94289 - CAFFEINE

1. IDENTIFICATION OF THE SUBSTANCE OR PREPARATION.

1.1 Identification of the substance or preparation.

Name: Caffeine
Bulk code: 94289
Valid from batch: 130822

1.2 Synonyms.

Caffeine anhydrous

2. DESCRIPTION

Appearance: crystalline powder or silky crystals
Color: white
Smell: Odorless
Origin: Chemical synthesis
Geographical origin: China

3. COMPOSITION/INFORMATION OF THE COMPONENTS.

Ingredients: Caffeine (≥98.5%)

Chemical name: 1, 3, 7-Trimethyl-3, 7-dihydro-1H-purine-2, 6-dione
Formula: $C_8H_{10}N_4O_2$
Molecular weight: 194.19 g/mol
CAS No: 58-08-2
CE No.: 200-362-1
Index No.: 613-086-00-5

4. PHYSICAL-CHEMICAL DATA.

For more detailed information, please refer to the analysis bulletin.

Solubility: Caffeine is sparingly soluble in water (20 g/L), soluble in boiling water, slightly soluble in ethanol and ether.

5. PROPERTIES/USES.

Active pharmaceutical ingredient.
Cosmetic active ingredient.
Food use.

As a pharmaceutical active ingredient:
It is the xanthine base with the greatest stimulating power of the CNS, acting first on the cerebral cortex, then on the bulb and finally on the spinal cord. Its mechanism of action is related to its capacity to inhibit the enzyme phosphodiesterase , which results in an increase in cAMP ; at low doses it antagonizes adenosine receptors .
It produces cardiac stimulation (positive inotropic effect) and reduction of peripheral arteriolar resistance , which compensates for its effects on blood pressure. At the cerebral level, it produces vasoconstriction, which is why its use as an antimigraine has been suggested . It stimulates skeletal muscles and respiratory control, increases gastric acid secretion and diuresis.
It is administered orally and rectally in the treatment of depressive states and mental fatigue, bronchial asthma, heart failure and headaches.

Topically, it has a local action without systemic effect, acting on the lipolysis of adipose tissue by inhibiting the enzyme phosphodiesterase . It is also used in atopic dermatitis.

As a cosmetic active ingredient:
It is used as a skin conditioning agent and as a perfumer .

6. DOSAGE.

As an active pharmaceutical ingredient:

- Oral route:
    - Treatment of asthenia: 50-100 mg every 6 hours, which may be increased depending on the clinical response up to a maximum of 1200 mg daily.
    - Associated with analgesics with acetylsalicylic acid , paracetamol or codeine in doses of 30-65 mg.
- Topical route:
    - Up to 30% for master formulation in atopic dermatitis therapies.

As a cosmetic active ingredient:

- Maximum quantity calculations should be based on the NOAEL data established by ECHA. (https://echa.europa.eu/es/brief-profile/-/briefprofile/100.000.329).

7. OBSERVATIONS.

The documentation corresponding to the regulatory part of the product that is available for it is the one reflected below.

The product has been handled in a NON-sterile room, therefore the product is NOT sterile.

NUTRITIONAL INFORMATION:

Energy / Nutrient	**Unit**	**Typical values per 100 g product**
Energy (total calories) -Energy from fat	Kcal or kJ Kcal or kJ	0
Protein	g	0
Carbohydrate (total), of which: -sugars -Polyols -starch	g g g g	0
Fat (total), of which: -Saturates -mono-unsaturates -polyunsaturates -Trans-fats -Cholesterol	g g g g g mg	0
Dietary Fibre	g	0
Sodium	mg	0
Potassium	mg	0
Calcium	mg	0
Ash	g	0
Moisture	g	0
Vitamin A	ug	0
Vitamin B	mg	0
Vitamin C	mg	0
Vitamin D	IU	0
Vitamin E	IU	0

ALLERGENS:

- Food allergens: The product does not contain the ingredients listed in Annex II of Regulation (EU) No 1169/2011 as follows:

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Allergens	Added as a base raw material or in a derivative form		Cross contamination(1)	
	Yes	No	Yes	No
Cereals containing gluten (i.e. wheat, rye, barley, oats, spelt, kamut or their hybridised strains) and products thereof, except (*): (a) wheat-based glucose syrups including dextrose ; (b) wheat-based maltodextrins ; (c) glucose syrups based on barley; (d) Cereals used for making distillates or ethyl alcohol of agricultural origin for spirit drinks and other alcoholic beverages.		No		No
Crustaceans and products thereof.		No		No
Eggs and products thereof.		No		No
Fish and products thereof, except (*): (a) Fish gelatine used as carrier for vitamin or carotenoid preparations; (b) Fish gelatine or Isinglass used as fining agent in beer and wine.		No		No
Peanuts and products thereof.		No		No
Soybeans and products thereof, except (*): (a) fully refined soybean oil and fat (And products thereof, insofar as the process that they have undergone is not likely to increase the level of allergenicity assessed by the EFSA for the relevant product from which they originated) (b) natural mixed tocopherols (E306), natural D-alpha tocopherol, natural D-alpha tocopherol acetate, natural D-alpha tocopherol succinate from soybean sources; (c) vegetable oils derived phytosterols and phytosterol esters from soybean sources; (d) plant stanol ester produced from vegetable oil sterols from soybean sources.		No		No
Milk and products thereof (including lactose), except (*): (a) whey used for making distillates or ethyl alcohol of agricultural origin for spirit drinks and other alcoholic beverages; (b) lactitol.		No		No

Allergens	Added as a base raw material or in a derivative form		Cross contamination(1)	
	Yes	No	Yes	No
Nuts, i.e. almonds (Amygdalus communis L.), hazelnuts (Corylus avellana), walnuts (Juglans regia), cashews (Anacardium occidentale), pecan nuts (Carya illinoiesis (Wangenh.) K. Koch), Brazil nuts (Bertholletia excelsa), pistachio nuts (Pistacia vera), macadamia nuts and Queensland nuts (Macadamia ternifolia), and products thereof, except (*): (a) nuts used for making distillates or ethyl alcohol of agricultural origin for spirit drinks and other alcoholic beverages.		No		No
Celery and products thereof.		No		No
Mustard and products thereof.		No		No
Sesame seeds and products thereof.		No		No
Sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre expressed as SO2.		No		No
Lupin and products thereof.		No		No
Molluscs and products thereof.		No		No

(1) Risk of cross contamination, may have traces.

LIFE :

4 years. For more detailed information, please consult the analysis bulletin.

STORAGE:

Store at room temperature (25±2ºC), in a cool, dry place, protected from light and with the container tightly closed.

LEGAL REQUIREMENTS:

The product complies with:

- Regulation (EU) No 231/2012 and its amendments.
- The manufacturer's primary objective is to ensure that its products and services meet the quality and safety requirements required by the various applicable legislations. This has led them to develop an integrated Quality Management System implemented in accordance with the activities carried out by the company and based on the application of Good Practices, taking the necessary measures to prevent fraud and adulteration, ensuring quality, efficacy and safety throughout the supply chain to the customer. The requirements of Regulation (EC) No. 178/2002 of the EU (General Food Legislation) and Regulation (EC) No. 852/2004 (Hygiene, HACCP system) have been established and are carried out in accordance with them and with the relevant national legislation, as appropriate. The manufacturer's HACCP system, based on the principles of Codex Alimentarius evaluates all possible physical, chemical and biological hazards throughout the supply chain.
- The “Plan for the control of allergens and substances that cause food intolerance” is included in the prerequisite program of said HACCP system, in compliance with Regulation (EU) No. 1169/2011 on food information provided to consumers.

BSE/TSE:

The product does not contain ingredients of ruminant origin or materials derived from or exposed to ruminants affected or under quarantine for Transmissible Spongiform Encephalopathy (TSE)/Bovine Spongiform Encephalopathy (BSE) and complies with EU legislation 999/2001.

GMO:

The product or any of its ingredients:

- They are non-GMO and do not contain any GMOs or any GMOs used in their production.
- The ingredients we supply do not require any mention of GMO on their labelling, according to Regulation (EC) No. 49/2000 of the Commission dated 10 January, and (ECC) No. 1829/2003 and (ECC) No. 1830/2003 of the European Parliament and of the Council.
- This product has not been genetically modified so there is no obligation to label GMO as defined by the aforementioned standards.

NANOMATERIALS:

According to the definition of " nanomaterials " in EU Regulation (EU) No. 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, the manufacturer indicates that no nanomaterials are used in the formulation or in the packaging material of the product.

RADIATION:

The product has not been sterilized by ionizing radiation at any point during the entire manufacturing process and therefore fully complies with the relevant legal regulations (Directive 1999/2/EC).
The product has not been irradiated or ionized.

ETHYLENE OXIDE:

The manufacturer does not use ethylene oxide (ETO), 2-Chloroethanol or any other chemical sterilizing agent during the manufacture, storage or transportation of the product.

Furthermore, it does not allow the use of ethylene oxide (ETO), 2-chloroethanol or any other chemical sterilizing agent by subcontractors involved in manufacturing, storage and transportation.

PESTICIDES:

Based on the knowledge of the production process, raw materials and equipment used, the possible pesticide residues in the above mentioned product comply with the European Legislation on pesticide residues, esp . Regulation (EC) No. 149/2008 and Regulation (EU) 2015/868 of 26 May 2015 amending Annexes II, III and V of Regulation (EC) No 396/2005.

RESIDUAL SOLVENTS:

The product complies with Directive E 2010/59/EU of 26 August 2010 amending Directive 2009/32/EC of the European Parliament and of the Council on the approximation of the laws of the Member States on extraction solvents used in the production of food and food ingredients. RD1101/2011

CONTAMINANTS/IMPURITIES:

Based on actual knowledge of the production process, raw materials and equipment used we do not expect any contaminants of dioxins, melamine , polycyclic aromatic hydrocarbons (PAH) and biphenyls. polychlorinated bicarbonate (PCB) in the product. (REGULATION (EU) 2023/915).

Based on the knowledge of the production process, raw materials and equipment used, the manufactured product meets the following requirements:

- REGULATION (EC) No- 1881/2006 and subsequent amendments as regards the maximum permitted level of the following pollutants:
  - Aflatoxin B1 <5ppb
  - Aflatoxins B1 + B2 + G1 + G2 <10ppb
  - Ochratoxin A <15ppb
  - Melamine
  - Dioxins
- REGULATION (EC) No 1933/2015 amending Regulation (EC) No 1881/2006 as regards maximum levels for polycyclic aromatic hydrocarbons , in particular:
  - Maximum level of 10 µ g /kg of benzo (a) pyrene
  - 50 µ g /kg for the sum of PAH4 (PAH4; benzo [a] pyrene , chrysene , benzo [a]anthracene and benzo [b] fluoranthene) in food supplements

Nitrosamines : Due to the manufacturing process, NMDA is either absent or below the detection limit in the product. Current in-process controls are sufficient for the manufacturing process, so detection of NDMA could be omitted from routine controls.

HEAVY METALS:

- Pb: <3.0 ppm
- Cd: <1.0 ppm
- Hg: <0.1ppm
- As: <1.0 ppm
- Heavy metals less than 10 ppm

VEGAN/VEGETARIAN:

The product is suitable for vegan/vegetarian use.

TESTED ON ANIMALS:

The above product has not been tested on animals at any stage of the manufacturing process, in line with the vegan philosophy and in line with Regulation (EU) No 211/2011 and any decisions adopted following EU Decision 2018/1701.

WADA:

According to the current World Anti-Doping Agency list, the ingredient is not a doping substance and is not a combination of doping substances. The ingredient does not contain any doping substances. The ingredient is not the result of a doping substance.

8. BIBLIOGRAPHY:

Pharmaceutical Monographs. COF Alicante, 1998.
" Martindale . The Extra Pharmacopoeia ". 30th Edition . Ed. The Pharmaceutical Press . London. (1993).
https://echa.europa.eu/es/brief-profile/-/briefprofile/100.000.329