SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Glucosamine 1250 mg Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 1250 mg glucosamine (as glucosamine hydrochloride).

Excipients: Sorbitol (E420)

Sodium

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Effervescent tablet.

Round, white to almost white effervescent tablets with lemon flavour.

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

Adults

1250 mg per day corresponding to one effervescent tablet Glucosamine 625 mg twice daily or one effervescent tablet Glucosamine 1250 mg once daily.

Before intake the effervescent tablets must be dissolved in at least 100 ml water (½ glass) and can be taken independently from meals.

Glucosamine is not indicated for the treatment of acute painful symptoms. Relief of symptoms (particularly pain relief) may not be experienced until after several weeks of treatment and in some cases even longer. If pain relief is not achieved after 2-3 months, continued treatment with glucosamine should be re-evaluated.

Elderly

Dose adjustment is not necessary in treatment of elderly.

Children and Adolescents

Glucosamine is not recommended for use in children and adolescents below 18 years, due to lack of data on safety and efficacy.

Impaired renal and/or hepatic function

As no studies have been conducted in patients with impaired renal and/or hepatic function, dosage recommendations cannot be given

4.3 Contraindications

Glucosamine is contraindicated in the following cases:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients who are allergic to shellfish as the active substance is extracted from shellfish.

4.4 Special warnings and precautions for use

Glucosamine should not be used in children and adolescents below the age of 18, due to lack of data on safety and efficacy.

A doctor should be consulted to rule out the presence of joint diseases for which other treatments should be considered.

In patients with impaired glucose tolerance, monitoring of the blood glucose levels and, where relevant, insulin requirements is recommended before start of treatment and periodically during treatment.

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

A report on exacerbated asthma symptoms triggered after initiation of glucosamine therapy is available (symptoms resolved after withdrawal of glucosamine). Asthmatic patients starting on glucosamine should therefore be aware of potential worsening of asthmatic symptoms.

Glucosamine contains sorbitol. Patients with hereditary problems of fructose intolerance should not take this medicine.

This medicinal product contains 320 mg sodium per tablet, equivalent to 16% of the WHO. Should be used with caution in patients with cardiac insufficiency.

4.5 Interaction with other medicinal products and other forms of interaction

Data on possible drug interactions with glucosamine are limited, but increased INR has been reported with coumarin anticoagulants (e. g. warfarin). Patients treated with anticoagulants should therefore be monitored closely when initiating or ending glucosamine therapy.

Concurrent treatment with glucosamine may increase the absorption and serum concentration of tetracyclines, but the clinical relevance of these interactions is probably limited.

Due to limited documentation on potential drug interactions with glucosamine, one should generally be aware of altered response or concentration of concurrently used medicinal products.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There is no adequate data from of the use of glucosamine in pregnant women.

From animal studies only insufficient data are available. Glucosamine should not be used during pregnancy.

Breast-feeding:

There is no data available on the excretion of glucosamine in human milk.The use of glucosamine during breast feeding is therefore not recommended as there are no data on the safety of the newborn.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. If light headedness, drowsiness, dizziness, nausea or vomiting occurs, car driving and operating machinery is not recommended.

4.8 Undesirable effects

The most common adverse reactions associated with treatment with glucosamine are described below. The reported adverse reactions are usually mild and transitory.

In the table below, all causality adverse events are listed by system organ class and frequency (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 (cannot be estimated from the available data)).

MedDRA System Organ Class	**Common (>1/100 to <1/10)**	**Uncommon (>1/1000 to <1/100)**	**Not known (cannot be estimated from the available data)**
Nervous system disorders	Headache Tiredness	-	Dizziness
Respiratory, thoracic and mediastinal disorders	-	-	Asthma / Asthma aggravated
Gastrointestinal disorders	Nausea Abdominal pain Indigestion Diarrhoea Constipation	-	Vomiting
Skin and subcutaneous tissue disorders	-	Rash Itching Flushing	Angioedema Urticaria
Metabolism and nutrition disorders	-	-	Diabetes mellitus inadequate control Hypercholesterolaemia
General disorders and administration site conditions	-	-	Oedema / Peripheral oedema

Cases of hypercholesterolemia, asthma, aggravated and diabetes mellitus inadequate control have been reported, but causality 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 Yellow Card Scheme, website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No case of overdose has been reported

The signs and symptoms caused by an accidental or intentional overdose with glucosamine may include headache, vertigo, disorientation, arthralgia, nausea, vomiting and diarrhoea.

In cases of overdose, treatment with glucosamine should be discontinued and standard supportive measures should be adopted as required.

In clinical studies, one in five young healthy subjects experienced headache after infusion of up to 30 g of glucosamine.

One case of overdose was reported in a 12-year old female who took orally 28 g of glucosamine hydrochloride. She developed arthralgia, vomiting and disorientation. The patient fully recovered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other anti-inflammatory and anti-rheumatic agents, non-steroidal anti-inflammatory drugs.

ATC-code: M01AX05

Glucosamine is an endogenous substance, a common 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 glucosaminoglycans and proteoglycans by chondrocytes and of hyaluronic acid by synoviocytes.

The mechanism of action of glucosamine in humans is unknown.

The period to onset of response cannot be established.

5.2 Pharmacokinetic properties

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

The available information on the pharmacokinetics of glucosamine is limited. The absolute bioavailability is unknown. The distribution volume is approximately 5 litres 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.

Glucosamine is mainly excreted via the hexosamine system independently of the cytochrome enzyme system.

5.3 Preclinical safety data

D-glucosamine has low acute toxicity.

Animal experimental data relating to toxicity during repeated administration, reproduction toxicity, mutagenicity and carcinogenicity is lacking for glucosamine. Therefore, a teratogenic effect cannot be excluded in this species.

Results from *in vitro* and *in vivo* studies in animals have shown that glucosamine reduces insulin secretion and induces insulin resistance, probably via glucokinase inhibition in the beta cells. Furthermore glucosamine causes an insulin resistance in the peripheral tissue. The clinical relevance of this fact is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid, anhydrous

Sodium hydrogen carbonate

Sodium carbonate, anhydrous

Sorbitol (E420)

Acesulfame potassium

Leucine

Lemon flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PP-tube with PE-cap with desiccant (silica gel)
Strip (paper/PE/aluminium/surlyn)

Pack sizes:

PP			tubes:
20	effervescent	tablets	(2x10)
15	effervescent	tablets	(1x15)
30	effervescent	tablets	(2x15)
90	effervescent	tablets	(6x15)
20	effervescent	tablets	(1x20)
40	effervescent	tablets	(2x20)

60 effervescent tablets (3x20)

Strips:
30 effervescent tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Medley Pharma Limited

Unit 2A,

Olympic Way

Sefton Business Park

Liverpool L30 1RD

UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 43870/0036

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/08/2011

10 DATE OF REVISION OF THE TEXT

04/12/2019