

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Dolenio 1178mg Film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 1884.60 mg of Glucosamine sulphate sodium chloride equivalent to 1500 mg Glucosamine sulphate or 1178 mg glucosamine.

Excipient: Sodium 151 mg.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White to off white, oval shaped, bi-convex film coated tablets with breakline on one side. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

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:

FOR ALL CMS EXCLUDING DK, FR & UK

One tablet daily

FOR DK, FR & UK ONLY

The recommended dose is 1178 mg of Glucosamine (1500 mg Glucosamine sulphate) to be taken once daily with a glass of water.

This quantity corresponds to:

1 tablet of Dolenio 1178 mg, once daily

Other strengths can be available and the corresponding dosages is:

2 tablets of Dolenio 589 mg to be taken together or 3 tablets of Dolenio 393 mg to be taken together, once daily.

Glucosamine is not indicated for the treatment of acute painful symptoms. Relief of symptoms (especially pain relief) may not be experienced until after several 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 re-evaluated.

Tablets can be taken with or without food.

Additional information on special populations:

Elders:

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.

Children and adolescents:

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

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 with this group.

4.3 Contraindications

Dolenio must not be used in patients who are allergic to shellfish as the active ingredient is obtained from shellfish.

Hypersensitivity to the active substance or to any of the excipients.

Children under 2 years of age.

4.4 Special warnings and precautions for use

A doctor should be consulted to rule out the presence of joint disease for which other treatment 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 known risk factor for cardiovascular disease, monitoring of the blood lipid levels is recommended, since hypercholesterolemia has been reported in a few cases in patients treated with glucosamine.

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

This medicinal product contains 6.52 mmol (or 151 mg) of sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Increased effect of coumarin anticoagulants (e.g. warfarin) during concomitant treatment with glucosamine has been reported. Patients treated with coumarin anticoagulants should therefore be monitored closely when initiating or ending glucosamine therapy.

Concurrent treatment with glucosamine may increase the absorption and serum concentrations of tetracyclines, but the clinical relevance of this interaction 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 medical products.

4.6 Pregnancy and lactation

Pregnancy:

There are inadequate data concerning 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 breastmilk. The use of glucosamine during breast feeding is therefore not recommended as there is no data on the safety of the child.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed.

If dizziness or drowsiness is experienced, car driving and the operating of machinery is not recommended.

4.8 Undesirable effects

The most common adverse reactions associated with treatment with glucosamine are nausea, abdominal pain, indigestion, constipation, and diarrhoea. In addition, headache, tiredness, rash, itching, and flushing have been reported. 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 $\geq 1/10$; common $\geq 1/100$ to $< 1/10$; uncommon $\geq 1/1,000$ to $< 1/100$; rare $\geq 1/10,000$ 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.

Dolenio may cause Hepatic enzyme elevation and rarely jaundice.

Patients with Diabetes mellitus

Blood glucose control worsened in patients with diabetes mellitus. Frequency not known.

4.9 Overdose

Signs and symptoms of accidental or intentional overdose with glucosamine might include headache, dizziness, disorientation, arthralgia, nausea, vomiting, diarrhoea or constipation.

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

In clinical trials one of five healthy young subjects experienced headache following infusion of glucosamin up to 30 g.

In addition, one case of overdose has been 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 antiinflammatory and antirheumatic agents, non-steroids.
ATC code: M01AX05

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

The mechanism of action of glucosamine is unknown.
The period to onset of response cannot be assessed.

5.2 Pharmacokinetic properties

Glucosamine is a relatively small molecule (molecular mass 179), which is easily dissolved in water and 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 unchanged in the urine.

The ADME (absorption, distribution, metabolism and excretion) profile for Glucosamine sulphate in man has not been completely elucidated.

5.3 Preclinical safety data

D-glucosamine has low acute toxicity.

Animal experimental data relating to toxicity during repeated administration, reproduction toxicity, mutagenicity or carcinogenicity is lacking for glucosamine. Results from *in vitro* or *in vivo* studies in animals have shown that glucosamine reduces insulin secretion and induces insulin resistance, probably via glucokinase inhibition in the beta cells. The clinical relevance is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet

Povidone K30
Macrogol 4000
Magnesium Stearate

Coating material

Hypromellose
Titanium Dioxide (E171)
Talc
Propylene glycol
Polysorbate 80

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

HDPE bottle with HDPE screw cap.

Alu/PVC/PVDC Blister packs

Pack-sizes:

20, 30, 60 and 90 film-coated tablets in HDPE bottle with HDPE screw cap.

4, 10, 20, 30, 45, 60, 90 film-coated tablets in Alu/PVC/PVDC Blister pack.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Blue Bio Pharmaceuticals Ltd.,
5th Floor, Beaux Lane House
Mercer Street Lower
Dublin2, Ireland

8. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

<[To be completed nationally]>