93148- CAPSULES 4 YELLOW

1. IDENTIFICATION OF THE SUBSTANCE OR PREPARATION.

1.1 Identification of the substance or preparation.

Name: Capsules 4 yellow
Code: 93148
Internal code: 55200
Valid from batch: 0130890

1.2 Synonyms.

No data available.

2. DESCRIPTION

Appearance: Two pieces hard gelatin. The gelatin used meets all the requirements of the European Pharmacopoeia and USP.
The hard gelatin capsule sections are freely separated before filling and the separated cap and body edges are cleanly and evenly cut without visible rough edges.

Size: 4
Head/body color: yellow/yellow
Head external diameter (mm): 5.33±0.03
Body external diameter (mm): 5.06±0.03
Odor: Odorless
Taste: Tasteless
Origin: Croatia.
Manufacturing method: Capsules are made from pharmaceutical grade bovine gelatin.

Approximate filling content of capsules in mg

Density / Size	0.6 g/ml	0.8 g/ml	1.0 g/ml	1.2 g/ml
4	126	168	210	252

3. COMPOSITION/INFORMATION OF THE COMPONENTS.

Capsule composition/ingredients:

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COMPONENT	PERCENTAGE HEAD	BODY PERCENTAGE
Water	14-15%	14-15%
Sunset Yellow E-110 (Colorant)	0.0044%	0.0044%
Quinolone Yellow E-104 (Colorant)	0.9197%	0.9197%
Titanium Dioxide E171 (opacifier)	1.33%	1.33%
Gelatin	Csp 100%	Csp 100%

Limitations: The composition data stated are target values based on laboratory scale development. Actual values may vary depending on colour.

The product is produced in an ISO certified plant.

Regulatory information under food legislation on the colour used:
Products to be consumed in the European Union use colours that comply with (EU) 231/2012 which sets specifications for food additives.
In this case, as in products to be consumed in the USA, the colorants are certified by the FDA in accordance with 21CFR parts 73 and 74 for food and drugs.
The amount of color additive used in the above product is in accordance with the ADI according to WHO/FAO as applicable.
Globally accepted colorants, such as iron oxides, when used meet the acceptance criteria of regulated markets such as the EU and the US.
Elemental iron content does not exceed 5 mg per day according to 21CFR part - 73.120 for food and part 73.1200 for medicine.

4. PHYSICAL-CHEMICAL DATA.

For more detailed information, please refer to the analysis bulletin.
Hard gelatin capsules disintegrate in less than 15 minutes .

5. PROPERTIES/USES.

The capsules are SUITABLE for human consumption.
Hard gelatin capsules are distributed worldwide and are designed for use in pharmaceutical products.
Oral use.
Not suitable for the production of food supplements or foods.
The capsules hard gelatin are soluble in hot water at 98.6 ° F ± 1.8 ° F (37 ° C ± 1 ° C).
Moisture content of gelatin capsules hard remains between 13% and 16% .

6. DOSAGE.

No data available.

7. OBSERVATIONS.

STORAGE:

Capsules are manufactured with carefully controlled moisture content and this must be taken into account to obtain the best filling performance; if the conditions are not respected, maintenance problems will arise. Capsules will be too dry and brittle and will shrink due to moisture loss, or they will become sticky and soft due to increased humidity.

The capsules maintain their characteristics as long as they are stored at temperatures between 15°C and 25°C, and at a relative humidity of 35% to 65% and the following precautions are taken:

- Capsules should not be exposed to direct sunlight or stored near sources of heat or moisture. They should be stored in a cool, dry place and allowed to equilibrate to conditions in the filling area before use.
- Capsules must be kept in their original packaging. The containers must be tightly closed during transport and storage to ensure their quality over time. In the event that a quantity of capsules is removed for any examination or for filling, it is essential to close the container perfectly.
- It is recommended that during capsule filling, only the number of capsules required be used, to avoid exposing them to the heat that filling machines generate. Filling areas should be between 20°C and 25°C and at a relative humidity between 45% and 55% to maintain the moisture content of the capsules in the desired range of 13% to 16%.

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

BSE/TSE:

Gelatin is manufactured by an alkaline process, according to the latest edition of Chapter 5.2.8 of the European Pharmacopoeia (EP), the EMEA note to Guideline 410/01 rev 03 and the latest edition of the EP gelatin monograph.
The manufacturer uses test methods described in the EP or methods that have been validated with the methods described in the EP. The gelatin is also statistically analyzed by an external laboratory to demonstrate compliance with the ICH Q3D guideline.
The gelatine used is a blend of pharmaceutical grade gelatine based on product quality requirements and regulations. All gelatine used complies with applicable pharmacopoeia and food standards. Bovine gelatine, when used, is derived from bones and hides of healthy animals that have been certified fit for human consumption by a veterinary officer at the slaughterhouse. Tissues used in the manufacture of gelatine are free from specified risk materials.
In addition, bovine gelatin complies with the following regulations applicable in the country of use of BSE such as:

• Regulation (EC) No 999/2001 and its amendments.

• Regulation (EC) No. 853/2004.
• USFDA, September 1997, Guidance for Industry on Sourcing and Processing Gelatin to Reduce the Potential Risk Posed by BSE in FDA-Regulated Products.
• USFDA 21 CFR parts 189, 589, 700 related to livestock materials prohibited in human food, drugs and cosmetics, and animal feed.
• USFDA 9 CFR Part 94.23 regarding the importation of gelatin from bovine animals.
• Commission Directive 2003/63/EC and Ph. Eur – 1483, certified by the certificate of suitability.
• Note on the Guide to minimizing the risk of agents of transmission of animal spongiform encephalopathy via products for human and veterinary use (EMA/410/01 Rev. 03).
• In addition, no ingredients of animal origin are used in the manufacturing of the above product.

Therefore, hard gelatin capsule shells do not pose any BSE risk.

GMO:
The hard gelatine capsule shells are not subject to, nor derived from, any genetic modification techniques as defined in Article 2(2) of European Directive 2001/187EC.
The ingredients used in the manufacture of the above product are not subject to or derived from any genetic modification techniques as defined above.
The ingredients used in the manufacturing of the above product can be traced back to their source.
The product does not contain GMO (Genetically Modified Organisms).
According to the above, the hard gelatin capsule shells comply with EC 298/2008 (previously 189/2003) and EC 1830/2003 on genetically modified food and feed.

NANOMATERIALS:
The product is not considered a nanomaterial according to the definition described in EC Directive 1169/2011.
In addition, the ingredients used in the above product are not manufactured as nanomaterials nor do nanotechnology use.

IRRADIATION:
The gelatin capsules have not been irradiated in any manufacturing or post- manufacturing process .

ETHYLENE OXIDE:
With regard to EC Regulation 396/2005 on maximum residual levels of pesticides in or on food and feed of animal or plant origin and its amendments, Directive 91/414/EEC, the manufacturer indicates:

- No ethylene oxide is used at any stage of the manufacturing process for Hard Gelatin Capsules.

- Samples of the hard gelatin capsules are analyzed for ethylene oxide residues with GC-MS with a LOD of 0.01 ppm. No ethylene oxide has been detected.
- The maximum residual level (MRLs) for ethylene oxide (sum of ethylene oxide and 2 -chloroethanol expressed as ethylene oxide) is 0.1 ppm for several foods listed under Annex II EU 396/2005.

Based on the above, the capsules comply with the specification for ethylene oxide (sum of ethylene oxide and 2 -chloroethanol expressed as ethylene oxide) as set out in Regulation EU 396/2005.

ADDITIVES:

The product does not contain preservatives.

RESIDUAL SOLVENTS:

Hard gelatin capsule shells do not contain any Class I and II solvents according to CPMP/ICH/283/95 and the current edition of USP General Chapter <467> on Residual Solvents.
The following Class III solvents (glacial acetic acid, isopropyl alcohol , ethyl alcohol and n-butyl alcohol) are likely to be present in the product in amounts less than 5000 ppm each. No other solvents are used in the manufacturing process.

ELEMENTAL IMPURITIES:

The product complies with:

- ICHQ3D Impurity Guide elementals , final version of April 26 , 2022.
- CDER and CBER Q3D impurity guide elementals for industry , August 2018.
- EMA/CHMP/ICH/353369/2013 ICH Q3D Guide to Impurities elementals March 22 , 2019 .
- EMA/CHMP/SWP/4446/ 2000 Limits Guideline specific for catalysis metallic or for reaction agents metallic .
- UPS <232> Impurity limit elementals .

The impurities elementals are monitored according to the monitoring program reduced for classes 1 and 2A using methods of analysis validated described in the versions current USP general chapter <233>.

By so much , the Hard gelatin capsules comply with the limits for Class 1 and Class 2A elements listed below :

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Elemental impurity	Symbol	Class IPEC	Limit (ppm)
Arsenic (inorganic)	As	1	1
Lead	Pb	1	1
Cadmium	Cd	1	0.5
Mercury (inorganic)	Hg	1	0.1
Cobalt	Co	2A	5
Nickel	Ni	2A	20
Vanandium	V	2A	10

Compliance with the regulations is based on three ICH Q3D components : the evaluation of the potentials impurities elementals , level comparison potentials with exposure daily allowed (PDE) for each element of toxicological concern and of the development of controls designed for limit the inclusion of impurities elemental in products medicinal by below the (PDEs).

CONTAMINANTS:

Melamine : The capsules do not contain melamine .
Aflatoxins : The capsules do not contain aflatoxins .
Pesticides: The capsules do not contain residual pesticides and are safe for human consumption.
Dioxins: The capsules do not contain dioxins.
PAH and PCB: The capsules do not contain PAH or PCB.

ALLERGENS:

- Food allergens: The capsules are gluten-free.

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ALLERGENS	*Y/N	COMMENTS
Gluten-containing cereals and products (wheat, barley, rye, oats, kamut , spelt and their hybridized varieties)	N	-
Crustaceans and derived products	N	-
Egg and egg products	N	-
Fish and fish products	N	-
Peanuts and derived products	N	-
Tree nuts and derived products	N	-
Soybeans and derived products	N	-
Milk and milk products (including lactose)	N	-
Nuts and derived products (almond, hazelnut, walnut, cashew, pecan, pistachio, Brazil nut, macadamia nut and Queensland nut)	N	-
Celery and derived products	N	-
Mustard and derived products	N	-
Sesame and derived products	N	-
Sulphite (E220 – 228) and sulphur dioxide [>= 10 ppm SO2]	N	Sulfur dioxide comes from used gelatin (SO_2 less than 50 ppm in gelatin)
Lupine and derived products	N	-
Mollusks and derived products	N	-
Dyes	N	Pharmaceutical and food grade colors are used as per customer requirements.
Antioxidants	N	-
Preservatives	N	Based on customer requirements.

*Y = YES, N = NO

Reference:
US FDA Guidance for Industry: Food Allergen Labeling and Consumer Protection Act 2004. Commission Regulation (EU) No 1169/2011 on the provision of food information to consumers.

NUTRITIONAL INFORMATION:

Gelatin used as the main ingredient in the manufacture of the shell of hard gelatin capsules has the following nutritional composition. Other additives used in manufacturing have no nutritional value:

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Ingredient: Gelatin
Protein: 87.17%
Carbohydrates: 0%
Fats: 0%
Total kCal : 349.

MANUFACTURER CERTIFICATIONS:

cGMP , ISO 9001:2015, 14001:2015, Kosher, Halal .