BONCARE PLUS
Module 1

1.6 PRODUCT INFORMATION

SPC – Summary of the Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

BONCARE PLUS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains

Methylsulfonylmethane USP	50 mg
Glucosamine Sulphate Potassium Chloride USP	750 mg
Chondroitin Sulphate Sodium USP	200 mg
Excipients	q.s

Colour: Ferric Oxide Red, Ferric oxide yellow

3. PHARMACEUTICAL FORM

Oral Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BONCARE PLUS is indicated in treatment of osteoarthritis are three supplements naturally found in the body that are essential to the metabolism of cartilage. These supplements, glucosamine and chondroitin sulfate, and methylsulfonylmethane have been claimed to ease pain and stiffness associated with osteoarthritis.

4.2 Posology and method of administration

As directed by Physician

4.3 Contraindications

Known hypersensitivity to **BONCARE PLUS** or any of the excipients.

4.4 Special warnings and special precautions for use

Pregnancy or breast-feeding: There is not enough reliable scientific information available to know if glucosamine sulfate is safe to take during pregnancy or while breast-feeding. Until more is known, do not take glucosamine sulfate while pregnant or breast-feeding.

Asthma: There is one report linking an asthma attack with taking glucosamine. It is not known for sure if glucosamine was the cause of the asthma attack. Until more is known, people with asthma should be cautious about taking products that contain

glucosamine.

Diabetes: Some early research suggested that glucosamine sulfate might raise blood sugar in people with diabetes. However, more recent and more reliable research now shows that glucosamine sulfate does not seem to affect blood sugar control in people with type 2 diabetes. Glucosamine appears to be safe for most people with diabetes, but blood sugar should be monitored closely.

Shellfish allergy:
Because some glucosamine sulfate products are made from the shells of shrimp, lobsters or crabs, there is concern that glucosamine products might cause allergic reactions in people who are allergic to shellfish. But allergic reactions in people with shellfish allergy are typically caused by the meat of shellfish, not the shell. There are no reports of allergic reactions to glucosamine in people who are allergic to shellfish. There is also some information that people with shellfish allergy can safely take glucosamine products.

4.5 Interaction with other medicinal products and other forms of Interaction
Do not take this combination with Warfarin (Coumadin) is used to slow blood clotting. Taking glucosamine sulfate along with some medications for cancer might decrease the effectiveness of these medications for cancer. Any person who is receiving chemotherapy should talk with their health provider before taking glucosamine sulfate.

4.6 Pregnancy and lactation

There is not enough reliable scientific information available to know if glucosamine sulfate is safe to take during pregnancy or while breast-feeding. Until more is known, do not take glucosamine sulfate while pregnant or breast-feeding.

4.7 Effects on ability to drive and use machines
It may cause drowsiness, do not drive a car or operate machinery while taking this medication.

4.8 Undesirable effects
It has some mild side effects including nausea, heartburn, diarrhea, and constipation. Uncommon side effects are drowsiness, skin reactions, and headache.

4.9 Overdose
Digestive upset.
Treatment: pump the stomach" or administer certain medications to induce vomiting

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Glucosamine Sulfate Potassium Chloride USP: Dietary Supplement

Chondroitin Sulfate Sodium USP: Dietary Supplement
Methyl Sulphonylmethane USP: Dietary Supplement

ATC code:
Glucosamine Sulfate Potassium Chloride USP:M01AX05
Chondroitin Sulfate Sodium USP: M01AX25
Methylsulphonylmethane USP: QA12CX99

Mechanism of action

Glucosamine Sulfate Potassium Chloride:

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 :

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.

Methyl Sulphonylmethane:

Methylsulfonylmethane has been proven to have anti-inflammatory and antioxidant mechanisms in an *in vitro* study in which human neutrophils were artificially stimulated to produce oxidative compounds, including hydrogen peroxide, superoxide, and hypochlorous acid. After cell lines were treated with either dimethyl sulfoxide or dimethyl sulfone , these free radical by-products were decreased. It has been suggested that polar solvents such as Methylsulfonylmethane and dimethyl sulfone have a chemopreventive mechanism that affects the interaction of tumor cells with the host immune response.7 Researchers examined DNA of dimethyl sulfoxide - treated cells and found these polar solvents create DMSO-induced nicks found in the DNA of folded genomes, suggesting these nicks may cause an untwisting of DNA, with resultant transcription of additional genes. Additional chemoprevention studies suggest Methylsulfonylmethane has no effect on cyclooxygenase (COX) activity or PGE2 activity, and operates on a COXindependent pathway in inducing differentiation. An early study of dimethyl sulfoxide and dimethyl sulfone demonstrates these agents reduce the binding, uptake, and degradation of low-density lipoproteins by cultured fibroblasts. A similar study showed dimethyl sulfoxide and dimethyl sulfone caused a dose-dependent suppression of growth and proliferation of cultured aortic smooth muscle and endothelial cells *in vitro*, the more substantial effect occuring in smooth muscle cells. In addition, dimethyl sulfone was a more potent inhibitor of cell growth than dimethyl sulfoxide and its effects were more irreversible than the effects of dimethyl sulfoxide.

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.

Methylsulfonylmethane: A study with Rhesus monkeys on metabolism and excretion of dimethyl sulfoxide found the primary metabolite dimethyl sulfone became detectable in serum approximately two hours after ingestion of dimethyl sulfoxide. With continued dimethyl sulfoxide ingestion, dimethyl sulfone maintained a steady concentration in the serum. When dimethyl sulfoxide was stopped after 14 days, the mean dimethyl sulfone concentration declined slowly over the subsequent 96 hours, and only trace amounts were detectable after five days. The decline in serum dimethyl sulfone was linear, and its half-life appeared to be about 38 hours.5 The authors observed that absorption in these animals was similar to humans, but elimination was quicker in the monkeys. Dimethyl sulfone has been shown to persist in the blood up to five times longer than dimethyl sulfoxide.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sr.No.	Raw materials	Pharmacopoeia
1.	Microcrystalline Cellulose	BP
2.	Lactose	BP
3.	Colloidal Anhydrous Silica	BP
4.	Sodium Lauryl Sulfate	BP
5.	Sodium starch glycolate (Type A)	BP
6.	Maize Starch	BP
7.	Purified Water	BP
8.	Povidone K-30	BP
9.	Croscarmellose Sodium	BP
10.	Magnesium Stearate	BP
11.	Propyl Gallate	BP
12.	Purified Talc	BP
13.	Insta Moistshield White (IC-MS-5486)	IHS
14.	Isopropyl Alcohol	BP
15.	Hypromellose	BP
16.	Dichloromethane	BP
17.	Ferric Oxide red	IHS
18.	Ferric Oxide yellow	IHS

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at a temperature below 30°C.

6.5 Nature and contents of container

10 Tablets in Alu / PVDC Blister & 3 such Blisters in a carton = 3 x 10's = 30 Tablet's

6.6 Instructions for use and handling

No special requirements

7. Marketing Authorisation Holder

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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
