STRIDE ADVANCED

TRM®

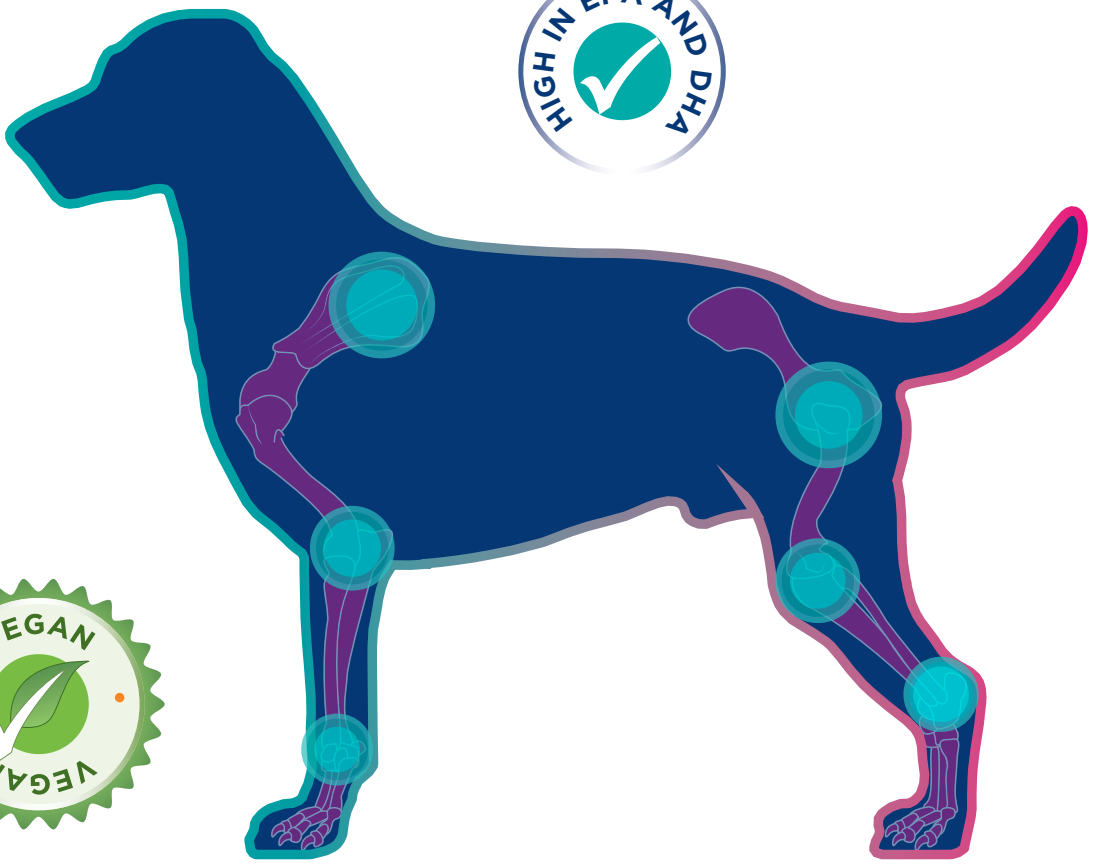
EXCELLENCE IN PET NUTRITION

STRIDE ADVANCED

For the support of the metabolism of joints in the case of osteoarthritis.

WITH HYALURONIC ACID

HIGH IN EPA AND DHA



VEGAN

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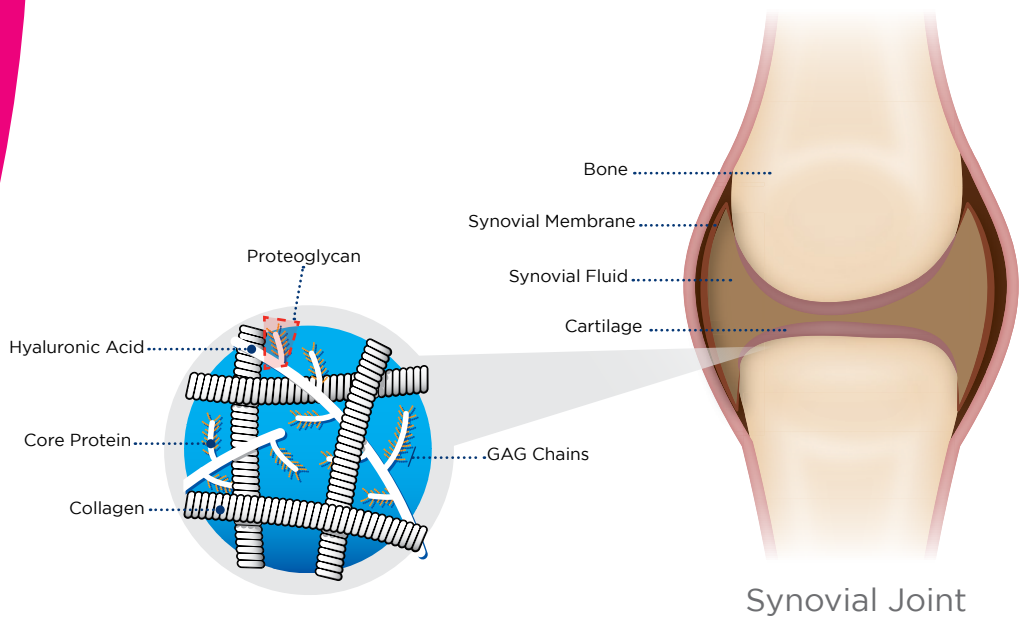
The Joint

The joint is where two or more bones meet. Each bone end is protected with a layer of cartilage; the entire joint is enclosed in the synovial capsule which is filled with synovial fluid. Bones provide a frame to support the body and protect the organs, muscles and blood vessels.

The Cartilage Matrix

The cartilage matrix is composed of collagen fibres and chondrocytes. Chondrocytes produce and maintain proteoglycans which are made up of proteins and **Glycosaminoglycan** (GAG chains).



Synovial Joint

Impaired function of skeletal joints can dramatically reduce joint flexion, movement and mobility. This seriously decreases a dog's life quality, with affected animals exhibiting decreased activity levels, stiffness and inability to partake in walks or play.

Predisposing factors can be:

- **Congenital**
  Certain breeds may also have a genetic predisposition towards skeletal joint diseases. Surveys have found 9.4% of Retrievers were affected by Hip Dysplasia (FCRSA Health Survey) while the cumulative hazard rate for cCHD in Boxers from 7 weeks to 8 years of age is 8.5% (Van Hagen et al.)

- **Developmental** (Osteochondrosis and Hip Dysplasia)
  Developmental problems will typically occur during periods of rapid growth between 3 and 9 months of age.

- **Traumatic** (fractures and dislocations).

- **Degenerative**
  Osteoarthritis by contrast occurs secondarily to developmental or traumatic conditions, and is characterized by progressive, degenerative changes in the joint structure. When any articular joint is damaged, inflammatory substances are released into the joint capsule, which in turn reduces the quality and quantity of Synovial fluid - the joint lubricant. Without the lubricant, the articular cartilage is in turn damaged and its protective cushion is no longer effective.

This cascade of events can contribute to a cycle of cartilage damage, inflammation and progressive loss of joint function. It is vital at this point to feed nutritional ingredients, which can support the Glycosaminoglycan (GAG) content of the cartilage, reduce the effect of the cartilage-chewing enzymes and improve the viscosity of the synovial fluid.

5 KEY INGREDIENTS
for the maintenance of Joint Health

- ✓ **Easy-to-feed liquid formulation for addition to dog's food.**
- ✓ **Contains no ingredients of animal origin.**
- ✓ **Palatable natural yeast flavouring.**
- ✓ **Proven in practice.**
- ✓ **No possibility of presence of animal prions or viruses; all ingredients from reliable and reproducible sources with highest purity.**
- ✓ **Chondroitin Sulphate in the formula has clinically proven bioavailability and substantial absence of unusually sulphated and over-sulphated disaccharides – made up of more than 75% C6S.**

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1. Chondroitin Sulphate

Chondroitin Sulphate (CS) is the most abundant GAG in the cartilage matrix. It stimulates the production of proteoglycans and is capable of binding large amounts of water. This enables the joint to withstand constant compression and concussion. It also inhibits cartilage-chewing enzymes which are present in damaged joints, and recent studies have shown that it can reduce the synthesis of nitric oxide in damaged cartilage tissue (Manerio, E. et al.)

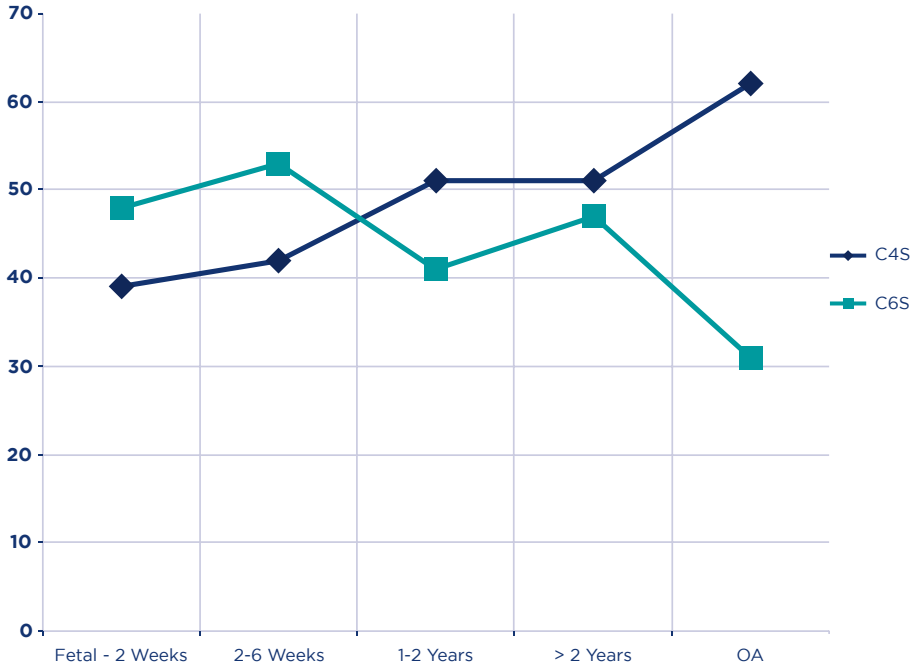
Most CS supplied to the market is extracted from cartilaginous feedstocks using organic solvents, with purification processes which may cause chemical degradation/desulphation and loss of activity along with an uncontrolled and unreliable supply chain of CS raw materials. This poses serious concerns about the quality and the safety of the ingredient.

STRIDE ADVANCED contains a non-animal CS characterized by high purity and obtained through a fermentation-derived manufacturing process. It promises to resolve the long-standing acknowledged problem of poor quality and potential safety issues of animal-derived CS.

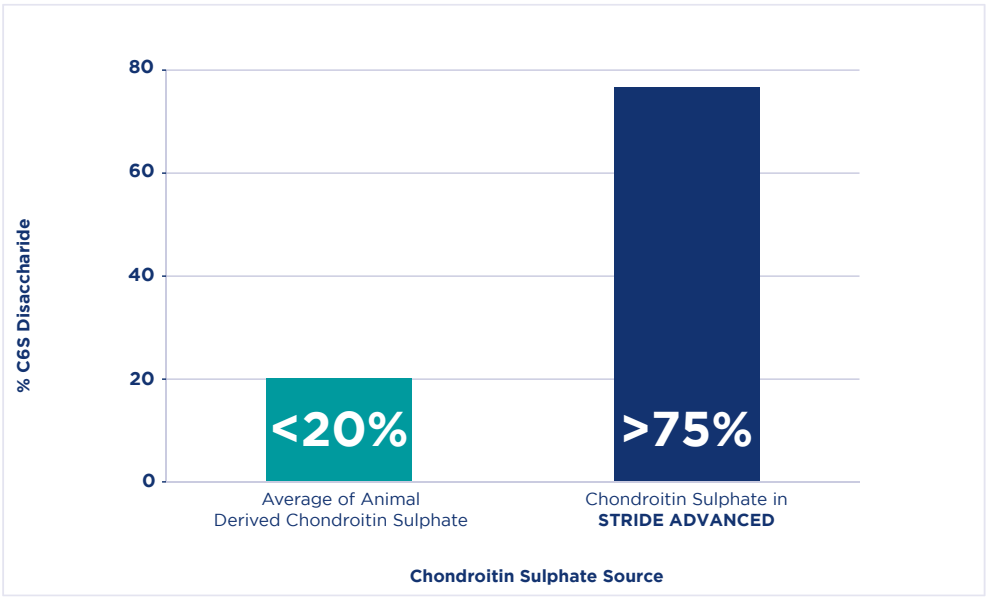
Scientific evidence reports a strong inverse correlation between age, osteoarthritis and variation in the sulphation patterns of CS in companion animals.

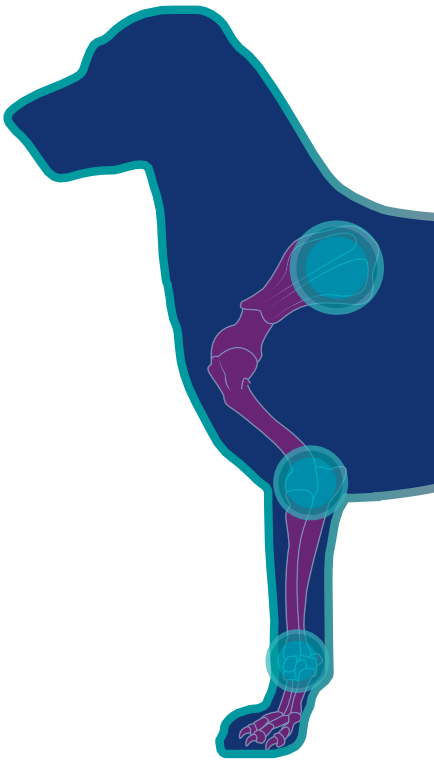
C6S tends to decrease with age and is lower in OA joints.

Sulphation of Chondroitin Sulphate in medial palmar carpal ligament in relation to age and osteoarthritis (OA) (Brown et al).



Chondroitin Sulphate utilised in **STRIDE ADVANCED** is made up of more than 75% of 6-Sulphated Disaccharides by comparison with most animal originating Chondroitin Sulphate which is made up of different Chondroitin Sulphate – mainly C4S (~70%) and only around 20% C6S.





2. Hyaluronic Acid

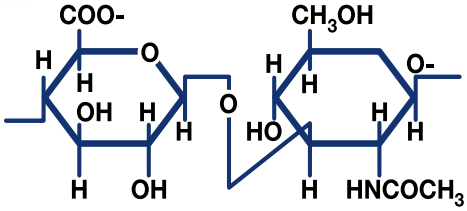
Hyaluronic Acid is a normal constituent of the joint. Its quantity and quality is reduced in the presence of synovitis and osteoarthritic cartilage.

One of its most important roles is to increase the viscosity of the synovial fluid; this reduces the friction between articular surfaces, thus ensuring a correct and smooth movement of the joint.

Biomechanical studies on canine tendons have shown a reduction in resistance when soaked in a solution of Hyaluronic Acid

(Akasaka, T. et al.).

The source of Hyaluronic Acid utilised in STRIDE ADVANCED is fermented from corn, and does not contain any ingredients originating from animals.



Structure of Hyaluronic Acid

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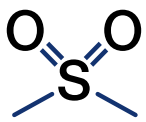
3. Methylsulphonylmethane (MSM)

MSM is a source of organic sulphur, which is easily absorbed and usable in the body. Sulphur is an important nutrient for the maintenance of healthy joints, tendons and ligaments and is needed for the synthesis of connective tissue. MSM is found in various foods and is used by the body to make important enzymes, antibodies, glutathione and connective tissues.



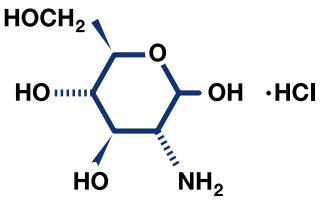
Structure of MSM

MSM is a useful nutritional adjunct in dogs with impaired joint function, and is usually combined with glucosamine as they work well together. It was reported by *Usha et al* that a combination of Glucosamine and MSM showed better efficacy than the individual feed materials fed separately.

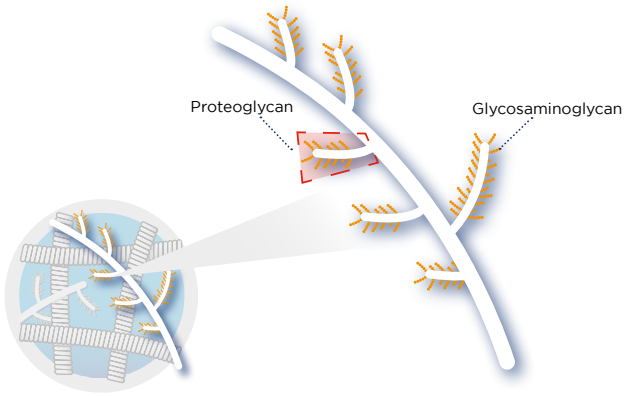
Studies have shown an improvement in physical function in subjects taking MSM (Kim et al).

4. Glucosamine HCl

Glucosamine is an amino sugar that is produced naturally in the body. It is a component of the proteoglycans (PGs) and glycosaminoglycans (GAGs) in the cartilage matrix.



Structure of Glucosamine



PGs are a major component of the extracellular matrix. They form large complexes to other proteoglycans, to hyaluran and to collagen. The majority of GAGs in the body are linked to core proteins, forming proteoglycans. GAGs are highly polar and attract water. They are therefore useful to the body as a lubricant or as a shock absorber.

The addition of Glucosamine in the diet stimulates the production of GAGs and PGs in the cartilage and helps promote cartilage health. Without adequate glucosamine, GAG synthesis would essentially cease and in turn cause proteoglycan synthesis to cease also.

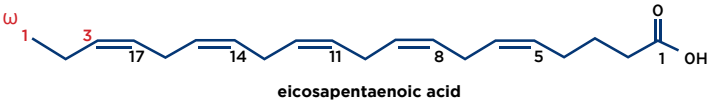
STRIDE ADVANCED contains Glucosamine **HCl**, which contains a significantly higher Glucosamine activity compared to the more commonly used Glucosamine **Sulphate**, and in vitro has been shown to increase mucopolysaccharide secretion compared to all other Glucosamine derivatives (Karzel et al.).

Pharmacokinetic studies on Glucosamine and Chondroitin in dogs indicated that 87% of an orally administrated dose of radio-labelled Glucosamine and 70% of the labelled Chondroitin are absorbed (Conte et al., Setnikar et al.).

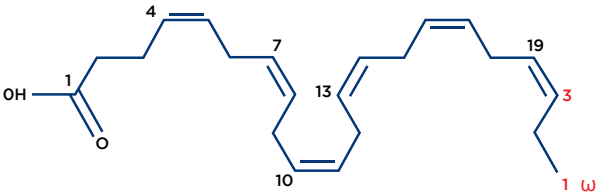
In canines, studies have shown that feeding Glucosamine in association with Chondroitin, prior to synovitis, supported an improvement in lameness scores (Canapp et al.), as well as an improvement in the quality of synovial fluid. (Johnson et al.).

5. EPA & DHA

Omega – 3's (ω-3's) are essential long chain polyunsaturated fatty acids (PUFA's) forming membrane components of various cells, thereby providing structural integrity. Alpha-linolenic acid (ALA), Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) are the most widely researched ω-3's for their benefits (Molfino et al., 2014). ALA, the most common ω-3, is converted into EPA and DHA within the body with a very low conversion of about 1 – 10% into EPA and 0.5 – 5% into DHA (Burdge, 2006, Brenna, 2002). Hence, an external source of high EPA and DHA is required to render their substantial health benefits.



eicosapentaenoic acid



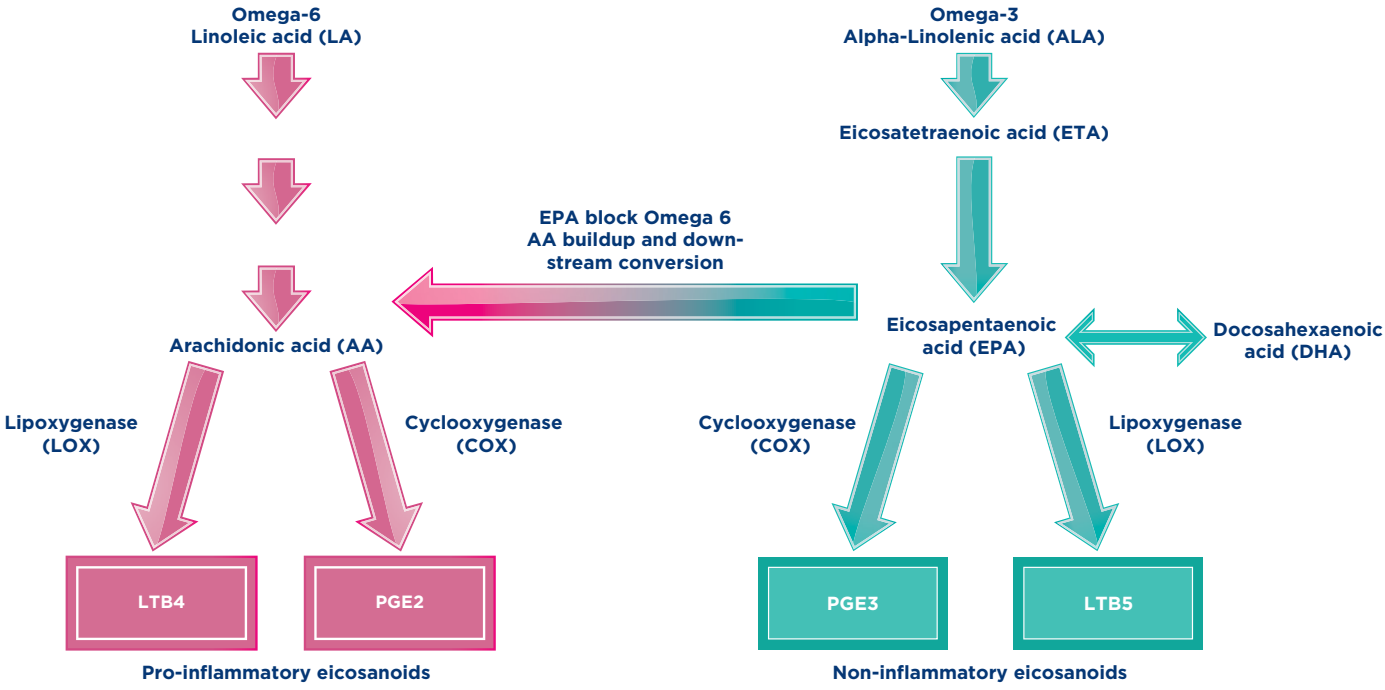
docosahexaenoic acid

By following a very systematic, interdependent pathway in maintaining the general wellbeing and homoeostasis in the body these macromolecules render various key benefits including osteo-articular health maintenance. In a prospective, randomized, double-blind, placebo-controlled trial involving 78 client owned dogs with clinical signs of Osteoarthritis of the stifle or coxofemoral joint, Mehler et al concluded all clinical outcomes for discomfort, lameness and joint severity and all blood parameters significantly improved compared to the placebo on feeding EPA + DHA omega oil for 84 days. This study involved orthopaedic examination and blood analysis at day 0, 42 and 84 with no major side effects at the end of the trial (Mehler et al., 2016).

In-vivo, intercalating with ω-6's metabolic conversions, EPA and DHA synthesise eicosanoids like prostaglandins (PGs, PGE3) and leukotrienes (LTs, (LTB5)) which have numerous physiological roles and modulate inflammatory pathways. Both, PGE3 and LTB5 are non-inflammatory mediators (Ricciotti & FitzGerald, 2011). Further, adequate levels of EPA and DHA act by:

- Competing with Arachidonic acid (AA) in the ω-6 pathway thereby downregulating the formation of pro-inflammatory mediator PGs (PGE2) and LTs (LTB4).
- Blocks AA build up and downstream conversion (particularly EPA).
- Producing non-inflammatory PGE3 and LTB5.

(ANSHEL,2006)



STRIDE ADVANCED incorporates Marine Algae Oil derived from Schizochytrium sp., a rich source with high levels of EPA and DHA. Thus, by rendering key benefits through their metabolic conversions in the body, these macromolecules help streamline signalling pathways, immune and non-inflammatory responses and regulate blood and heart vitals.

STRIDE ADVANCED is a complementary (dietetic) feed for dogs for the support of the metabolism of joints in the case of osteoarthritis.
It is a vegan formulation containing Glucosamine HCL, MSM, fermented Chondroitin to maximise the C6 isomer component, high molecular weight Hyaluronic Acid and sustainably farmed Algal Oil with a very high concentration of EPA and DHA

Instructions for proper use:

Feed initially for up to 3 months. It is recommended that advice from a veterinarian be sought before use and before extending the period of use. Add to the normal feed ration; feed each dog individually.

Feeding Instructions first 14 days		**Feeding Instructions Long Term**	
Small dogs (up to 10kg):	4 ml	**Small dogs (up to 10kg):**	2 ml
Medium dogs (10-25kgs):	8 ml	**Medium dogs (10-25kgs):**	4 ml
Large dogs (25-40kgs):	12 ml	**Large dogs (25-40kgs):**	6 ml
Very large dogs (over 40kgs):	16 ml	**Very large dogs (over 40kgs):**	8 ml

The dosing pump attached to this container dispenses 2 ml.
Alternatively for large dog doses a graduated measuring cup is enclosed.

Composition	**per 100ml**
Glucosamine HCl	16,675 mg
Marine Algae Oil	5,000 mg
Chondroitin Sulphate	3,562 mg
Methyl sulphonyl methane	3,000 mg
Hyaluronic Acid	149 mg
Additives	
Vitamin E	100 iu

Analytical Constituents:

Crude protein 6.4%, Crude fat 5%, Crude ash 1.1%, Crude fibre 0.2%, Sodium 0.31%, Moisture 73.8%, Omega 3 fatty acids 33 g per kg, Eicosapentaenoic acid 8 g per kg, Docosahexaenoic acid 23 g per kg, Vitamin E 1,000 iu per kg

PRESENTATION: **200ML** **500ML**

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