SAFETY DATA SHEETS

This SDS packet was issued with item: 078049792

The safety data sheets (SDS) in this packet apply to the individual products listed below. Please refer to invoice for specific item number(s).

078360460

Safety Data Sheet

According To Federal Register / Vol. 77, No. 58 / Monday, March 26, 2012 / Rules And RegulationsRevision Date: 05/26/2016Date of Issue: 05/26/2016

Version: 1.0

SECTION 1: IDENTIFICATION	N
1.1. Product Identifier	
Product Form: Mixture	
Product Name: Goodwinol Oint	ment
1.2. Intended Use of the I	Product
Use of the Substance/Mixture:	A topical skin ointment to be used on dogs.
1.3. Name, Address, and	Telephone of the Responsible Party
Company	Manufacturer
Goodwinol Products Corp	Vita-Herb Nutriceuticals, Inc.
41710 County Road 29	1012 Segovia Circle
Pierce, CO 80650	Placentia, CA 92870
T (970) 834-1229	Т (714) 632 - 3726
1.4. Emergency Telephon	e Number
Emergency Number	: ChemTel 1-800-255-3924
SECTION 2: HAZARDS IDEN	TIFICATION
2.1. Classification of the S	Substance or Mixture
GHS-US Classification	
Acute Tox. 4 H33	32
(Inhalation:dust,mist)	
Skin Sens. 1 H3	17
Asp. Tox. 1 H30	04
Aquatic Acute 1 H40	00
Aquatic Chronic 3 H4:	12
Full text of hazard classes and H	-statements : see section 16
2.2. Label Elements	
GHS-US Labeling	
	GH507 GH508 GH509
Signal Word (GHS-US)	: Danger
Hazard Statements (GHS-US)	: H304 - May be fatal if swallowed and enters airways.
	H317 - May cause an allergic skin reaction.
	H332 - Harmful if inhaled.
	H400 - Very toxic to aquatic life.
	H412 - Harmful to aquatic life with long lasting effects.
Precautionary Statements (GHS	-US) : P261 - Avoid breathing vapors, mist, spray.
	P271 - Use only outdoors or in a well-ventilated area.
	P272 - Contaminated work clothing must not be allowed out of the workplace.
	P273 - Avoid release to the environment.
	P280 - Wear protective gloves, protective clothing, and eye protection.
	P301+P310 - II Swallowed: Infinedialely Call a poison center of doctor.
	P302+P352 - II OII SKIII. Wash with pienty of water.
	comfortable for breathing
	P212 - Call a poison center or doctor if you feel unwell
	P321 - Specific treatment (see section 4 on this SDS)
	P331 - Do NOT induce vomiting.
	P333+P313 - If skin irritation or rash occurs: Get medical advice/attention
	P363 - Wash contaminated clothing before reuse.
	P391 - Collect spillage.
	P405 - Store locked up.
	P501 - Dispose of contents/container in accordance with local, regional. national.
	and international regulations.

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2.3. Other Hazards

Exposure may aggravate pre-existing eye, skin, or respiratory conditions.

2.4. Unknown Acute Toxicity (GHS-US)

No data available

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substance

Not applicable

3.2. Mixture

Name	Product Identifier	%
Paraffin oils	(CAS No) 8012-95-1	30.8333
Paraffin waxes and Hydrocarbon waxes	(CAS No) 8002-74-2	2.9231
Benzoic acid, 4-amino-, ethyl ester	(CAS No) 94-09-7	2.0462
Rotenone	(CAS No) 83-79-4	1.2484
3,5,7-Triaza-1-azoniatricyclo[3.3.1.13,7]decane, 1-(3-chloro-2-propenyl)-, chloride	(CAS No) 4080-31-3	0.1
SECTION 4: FIRST AID MEASURES		

4.1. Description of First-aid Measures

First-aid Measures General: Never give anything by mouth to an unconscious person. If you feel unwell, seek medical advice (show the label where possible).

First-aid Measures Inhalation: When symptoms occur: go into open air and ventilate suspected area. Remove to fresh air and keep at rest in a position comfortable for breathing. Get medical advice/attention.

First-aid Measures After Skin Contact: Remove contaminated clothing. Drench affected area with water for at least 15 minutes. Obtain medical attention if irritation develops or persists.

First-aid Measures After Eye Contact: Rinse cautiously with water for at least 15 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention.

First-aid Measures After Ingestion: Do NOT induce vomiting. Rinse mouth. Immediately call a POISON CENTER or doctor/physician.

4.2. Most Important Symptoms and Effects Both Acute and Delayed

Symptoms/Injuries: Harmful if inhaled. Skin sensitization. May be fatal if swallowed and enters airways.

Symptoms/Injuries After Inhalation: Inhalation is likely to cause adverse health effects including but not limited to: irritation, difficulty breathing, and unconsciousness.

Symptoms/Injuries After Skin Contact: May cause an allergic skin reaction.

Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.

Symptoms/Injuries After Ingestion: Aspiration into the lungs can occur during ingestion or vomiting and may cause lung injury. **Chronic Symptoms:** None known.

4.3. Indication of Any Immediate Medical Attention and Special Treatment Needed

If exposed or concerned, get medical advice and attention. If medical advice is needed, have product container or label at hand.

SECTION 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing Media

Suitable Extinguishing Media: Water spray, fog, carbon dioxide (CO₂), alcohol-resistant foam, or dry chemical.

Unsuitable Extinguishing Media: Do not use a heavy water stream. Use of heavy stream of water may spread fire.

5.2. Special Hazards Arising From the Substance or Mixture

Fire Hazard: Not considered flammable but may burn at high temperatures.

Explosion Hazard: Product is not explosive.

Reactivity: Hazardous reactions will not occur under normal conditions.

5.3. Advice for Firefighters

Precautionary Measures Fire: Exercise caution when fighting any chemical fire.

Firefighting Instructions: Use water spray or fog for cooling exposed containers.

Protection During Firefighting: Do not enter fire area without proper protective equipment, including respiratory protection.

Hazardous Combustion Products: Carbon monoxide. Carbon dioxide. Nitrogen oxides. Hydrocarbons. Sulfur oxides.

Other Information: Do not allow run-off from fire fighting to enter drains or water courses.

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SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal Precautions, Protective Equipment and Emergency Procedures

General Measures: Avoid breathing (vapor, mist, spray). Do not get in eyes, on skin, or on clothing.

6.1.1. For Non-Emergency Personnel

Protective Equipment: Use appropriate personal protection equipment (PPE).

Emergency Procedures: Evacuate unnecessary personnel.

6.1.2. For Emergency Personnel

Protective Equipment: Equip cleanup crew with proper protection.

Emergency Procedures: Upon arrival at the scene, a first responder is expected to recognize the presence of dangerous goods, protect oneself and the public, secure the area, and call for the assistance of trained personnel as soon as conditions permit. Ventilate area.

6.2. Environmental Precautions

Prevent entry to sewers and public waters. Avoid release to the environment. Collect spillage.

6.3. Methods and Materials for Containment and Cleaning Up

For Containment: Contain any spills with dikes or absorbents to prevent migration and entry into sewers or streams. As an immediate precautionary measure, isolate spill or leak area in all directions. Ventilate area.

Methods for Cleaning Up: Clean up spills immediately and dispose of waste safely. Transfer spilled material to a suitable container for disposal. Contact competent authorities after a spill.

6.4. Reference to Other Sections

See Section 8 for exposure controls and personal protection and Section 13 for disposal considerations.

SECTION 7: HANDLING AND STORAGE

7.1. Precautions for Safe Handling

Precautions for Safe Handling: Wash hands and other exposed areas with mild soap and water before eating, drinking or smoking and when leaving work. Avoid prolonged contact with eyes, skin and clothing. Avoid breathing vapors, mist, or spray. Use only outdoors or in a well-ventilated area.

Hygiene Measures: Handle in accordance with good industrial hygiene and safety procedures.

7.2. Conditions for Safe Storage, Including Any Incompatibilities

Technical Measures: Comply with applicable regulations.

Storage Conditions: Keep container closed when not in use. Store in a dry, cool place. Keep/Store away from direct sunlight, extremely high or low temperatures and incompatible materials.

Incompatible Products: Strong acids, strong bases, strong oxidizers.

7.3. Specific End Use(s)

A topical skin ointment to be used on dogs.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control Parameters

For substances listed in section 3 that are not listed here, there are no established exposure limits from the manufacturer, supplier, importer, or the appropriate advisory agency including: ACGIH (TLV), AIHA (WEEL), NIOSH (REL), or OSHA (PEL).

Rotenone (83	3-79-4)	
USA ACGIH	ACGIH TWA (mg/m³)	5 mg/m ³ (commercial)
USA ACGIH	ACGIH chemical category	Not Classifiable as a Human Carcinogen commercial
USA NIOSH	NIOSH REL (TWA) (mg/m³)	5 mg/m ³
USA IDLH	US IDLH (mg/m ³)	2500 mg/m ³
USA OSHA	OSHA PEL (TWA) (mg/m³)	5 mg/m ³
Paraffin wax	es and Hydrocarbon waxes (8002-74-2)	
USA ACGIH	ACGIH TWA (mg/m³)	2 mg/m³ (fume)
USA NIOSH	NIOSH REL (TWA) (mg/m ³)	2 mg/m³ (fume)
Paraffin oils	(8012-95-1)	
USA ACGIH	ACGIH TWA (mg/m ³)	5 mg/m ³ (excluding metal working fluids, highly & severely refined-
		inhalable fraction)
USA ACGIH	ACGIH chemical category	Not Classifiable as a Human Carcinogen highly and severely refined,
		Suspected Human Carcinogen highly and severely refined
USA NIOSH	NIOSH REL (TWA) (mg/m³)	5 mg/m ³
USA NIOSH	NIOSH REL (STEL) (mg/m ³)	10 mg/m³
USA IDLH	US IDLH (mg/m ³)	2500 mg/m ³

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USA OSHA	OSHA PEL (TWA) (mg/m ³)	5 mg/m ³	
8.2. Exp	osure Controls		
Appropriate Personal Pro	Engineering Controls	 Emergency eye wash fountains and safety showers should be available in the immediate vicinity of any potential exposure. Ensure adequate ventilation, especially in confined areas. Ensure all national/local regulations are observed. Gas detectors should be used when toxic gases may be released. Gloves. Protective clothing. Protective goggles. Insufficient ventilation: wear respiratory protection. 	
Materials for Protective Clothing : Chemically resistant materials and fabrics.		: Chemically resistant materials and fabrics.	
Hand Protec	tion	: Wear protective gloves.	
Eye Protecti	on	: Chemical safety goggles.	
Skin and Body Protection : Wear suitable protective clothing.		: Wear suitable protective clothing.	
Respiratory	Protection	: If exposure limits are exceeded or irritation is experienced, approved respiratory protection should be worn. In case of inadequate ventilation, oxygen deficient atmosphere, or where exposure levels are not known wear approved respiratory protection.	
Other Inform	nation	: When using, do not eat, drink or smoke.	
SECTION 9 :	PHYSICAL AND CHEMIC	AL PROPERTIES	
9.1. Info	ormation on Basic Physical	and Chemical Properties	
Physical Stat	te	: Liquid	
Appearance		: Light tan to dark rust color	
Odor		: Lanolin	
Odor Threshold : No data available		: No data available	
рН		: No data available	
Evaporation	Rate	: No data available	
Melting Poir	nt	: No data available	
Freezing Poi	nt	: No data available	
Boiling Poin	t	: No data available	
Flash Point		: No data available	
Auto-ignitio	n Temperature	: No data available	
Decomposit	ion Temperature	: No data available	
Flammabilit	y (solid, gas)	: No data available	
Vapor Press	ure	: No data available	
Relative Vap	oor Density at 20°C	: No data available	
Relative Der	nsity	: No data available	
Solubility		: Water: Not soluble	
Partition Co	efficient: N-Octanol/Water	: No data available	
Viscosity		: No data available	
9.2. Oth	er Information No addition	al information available	
SECTION 10	D: STABILITY AND REACT	VITY	
10.1. Rea	activity: Hazardous reactions	s will not occur under normal conditions.	
10.2. Che	emical Stability: Stable unde	r recommended handling and storage conditions (see section 7).	
10.2 Doc	cibility of Hazardous Boastia	ne Hazardous polymorization will not assur	

10.3. Possibility of Hazardous Reactions: Hazardous polymerization will not occur.

- **10.4.** Conditions to Avoid: Direct sunlight, extremely high or low temperatures, and incompatible materials.
- 10.5. Incompatible Materials: Strong acids, strong bases, strong oxidizers.

10.6. Hazardous Decomposition Products: None known.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on Toxicological Effects

Acute Toxicity: Inhalation:dust,mist: Harmful if inhaled.

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Goodwinol Ointment		
ATE (Dust/Mist)	4.86 mg/l/4h	
Rotenone (83-79-4)		
LD50 Oral Rat	60 mg/kg	
LD50 Dermal Rabbit	100 mg/kg	
Paraffin waxes and Hydrocarbon waxes (8002-74-	2)	
LD50 Oral Rat	> 3750 mg/kg	
LD50 Dermal Rabbit	> 3600 mg/kg	
Paraffin oils (8012-95-1)		
LD50 Oral Rat	> 24 g/kg	
LC50 Inhalation Rat	2062 ppm/4h	
3,5,7-Triaza-1-azoniatricyclo[3.3.1.13,7]decane, 1-(3-chloro-2-propenyl)-, chloride (4080-31-3)		
LD50 Oral Rat	500 mg/kg	
LD50 Dermal Rabbit	565 mg/kg	
Benzoic acid, 4-amino-, ethyl ester (94-09-7)		
LD50 Oral Rat	3042 mg/kg	

Skin Corrosion/Irritation: Not classified

Serious Eye Damage/Irritation: Not classified

Respiratory or Skin Sensitization: May cause an allergic skin reaction.

Germ Cell Mutagenicity: Not classified

Carcinogenicity: Not classified

IARC group

Reproductive Toxicity: Not classified

Specific Target Organ Toxicity (Single Exposure): Not classified

Specific Target Organ Toxicity (Repeated Exposure): Not classified

Aspiration Hazard: May be fatal if swallowed and enters airways.

Symptoms/Injuries After Inhalation: Inhalation is likely to cause adverse health effects including but not limited to: irritation, difficulty breathing, and unconsciousness.

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Symptoms/Injuries After Skin Contact: May cause an allergic skin reaction.

Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.

Symptoms/Injuries After Ingestion: Aspiration into the lungs can occur during ingestion or vomiting and may cause lung injury. Chronic Symptoms: None known.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity		
Ecology - General	: Very toxic to aquatic life. Harmful to aquatic life with long lasting effects.	
Rotenone (83-79-4)		
LC50 Fish 1	0.004 mg/l (Exposure time: 96 h - Species: Pimephales promelas [flow-through])	
EC50 Daphnia 1	0.0025 - 0.0055 mg/l (Exposure time: 48 h - Species: Daphnia magna [Static])	
LC50 Fish 2	0.0028 - 0.004 mg/l (Exposure time: 96 h - Species: Pimephales promelas [static])	
EC50 Daphnia 2	0.007 - 0.01 mg/l (Exposure time: 48 h - Species: Daphnia magna [Flow through])	
3,5,7-Triaza-1-azoniatricyclo[3.3.1.13,7]dec	ane, 1-(3-chloro-2-propenyl)-, chloride (4080-31-3)	
LC50 Fish 1	59 mg/l (Exposure time: 96 h - Species: Lepomis macrochirus)	
EC50 Daphnia 1	42 mg/l (Exposure time: 96 h - Species: Daphnia)	
Benzoic acid, 4-amino-, ethyl ester (94-09-7	7)	
LC50 Fish 1	34.6 - 36.1 mg/l (Exposure time: 96 h - Species: Pimephales promelas [flow-through])	
LC50 Fish 2	24.9 - 26.9 mg/l (Exposure time: 96 h - Species: Pimephales promelas [static])	
12.2. Persistence and Degradability		
Goodwinol Ointment		
Persistence and Degradability May cause long-term adverse effects in the environment.		
12.3. Bioaccumulative Potential		
Goodwinol Ointment		
Bioaccumulative Potential	Not established.	

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Other Information

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Rotenone (83-79-4)		
Log Pow	4.1	
Benzoic acid, 4-amino-, ethyl ester (94-09-7)		
Log Pow	1.86	

12.4. Mobility in Soil No additional information available

12.5. Other Adverse Effects

: Avoid release to the environment.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste Treatment Methods

Waste Disposal Recommendations: Dispose of contents/container in accordance with local, regional, national, and international regulations.

Additional Information: Container may remain hazardous when empty. Continue to observe all precautions.

Ecology - Waste Materials: Avoid release to the environment. This material is hazardous to the aquatic environment. Keep out of sewers and waterways.

SECTION 14: TRANSPORT IN	IFORMATION	
14.1. In Accordance with	DOT	
Proper Shipping Name	: HAZARDOUS WASTE, L	IQUID, N.O.S.
Hazard Class	: 9	ALL
Identification Number	: NA3082	Anny
Label Codes	: 9	9
Packing Group	: 111	
Marine Pollutant	: Marine pollutant	
ERG Number	: 171	
14.2. In Accordance with	IMDG	
Proper Shipping Name	: ENVIRONMENTALLY H	AZARDOUS SUBSTANCE, LIQUID, N.O.S.
Hazard Class	: 9	
Identification Number	: UN3082	
Packing Group	: 111	
Label Codes	: 9	
EmS-No. (Fire)	: F-A	AUIN
EmS-No. (Spillage)	: S-F	3
Marine Pollutant	: Marine pollutant	
14.3. In Accordance with	ΙΑΤΑ	
Proper Shipping Name	: ENVIRONMENTALLY H	AZARDOUS SUBSTANCE, LIQUID, N.O.S.
Packing Group	: 111	
Identification Number	: UN3082	atta.
Hazard Class	: 9	Anny.
Label Codes	: 9	9
ERG Code (IATA)	: 9L	
SECTION 15: REGULATORY	INFORMATION	
15.1. US Federal Regulation	ons	
Goodwinol Ointment		
SARA Section 311/312 Hazard Classes Immediate (acute) health hazard		
Paraffin waxes and Hydrocarbon waxes (8002-74-2)		
Listed on the United States TSCA (Toxic Substances Control Act) inventory		
Paraffin oils (8012-95-1)		
Listed on the United States TSCA (Toxic Substances Control Act) inventory		

3,5,7-Triaza-1-azoniatricyclo[3.3.1.13,7]decane, 1-(3-chloro-2-propenyl)-, chloride (4080-31-3) Listed on the United States TSCA (Toxic Substances Control Act) inventory

Subject to reporting requirements of United States SARA Section 313

SARA Section 313 - Emission Reporting 1.0 %

Benzoic acid, 4-amino-, ethyl ester (94-09-7)

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Listed on the United States TSCA (Toxic Substances Control Act) inventory

15.2. US State Regulations

Rotenone (83-79-4)

U.S. - Massachusetts - Right To Know List

U.S. - New Jersey - Right to Know Hazardous Substance List

U.S. - Pennsylvania - RTK (Right to Know) List

Paraffin waxes and Hydrocarbon waxes (8002-74-2)

U.S. - Massachusetts - Right To Know List

U.S. - New Jersey - Right to Know Hazardous Substance List

U.S. - Pennsylvania - RTK (Right to Know) List

Paraffin oils (8012-95-1)

U.S. - Massachusetts - Right To Know List

U.S. - New Jersey - Right to Know Hazardous Substance List

U.S. - Pennsylvania - RTK (Right to Know) List

3,5,7-Triaza-1-azoniatricyclo[3.3.1.13,7]decane, 1-(3-chloro-2-propenyl)-, chloride (4080-31-3)

U.S. - New Jersey - Right to Know Hazardous Substance List

SECTION 16: OTHER INFORMATION, INCLUDING DATE OF PREPARATION OR LAST REVISION

Revision Date

: 05/26/2016

Other Information

. US/20/2010

: This document has been prepared in accordance with the SDS requirements of the OSHA Hazard Communication Standard 29 CFR 1910.1200

GHS Full Text Phrases:

Acute Tox. 4 (Inhalation:dust,mist)	Acute toxicity (Inhalation:dust,mist) Category 4
Aquatic Acute 1	Hazardous to the aquatic environment - Acute Hazard Category 1
Aquatic Chronic 3	Hazardous to the aquatic environment - Chronic Hazard Category 3
Asp. Tox. 1	Aspiration hazard Category 1
Skin Sens. 1	Skin sensitization Category 1
H304	May be fatal if swallowed and enters airways
H317	May cause an allergic skin reaction
H332	Harmful if inhaled
H400	Very toxic to aquatic life
H412	Harmful to aquatic life with long lasting effects

This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product.

SDS US (GHS HazCom)



Canine post surgical lavage Canine synovial fluid replacement



Product Information

- Designed for Canine synovial fluid (SF) replacement
- Tested as post surgical lavage and SF replacement
- High molecular weight (MW) Hyaluronic Acid (HA)
- MW = 1.5-3M Daltons
- 15mg HA, 9mg Sodium Chloride, 1.0mL water
- 1mL in a sterile syringe
- Active components exhibit similar properties as SF
- Manufactured in an FDA approved human facility



Synovial fluid replacement of canine knee

Item Number: 001000



Clinical studies beign performed by Sherman Canapp, DVM, DACVS, DACVSMR at VOSM.



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Evervisc

Instructions for Use

Description: Evervisc sterile gel is a commercially available canine formulation of high molecular weight hyaluronic acid used for post-surgical lavage of synovial components.

Composition: Evervisc is made of a high molecular weight polysacchride composed of repeating disaccharide units of sodium glucuronate and N-acetylglucosamine.

Each syringe contains the following in a 1 ml dose sterile-filled into a syringe:

Hyaluronic Acid Sodium Chloride Water for Injection 15 mg 9 mg q.s. up to 1.0 mL

Contents: Each 1 mL syringe contains 15mg of high molecular weight hyaluronic acid.

Storage: Store at room temperature. Do not freeze.

Properties: Hyaluronic acid is an important component of synovial fluid. The active components in Evervisc exhibit viscoelastic properties similar in nature to synovial fluid. Introducing Evervisc into the synovial space as a post-surgical lavage and fluid replacement will assist in the normalization of the joint post-surgery.

Directions: Instill or inject Evervisc medical device up to 8 weeks following arthroscopy or surgery. Quantity to be determined by a Veterinary Surgeon. Treatment may be repeated as necessary. Properly discard of the syringe and any Evervisc remaining in the syringe after injection.

Warning: Keep out of reach of children. Do not reuse syringe.

How supplied: Single sterile syringe containing 1ml Evervisc within a sterile pouch.

Distributor:

Everost, Inc. Sturbridge, MA 01566, USA 1.855.EVEROST (383-7678)

Manufacturer:

Anika Therapeutics, Inc. Bedford, MA 01730, USA 1.800.457.9000

AML 500-302/A



EVERVISC POST-SURGICAL INJECTIONS

WHAT IS EVERVISC?

Evervisc is a post-surgical injection used as a synovial fluid replacement. It exhibits similar viscoelastic properties to that of synovial fluid. Each dosage contains 15mg high molecular weight hyaluronic acid (HA), 9mg of sodium chloride and up to 1.0mL of water. The most important component in both synovial fluid and Evervisc is HA. It coats, protects and lubricates the joints, allowing for pain free movement.

WHY USE HIGH MOLECULAR WEIGHT HA?

High molecular weight HA is a better lubricant and shock absorber and has a longer half-life than low molecular weight HA. High molecular weight binds very readily with water and creates an extremely viscous and Jell-O like substance, making it a good lubricant and shock absorber for joints. Low molecular weight HA does not create as viscous a substance, therefore is a poor lubricant and shock absorber. Low molecular weight HA within arthritic synovial fluid is the reason people with OA experience cartilage degradation and pain. The synovial fluid is so thin the articular cartilage rubs together and becomes weak. High molecular weight HA in post-surgical substitutes is also important because it has a long half-life in the body. Because post-surgical injections are foreign to the body they are cleared rapidly from the joints by lymphatics, which are small thin channels similar to blood vessels that carry tissue fluid from the body and drain it back into the blood stream. The average half-life of hyaluronic acid is about 20 hours in a healthy knee and 12 hours in an inflamed knee. By increasing the molecular weight of HA within the injection, the half-life is increased, so the injection will stay in the knee for 2-3 days versus one. Therefore the injection has more time in the joint to exhibit its beneficial effects.

BENEFITS OF EVERVISC

The HA in Evervisc works in five main ways to enhance the benefits and recovery of surgery. HA replenishes the synovial fluid lost during surgery, acts as a pain killer, an anti-inflammatory, stimulates the production of natural HA by synoviocytes and is convenient.

Prior to surgery, irrigation fluid is used to clean loose cartilage and debris from the joint. In doing so irrigation fluid also removes the synovial fluid and the HA layer that coats joint tissue and cartilage. Even though the irrigation fluid is drained after surgery some may reside in the knee. Continuous contact between the cartilage and irrigation fluid can lead to detrimental effects on both the chondrocytes, the cells that make up healthy cartilage, and cartilage metabolism. A synovial fluid substitute coats the articular cartilage and protects it from left over irrigation fluid. A lack of synovial fluid can also cause the cartilage and joint tissues rub together and become weak. By replenishing the joint with a synovial fluid substitute the cartilage and joint tissue in the knee is coated by HA and protected.

Evervisc also acts as a pain killer. Due to its viscoelasticity Evervisc has the ability to shield nerve endings and mechanoreceptors, sensory nerves that detect pain. The HA in Evervisc also inhibits increased vascular permeability induced by substance P. Substance P is a small peptide involved in the transmission of pain signals. Increasing vascular permeability allows an increased flow of fluid into the tissue, leading to swelling. It is chemicals released during the inflammatory process that cause nerve ending stimulation and pain. HA inhibits the increased vascular permeability induced by substance, relieving pain.

Evervisc also act as an anti-inflammatory. The HA in the injection binds to HA binding proteins on the cartilage surface and HA receptors on the synovial membrane. This creates a barrier that protects underlying tissue from damage caused by free radicals and pro-inflammatory cytokines produced by the inflammatory process following surgery. The barrier also helps protect against cartilage and tissue degradation as well as preventing inflammation of the joint.

The exogenous HA in Evervisc leads to the production of endogenous HA. Studies have shown HA within the knee days after the injections have been cleared from the joints by lymphatics. Leading to the conclusion that the exogenous HA stimulates the natural production of HA by synoviocytes. This allows for quicker and longer lasting results.

Lastly, studies have shown just one injection has effects lasting up to 6 month or longer while other post-surgical treatments require pills every day or continual treatments. Post-surgical injections are given directly after surgery and by the veterinarian, therefore are very convenient for the dog owner.



TESTING POST-SURGICAL INJECTIONS IN DOGS

Overall about 70% of dogs experience beneficial and lasting effects from post-surgical injections. The less chondral damage there is prior to surgery the longer the results tend to last. A study comparing the results of one, two and no post-surgical injections in dogs had very promising results. The five main parameters measured in the study were lameness, weight bearing, pain on palpation, change in serum CS-WF6 levels, and change in serum HA levels. CS-WF6 is a serum found in the joints that is linked to the degradation of cartilage. The study had three random groups. Each group had around the same number of each dog breed and 5 breeds of dogs were observed. Group 1 was given injections directly after surgery, group 2 was given one injection directly after surgery and another at the one week mark, while group 3 received no post-surgical injections. It lasted one month. At one week there were no significant differences in any of the five categories; the dogs given post-surgical injections had slightly lower levels of CS-WF6 in their joints at the one week mark. At this point the dogs in group 2 were given their second injections. During weeks 2, 3 and 4, all the groups showed progressive results in weight bearing, lameness and pain on palpation. However groups 1 and 2 had significantly more progress in all three categories, pulling farther and farther away from group 3 each week. Groups 1 and 2 also showed continuously decreasing amounts of CS-WF6, while group 3 levels increased with each week. From weeks 0-2 all three groups had decreasing levels of HA. At week 2 groups 1 and 2 began showing increasing levels of HA, regardless of the fact that the injections had already been cleared from the joints by lymphatics. Group 3 levels of HA continued to decrease. Overall group 2 did slightly better than group 1, but the differences were very small. All this leads to the conclusion that post-surgical injections result in less cartilage degradation, stimulation of endogenous HA, and faster pain relief/recovery in dogs. Many other recent studies have had very similar results and concluded these benefits can last up to a year or two.

WHY USE EVERVISC OVER OTHER ANALGESIC TECHNIQUES?

There are various other analgesic techniques used to treat pain following arthroscopic knee surgery. This includes systemic drugs, central and peripheral blocking agents, oral NSAIDs (nonsteroidal anti-inflammatory drugs), and intra-articular drug administration, however their analgesic effects are short lived. NSAIDs provide the most relief out of all of these methods, but there use is limited due to its gastric side effects. Post-surgical injections provide long lasting pain relief as well as having minimal harmful side effects.

SIDE EFFECTS

The most common side effect to a post-surgical injection is swelling and pain at the injection site. This should go away on its own after a few days. More serious, but very rare, side effects include pseudosepsis and liver damage. Pseudosepsis is a noninfectious disorder that mimics sepsis. It can be detected by pain and inflammation of the joint 24-72 hours after injection, a worsening of pain after each injection, a lack of infectious agents and calcium pyrophosphate crystals in synovial fluid and an increase in the number of mononuclear cells in synovial fluid from the surrounding membrane. Usually pseudosepsis is not self-limited and requires clinical intervention in the form NSAIDs (nonsteroidal anti-inflammatory drugs), or intra-articular steroid injections. There is no way to determine if a patient will develop pseudosepsis, but it is treatable and does not cause the body any permanent damage. Both side effects are linked to high molecular weight hyaluronic acid. This presents a problem because high molecular weight HA is the key component in the injections that cause them to work. Therefore in order to decrease the chance of side effects it is better to give more weekly injections of a molecular weight around 860-1000 kDaltons instead of giving less injections of HA with a molecular weight around 2300 kDaltons. The concentration of the HA in the injection also makes a difference. The higher the concentration of HA in the injection and the higher the molecular weight, the more likely it is for these side effect to occur.

CONCLUSIONS

After arthroscopic surgery, post-surgical injections are used in order to replenish the synovial fluid lost during surgery, act as a pain killer, an anti-inflammatory, and stimulate the production of natural HA by synoviocytes. Post-surgical injections have little harmful side effects and relieves pain better than other analgesic drugs. As little as one injection can have long-term, beneficial effects. Recent studies have only focused on post-surgical injections in dogs' knees, more testing needs to be done to see if it is suitable for other parts of the body.