

9892-CAPSUCEL EXCIPIENT FOR CAPSULES**1. IDENTIFICATION OF THE SUBSTANCE OR PREPARATION****1.1. Identification of the substance or preparation**

Name: Capsucel excipient for capsules

Bulk code: 9892

Internal code: 405520

Valid from lot: 0129767

1.2. Synonyms

Microcrystalline cellulose

2. DESCRIPTION.

Appearance: Fine powder

Color: White

Smell: No smell

Origin: Purified wood pulp. Pine and fir trunks are used. It is natural, and no artificial or synthetic ingredients are used.

Geographical origin: China.

3. COMPOSITION/INFORMATION OF COMPONENTS.

microcrystalline cellulose .

Formula: $(C_6H_{10}O_5)_n$

CAS: 9004-34-6

Ce: 232-674-9

INCI: Microcrystalline cellulose

Method of production: Capsucel consists of purified, partially depolymerized microcrystalline cellulose prepared by alpha cellulose treatment, obtained as pulp from fibrous plant material, with acidic minerals. In the manufacturing process, acid hydrolysis of cellulose in wood pulps is performed with nitric acid. After hydrolysis, process water (in the form of reverse osmosis water) together with ammonia water are used to wash and neutralize the residual acid in the product. The water washes and removes the hemicellulose from the hydrolysis and the nitrate salt generated in the neutralization process. The nitric acid spent after being filtered and reinforced is recycled for reuse. The product is then dried and sieved before being analyzed.

4. PHYSICAL-CHEMICAL DATA.

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

Solubility: The product is practically insoluble in water, acetone, ethanol, toluene, dilute acids and in 5% sodium hydroxide solution.

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Slightly hygroscopic

5. PROPERTIES/USES.

Excipient for pharmaceutical use.

Oral use.

Not valid for the production of food supplements or foods.

Capsucel can be used both in the production of capsules and in direct compression in the manufacture of tablets, due to its excellent rheological properties .

6. DOSAGE.

No data available.

7. OBSERVATIONS.

STORAGE:

Store at room temperature ($25 \pm 2^\circ\text{C}$) in a cool, dry place, protected from light, with the container tightly closed, in dry and ventilated places.

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

BSE/TSE:

The product complies with the Note for guidance on minimising the risk of transmission of animal spongiform encephalopathy agents via human and veterinary medicinal products (EMA/410/01 Rev. 3 – July 2011).

No animal materials are used in the manufacture of the above mentioned product, neither during manufacturing nor other processes. Lubricants and cleaning agents are BSE/TSE free.

The product does not come into contact with animal products either during storage or during transport.

Therefore, the product is BSE/TSE free.

GMO:

No GMO additives are used in the plantation of the wood from which the cellulose is obtained.

Furthermore, no additives are used in our manufacturing process, whether GMO or originating from GMO. Therefore, it does not need to be labelled under the GMO labelling rules according to Directive 2001/18/EC, Regulation EC 1829/2003 and Regulation EC 1830/2003.

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CMR:

The product is not a CMR substance.

NANOMATERIALS:

The product is not considered a nanomaterial as defined in Recommendations 2011/696/EU, point 2, the definition of engineered nanomaterial listed in Regulation (EU) 1169/2011, Article 2 Definitions, point 2 (t), and Regulation (EU) 2015/2283, Article 3 Definitions, point 2 (f). No nanotechnology is used in the manufacturing process.

RADIATION:

The product complies with EC Regulations on radioactivity and irradiation. The product has not been treated with ionizing radiation during the manufacturing process.

ETHYLENE OXIDE:

The product does not contain ethylene oxide in accordance with Regulation (EU) No 2015/868 amending Annexes II, III and V to Regulation (EC) No 396/2005 and of the Council as regards maximum residue levels for ethylene oxide. Ethylene oxide is not used at all in the production of microcrystalline cellulose or in the production of raw materials used for microcrystalline cellulose , nor in storage or transport, nor in any treatment such as sterilisation performed with ethylene oxide or ethanol.

PESTICIDES:

The product complies with Regulation 839/2008 on pesticides in foodstuffs and with Regulation (EC) No 396/2005 which sets maximum levels of pesticides.

RESIDUAL SOLVENTS:

No organic solvents are used in the manufacturing process. Only water is used throughout the entire process. The product complies with ICH Q3C (R6) Guideline on impurities: Guideline for Residual Solvents (dated July 22, 2019), General Monographs 5.4 Residual Solvents of the current EP and General Chapter <467> Residual Solvents of the current USP/NF, official as of December 1, 2020.

CONTAMINANTS/IMPURITIES:

- Aflatoxins : The product is free of aflatoxins .
- Nitrosamines : Nitric acid is used during the manufacturing process and the product has therefore been assessed according to CMDh /404/2019, EMA/189634/2019 and EMA/217823/2019. The criteria assessed are listed below:
 1. Purified wood pulp as raw material is used in the manufacture of the product.
 2. In the manufacturing process, nitric acid is the reagent used in hydrolysis. In the neutralization process, water is used to wash away the nitrate salt and hemicellulose , and ammonia water is used to neutralize the residual acid in the final product.

Prior to the neutralization process, the nitric acid reagent used in the hydrolysis process is separated, filtered and recycled. There is no risk of cross contamination with other agents.

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Residual nitric acid from the hydrolysis process and nitrate salts generated in the neutralization process are found at negligible levels, if present at all, in the final product. Therefore, the potential to act as nitrosating agents is low.

nitrosatable substances [e.g. secondary amines (cyclic and acyclic), tertiary amines (cyclic and acyclic), N- methylmorpholine (NMM), tributylamine (TBA), hydrazine derivatives , N-methyl-2-pyrrolidinone, N- chloroalkylamines , N- alkylcarbamates , any tertiary amides (cyclic and acyclic), or any other amide-type solvents] used or present in the process.

Given the absence of nitrosatable substances and the low probability of the presence of nitrosating agents in CAPSUCEL, it is concluded that there is a low risk of N- nitrosamine impurities in the product.

- The product complies with current Regulation 1881/2006 on contaminants in food and food categories:
 - o Nitrates
 - o Mycotoxins
 - o Dioxins
 - o PCBs
 - o 3MCPD
 - o PAH
- Melamine : Melamine is not used in the manufacturing process and is not intentionally added so it is not expected to be present.
- ICHQ3D: The product complies with the elemental impurity limits <232> of the US Pharmacopeia, EMEA/CHMP/SWP/4446/2000, Guideline on specification limits for residues of metal catalysts or metal reagents, European Pharmacopoeia 5.20 Metal catalysts or metal reagent residues, ICH Q3D Guideline for Elemental Impurities and Implementation of ICH Q3D in the Certification Procedure (PA/PH/CEP (16) 23, August 2016) Annex I.

Element	Classes	Added intentionally	Conclusion (maximum level)	Analytical result
CD	1	No	<0.15 ppm	Not detected
Pb	1	No	<0.15 ppm	Not detected
Ace	1	No	<0.45 ppm	Not detected
Hg	1	No	<0.9 ppm	Not detected
Co	2A	No	<1.5 ppm	Not detected

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V	2A	No	<3 ppm	Not detected
Neither	2A	No	<6 ppm	0.0249
TI	2B	No	<0.24 ppm	Not detected
Au	2B	No	<3 ppm	Not detected
P.S	2B	No	<3 ppm	Not detected
Go	2B	No	<3 ppm	Not detected
You	2B	No	<3 ppm	Not detected
Rh	2B	No	<3 ppm	Not detected
Ru	2B	No	<3 ppm	Not detected
HE	2B	No	<4.5 ppm	Not detected
Ag	2B	No	<4.5 ppm	Not detected
Pt	2B	No	<3 ppm	Not detected
Li	3	No	<16.5 ppm	Not detected
Sb	3	No	<36 ppm	Not detected
Ba	3	No	<42 ppm	0.121
Mo	3	No	<90 ppm	Not detected
Cu	3	No	<90 ppm	Not detected
Sn	3	No	<180 ppm	Not detected
Cr	3	No	<330 ppm	0.0327

- The product is manufactured without the use of the following products, nor does it come into contact with them either during storage or during transport:

1	Acetonitrile	13	Di(2-ethylhexyl) phthalate (DEHP)
2	Aspirin	14	Phenylalanine
3	Benzene	15	Phenylenediamine
4	Benzoic acid	16	Phthalates
5	Benzopyrens	17	Polychlorinated biphenyls (PCB)
6	Citric acid	18	Polycyclic aromatic hydrocarbons (PAHs)
7	Diethylene glycol	19	Polyvinyl chloride (PVC)
8	Propylene glycol	20	Sorbic acid
9	Dioxin	21	Sulfur Dioxide

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10	Iodine	22	Sulphite
11	Parabens (E211-E219)	23	Vanillin
12	Peroxides		

The product is also free of:

1	Alginates	15	Heparin
2	Artificial colors	16	Histamine
3	Artificial flavors	17	Hormone
4	Caramel Pigment	18	Inulin
5	Casein	19	Lactose
6	Citrus	20	Latex
7	Dextrin	21	Sorbitol
8	Dextrose	22	Starch
9	Fructose	23	Sucrose
10	Gelatin	24	Sugar alcohols
11	Glucose	25	Soy
12	Glutamate	26	Tartrazine (FD&C Yellow No. 5 - E102)
13	Gluten	27	Wheat
14	Glycerin	28	Yeast

HEAVY METALS:

The product complies with current Regulation 1831/2003 on contaminants in food and food categories. (Pb < 10ppm).

ALLERGENS:

- **Food allergens:** The product complies with EU Regulation No. 1169/2011 and is free of the following allergens corresponding to Annex II of the aforementioned legislation:
 - Cereals containing gluten, namely: wheat, rye, barley, oats, spelt, kamut or their hybrid strains, and derived products.
 - Crustaceans and derived products.
 - Eggs and derived products.
 - Fish and derived products.
 - Peanuts and derived products.
 - Soybeans and derived products ..
 - Milk and milk products (including lactose).
 - Nuts, namely: almonds (Amygdalus communis L.), hazelnuts (Corylus avellana), walnuts (Juglans regia), cashews (Anacardium Occidentale), pecans (Carya illinoensis (Wangenh .) K.

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Koch), Brazil nuts (Bertholletia excelsa), pistachios (Pistacia vera), macadamia or Queensland nuts (Macadamia ternifolia), and derived products.

- Celery and derived products.
- Mustard and derived products.
- Sesame seeds and derived products.
- Sulfur dioxide and sulfites in concentrations greater than 10 mg/kg or 10 mg/liter in terms of total SO₂.
- Lupine and derived products.
- Molluscs and derived products.

HALAL:

The product is HALAL certified.

KOSHER:

The product is KOSHER certified.

VEGAN/VEGETARIAN:

The product does not contain any animal products, making it suitable for vegan-vegetarian consumption.

NUTRITIONAL INFORMATION:

Item	Unit	Result
Calories	Kcal/100g	200.1
Proteins	g/100g	0.2
Fats	g/100g	0.3
- Saturated fatty acids	g/100g	Not detected
- Trans fatty acids	g/100g	Not detected
Cholesterol	mg/100g	Not detected
Carbohydrates	g/100g	98.3
- Sugars	g/100g	Not detected
- Dietary fiber	g/100g	98.3
Sodium	mg/100g	2.2
Humidity	g/100g	1.2
Ashes	g/100g	Not detected

TESTED ON ANIMALS:

The product has not been tested on animals.

PALM OIL:

The product is free of palm oil.

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The product is exempt from CITES cataloging because it is not a product manufactured under the Convention on International Trade in Endangered Species of Wild Fauna and Flora.

REACH:

Exempt.

TARIFF ITEM:

39129090.