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Dona® 1500 mg, Powder for Oral Solution

1. NAME OF THE MEDICINAL PRODUCT

Dona® 1500 mg, powder for oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains: 1884 mg of glucosamine hemisulfate sodium chloride (1:1), equivalent to 1500 mg of glucosamine hemisulfate, equivalent to 1178 mg of glucosamine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of symptoms in mild to moderate osteoarthritis of the knee.

4.2 Posology and method of administration

Posology:

Unless otherwise prescribed by the doctor, the usual dosage is:
1 sachet daily.

Glucosamine is not indicated for the treatment of acute painful symptoms. Relief of symptoms (especially pain relief) may not be experienced until after some weeks of treatment and in some cases even longer.
If no relief of symptoms is experienced after 2-3 months, continued treatment with glucosamine should be reconsidered.

Additional information on special populations:

Children and Adolescents:
Glucosamine should not be used in children and adolescents below the age of 18 years, since efficacy and safety of the use have not been established.

Elderly:
No specific studies have been performed in the elderly, but according to clinical experience dosage adjustment is not required when treating otherwise healthy elderly patients.

Impaired renal and/or liver function:
In patients with impaired renal and/or liver function no dose recommendations can be given, since no studies have been performed.

Method of administration

The contents of one sachet (dissolved in a glass of water) should be taken preferably at meals.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Contains aspartame as a source of phenylalanine and may therefore be harmful for patients with phenylketonuria.
Contains sorbitol, patients with rare hereditary problems of fructose intolerance should not take Dona® 1500 mg, Powder for Oral Solution.

Dona® 1500 mg, Powder for Oral Solution, must not be given to patients who are allergic to shellfish as the active ingredient is obtained from shellfish.

4.4 Special warnings and precautions for use

Glucosamine should not be used in children and adolescents below the age of 18 years since safety and efficacy of use have not been established.
A doctor must be consulted to rule out the presence of joint diseases for which other treatment should be considered.

Caution is advised when treating patients with impaired glucose tolerance. Closer monitoring of blood sugar levels and, where relevant, insulin requirements may be necessary at the beginning of treatment and at regular intervals during treatment.

In patients having a known risk factor of cardiovascular disease monitoring of blood lipid levels is recommended, since hypercholesterolemia has been observed in a few cases in patients treated with glucosamine.

Exacerbation of asthma symptoms triggered after initiation of glucosamine treatment has been described in one report (these symptoms resolved after withdrawal of glucosamine). Therefore, asthmatic patients starting on glucosamine should be aware of potential worsening of symptoms.

One sachet contains 6.6 mmol (151 mg) of sodium. To be taken into consideration by patients on a controlled sodium (low in sodium/salt) diet.

No special studies were performed in patients with renal or hepatic insufficiency. The toxicological and pharmacokinetic profile of the product does not indicate limitations for these patients. However, the administration in patients with severe hepatic or renal insufficiency should be made under medical supervision

4.5 Interaction with other medicinal products and other forms of interaction

No specific drug interaction studies have been performed. However, the physico-chemical and pharmacokinetic properties of glucosamine sulfate suggest a low potential for interactions. In addition glucosamine sulfate was found not to inhibit nor to induce any of the mayor human P450 enzymes: CYP1A2, CYP2E1, CYP2C19, CYP2C9, CYP2D6, CYP3A4. In fact the compound does not compete for absorption mechanisms and, after absorption, does not blind to plasma proteins, while its metabolic fate as an endogenous substance incorporated in proteoglycans or degradated independently of the cytochrome enzyme system, is unlikely to give rise to drug interactions.

However, and increased effect of cumarinic anticoagulants during concomitant treatment with glucosamine sulfate has been reported. Therefore, a closer monitoring of the coagulation parameters may be considered in these patients when initiating or ending glucosamine therapy.

The oral administration of glucosamine sulfate can enhance the gastrointestincal absorption of tetracyclines.

Steroidal or non-steroidal analgesic or anti-inflammatory agents can be administered together with glucosamine sulfate.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is only limited amount of data from the use of glucosamine in pregnant women. From animal studies only insufficient data is available. dona® 1500 mg, Powder for Oral Solution, should not be used during pregnancy.

Lactation

It is not known whether or not glucosamine is excreted in human milk. Use of glucosamine during lactation is not recommended as there is no data available on the safety for the newborn.

4.7 Effects on ability to drive and use machines

Studies on the effects on the ability to drive and use machines have not been performed. If dizziness or drowsiness is experienced, driving a car or operating machinery is not recommended.

4.8 Undesirable effects

Evaluation of the undesirable effects is based on the following frequency information:

Very common: ≥ 1/10
Common: ≥ 1/100 to < 1/10
Uncommon: ≥ 1/1 000 to < 1/100
Rare: ≥ 1/10 000 to < 1/1 000
Very rare: ≤ 1/10 000
Not known: (Frequency cannot be estimated from the available data).

The most common side effects associated with treatment with glucosamine are nausea, abdominal pain, dyspepsia, flatulence, constipation, diarrhoea, headache, tiredness and somnolence. The reported undesirable effects are usually mild and transitory.
In the following table, adverse reactions have been grouped on the basis of MedDRA Classification.

Organ System Class	**Very common > 1/10**	**Common from > 1/100 to < 1/10**	**Uncommon from > 1/1,000 to < 1/100**	**Rare from > 1/10,000 to < 1/1,000**	**Very rare < 1/10,000**	**Unknown***
Immune system disorders						Allergic reaction
Metabolism and nutrition						Inadequate control of glycemia in diabetes
Mental disorders						Insomnia
Nervous system disorders		Headache Somnolence				Dizziness
Eye disorders						Visual disturbances
Heart disorders						Arrhythmias, including tachycardia
Vascular disorders			Flushing			
Respiratory, thoracic and mediastinal disorders						Asthma Exacerbation of asthma

Gastro-intestinal disorders		Nausea Abdominal pain Dyspepsia Flatulence Diarrhoea Constipation				Vomiting
Hepatobiliary disorders						Increase in the level of "liver" enzymes in the blood and lcterus***
Skin and subcutaneous tissue disorders			Erythema Pruritus Rash			Angioedema Urticaria
General disorders and administration site conditions		Tiredness				Oedema Peripheral oedema
Investigations						Increase "liver" enzymes, blood glucose levels, increased bood pressure, fluctuations in the MGO

*Which frequency cannot be estimated by the available data

**Severe allergic reactions to glucosamine may develop in predisposed patients.

***There have been reported cases of increased "liver" enzymes and the development of jaundice has been reported, but the cause-and-effect relationship with the intake of glucosamine has not been established.

Isolated spontaneous cases of hypercholesterolemia have been reported; however, a causal relationship has not been established.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Bundesinstitut fuer Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, Germany, website: http://www.bfarm.de.

4.9 Overdose

No cases of overdosage have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Other anti-inflammatory and anti-rheumatic agents, non-steroids.
ATC code: M01AX05

Glucosamine is an endogenous substance and a normal constituent of the polysaccharide chains of cartilage matrix and synovial fluid glucosaminoglycans. In vitro and in vivo studies have shown that glucosamine stimulates the synthesis of physiological glycosaminoglycans and proteoglycans by chondrocytes, and of hyaluronic acid by synoviocytes.

The mechanism of action of glucosamine in humans is unknown. The period to the onset of action cannot be assessed.

5.2 Pharmacokinetic properties

Glucosamine is a relatively small molecule (molecular weight: 179) which is easily dissolved in water and soluble in hydrophilic organic solvents.

The available information on the pharmacokinetics of glucosamine is limited. Absolute bioavailability is unknown. The volume of distribution is approximately 5 liters, and the half-life after intravenous administration is approximately 2 hours. Approximately 38% of an intravenous dose is excreted in the urine as unchanged substance.

5.3 Preclinical safety data

Non-clinical safety data revealed no special hazard of glucosamine sulfate for humans based on conventional studies of repeat-dose toxicity, toxicity to reproduction and development and genotoxicity.

Studies on the carcinogenic potential are not available.

Preclinical results from *in vitro* studies and *in vivo* studies have shown that intravenous administration of high glucosamine doses reduces insulin secretion, probably by inhibiting glucokinase in the beta cells, and induces insulin resistance in peripheral tissues. The clinical relevance of these findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aspartame, Sorbitol (Ph. Eur.), Citric acid, Macrogol 4000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.
Keep medicines out of the sight and reach of children.

6.5 Nature and contents of container

Each sachet consists of three-layered material made of paper, aluminium and polyethylene.
Packs containing 10 (N1), 30 (N2) or 90 (N3) sachets with powder for oral solution.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

MEDA Pharma GmbH & Co. KG
Benzstrasse 1
61352 Bad Homburg (Germany)
Tel.: (06172) 888 01
Fax: (06172) 888 27 40
Email: medinfo@medapharma.de

8. MARKETING AUTHORIZATION NUMBER(S)

57863.00.00

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

14 February 2007

10. DATE OF REVISION OF THE TEXT

March 2018

11. GENERAL CLASSIFICATION FOR SUPPLY

Pharmacy-only medicine