

## Summary of Product Characteristics

### 1 NAME OF THE MEDICINAL PRODUCT

Arthrimel Once Daily 1500mg Powder for Oral Solution

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 1884 mg of glucosamine sulfate and sodium chloride equivalent to 1500 mg of glucosamine sulfate and 384 mg of sodium chloride or to 1178 mg glucosamine.

Excipients:

Each sachet contains 2.5 mg aspartame, 2,023.5 mg sorbitol and 6.57 mmol (or 151 mg) sodium.

For a full list of excipients, see section 6.1

### 3 PHARMACEUTICAL FORM

Powder for oral solution.

Off-white to yellowish homogeneous powder.

### 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

One sachet, dissolved in a glass of water, once daily for relief of symptoms.

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.

Sachets can be taken with or without food.

Additional information on special populations.

##### *Children and Adolescents*

Arthrimel is not recommended for use in children and adolescents below the age of 18 years (see section 4.4).

##### *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.

### 4.3 Contraindications

Known hypersensitivity to glucosamine or to any of the excipients.

Arthrimel must not be given to patients who are allergic to shellfish as the active substance is obtained from shellfish.

### 4.4 Special warnings and precautions for use

The presence of joint diseases for which other treatment should be considered must be ruled out.

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 is 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 has been described (symptoms resolved after withdrawal of glucosamine). Asthmatic patients starting on glucosamine should therefore be aware of potential worsening of symptoms.

Glucosamine should not be used in children and adolescents under the age of 18 years safety and efficacy have not been established.

This medicinal product contains 6.57 mmol (or 151 mg) sodium per sachet. To be taken into consideration by patients on a controlled sodium diet.

The medicinal product contains aspartame, which is a source of phenylalanine. It may be harmful for people with phenylketonuria.

The medicinal product contains sorbitol: patients with rare hereditary problems of fructose intolerance, should not take this medicine.

### 4.5 Interaction with other medicinal products and other forms of interaction

Data on possible drug interactions with glucosamine is limited, but increased INR with coumarin anticoagulants (warfarin and acenocoumarol) 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 concentration of tetracyclines, but the clinical relevance of this interaction is probably limited.

Concurrent treatment with glucosamine may decrease the absorption of penicilline V and chloramphenicol.

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 the use of glucosamine in pregnant women. From animal studies only insufficient data are available, Glucosamine should therefore 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 breastfeeding is therefore not recommended as there is 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 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 (frequency cannot be estimated from the available data)).

System Organ Class	Common	Uncommon	Not known
<b>Metabolism and nutrition disorders</b>			Hypercholesterolaemia, blood glucose control worsened especially in patients with diabetes mellitus/diabetes mellitus inadequate control
<b>Nervous system disorders</b>	Headache, tiredness		Dizziness-
<b>Respiratory, thoracic and mediastinal disorder</b>			Asthma/asthma aggravated
<b>Gastrointestinal disorders</b>	Nausea, abdominal pain, indigestion, diarrhoea, constipation		Vomiting
<b>Hepatobiliary disorders</b>			Hepatic enzyme elevation and jaundice
<b>Skin and subcutaneous tissue disorders</b>		Rash, itching, flushing	Angioedema, urticaria
<b>General disorders and administration site conditions</b>			Oedema/ peripheral oedema

## 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 cases 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 glucosamine 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 anti-inflammatory and anti-rheumatic 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 in humans 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 in the urine as unchanged substance.

### 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.

Results from *in vitro* studies 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. The clinical relevance is unknown.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Aspartame (E951)  
Sorbitol (E420)  
Citric acid, anhydrous  
Macrogol 4000  
Colloidal anhydrous silica

### 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**

Paper/Aluminium/PE sachets.

Pack sizes of 10, 20, 30, 40, 60, 90 and 180 sachets.

Not all pack-sizes may be marketed.

### **6.6 Special precautions for disposal and other handling**

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

## **7 MARKETING AUTHORISATION HOLDER**

Clonmel Healthcare Limited  
Waterford Road  
Clonmel  
Co. Tipperary  
Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA 126/149/4

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 13th November 2009

## **10 DATE OF REVISION OF THE TEXT**

May 2010