



GUINAMA. Laboratory distributor of raw materials for the pharmaceutical and cosmetics industries.

Type of document:

TECHNICAL DATA SHEET

Review date:

14.09.2022

Version:

7.0

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

1.2. Synonyms

Microcrystalline cellulose

2. DESCRIPTION

Appearance: Fine powder.

Colour: White

Odour: Odourless.

Flavour: Flavourless.

Origin: Purified wood pulp. The trunk of the pine and spruce is used. It is natural, and no artificial or synthetic ingredients are used.

Geographical origin: China.

3. COMPOSITION/INFORMATION ON COMPONENTS

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

CAS: 9004-34-6

INCI: Microcrystalline cellulose

Components: Microcrystalline cellulose

Method of production:

CAPSUCEL consists of purified, partially depolymerised microcrystalline cellulose prepared by treating alpha cellulose, obtained as a pulp from fibrous plant material, with mineral acids. In the manufacturing process, the acid hydrolysis of cellulose in wood pulps is performed with nitric acid. After hydrolysis, the process water (in the form of reverse osmosis water) together with the ammonia water, are used to wash and neutralise the residual acid in the product. The water washes and removes the hemicellulose from the hydrolysis and the nitrate salt generated in the neutralisation process. After being filtered and reinforced, the used nitric acid is recycled for reuse. The product is then dried and sieved, before being analysed.

During the manufacturing process, the product has a hazard analysis and critical control points (HACCP) system and safety procedures in accordance with Commission Regulations (EC) Nos 852/2004, 853/2004, 854/2004, 178/2002, making it suitable for food applications.



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4. PHYSICO-CHEMICAL DATA

For more information, see the analysis report.

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

Slightly hygroscopic.

5. PROPERTIES/USES

Excipient for pharmaceutical use.

Food additive use.

The product is classified as a food additive on the basis of Commission Regulation (EU) No 231/2012, which shall not apply to this provision in accordance with Article 1, point 5, (e), (i) of Regulation (EC) No 1272/2008.

The product is compliant with the following specification required by the current E460(i) set forth by commission of the European Communities Directive EC 629/2008, EU 231/2012 and its subsequent amendment EU 2018/75.

The GUINAMA Capsucel excipient for capsules is an inert excipient, made from microcrystalline cellulose, used as an essential ingredient in the manufacture of capsules and tablets. Its function as a binder/diluent/disintegrant makes it a first choice in manual or semi-automatic encapsulation processes, as well as in the manufacture of tablets, both in wet granulation and in direct compression.

With Capsucel excipient for capsules, spheronisation processes have been adopted that enhance the fluidity of the powder, facilitating the filling of gelatine capsules.

The main features of Capsucel include:

- Improved solids rheology due to its sphericity. Improved fluidity compared to regular microcrystalline cellulose.
- Low coefficient of friction.
- Active ingredients are more easily mixed and added due to an optimal range of particle size distribution.
- Excellent compressibility in the manufacture of lozenges and tablets.
- Rapid disintegration in tablets.



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6. DOSAGE

For preparing capsules, GUINAMA CAPSUCEL excipient for capsules can be dosed as the only excipient together with the active ingredient(s), and given its flow capacity, other lubricants such as magnesium stearate or talc are unnecessary.

Preliminary checks should be conducted prior to preparing tablets; however, its binding and disintegrating capacity make it the ideal excipient to use in tablets.

7. REMARKS

STORAGE:

Store at room temperature ($25\pm 2^{\circ}\text{C}$) in a dry, well-ventilated place away from sunlight in a full and tightly closed container.

The documentation available related to the product's regulatory compliance is included below.

BSE/TSE:

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

Materials of animal origin are not used in the manufacture of the above-mentioned product, neither during the manufacture 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.

GMOs:

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

In addition, no additives are used in our manufacturing process, whether GMOs or derived from GMOs. It is therefore not necessary to label it under the GMO labelling rules in accordance with Directive 2001/18/EC, Regulation (EC) No 1829/2003 and Regulation (EC) No 1830/2003.

CMR substances:

The product is not a CMR substance.



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NANOMATERIALS:

The product is not considered a nanomaterial as defined in Recommendations 2011/696/EU, Point 2, the definition of artificial nanomaterial listed in Regulation (EU) 1169/2011, Article 2 Definitions, Point 2 (t), and Regulation (EU) 2015/2283, Article 3 Definitions, Point 2 (f). Nanotechnology is not used in the manufacturing process.

RADIATION:

The product is compliant with EC Regulations on radioactivity and irradiation. The product has not been treated with ionising radiation in the manufacturing process.

PESTICIDES:

The product is compliant with Regulation 839/2008 on pesticides in food products and with Regulation (EC) No 396/2005 setting maximum levels of pesticides.

RESIDUAL SOLVENTS:

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

IMPURITIES:

Aflatoxins:

The product is free of aflatoxins.

Nitrosamines:

Nitric acid is used in the manufacturing process, therefore, the product has been assessed based on 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 neutralisation process, water is used to wash and remove nitrate salt and hemicellulose and ammonia water is used to neutralise residual acid in the final product.

Prior to the neutralisation process, the nitric acid reagent used in the hydrolysis, filtration and recycling process is separated. There is no risk of cross-contamination with other agents.

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

3. There are no nitrosatable substances [e.g., secondary amines (cyclic and acyclic), tertiary amines (cyclic and acyclic), N-methylmorpholine (NMM), tributylamine (TBA), hydrazine derivatives, N-methyl-



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2-pyrrolidinone, N-chloroalkylamines, N-alkylcarbamates, any tertiary amide (cyclic and acyclic), or any other amide-type solvent] used or present in the process.

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

The product is analysed annually to confirm that it is compliant with Commission Regulation (EC) No 1881/2006 setting maximum levels for nitrites in foodstuffs.

3MCPD:

The product is compliant with the current Regulation 1881/2006 on contaminants in foodstuffs and food categories.

Dioxins:

The product is compliant with the current Regulation 1881/2006 on contaminants in foodstuffs and food categories.

PCBs:

The product is compliant with the current Regulation 1881/2006 on contaminants in foodstuffs and food categories.

PAHs:

The product is compliant with the current Regulation 1881/2006 on contaminants in foodstuffs and food categories.

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 nor in the production of the raw materials used for microcrystalline cellulose, nor in storage or transport, nor in any treatment such as sterilisation performed with ethylene oxide or ethanol.

Heavy metals:

The product is compliant with the current Regulation 1881/2006 on contaminants in foodstuffs and food categories.

Melamine:

Melamine is not used in the manufacturing process and is not intentionally added, and therefore is not expected to be present.

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ICHQ3D:

The product is compliant with the elemental impurity limits <232> of the US Pharmacopoeia, EMEA/CHMP/SWP/4446/2000, the Guideline on Specification Limits for Metal Catalyst or Metal Reagent Residues, the European Pharmacopoeia 5.20 Metal Catalyst or Metal Reagent Residues, the ICH Q3D Guideline for Elemental Impurities and the Implementation of ICH Q3D in the Certification Procedure (PA/PH/CEP (16) 23, August 2016) Annex I.

Element	Class	Intentionally added	Conclusion (maximum level)	Analytical result
Cd	1	No	<0.15 ppm	Not detected
Pb	1	No	<0.15 ppm	Not detected
As	1	No	<0.45 ppm	Not detected
Hg	1	No	<0.9 ppm	Not detected
Co	2A	No	<1.5 ppm	Not detected
V	2A	No	<3 ppm	Not detected
Ni	2A	No	<6 ppm	0.0249
Tl	2B	No	<0.24 ppm	Not detected
Au	2B	No	<3 ppm	Not detected
Pd	2B	No	<3 ppm	Not detected
Ir	2B	No	<3 ppm	Not detected
Os	2B	No	<3 ppm	Not detected
Rh	2B	No	<3 ppm	Not detected
Ru	2B	No	<3 ppm	Not detected
Se	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

CONTAMINANTS:

The product is manufactured without using 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	Sulphur dioxide
10	Iodine	22	Sulphite
11	Parabens (E211-E219)	23	Vanillin
12	Peroxides		



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The product is also free of:

1	Alginates	15	Heparin
2	Artificial colours	16	Histamine
3	Artificial flavours	17	Hormones
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	Gelatine	24	Sugar alcohols
11	Glucose	25	Soya
12	Glutamate	26	Tartrazine (FD&C Yellow No 5 - E102)
13	Gluten	27	Wheat
14	Glycerine	28	Yeast

ALLERGENS:

FOOD ALLERGENS:

The product is free of food allergens based on Regulation (EU) 1169/2011, Annex II, substances or products causing allergies or intolerances.

HALAL:

The product is HALAL certified.

KOSHER:

The product is KOSHER certified.

VEGAN/VEGETARIAN:

The product does not contain animal-derived products and thus is suitable for vegan-vegetarian consumption.

TESTED ON ANIMALS:

The product has not been tested on animals.

PALM OIL:

The product is free of palm oil.



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CITES:

The product is exempt from CITES cataloguing.

REACH:

Exempt.

TARIFF ITEM NUMBER:

39129090.