



Innovation you can build on™

ACTIVE

Product Information File

ACTIVE

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RECOMMENDATIONS:

The information in this publication is believed to be accurate and is given in good faith but no representation or warranty as to its completeness or accuracy is made. Suggestions for uses or applications are only opinions. Users are responsible for determining the suitability of these products for their own particular purpose.

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1. PRODUCT INFORMATION

Description

ACTIVE supports the activation of the cutaneous repair process, and in particular at the level of the fragile and UV-damage prone papillary dermis. **ACTIVE** promotes wrinkle smoothing and improves tone and elasticity.

ACTIVE is an association of 2 palmitoylated matrikines: Pal-Gly-His-Lys and Pal-Gly-Gln-Pro-Arg.



INCI Name

Glycerin (and) Water (Aqua) (and) Butylene Glycol (and) Carbomer (and) Polysorbate 20 (and) Palmitoyl Tripeptide-1⁽¹⁾ (and) Palmitoyl Tetrapeptide-7.

(1): Previous INCI Name Palmitoyl Oligopeptide which has been revised in Palmitoyl Tripeptide-1 in September 2013.

Proven cosmetic activity

In vitro

Study on senescence markers

Study of *de novo* matrix synthesis by human fibroblasts

Gene activation study (DNA Array method)

In vivo

Tests on female panelists

Tests on male panelists

Tests on female panelists (High resolution ultrasound and confocal laser microscopy)

Ex vivo

Study on skin explants

Formulation guidelines

Appearance: whitish opalescent gel

Solubility: water soluble

Recommended use level: 3%

Storage

Conditions: Long term storage recommended at 4-7°C.

Re-evaluation date: 24 months from the date of manufacturing, if the storage conditions are respected.

Specifications

See selling specifications or contact your local sales representative.

Patents

WO 2005/048968; EP 1 686 957; US 6,974,799; JP 4256389; CN 1893911; KR 20060122844

For further information, please contact your local sales representative or refer to our technical dossier available upon request.

2. MANUFACTURER / SUPPLIER INFORMATION

Supplier and/or Manufacturer

Certifications

is certified ISO 14001:2004, ISO 9001:2008, OHSAS 18001-2007 and EFfCI GMP.

Good Manufacturing Practices

realizes their activities according to Good Manufacturing Practices for Cosmetic Ingredients and makes sure they are correctly implemented thanks to external audits.

Sustainability

According to its policy, is in favor of sustainable development based on the following objectives:

- decrease of energy and water consumption,
- respect of protected species (according to Washington's convention),
- promotion of recycling of waste,
- use of cell plant culture to minimize the impact on the environment,
- use of renewable and sustainable raw materials whenever possible.

ambition is to raise awareness about social and environmental responsibility of every actor along the value chain and to favor shared commitments to progress. In particular:

- to pursue traceability of raw materials, their processing, and of all those involved in these domains,
- to encourage sustainable partnerships between all those involved in the supply chain.

Moreover, respects the Corporate Social Responsibility (C.S.R.) policy developed by CRODA and has also signed the "Cosmetic Valley Charter for Sustainability".

3. COMPOSITION AND MANUFACTURING PROCESS**Composition**

INCI Name (PcPc)	CAS Nr	%	Origin*	Function
Glycerin	56-81-5	qsp 100	V	Solvent
Water	7732-18-5	≈ 25		Solvent
Butylene Glycol	107-88-0	≈ 20	S	Solvent
Carbomer	9003-01-4	≈ 1	S	Viscosity increasing agent
Polysorbate 20	9005-64-5	≈ 0.5	S,V	Surfactant
Palmitoyl Tripeptide-1 ⁽¹⁾	147732-56-7	≈ 0.01	S	Skin conditioning agent
Palmitoyl Tetrapeptide-7	221227-05-0	≈ 0.005	S	Skin conditioning agent
<i>Manufacturing additive:</i>				
Sodium Lactate	72-17-3	max 1	B	pH buffer
<i>Preservative: /</i>				

* V: vegetable, S: synthetic, B: biotechnology, Mi: mineral

(1): Previous INCI Name Palmitoyl Oligopeptide which has been revised in Palmitoyl Tripeptide-1 in September 2013.

Country of origin**Simplified manufacturing process**

ACTIVE is a mixture of Glycerin, Water, Butylene Glycol, Carbomer, Polysorbate 20, Palmitoyl Tripeptide-1 and Palmitoyl Tetrapeptide-7.

Palmitoyl Tripeptide-1 (Pal GHK) and Palmitoyl Tetrapeptide-7 (Pal GQPR) are obtained by chemical synthesis: for each peptide, coupling of aminoacids followed by a last coupling with palmitic acid.

The both peptides are solubilized in a jellified excipient.

4. REGULATORY INFORMATION

All information provided in this dossier has been compiled to the best of our current knowledge.

Chemical Inventory Status / REACH

INCI Name (PcPc)	CAS Nr	Chemical Inventory								REACH	
		Europe EINECS Nr	US TSCA	Canada DSL/NDSL /ICL	China IECSC	Korea KECI	Japan ENCS /MITI Nr	Australia AICS	Exemption if any	Pre- registered	Registered
Glycerin	56-81-5	200-289-5	X	DSL	X	X	X	X	Annex V.9		
Water	7732-18-5	231-791-2	X	DSL	X	X	X	X	Annex IV		
Butylene Glycol	107-88-0	203-529-7	X	DSL	X	X	X	X		Yes	01-2119455875-25
Carbomer	9003-01-4	n/a	X	DSL	X	X	X	X	Polymer		
Polysorbate 20	9005-64-5	n/a	X	DSL	X	X	X	X	Polymer		
Palmitoyl Tripeptide-1	147732-56-7	n/a	X	ICL	-	-	-	X	<1t/year		
Palmitoyl Tetrapeptide-7	221227-05-0	n/a	X	ICL	-	-	-	-	<1t/year		
Sodium Lactate	72-17-3	200-772-0	X	DSL	X	X	X	X	Annex V.4		

X: listed or exempt

-: unknown

Cosmetic use covered according to the Cosmetics Europe (formerly COLIPA) use mapping.

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Cosmetic Status

- Europe: ACTIVE complies with the Regulation (EC) No 1223/2009 of the European Parliament and of the Council.
- United States of America: ACTIVE complies with the Code of Federal Regulation (CFR) title 21.
- Canada: ACTIVE complies with the Cosmetic Regulation C.R.C., c 869.
- MERCOSUR (Argentina, Brazil, Paraguay, Uruguay and Venezuela): ACTIVE complies with cosmetic regulation in force.
- CAN (Bolivia, Colombia, Ecuador and Peru): ACTIVE complies with cosmetic regulation in force.
- ASEAN (Indonesia, Malaysia, the Philippines, Singapore, Thailand, Brunei, Burma (Myanmar), Cambodia, Laos and Vietnam): ACTIVE complies with the ASEAN Cosmetic Directive.
- South Korea: ACTIVE complies with the Korean Cosmetic Products Act (KCPA).
- Japan: ACTIVE complies with the Standards for Cosmetics.
- China: ACTIVE complies with the Hygienic Standard 2007. All the ingredients of ACTIVE are listed IECIC 2014.

Biodiversity

RSPO: ACTIVE contains Glycerin obtained from rapeseed but can be obtained from palm, palm kernel, coconut or other plants (except from Jatropha).

We confirm that our suppliers of Glycerin are members of the Roundtable on Sustainable Palm Oil (RSPO).

CITES / IUCN: ACTIVE does not contain endangered species, according to the Convention on International Trade in Endangered Species of wild fauna and flora (CITES) list and the International Union or Conservation of Nature (IUCN) red list of threatened species, and is not subject to the Convention of Washington to our knowledge to date.

The plant raw materials used are not parts of Annexes I, II and III of the Convention of Washington.

Nanomaterial

ACTIVE is not a nanomaterial and does not contain nanomaterial, according to the Cosmetic Regulation (EC) No 1223/2009 definition of a nanomaterial:

'Nanomaterial' means an insoluble or biopersistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.

GMO

ACTIVE does not contain and is not produced from genetically modified organisms (GMO).

BSE / TSE

None of the ingredients used for the production of ACTIVE are of bovine, ovine, equine or porcine origin. Therefore, Bovine Spongiform Encephalopathy (BSE) / Transmitting Spongiform Encephalopathy (TSE) risk, as defined in the European Commission Decision 97/534/EC and EMEA/410/10, does not concern this product.

5. IMPURITIES AND OTHER RESIDUES

Note: This information is based on the knowledge of our raw materials and of the manufacturing process of the product. Analyses are not part of the product's specifications and are thus not performed in routine.

Allergens

According to its manufacturing process, ACTIVE does not contain any of the 26 allergenic substances as defined in the Annex III of the Cosmetics Regulation (EC) No 1223/2009 (analysis not performed).

Pesticides

According to its manufacturing process, ACTIVE does not contain any pesticides (analysis not performed).

Heavy metals

Elements		Results (mg/kg) ICP-MS based on ISO 17294
Arsenic	(As)	<0.10
Cadmium	(Cd)	<0.10
Lead	(Pb)	<0.10
Mercury	(Hg)	<0.10
Chromium	(Cr)	<0.20
Antimony	(Sb)	<0.50
Molybdenum	(Mo)	<0.50
Tin	(Sn)	<0.50
Nickel	(Ni)	<0.50
Cobalt	(Co)	<0.10
Barium	(Ba)	<0.20

CMR

ACTIVE does not contain any ingredients classified CMR category 1A, 1B or 2 (Carcinogen, Mutagen, toxic for the Reproduction) according to the Regulation (EC) No 1272/2008 and adaptations. Nevertheless, potential traces of these substances are technically unavoidable due to the presence of Polysorbate 20.

ACTIVE fulfils the requirements of the article 15 of the Cosmetics Regulation (EC) No 1223/2009 and its amendments.

Residual Solvents

ACTIVE complies with ICH guideline for residual solvents CPMP/ICH/283/95 and Chapter <467> of USP/NF: Residual Solvents Limits.

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VOC

ACTIVE does not contain one or more intentionally added Volatile Organic Compounds (VOC) in compliance with the Swiss ordinance and the definition of California. Nevertheless, potential traces of Ethyl Acetate and Cyclohexane are technically unavoidable due to the presence of Carbomer.

SVHC

No Substances of Very High Concern (SVHC) listed in annex 14 of the Regulation (EC) 1907/2006, or listed in candidate list published by ECHA of which we regularly follow the updates, are intentionally added in the manufacturing process of ACTIVE. Therefore, ACTIVE would not be expected to contain these substances.

Proposition 65

The ingredients constituting ACTIVE are not known to the State of California to cause cancer or reproductive toxicity as listed under Proposition 65 State Drinking Water and Toxic Enforcement Act of which we regularly follow the updates.

Phthalates

The following Phthalates are not intentionally added in the manufacturing process of ACTIVE. Therefore, ACTIVE would not be expected to contain these substances:

Substances		CAS Nr
Dibutyl Phthalate	(DBP)	84-74-2
Diethylhexyl Phthalate	(DEHP)	117-81-7
Benzyl Butyl Phthalate	(BBP)	85-68-7
Di-n-pentyl Phthalate	(DnPP)	131-18-0
bis(2-Methoxyethyl) Phthalate	(DMEP)	117-82-8
Diisopentyl Phthalate	(DiPP)	605-50-5
n-Pentyl Isopentyl Phthalate	(DPP)	84777-06-0
Diisobutyl Phthalate	(DiBP)	84-69-5

Glycol Ethers

The following Glycol Ethers are not intentionally added in the manufacturing process of ACTIVE. Therefore, ACTIVE would not be expected to contain these substances:

Substances		CAS Nr
2-Methoxyethanol / Ethylene Glycol Monomethyl Ether	(EGME)	109-86-4
2-Methoxyethyl Acetate / Methylglycol Acetate	(EGMEA)	110-49-6
2-Ethoxyethanol	(EGEE)	110-80-5
2-Ethoxyethyl Acetate	(EGEEA)	111-15-9
1,2-Dimethoxyethane / Ethylene Glycol Dimethyl Ether	(EGDME)	110-71-4
Oxybis(2-Methoxyethyl) / Dimethoxydiglycol	(DEGDME)	111-96-6
1,2-bis(2-Methoxyethoxy)ethane / Triethylene Glycol Dimethyl Ether	(TEGDME)	112-49-2
2-Butoxyethanol	(EGBE)	111-76-2
2-(2-Butoxyethoxy)ethanol	(DEGBE)	112-34-5
2-(2-Ethoxyethoxy)ethanol	(DEGEE)	111-90-0

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Diethylene Glycol

Glycerin used for the production of ACTIVE is compliant with the USP monograph (DEG: < 0.10%).

Formaldehyde

Formaldehyde and Formaldehyde releasers (as described by the SCCNFP opinions 586/02 and 587/02) are not intentionally added in the manufacturing process, and so are not expected in ACTIVE.

Packaging

The packaging of ACTIVE is in compliance with Regulation (EC) No 1935/2004 of the European parliament and of the Council of October 27th, 2004 on materials and articles intended to come into contact with food.

6. MICROBIOLOGICAL INFORMATION

Specifications

Total aerobic microbial count <100 cfu/g

Total combined yeasts / moulds count <10 cfu/g

Challenge Test

Strains	D7 (cfu/g)	D14 (cfu/g)	D28 (cfu/g)
Bacteria	<10	<10	<10
Yeast/mould	<10	<10	<10
<i>Aspergillus. niger</i>	100	<10	<10

Internal test method

7. TOXICOLOGICAL INFORMATION**Animal testing**

ACTIVE has not been tested on animals.

Since 1998 and according to CRODA's policy, has decided not to perform any animal testing on its products (except for other specific regulatory purposes).

Toxicological tests results

Local toxicity	
<u>Cutaneous primary tolerance</u> (Patch-test) October 31 st , 2003 Dilution to 50%	Non irritant
<u>Ocular irritation</u> (HETCAM) October 24 th , 2003 Dilution to 50%	Slightly irritant
<u>Ocular irritation</u> (Neutral Red Release Method) October 24 th , 2003	Slightly cytotoxic
Allergenicity	
<u>Sensitization</u> (HRIPT) December 12 th , 2003 Dilution to 50%	Non sensitizing
Systemic toxicity	
<u>Mutagenicity</u> (Ames test) November 4 th , 2003	Non mutagenic

Complete reports and Expert's certificates are available upon request.

NOAEL

INCI Name (PcPc)	DA $\mu\text{g}/\text{cm}^2$ (%)	NOAEL ^(a) / NOEL ^(b) (mg/kg/day)	Read across
Glycerin	100	8000 ^(b) [1]	No
Water	n/a	n/a	No
Butylene Glycol	100	3000 ^(a) [2]	No
Carbomer	100	Safe for use [3]	No
Polysorbate 20	100	1000 ^(a) [4]	Polysorbates
Palmitoyl Tripeptide-1 ⁽¹⁾	10	[5]	No
Palmitoyl Tetrapeptide-7	100	0.96 ^(a) [6]	Tuftsins [7]

References for NOAELs:

- [1] EFSA Panel on Contaminants in the Food Chain (CONTAM): Scientific Opinion on the abiotic risks for public and animal health of glycerine as co-product from the biodiesel production from Category 1 animal by-products (ABP) and vegetable oils. EFSA Journal 2010; 8(12): 1934.
- [2] 1,3-Butanediol USEPA - HPV Challenge Program Submission- December 17, 2002.
- [3] Cosmetic Ingredient Expert Review Panel (1982) Final Report on the Safety Assessment of Carbomers-934, -910, -934P, -940, -941, and -962. International Journal of Toxicology (1982), Vol. 1, No. 2, pp. 109-141.
- [4] Food Safety Commission (2007) Evaluation Report of Food Additives Polysorbates (Polysorbates 20, 60, 65 and 80).
- [5] To the best of our current knowledge, NOAEL data are not available in literature for this ingredient and can only be determined with animal experimentations. Since 1998 and according to CRODA's policy, has decided not to perform any animal testing on its products (except for other specific regulatory purposes). Palmitoyl GHK (INCI name: Palmitoyl Tripeptide-1) has been worldwide used up to 1000 ppm in several products since 1996 without any complaint concerning its innocuousness.
- [6] Catane *et al*, (1983). Toxicology and antitumor activity of tuftsins, Annals of New York Academy of Science, 419(1), pp. 251-260.
- [7] Veretennikova NI, Chipens GI, Nikiforovich GV, Betinsh YR. (1981) Rigin, another phagocytosis-stimulating tetrapeptide isolated from human IgG. Confirmations of a hypothesis. Int J Pept Protein Res. 17 (4), pp. 430-435.

Product Information File

ACTIVE

Date

July 3rd, 2014

Rev #

0

Signed by:

Brice LECLERC

Regulatory Affairs Manager

A handwritten signature in black ink, appearing to be 'Brice Leclerc', written over a faint rectangular stamp.



Cosmetic

ACTIVE INGREDIENTS

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