

PENTAPHARM SERVICE CENTER COSMETICS

Formulation Guidelines for ALPAFLOR[®] GIGAWHITE[™] (Code no 910-02)

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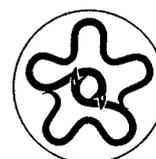
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SUMMARY

ALPAFLOR[®] GIGAWHITE[™] was tested with different groups of raw materials like preservatives, hydrocolloids, sunscreens, commonly used water-soluble substances and various PENTAPHARM actives.

INTRODUCTION

ALPAFLOR[®] GIGAWHITE[™] is a plant-derived, preservative-free, water-soluble, clear, amber-coloured and ready to use solution. ALPAFLOR[®] GIGAWHITE[™] is a skin lightener that significantly reduces the colour and size of age spots.

PENTAPHARM has screened a wide range of common ingredients to test their compatibility with ALPAFLOR[®] GIGAWHITE[™].

The following guideline gives an overview of those raw materials tested and found to be either compatible or incompatible with ALPAFLOR[®] GIGAWHITE[™].

GENERAL RECOMMENDATIONS

- Dosage:** For skin care preparations, concentrations of 3 to 5% ALPAFLOR[®] GIGAWHITE[™] are recommended.
- Processing:** ALPAFLOR[®] GIGAWHITE[™] can be processed either cold or warm (up to 2 hours at 60°C) and is incorporated into the aqueous phase of a cosmetic formulation.
- pH:** The optimal pH for the formulation with ALPAFLOR[®] GIGAWHITE[™] ranges from 3.0 to 5.5.
- Ethanol:** ALPAFLOR[®] GIGAWHITE[™] is compatible with ethanol at concentrations up to 50%.
- Storage:** between 15 and 25°C in the original sealed container, protected from light and in a clean place.



TEST PROCEDURE

The different raw materials were tested with 5% ALPAFLOR® GIGAWHITE™ in aqueous solutions.

The raw materials to be tested were used in concentrations according to the manufacturer's indications. **Should these raw materials be used at other concentrations, we recommend to eventually re-test their stability with ALPAFLOR® GIGAWHITE™.**

The compatibility test was not performed for raw materials whose optimal pH-ranges were too divergent.

The samples were stored at 4°C, room temperature and 40°C. The samples were judged after 1 month and again after 3 months according to the following criteria: pH value, odour, colour, appearance, viscosity.

The results of these compatibility tests are split into three groups:

- **Recommended substances:** without or with very slight turbidity, stable pH value, no odour or colour development, stable viscosity.
- **Compatible substances:** with slight turbidity, stable pH value or slight variation, no odour or colour development, stable viscosity.
- **Substances with limited compatibility:** high turbidity, and/or unstable pH value, and/or odour or colour development, and/or unstable viscosity.

However, if these substances with limited compatibility are used with ALPAFLOR® GIGAWHITE™ in an emulsion or/and in lower concentration, improved compatibility might result.



PRESERVATIVES

RECOMMENDED PRESERVATIVES

Product Name / Supplier	% Wt.	INCI Name
Nipastat Sodium / Nipa	0.1	Methylparaben, Butylparaben, Ethylparaben, Propylparaben
Phenoxyetol / Nipa	1.0	Phenoxyethanol
Nipaguard PDU / Nipa	0.5	Diazolidinyl Urea
Unicide U-13 / Lipo	0.6	Imidazolidinyl Urea
Glydant 2000 / Lonza	0.4	DMDM Hydantoin
Isocil PC / Lonza	0.1	Methylchloroisothiazolinone, Methylisothiazolinone
Glycacil 2000 / Lonza	0.8	Iodopropynyl Butylcarbamate
Benzyl Alcohol / VWR	1.0	Benzyl Alcohol
Benzoic Acid / VWR	0.2	Benzoic Acid

With ALPAFLOR[®] GIGAWHITE[™], these preservatives formed stable aqueous solutions without turbidity.

COMPATIBLE PRESERVATIVES

Product Name / Supplier	% Wt.	INCI Name	Observations
Potassium Sorbate / CFS-Schweizerhall	0.5	Potassium Sorbate	Slight coloration at 40°C
Geogard 221 / Lonza	0.8	Dehydroacetic Acid (and) Benzyl Alcohol	Slight coloration at 40°C
Irgasan DP300 / Ciba	0.3	Triclosan	Slight coloration

PRESERVATIVES WITH LIMITED COMPATIBILITY

Product Name / Supplier	% Wt.	INCI Name	Observations
Spectradyne / Lonza	0.3	Chlorhexidine Digluconate	Precipitate



HYDROCOLLOIDS

RECOMMENDED HYDROCOLLOIDS

Product Name / Supplier	% Wt.	INCI Name
Pemulen TR-1 / Noveon	1.0	Acrylates / C10-30 Alkyl Acrylate Crosspolymer
Natrosol 250 HHX / Hercules	2.5	Hydroxyethyl Cellulose
Sepigel 305 / Seppic	3.0	Polyacrylamide (and) C13-14 Isoparaffin (and) Laureth-7
Structure XL / National Starch	5.0	Hydroxypropyl Starch Phosphate

These hydrocolloids formed stable gels with ALPAFLOR® GIGAWHITE™.

COMPATIBLE HYDROCOLLOIDS

Product Name / Supplier	% Wt.	INCI Name	Observations
Keltrol RD / Kelco	3.0	Xanthan Gum	Slight pH decrease at 40°C

HYDROCOLLOIDS WITH LIMITED COMPATIBILITY

Product Name / Supplier	% Wt.	INCI Name	Observations
Carbopol ETD 2001 / Noveon	0.5	Carbomer	Viscosity decrease
Stabileze QM / ISP	0.5	PVM/MA Decadiene Crosspolymer	Viscosity decrease
Aristoflex AVC / Clariant	1.0	Ammonium Acryloyldimethyltaurate / VP Copolymer	Viscosity decrease

DETERGENTS

RECOMMENDED DETERGENTS

Product Name / Supplier	% Wt.	INCI Name
Genapol LRO liquid / Clariant	20.0	Sodium Laureth Sulfate
Tego Betain F / Degussa	20.0	Cocamidopropyl Betain
Rewopol SB FA 30 / Rewo	20.0	Disodium Laureth Sulfosuccinate
Rewoteric AMCAS / Rewo	20.0	Cocamidopropyl Hydroxysultaine
Rewoteric AM2CNM / Rewo	20.0	Disodium Cocoamphodiacetate

With ALPAFLOR® GIGAWHITE™, these detergents formed stable solutions, without turbidity.



DETERGENTS WITH LIMITED COMPATIBILITY

Product Name / Supplier	% Wt.	INCI Name	Observations
Plantacare 2000 UP / Cognis	20.0	Decyl Glucoside	Precipitate

MISCELLANEOUS SUBSTANCES

RECOMMENDED MISCELLANEOUS SUBSTANCES

Product Name / Supplier	% Wt.	INCI Name
D-Panthenol 50P	2.0	Panthenol
EDTA	0.1	EDTA
Glycerin 86.5%	20.0	Glycerin
Propylene Glycol	20.0	Propylene Glycol
1,3-Butandiol	20.0	Butylene Glycol
Cremophor RH 410	5.0	PEG-40 Hydrogenated Castor Oil
Glycine	2.0	Glycine
L-Glutamic Acid	2.0	Glutamic Acid
Lactic Acid	2.0	Lactic Acid
Citric Acid	2.0	Citric acid

These miscellaneous substances formed stable, clear to very slightly turbid solutions with ALPAFLOR® GIGAWHITE™.

COMPATIBLE MISCELLANEOUS SUBSTANCES

Product Name / Supplier	% Wt.	INCI Name	Observations
Sodium Metabisulfite	0.1	Sodium Metabisulfite	Slight pH decrease
EDG Plus	5.0	Ethoxydiglycol	Slight pH decrease at 40°C
Glycolic Acid	2.0	Glycolic Acid	Slight turbidity at 40°C

MISCELLANEOUS SUBSTANCES WITH LIMITED COMPATIBILITY

Product Name / Supplier	% Wt.	INCI Name	Observations
L-Lysine	2.0	Lysine	Precipitate



PENTAPHARM ACTIVES

RECOMMENDED PENTAPHARM ACTIVES

Product Name	Product Code	% Wt.	INCI Name
ALPAFLOR [®] NECTAPURE	911-02	5.0	Glycerin, Water, Buddleja davidii Extract, Thymus vulgaris (Thyme) Extract
ALPHA-ARBUTIN	336-01	2.0	Alpha-Arbutin
CEPHALIPIN	293-01	5.0	Cephalins, Disodium Cocoamphodiacetate
HYASOL-BT	296-04	5.0	Sodium Hyaluronate
MELFADE [®] -J	308-02	5.0	Water, Arctostaphylos Uva Ursi Leaf Extract, Glycerin, Magnesium Ascorbyl Phosphate
PENTACARE-HP	305-02	5.0	Water, Ceratonia Siliqua Gum, Hydrolyzed Casein
PENTACARE-NA	319-01	5.0	Hydrolyzed Wheat Gluten, Ceratonia Siliqua Gum
PENTAGLYCAN	181-01	5.0	Glycosaminoglycans
PENTAVITIN [®]	180-01	5.0	Saccharide Isomerate
PHYTALURONATE [®]	298-01	5.0	Ceratonia Siliqua Gum
REVITALIN [®] -BT	291-01	5.0	Glycoproteins
SERICIN	303-02	5.0	Sericin

These water-soluble PENTAPHARM actives formed stable, clear solutions with ALPAFLOR[®] GIGAWHITE™.

COMPATIBLE PENTAPHARM ACTIVES

Product Name	Product Code	% Wt.	INCI Name	Observations
ALPAFLOR [®] EDELWEISS GC	900-01	5.0	Leontopodium Alpinum Extract	Slight coloration at 40°C
IMMUCELL [®]	302-01	5.0	Glycoproteins	Slight turbidity
SETAKOL [®]	320-01	5.0	Hydrolyzed Sericin	Slight pH decrease

With ALPAFLOR[®] GIGAWHITE™, these water-soluble PENTAPHARM actives formed solutions that developed a slight turbidity or a slight pH variation during the stability tests.



PENTAPHARM ACTIVES WITH LIMITED COMPATIBILITY

Product Name	Product Code	% Wt.	INCI Name	Observations
COLHIBIN	801057	5.0	Hydrolyzed Rice Protein	Precipitate
DISMUTIN [®] -BT	313-01	1.0	Superoxide Dismutase	Decrease of SOD activity
LACTOMIDE	309-01	5.0	Milk Lipids, Ceramide 3	Precipitate
MELAWHITE [®]	282-01	5.0	Leukocyte Extract, Water	Precipitate
PEPHA [®] -NUTRIX	800272	5.0	Colostrum Whey	Precipitate
PEPHA [®] -TIGHT	800356	5.0	Algae Extract, Pullulan	Precipitate
PEPHA [®] -TIMP	800420	5.0	Human Oligopeptide-20	Precipitate
SYN [®] -COLL	800421	5.0	Glycerin, Palmitoyl Tripeptide-5	Precipitate

The compatibility test was not performed for Pentapharm active ingredients whose optimal pH-ranges were too divergent from each other (EASHAVE, ELHIBIN[®], FITOBROSIDE, IRICALMIN, PREREGEN[®], REGU[®]-AGE).

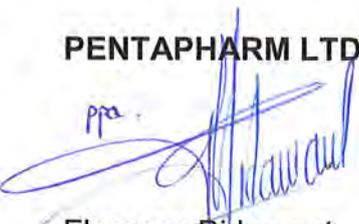
DISCUSSION

ALPAFLOR[®] GIGAWHITE[™] is easy to formulate in gels, cream gels and emulsions.

Some of the tested substances showed a limited compatibility in aqueous solution with ALPAFLOR[®] GIGAWHITE[™]. This does not necessarily mean that they cannot be used in combination with ALPAFLOR[®] GIGAWHITE[™] in emulsions: the formula and/or the concentrations have to be carefully evaluated in detail to ensure the stability of the product.

We are open to discuss any questions connected with the formulation of ALPAFLOR[®] GIGAWHITE[™] and any additional information to these guidelines would be welcome.

PENTAPHARM LTD.


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Cosmetic Application

SKIN WHITENING FORMULATION - IN VIVO STUDY (ALPAFLOR® GIGAWHITE™)

Description This formulation was developed for the in vivo skin lightening study with GIGAWHITE™. The formulation is enhancing the activity and should be considered to guarantee the performance. A UV-filter formulation should be applied for an adequate UV-protection.

Item	Ingredients	INCI Name	% w/w	Suppl.
1	A) Brij 721	Steareth-21	5.60	5
2	Brij 72	Steareth-2	1.90	5
3	Cetyl Alcohol	Cetyl Alcohol	3.00	
4	Oleic acid	Oleic acid	6.00	
5	Paraffin Oil	Mineral Oil	7.00	
6	Isopropyl Myristate	Isopropyl Myristate	7.00	
7	Trivalin SF	Ethoxydiglycol	5.00	70
8	B) Deionized Water	Water	54.00	
9	C) Propylene Glycol	Propylene Glycol	5.00	
10	Phenonip	Phenoxyethanol, Methylparaben, Ethylparaben, Butylparaben, Propylparaben, Isobutylparaben	0.50	11
11	D) ALPAFLOR® GIGAWHITE™	Water, Glycerin, Malva Sylvestris (Mallow) Extract, Mentha Piperita (Peppermint) Leaf Extract, Primula Veris Extract, Alchemilla Vulgaris Extract, Veronica Officinalis Extract, Melissa Officinalis Leaf Extract, Achillea Millefolium Extract	5.00	1

Procedure

Heat the ingredients of fatty phase A) to 70°C.
 Heat the ingredients of water phase B) to 75°C.
 Under stirring add phase B) to phase A), cool to 50°C, homogenize and cool to 30°C.
 Finally incorporate phases C) and D) one after the other and stir cold.

Suppliers

- 1) PENTAPHARM, CH
- 5) Uniqema, B
- 11) Nipa Laboratories, GB
- 70) Trivent Chem. Co., USA

We recommend to adjust the formulation and manufacture to the local conditions, to the raw materials available and to the current patent situation. Although this formulation has been designed with utmost care, we cannot assume any responsibility.



Cosmetic Application

SKIN WHITENING LOTION (ALPAFLOR® EDELWEISS GC / ALPAFLOR® GIGAWHITE™ / ALPHA-ARBUTIN / DISMUTIN®-BT / PENTAVITIN®)

Description This light lotion is formulated with PENTAPHARM's powerful whitening actives ALPHA-ARBUTIN and GIGAWHITE™. DISMUTIN®-BT and EDELWEISS GC protect the skin from harmful environmental influences and PENTAVITIN® has moisturizing properties.

Item	Ingredients	INCI Name	% w/w	Suppl.
1	A) Tego Care PS	Methyl Glucose Sesquistearate	3.00	6
2	Brij 700	Steareth-100	0.50	64
3	Cetyl Alcohol	Cetyl Alcohol	2.00	
4	Tegosoft MM	Myristyl Myristate	3.00	6
5	Tegosoft OP	Ethylhexyl Palmitate	3.50	6
6	Tegosoft liquid	Cetearyl Ethylhexanoate	5.50	6
7	Dow Corning 2-1184 Fluid	Dimethicone, Trisiloxane	4.00	16
8	Dow Corning 345 Fluid	Cyclomethicone	1.50	16
9	Tinosorb OMC	Ethylhexyl Methoxycinnamate	2.00	35
10	B) Water	Aqua	63.90	
11	ALPHA-ARBUTIN	Alpha-Arbutin	0.20	1
12	Glycerin	Glycerin	5.00	
13	Preservative	[q.s.]		
14	C) Tinosorb M	Methylene Bis-Benzotriazolyl Tetramethylbutylphenol	2.00	35
15	D) ALPAFLOR® GIGAWHITE™	Water, Glycerin, Malva Sylvestris (Mallow) Extract, Mentha Piperita (Peppermint) Leaf Extract, Primula Veris Extract, (etc...)	1.00	1
16	PENTAVITIN®	Saccharide Isomerase	1.00	1
17	DISMUTIN®-BT	Superoxide Dismutase	0.10	1
18	ALPAFLOR® EDELWEISS GC	Leontopodium Alpinum Extract	0.50	1
19	Dry Flo AF	Corn Starch Modified	1.00	103
20	E) Lactic Acid	Lactic Acid	0.30	

Procedure

Heat phases A) and B) separately to 75°C.
 Add phase A) to phase B). Homogenise.
 Add phase C) under stirring.
 At approx. 30°C, add ingredients of phases D) one after the other and mix to obtain a homogeneous lotion.
 Adjust the pH at approx. 5.0 with phase E).

Suppliers

- | | |
|----------------------------|---------------------------|
| 1) PENTAPHARM, CH | 64) Uniqema, B |
| 6) Degussa, GER | 103) National Starch, USA |
| 16) Dow Corning, USA | |
| 35) Ciba Specialty Ch., CH | |

We recommend to adjust the formulation and manufacture to the local conditions, to the raw materials available and to the current patent situation. Although this formulation has been designed with utmost care, we cannot assume any responsibility.