1.6 PRODUCT INFORMATION

SPC – Summary of the Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

CHONDROFLEX (Glucosamine & Chondroitin Capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Glucosamine Sulfate Potassium Chloride USP	500 mg
Chondroitin Sulphate Sodium USP	400 mg
Excipients	q.s.

3. PHARMACEUTICAL FORM

Oral Capsule, A Blue/ Blue coloured Size '00' hard gelatin capsule shell, containing off white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CHONDROFLEX (Glucosamine & Chondroitin Capsules) is indicated for
Treatment of all types of osteoarthritis & other painful and degenerative joint conditions.
CHONDROFLEX reduces joint pain, improves joint mobility, and stops progression of the disease process.
To improve movement of joints in elderly and decrease pain of musculoskeletal disorders. **CHONDROFLEX** works as a complementary agent to standard therapy to limit cartilage damage.
For athletes and those undergoing regular physical exercises, intensive sports, or heavy weight lifting to preserve joint structure & repair traumatic damage. **CHONDROFLEX** ensures painless flexible movement of different joints such as back, knee, elbow, ankle and wrist.
As adjuvant therapy in treatment of rheumatoid arthritis.

4.2 Posology and method of administration

1 Capsule 3 times daily

Method of administration
To be taken orally**.**

4.3 Contraindications

Hypersensitivity to CHONDROFLEX is a contraindication. In addition, CHONDROFLEX should not be used if you have the following conditions:

- Children
- Hypersensitivity

4.4 Special warnings and special precautions for use

Before using this drug, inform your doctor about your current list of medications, over the counter products (e.g. vitamins, herbal supplements, etc.), allergies, pre-existing diseases, and current health conditions (e.g. pregnancy, upcoming surgery, etc.). Some health conditions may make you more susceptible to the side-effects of the drug. Take as directed by your doctor or follow the direction printed on the product insert. Dosage is based on your condition. Tell your doctor if your condition persists or worsens. Important counseling points are listed below.

- Ask your doctor about reliable Chondroitin brands, since some products contain excess amount of manganese
- Asthma
- Blood clotting disorders
- Do not drive or operate machinery
- Pregnant or breastfeeding
- Prostate cancer

4.5 Interaction with other medicinal products and other forms of Interaction

If you use other drugs or over the counter products at the same time, the effects of Flexibel Capsule may change. This may increase your risk for side-effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that you doctor can help you prevent or manage drug interactions. Flexibel Capsule may interact with the following drugs and products:

- Antimitotic chemotherapy
- Warfarin

4.6 Pregnancy and lactation

Pregnancy

- Glucosamine Sulphate: Please consult with your doctor for case-specific recommendations.
- Chondroitin: Please consult with your doctor for case-specific recommendations.

Lactation

- Glucosamine Sulphate: Please discuss the risks and benefits with your doctor.
- Chondroitin: Please discuss the risks and benefits with your doctor.

4.7 Effects on ability to drive and use machines

If you experience drowsiness, dizziness, hypotension or a headache as side-effects when using Chondroflex Capsule medicine then it may not be safe to drive a vehicle

or operate heavy machinery. One should not drive a vehicle if using the medicine makes you drowsy, dizzy or lowers your blood-pressure extensively. Pharmacists also advise patients not to drink alcohol with medicines as alcohol intensifies drowsiness side-effects. Please check for these effects on your body when using Chondroflex Capsule. Always consult with your doctor for recommendations specific to your body and health conditions.

4.8 Undesirable effects

The most commonly reported side-effects of Chondroflex Capsule are gas, bloating, cramps, mild stomach pain, nausea, and diarrhea.

The following is a list of possible side effects that may occur from the use of Chondroflex Capsule. This is not a comprehensive list. These side-effects are possible, but do not always occur. Some of the side-effects may be rare but serious. Consult your doctor if you observe any of the following side-effects, especially if they do not go away.

- Gas
- Bloating
- Cramps
- Mild stomach pain
- Nausea
- Diarrhea
- Constipation
- Headache
- Swollen eyelids
- Leg swelling
- Hair loss
- Skin rash
- Irregular heartbeat

4.9 Overdose

Do not use more than prescribed dose. Taking more medication will not improve your symptoms; rather they may cause poisoning or serious side-effects. Please consult your physician or pharmacist or product package for more information.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Non-steroidal anti-inflammatory and antirheumatic drug

ATC code:

Glucosamine Sulfate Potassium Chloride USP: M01AX05
Chondroitin Sulfate Sodium USP: M01AX25

CHONDROFLEX

(Glucosamine & Chondroitin Capsules)

Module 1

Glucosamine Sulfate Potassium Chloride:

ACTIONS

The actions of supplemental glucosamine have yet to be clarified. It may play a role in the promotion and maintenance of the structure and function of cartilage in the joints of the body. Glucosamine may also have anti-inflammatory properties.

MECHANISM OF ACTION

Until the specific actions of supplemental glucosamine are determined, the mechanism of action in relieving arthritic pain and in repair of cartilage is a matter of speculation. However, we do know a great deal about the biochemistry of the molecules in which glucosamine is found. Biochemically, glucosamine is involved in glycoprotein metabolism. Glycoproteins, known as proteoglycans, form the ground substance in the extra-cellular matrix of connective tissue. Proteoglycans are polyanionic substances of high-molecular weight and contain many different types of heteropolysaccharide side-chains covalently linked to a polypeptide-chain backbone. These polysaccharides make up to 95% of the proteoglycan structure. In fact, chemically, proteoglycans resemble polysaccharides more than they do proteins.

The polysaccharide groups in proteoglycans are called glycosaminoglycans or GAGs. GAGs include hyaluronic acid, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparin and heparan sulfate. All of the GAGs contain derivatives of glucosamine or galactosamine.

Glucosamine derivatives are found in hyaluronic acid, keratan sulfate and heparan sulfate. Chondroitin sulfate contains derivatives of galactosamine.

The glucosamine-containing glycosaminoglycan hyaluronic acid is vital for the function of articular cartilage. GAG chains are fundamental components of aggrecan found in articular cartilage. Aggrecan confers upon articular cartilage shock-absorbing properties. It does this by providing cartilage with a swelling pressure that is restrained by the tensile forces of collagen fibers. This balance confers upon articular cartilage the deformable resilience vital to its function.

In the early stages of degenerative joint disease, aggrecan biosynthesis is increased. However, in later stages, aggrecan synthesis is decreased, leading eventually to the loss of cartilage resiliency and to most of the symptoms that accompany osteoarthritis. During the progression of osteoarthritis, exogenous glucosamine may have a beneficial role. It is known that, *in vitro*, chondrocytes do synthesize more aggregan when the culture medium is supplemented with glucosamine. N-acetylglucosamine is found to be less effective in these *in vitro* studies. Glucosamine has also been found to have antioxidant activity and to be beneficial in animal models of experimental arthritis.

The counter anion of the glucosamine salt (i.e. chloride or sulfate) is unlikely to play any role in the action or pharmacokinetics of glucosamine. Further, the sulfate in glucosamine sulfate supplements should not be confused with the glucosamine sulfate found in such GAGs as keratan sulfate and heparan sulfate. In the case of the

supplement, sulfate is the anion of the salt. In the case of the above GAGs, sulfate is present as an ester. Also, there is no glucosamine sulfate in chondroitin sulfate.

Chondroitin Sulfate Sodium:

ACTIONS

The action of orally administered chondroitin sulfate has yet to be clarified. Possible actions include promotion and maintenance of the structure and function of cartilage (referred to as chondroprotection), pain relief of osteoarthritic joints and anti-inflammatory activity.

MECHANISM OF ACTION

Until the specific actions of supplemental chondroitin sulfate are determined, the mechanism of action is a matter of speculation. However, much is known about the biochemistry and physiology of chondroitin sulfate and similar molecules. Glycoproteins known as proteoglycans form the ground substance in the extracellular matrix of connective tissue. Proteoglycans are polyanionic substances of high molecular weight and contain heteropolysaccharide-side-chains covalently linked to a polypeptide-chain backbone. The polysaccharides, which include chondroitin sulfate and hyaluronic acid, make up as much as 95% of the proteoglycan structure.

The polysaccharides in proteoglycans are called glycosaminoglycans or GAGs. Chondroitin sulfate and hyaluronic acid are vital for the structure and function of articular cartilage. Chondroitin sulfate and hyaluronic acid are fundamental components of aggrecan found in articular cartilage. Aggrecan confers upon articular cartilage shock-absorbing properties. It does this by providing cartilage with a swelling pressure that is restrained by the tensile force of collagen fibers. This balance confers upon articular cartilage the deformable resilience vital to its function. Hyaluronic acid, which is also found in synovial fluid, has lubricating properties for the joint.

In the progression of degenerative joint disease or osteoarthritis, aggrecan synthesis is decreased, leading to the loss of cartilage resiliency and the pain and other symptoms that accompany osteoarthritis.

Intra-articular injections of hyaluronic acid, an FDA-approved drug, can relieve joint pain and improve mobility. This type of therapy is called viscotherapy and is believed to act by improving joint lubrication. If chondroitin sulfate were delivered into joints, some similar effects would be expected. Animal studies have shown that parenterally administered chondroitin sulfate does get into cartilage tissue as does orally administered chondroitin sulfate. There is some human data suggesting orally administered chondroitin sulfate, particularly low-molecular-weight chondroitin sulfate, is also delivered to articular tissue. There is some indication that orally administered chondroitin sulfate leads to increases in hyaluronic acid and viscosity of synovial fluid, as well as decreases in collagenase in synovial fluid. That is,

glucosamine delivered into joints may inhibit enzymes involved in cartilage degradation and enhance the production of hyaluronic acid.

5.2 Pharmacokinetic properties

Glucosamine sulfate potassium chloride: In humans, about 90 percent of glucosamine, administered as an oral dose of glucosamine sulfate potassium chloride, is absorbed from the digestive tract. After an oral dose, glucosamine concentrates in the liver, where it is either incorporated into plasma proteins, degraded into smaller molecules, or utilized for other biosynthetic processes. Elimination of glucosamine is primarily through the urine, with a small amount of glucosamine or its derivatives eliminated in the feces.

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, Ronca et al. reported that chondroitin sulfate is not rapidly absorbed in the gastro-intestinal tract and a high content of labeled chondroitin sulfate is found in the synovial fluid and cartilage.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sr. No.	Raw Material	Pharmacopoeia
1.	Purified Talc	BP
2.	Colloidal Anhydrous Silica	BP
3.	A Blue/ Blue coloured Size '00' Capsules	IHS

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at below 30^0C

6.5 Nature and contents of container

10 Capsule in Blister & 3 such Blisters in a carton = 3 x 10 = 30 Capsule

6.6 Instructions for use and handling

No special requirements

7. Marketing Authorisation Holder

Aurochem Laboratories (India) Pvt. Ltd.
333, Gundecha Industrial Complex, 3rd Floor, Akurli Road.
Kandivali (E), Mumbai - 400101,
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Tel: +(91)-(22)-2885 8503/04/05
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8. Marketing Authorisation Number (S)

Form 25A in KD/771-A

9. Date of First Authorisation/Renewal of the Authorisation

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10. Date of Revision of the Text
