) with the exception of cosmetics applied on a full body area (body lotion).

Following the SCCS opinion, a discussion was held at the Working Group on Cosmetic Products on 28 February 2018 with a view to a COM proposal for a draft Regulation on Climbazole as preservative and as an anti-dandruff in rinse-off shampoos. During this discussion, Cosmetics Europe highlighted that Climbazole should also be safe for use as a preservative in rinse-off shampoos at 0.5%.

Further to concerns raised by Member States on this specific use, a re-assessment on the safety of Climbazole as a preservative in rinse-off shampoos is needed. At the same time, considering the need to evaluate the aggregate exposure for cosmetics, it is appropriate to re-assess the use of Climbazole for the different categories of relevant products and concentrations as follows.

[1] http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_027.pdf
[2] http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_164.pdf
[3] http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_120.pdf
[4] http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_121.pdf

Terms of reference

(1) In light of the SCCS addendum (SCCS/1590/17), does the SCCS consider safe the use of Climbazole (CAS 38083-17-9) when used in cosmetic products in the following specified concentrations under an aggregate exposure scenario for cosmetics:

- *As a cosmetic preservative in face cream up to a concentration of 0.2%;?*
- *As a cosmetic preservative in hair lotion up to a concentration of 0.2%;*
- *As a cosmetic preservative in foot care up to a concentration of 0.2%;*
- *As a cosmetic preservative in rinse-off shampoo up to a concentration of 0.5%;*
- *As an anti-dandruff agent in rinse-off shampoo up to a concentration of 2.0%.*

(2) If not, what is according to the SCCS, the maximum concentration considered safe for use of Climbazole (CAS 38083-17-9) as a cosmetic preservative respectively in face cream, hair lotion, foot care and rinse-off shampoo as well as anti-dandruff agent in rinse-off shampoo under an aggregate exposure scenario for cosmetics?

2. OPINION

In the current mandate and in light of the SCCS Addendum (SCCS/1590/17), the SCCS is being asked to re-evaluate the safety levels of Climbazole in different specified concentrations in different cosmetic formulations (as preservative in face cream, hair lotion, foot care, rinse-off shampoo and as antidandruff agent in rinse-off shampoo) under an aggregate exposure scenario for cosmetics.

2.1 Relevant Information taken from the previous opinions

Calculation for the use of Climbazole at 2% as an anti-dandruff agent in shampoo

Dermal absorption through human skin	A (µg/cm²)	=	0.506 µg/cm²
Skin Area surface (area hand + ½ area head)	SAS (cm²)	=	1440 cm²
Frequency of application of the finished product	F (day^{-1})	=	1.00
Typical human body weight		=	60 kg
Systemic exposure dose (SED)			
A x (10^{-3}mg/µg) x SAS x F /60		=	0.0121 mg/kg bw
No observed effect level (90 day, oral, rat)	NOEL	=	5 mg/kg bw/day

Margin of Safety	NOEL/ SED	=	413

Calculation for the use of Climbazole as preservative at 0.2% in aqueous hair lotions

Dermal absorption through human skin*	A (µg/cm²)	=	0.687 µg/cm²
Skin area surface (area hand + ½ area head)	SAS (cm²)	=	1440 cm²
Frequency of application of the finished product	F (day-1)	=	1.00
Typical human body weight		=	60 kg
Systemic exposure dose (SED)			
A x (10^{-3}mg/µg) x SAS x F / 60 kg		=	0.0164 mg/kg bw
No observed effect level (90 day, oral, rat)	NOEL	=	5 mg/kg bw/day

Margin of Safety	NOEL / SED	=	303

Calculation for the use of Climbazole as preservative at 0.2% in a cosmetic face cream: application 2.14 times/day according to frequency of application per product type by Bremmer et al. (2006a, 2006b) and SCCS/1564/15

Dermal absorption through human skin	A (µg/cm²)	=	0.687 µg/cm²
Skin area surface (1/2 area head female)	SAS (cm²)	=	565 cm²
Frequency of application of the finished product	F (day^{-1})	=	2.14
Typical human body weight		=	60 kg
Systemic exposure dose (SED)			
A x (10^{-3}mg/µg) x SAS x F / 60 kg		=	0.0138 mg/kg bw
No observed effect level (90 day, oral, rat)	NOEL	=	5 mg/kg bw/day

Margin of Safety	NOEL / SED	=	361

Calculation for the use of Climbazole as preservative at 0.5% in leave-on body lotion: application 2.28 times/day (according to frequency of application per product type by Bremmer et al. (2006a, 2006b) and SCCS/1564/15

Dermal absorption through human skin	A (µg/cm²)	=	1.719 µg/cm²
Skin area surface (whole body)	SAS (cm²)	=	18,000 cm²
Frequency of application of the finished product	F (day^{-1})	=	2.28
Typical human body weight		=	60 kg
Systemic exposure dose (SED)			
A x (10^{-3}mg/µg) x SAS x F / 60 kg		=	1.175 mg/kg bw
No observed effect level (90 day, oral, rat)	NOEL	=	5 mg/kg bw/day

Margin of Safety	NOEL/ SED	=	4

Calculation for the use of Climbazole as preservative up to 0.2% in foot care products

Dermal absorption through human skin*	A (µg/cm^2)	=	0.687 µg/cm²
Skin area surface (feet, Ref. 2)	SAS (cm^2)	=	1170 cm^2
Frequency of application of the finished product	F (day^{-1})	=	1.00
Typical human body weight		=	60 kg
Systemic exposure dose (SED)			
A x (10^{-3}mg/µg) x SAS x F/ 60 kg		=	0.0133 mg/kg bw
No observed effect level (90 day, oral, rat)	NOEL	=	5 mg/kg bw/day

Margin of Safety	NOEL / SED	=	373

* dermal absorption A (µg/cm^2) has been proportionally adjusted for the lowered concentration of Climbazole

2.2 Current Request

In a current request, the applicant requests the extension of the use of Climbazole as preservative at maximal concentration of 0.5% in shampoos. The following calculation of the MoS for that particular application is as follows:

Calculation for the use of Climbazole at 0.5 % as preservative in shampoo

Dermal absorption through human skin	A (µg/cm²)*	=	0.126 µg/cm²
Skin Area surface (area hand + ½ area head)	SAS (cm²)	=	1440 cm²
Frequency of application of the finished product	F (day^{-1})	=	1.00
Typical human body weight		=	60 kg
Systemic exposure dose (SED)			
A x (10^{-3}mg/µg) x SASx F / 60 kg		=	0.0030 mg/kg bw
No observed effect level (90 day, oral, rat)	NOEL	=	5 mg/kg bw/day

Margin of Safety	NOEL/ SED	=	1653

* dermal absorption A (µg/cm2) has been proportionally adjusted for the requested, lowered concentration of Climbazole

The individual uses of Climbazole and under an aggregate exposure scenario (Table 1 and 2), except its use as preservative up to 0.5% for whole body applications (MoS= 4), are considered safe:

- as an anti-dandruff compound up to 2% in cosmetic shampoos (MoS= 413),
- as a preservative compound up to 0.5 % in cosmetic shampoos (MoS= 1653),
- as preservative up to 0.2% in an aqueous hair lotion (MoS= 196),
- as preservative up to 0.2% in a face cream (MoS= 144),
- as preservative up to 0.2 % in foot care (MoS= 241).

Table 1 Combined use of Climbazole as preservative at a maximum concentration of 0.2% in leave-on and rinse-off cosmetic products and as an anti-dandruff agent in shampoo at 2%; realistic frequency of use values and conservative absorption values +1SD were taken into consideration;

Product type	Inclusion %	A* (ug/cm^2)	SAS (cm^2)	F (day^{-1})	bw (kg)	SED	NOEL (mg/kg/day)	MoS
Shampoo (anti-dandruff)	2	0.506	1440	1	60	0.0121	5	413
hair lotion	0.2	0.687	1440	1	60	0.0164	5	304
face cream	0.2	0.687	565	2.14	60	0.0138	5	361
foot care	0.2	0.687	1170	1	60	0.0133	5	375
shampoo + hair lotion						0.0285	5	175
shampoo + face cream						0.0259	5	193
shampoo + foot care						0.0254	5	196
hair lotion + face cream						0.0302	5	165
hair lotion + foot care						0.0297	5	168
face cream + foot care						0.0271	5	184
shampoo + hair lotion + face cream						0.0423	5	118
shampoo + hair lotion + foot care						0.0418	5	119
shampoo + face cream + foot care						0.0392	5	127
hair lotion + face cream + foot care						0.0435	5	114
Shampoo(2%) + hair lotion + face cream + foot care						0.0556	5	89

*Dermal absorption values were proportionally adjusted.
NOTE: only cosmetic products with MoS ≥ 100 were included in combined-use calculations.

Tab. 2 Combined use of Climbazole as preservative at a maximum concentration of 0.2% in leave-on cosmetic products and 0.5% in shampoo; realistic frequency of use values and conservative absorption values +1SD were taken into consideration;

Product type	Inclusion %	A* (ug/cm^2)	SAS (cm^2)	F (day^{-1})	bw (kg)	SED	NOEL (mg/kg/day)	MoS
Shampoo (preservative)	0.5	0.126	1440	1	60	0.0030	5	1653
hair lotion	0.2	0.687	1440	1	60	0.0164	5	304
face cream	0.2	0.687	565	2.14	60	0.0138	5	361
foot care	0.2	0.687	1170	1	60	0.0133	5	375
shampoo + hair lotion						0.0195	5	256
shampoo + face cream						0.0168	5	296
shampoo + foot care						0.0164	5	304
hair lotion + face cream						0.0303	5	165
hair lotion + foot care						0.0298	5	168
face cream + foot care						0.0272	5	184
shampoo + hair lotion + face cream						0.0333	5	149
shampoo + hair lotion + foot care						0.0329	5	151
shampoo + face cream + foot care						0.0302	5	165
hair lotion + face cream + foot care						0.0437	5	114
Shampoo(0.5%) + hair lotion + face cream + foot care						0.0467	5	106

*Dermal absorption values were proportionally adjusted.
NOTE: only cosmetic products with MoS ≥ 100 were included in combined-use calculations.

3.3 Discussion

In light of the addendum (SCCS/1590/17), the SCCS recalculated the SED and MoS values according to the principles of the Notes of Guidance [SCCS/1564/15]. The proposed concentrations of Climbazole as a cosmetic preservative:
- in face cream up to a concentration of 0.2%;
- in hair lotion up to a concentration of 0.2%;
- in foot care up to a concentration of 0.2%;
- in rinse-off shampoo up to a concentration of 0.5%;

are considered safe as well individually as under a conservative deterministic aggregate exposure scenario (as preservative in shampoo(0.5%) + hair lotion + face cream + foot care).

When Climbazole is present as an anti-dandruff agent in rinse-off shampoo up to a concentration of 2.0%, it is considered to be safe as well individually as under a conservative deterministic aggregate exposure scenario (as anti-dandruff in shampoo (2%) + hair lotion + face cream + foot care).

The SCCS used the 4-cosmetic products combination in its calculation as it considers that the 5-cosmetic products combination including the combined use of both shampoos (as preservative only and with anti-dandruff action) is unrealistic.

3. CONCLUSION

(1) In light of the SCCS addendum (SCCS/1590/17), does the SCCS consider safe the use of Climbazole (CAS 38083-17-9) when used in cosmetic products in the following specified concentrations under an aggregate exposure scenario for cosmetics:

- *As a cosmetic preservative in face cream up to a concentration of 0.2%;*
- *As a cosmetic preservative in hair lotion up to a concentration of 0.2%;*
- *As a cosmetic preservative in foot care up to a concentration of 0.2%;*
- *As a cosmetic preservative in rinse-off shampoo up to a concentration of 0.5%;*
- *As an anti-dandruff agent in rinse-off shampoo up to a concentration of 2.0%.*

  - The SCCS considers the specified concentrations when used as preservative, for the individual cosmetic products as well as for their combinations under aggregate exposure scenario as safe

  - When Climbazole is used as an anti-dandruff agent up to 2%, the 4-cosmetic products combination (with hair lotion, face cream and foot care) is also considered as safe

  - The SCCS therefore considers that the use of climbazole up to a concenration of 2% in shampoos is safe for the consumer, either as anti-dandruff agent or as a preservative agent in combination with other uses and at concentrations as listed above.

(2) If not, what is according to the SCCS, the maximum concentration considered safe for use of Climbazole (CAS 38083-17-9) as a cosmetic preservative respectively in face cream, hair lotion, foot care and rinse-off shampoo as well as anti-dandruff agent in rinse-off shampoo under an aggregate exposure scenario for cosmetics?

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4. MINORITY OPINION

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