# TRIPAXIL
## GLUCOSAMINE + CHONDROITIN & MSM CAPSULE

**Composition:**
Each capsule contains:

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|---|---|
| Glucosamine Sulphate Sodium Chloride<br>(equivalent to Glucosamine Sulphate 250mg)<br>(Derived from seafood) | 314mg |
| Chondroitin Sulphate Sodium<br>(Derived from chicken) | 200mg |
| Methylsulfonylmethane (MSM) | 100mg |

**Source of Capsule:** Bovine

**Product Description:**
White colour powder is filled in scarlet bovine capsule.
Capsule size: 0
No marking on the capsule.

**Indication:**
As adjuvant therapy for osteoarthritis

**Recommended Dose:**
**Light or moderate osteoarthritis symptoms:**
2 capsules to be taken twice daily for at least 6 weeks (or according to medical prescription).
**Severe osteoarthritis symptoms:**
**Initial therapy:** 2 capsules to be taken three times daily for at least 8 weeks (or according to medical prescription).
**Follow up therapy:** 2 capsules to be taken twice daily. Maintenance therapy should be followed for 3- 4 months (or according to medical prescription).

The treatment should be repeated every other 6 months or less according to medical prescription.

**Pharmacodynamics:**
*Glucosamine*
Glucosamine is a natural substance found in chitin, mucoproteins, and mucopolysaccharides. It is involved in the manufacture of glycosaminoglycan, which forms cartilage tissue in the body; glucosamine is also present in tendons and ligaments. Glucosamine must be synthesized by the body but the ability to do this decline with ages. Glucosamine and its salts have therefore been advocated in the treatment of rheumatic disorders including osteoarthritis.
Glucosamine also acts to improve the viscosity of synovial fluid by increasing synovial fluid production, thereby providing lubricant activity.

*Chondroitin sulfate*
The effect of chondroitin sulfate in patients with osteoarthritis is likely the result of a number of reactions including its anti-inflammatory activity, the stimulation of the synthesis of proteoglycans and hyaluronic acid, and the decrease in catabolic activity of chondrocytes inhibiting the synthesis of proteolytic enzymes, nitric oxide, and other substances that contribute to damage cartilage matrix and cause death of articular chondrocytes. A recent review summarizes data from relevant reports describing the biochemical basis of the effect of chondroitin sulfate on osteoarthritis articular tissues. The rationale behind the use of chondroitin sulfate is based on the belief that osteoarthritis is associated with a local deficiency in some natural substances, including chondroitin sulfate.
Recently, new mechanisms of action have been described for chondroitin sulfate. In an in vitro study, chondroitin sulfate reduced the IL-1β-induced nuclear factor-kB (NF-κB) translocation in chondrocytes. In addition, chondroitin sulfate has recently shown a positive effect on osteoarthritic structural changes occurred in the subchondral bone.

*Methylsulfonylmethane (MSM)*

Methylsulfonylmethane (MSM) is an organic sulphur-containing compound. It is an oxidation product of the organic solvent, dimethyl sulfoxide (DMSO). DMSO has been used in the treatment of arthritis and connective tissue injuries because cartilage has a high content of sulphur, and sulphur is needed for the formation of connective tissue, MSM as a source of sulphur could be useful in the management of conditions such as osteoarthritis and joint injuries where there is degeneration or destruction of cartilage.

**Pharmacokinetics:**

*Glucosamine*

*Absorption*

After oral administration, bioavailability is low due to first-pass hepatic metabolism 26%. The gastrointestinal absorption is close to 90%.

*Distribution*

Glucosamine is not protein-bound, but rather incorporates into plasma proteins (primarily globulins)
Volume of distribution: 2.5 Liters.

*Metabolism*

- Liver extensive

The first-pass effect in the liver in which more than 70% of glucosamine is metabolized.

*Excretion*

Renal Excretion, 10%
Feces, 11%
Part of a dose of glucosamine sulfate is eliminated as carbon dioxide via expired air.

*Chondroitin Sulfate*

Pharmacokinetic studies performed on humans and experimental animals after oral administration of chondroitin sulfate revealed that it can be absorbed orally. Chondroitin sulfate shows first-order kinetics up to single doses of 3,000 mg. Multiple doses of 800 mg in patients with osteoarthritis do not alter the kinetics of chondroitin sulfate. The bioavailability of chondroitin sulfate ranges from 15% to 24% of the orally administered dose. More particularly, on the articular tissue reported that chondroitin sulfate is not rapidly absorbed in the gastro-intestinal tract and a high content of labelled chondroitin sulfate is found in the synovial fluid and cartilage.

*Methylsulfonylmethane (MSM)*

A study with Rhesus monkeys on metabolism and excretion of DMSO found the primary metabolite DMSO2 became detectable in serum approximately two hours after ingestion of DMSO. With continued DMSO ingestion, DMSO2 maintained a steady concentration in the serum. When DMSO was stopped after 14 days, the mean DMSO2 concentration declined slowly over the subsequent 96 hours, and only trace amounts were detectable after five days. The decline in serum DMSO2 was linear, and its half-life appeared to be about 38 hours. The authors observed that absorption in these animals was similar to humans, but elimination was quicker in the monkeys. DMSO2 has been shown to persist in the blood up to five times longer than DMSO.

**Contraindication:**

It is contraindicated in patient with hypersensitivity to glucosamine sulphate, chondroitin sulphate and methylsulfonylmethane.

As the active ingredient is obtained from seafood, the product should not be given to patients who are allergic to seafood.

**Warning and Precaution:**

This product treats the underlying cause of osteoarthritis and the therapeutic effect can only be seen after a few weeks. Therefore, it is advisable to take an analgesic/anti-inflammatory drug if required during the first few weeks of therapy with this product.

Safety and effectiveness have not been established in children (<18 years), therefore children (<18 years) should avoid using this product.

The administration in patients with severe hepatic or renal insufficiency should be made under medical supervision.

A doctor should be consulted in order to exclude the presence of other joint conditions/ diseases for which an alternative treatment should be considered.

**Interactions with Other Medicaments:**

1) Effects on glucose metabolism & antidiabetic agents: It has been hypothesized that glucosamine may impair insulin secretion through competitive inhibition of glucokinase in pancreatic beta cells and/or alteration of peripheral glucose uptake. Glucosamine may increase insulin resistance and consequently affect glucose tolerance. It may reduce antidiabetic agent effectiveness e.g. when used with these antidiabetic agents: Acarbose, Acetohexamide, Chlorpropamide, Glipizidede, Glyburide, Metformin, Miglitol, Pioglitazone, Repaglinide, Rosiglitazone, Glimepiride, Tolbutamide, Troglitazone, Glucosamine is likely safe in patients with well-controlled diabetes (HbA1c less than 6.5%) taking one or two oral antidiabetic medications or controlled by diet only. In patients with higher HbA1c levels or those taking insulin, monitor blood glucose levels closely/more frequently.
2) Reduced effectiveness when used with glucosamine: Doxorubicin, Etoposide, Teniposide.
3) Warfarin
   - Elevations of International Normalized Ratio serum values and potentiation of anticoagulant effects.
   - If concomitant therapy is necessary, the patient's INR should be more closely monitored.
4) Avoid combination with chitosan as it may form complexes with chondroitin sulfate, thus decreasing its absorption.

**Pregnancy & Lactation:**
Available evidence is inconclusive or inadequate for use in pregnant or lactating mothers. Until more information is available, this product should only be used under medical supervision in pregnancy and lactating mothers if the potential benefit to the mother justifies the potential risk to the fetus.

Administration during the first 3 months of pregnancy must be avoided.

**Side Effect:**
Cardiovascular: Peripheral oedema, tachycardia were reported in a few patients following larger clinical trials investigating oral administration in osteoarthritis. Causal relationship has not been established.

Central nervous system: Drowsiness, headache, insomnia have been observed rarely during therapy (less than 1%).

Gastrointestinal: Nausea, vomiting, diarrhea, dyspepsia or epigastric pain, constipation, heartburn and anorexia have been described rarely during oral therapy with glucosamine.

Skin: Skin reactions such as erythema and pruritus have been reported with therapeutic administration of glucosamine.

**Symptoms of Overdosage and Treatment:** Not known

**Packing:** 60's

**Storage Condition:**
Store below 30°C. Protect from light and moisture.
Keep out of reach of children.
Jauhkan daripada capaian kanak- kanak.

**Shelf Life:** Please refer to the packaging. Do not use beyond the expiry date.

The information contained in this leaflet is limited. For further information, please consult your pharmacist or doctor.

**Product Registration Holder:**
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**Manufacturer:**
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