

mobility can make life remarkable

Let's talk about why Adequan® Canine is the right choice for your dog.

There's nothing else like Adequan® Canine for dogs:

- Treats the disease, not just the signs of osteoarthritis (OA)¹
- Helps repair damaged cartilage
- Relied on by veterinarians for 20+ years
- Not a supplement, not just for pain

INDICATIONS Adequan® Canine is recommended for intramuscular injection for the control of signs associated with non-infectious degenerative and/or traumatic arthritis of canine synovial joints.

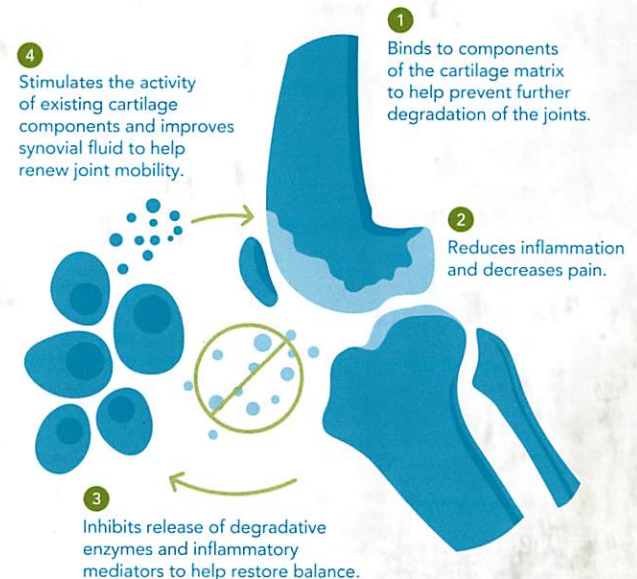
It works differently by preventing further joint damage and may help:¹

- **restore** joint lubrication
- **relieve** inflammation
- **renew** the building blocks of healthy cartilage

IMPORTANT SAFETY INFORMATION Adequan® Canine should not be used in dogs who are hypersensitive to PSGAG or who have a known or suspected bleeding disorder. It should be used with caution in dogs with renal or hepatic impairment. Adverse reactions in clinical studies (transient pain at injection site, transient diarrhea, and abnormal bleeding) were mild and self-limiting. In post approval experience, death has been reported in some cases; vomiting, anorexia, depression/lethargy and diarrhea have also been reported. The safe use of PSGAG in breeding, pregnant or lactating dogs has not been evaluated. *Please see Full Prescribing Information on back or at adequancanine.com.*

How Adequan® Canine Works^{1,2} (polysulfated glycosaminoglycan)

The specific mechanism of action of Adequan® in canine joints is not known.¹



1. Adequan® Canine Package Insert, Rev 1/19.

2. Adequan® Canine (polysulfated glycosaminoglycan) NADA 141-038 FOI Summary, 1997.

Adequan® Canine
polysulfated glycosaminoglycan

A multi-modal plan for your dog's mobility.

Along with Adequan® Canine, let's include:

- _____
- _____
- _____

Put your dog's treatment dates on the calendar. Twice a week, up to 4 weeks is recommended:

Wk #1: Visit #1 _____	Visit #2 _____	Wk #3: Visit #1 _____	Visit #2 _____
Wk #2: Visit #1 _____	Visit #2 _____	Wk #4: Visit #1 _____	Visit #2 _____



Brand of Polysulfated Glycosaminoglycan
Solution 100 mg/mL in a 5 mL preserved
Multiple dose vial for intramuscular use in dogs.



Description: The active ingredient in Adequan® Canine is polysulfated glycosaminoglycan (PSGAG). Polysulfated glycosaminoglycan is a semi-synthetic glycosaminoglycan prepared by extracting glycosaminoglycans (GAGs) from bovine tracheal cartilage. GAGs are polysaccharides composed of repeating disaccharide units. The GAG present in PSGAG is principally chondroitin sulfate containing 3 to 4 sulfate esters per disaccharide unit. The molecular weight for PSGAG used in the manufacture of Adequan® is 3,000 to 15,000 daltons.

Each ml of Adequaph® contains 100 mg of PSGLG, 0.9% *in vivo* benzyl alcohol as a preservative, and water for injection q.s. to 1 ml. Sodium hydroxide and/or hydrochloric acid is added when necessary to adjust pH. The solution is clear, colorless to slightly yellow.

[illegible]

synthesis by synovial membrane cells *in vitro*. Absorption, distribution, metabolism, and excretion of PSGAG following intramuscular injection have been studied in several species, including rats, rabbits, humans, horses and dogs.

Studies in rabbits showed maximum blood concentrations of PS6G following intravenous injection, and that the drug was distributed to all tissues studied, including articular cartilage, synovial fluid, adrenals, thyroid, peritoneal fluid, lungs, eyes, spinal cord, kidneys, brain, liver, spleen, bone marrow, skin, and heart.

Following intramuscular injection of PS-GAG in humans, the drug was found to be bound to serum proteins. PS-GAG binds to both albumin and α_2 and β_2 -globulins and the extent of the binding is suggested to be 30 to 40%. Therefore, the drug may be present in both bound and free form in the bloodstream. Because of its relatively low molecular weight, the synovial membrane is not a significant barrier to distribution of PS-GAG from the bloodstream to the synovial fluid. Distribution from the synovial fluid to the cartilage takes place by diffusion, in the articular cartilage the drug is deposited into the cartilage matrix.

Serum and synovial fluid distribution curves of PSGAG have been studied in dogs and appear similar to those found in humans and rabbits.

Metabolism may also occur in the kidneys. PSGAG administered intramuscularly and not protein excreted in the feces.

Toxicity: In a study by Goss et al., male rats were administered either 0.6% saline solution or PSGAG at a dose of 5 mg, 15 mg, or 50 mg per kg body weight twice weekly for 2 weeks. PSGAG doses represented approximately 1X, 3X, and 10X the recommended dosage of 2 mg/kg and more than 3 times the recommended 4-week duration of treatment. Necropsies were performed on all animals.

[illegible]

Effectivity of Adequan® Canine was demonstrated in two studies. A laboratory study using radiolabelled PSGAG established distribution of PSGAG into canine serum and synovial fluid following a single intramuscular injection of 2 mg/kg. A clinical trial that was conducted in dogs diagnosed with radiographically-confirmed traumatic and/or degenerative joint disease of 1 or 2 joints. Joints evaluated included hips, stifles, shoulders, hocks and elbows. Fifty-one dogs were randomly assigned to receive either Adequan® Canine at 2 mg/kg of body weight or 0.9% saline. Efficacy of Adequan® Canine was measured using a visual analogue scale (VAS) and a modified

Both treatment groups were administered intramuscular infection twice weekly for 4 weeks (8 injections) [16]. Injections were administered by intramuscular injection and evaluating the dogs were unaware of the treatment assignment. A total of 71 limbs in 51 dogs were evaluated. Of these, 35 limbs in 24 dogs were in the Adequan® Canine treated group. Each lame limb was scored for lameness at a walk, lameness at a trot, pain, range of motion, and functional disability. The scores for the individual lameness treatment were summed to determine a total orthopedic score. At the end of the treatment period, dogs treated with Adequan® Canine showed a statistically significant improvement in range of motion and total orthopedic score over placebo treated control dogs.

Contraindications: Do not use in dogs showing hypersensitivity to PSGAG. PSGAG is a synthetic hyaluronan; do not use in dogs with known or suspected bleeding disorders.

Precautions: The safe use of Adequan® Canine used in breeding, pregnant, or lactating dogs has not been evaluated. Use with caution in dogs with renal or hepatic impairment.

These included transient pain at the injection site (1 incident), transient diarrhoea (1 incident each in 2 dogs), and abnormal bleeding (1 incident). These effects were mild and self-limiting and did

not require interruption of therapy.
Post Approval Experience (2014)

the following adverse events are based on voluntarily, post-approval reporting, and may not be representative of the frequency or establish a causal relationship to product exposure using these data. The event frequency are reported to FDA/CVM. It is not always possible to reliably estimate the adverse reactions are reported to FDA/CVM.

signs reported are listed in decreasing order of reporting frequency. Vomiting, anorexia, depression/lethargy, diarrhea. In some cases, death has been reported.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

DOSEAGE AND ADMINISTRATION: Practice aseptic techniques in withdrawing each dose to decrease the possibility of post-injection bacterial infections. Adequately clean and disinfect the stopper prior to entry with a sterile needle and syringe. Use only sterile needles, and use each needle only once.

The recommended dose of Adequan® Caine is 2 mg/lb body weight (.02 mL/lb. or 1 mL per lb.) administered intramuscularly once daily for 7-10 days. The recommended dose may be repeated after 6 weeks.

The vial stopper may be punctured a maximum of 10 times.

50 lb), by intramuscular injection only, twice weekly for up to 4 weeks (maximum of 8 injections). Do not exceed the recommended dose or therapeutic regimen. Do not mix Adequan® Canine with

Storage Conditions: Store at 20° to 25°C (68° to 77°F) excursions permitted to 15° to 30°C (59° to 86°F). (See USP Controlled Room Temperature). Avoid prolonged exposure to temperatures ≥ 40°C (104°F).

Uses within 28 days of first puncture and puncture a maximum of 10 times. Dispose of spent needles in accordance with all federal, state and local environmental laws.

How Supplied: Adequan® Canine Solution 100 mg/mL in a 5 mL preserved multiple dose vial. NDC 10797-975-02 5 mL Multiple Dose Vials. Packaged 2 vials per box

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ANIMAL HEALTH

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NADA 141-038, Approved by FDA
Made in U.S.A.
Rev. 1/19
IN975

IN975
MG #44454



restore relieve renew rethink

Discover if Adequan® Canine (polysulfated glycosaminoglycan) is the right choice for your patients.

feature #1

Only FDA-approved, disease-modifying osteoarthritis (OA) drug that's never been duplicated.¹

benefit #1

Enters the joints quickly, within 2 hours, to help control the signs associated with non-infectious degenerative and/or traumatic arthritis of canine synovial joints.² It delivers therapeutic concentrations in synovial fluid and articular cartilage which last up to 3 days.²

The specific mechanism of action of Adequan® in canine joints is not known.¹

feature #2

Provides fast relief and reliable protection to help **renew** joint mobility.

benefit #2

Adequan® Canine (polysulfated glycosaminoglycan) inhibits cartilage loss in a dog's synovial joints, and may help to:¹

- **restore** joint lubrication
- **relieve** inflammation
- **renew** the building blocks of healthy cartilage

feature #3

Used early for OA, it may help dogs stay active longer and keep moving throughout life's adventures.

benefit #3

Efficacy demonstrated in two clinical studies, which showed Adequan® Canine inhibits the enzymes that can break down cartilage, leading to reduced joint damage and slowing the progression of OA.¹

The difference between feeling better and getting better.®

Adequan® Canine brand of polysulfated glycosaminoglycan (PSGAG)

INDICATIONS Adequan® Canine is recommended for intramuscular injection for the control of signs associated with non-infectious degenerative and/or traumatic arthritis of canine synovial joints. **IMPORTANT SAFETY INFORMATION** Adequan® Canine should not be used in dogs who are hypersensitive to PSGAG or who have a known or suspected bleeding disorder. It should be used with caution in dogs with renal or hepatic impairment. Adverse reactions in clinical studies (transient pain at injection site, transient diarrhea, and abnormal bleeding) were mild and self-limiting. In post approval experience, death has been reported in some cases; vomiting, anorexia, depression/lethargy and diarrhea have also been reported. The safe use of PSGAG in breeding, pregnant or lactating dogs has not been evaluated. **Caution:** Federal law restricts this drug to use by or on the order of a licensed veterinarian. For additional safety information, please see Full Prescribing Information at adequancanine.com.

1. Adequan® Canine Package Insert, Rev. 1/19.

2. Adequan® Canine (polysulfated glycosaminoglycan) NADA 141-038 FOI Summary, 1997.

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For more information on this product.

website: adequancanine.com

call: 800-458-0163

email: cs@americanregent.com

What does Adequan® Canine offer?

Product Features	Adequan® Canine*	Oral Joint Supplements**	NSAIDs
Only FDA-approved disease-modifying osteoarthritis drug (DMOAD) for dogs ¹	✓	✗	✗
FDA-reviewed studies with proven efficacy results for treating the OA disease process in dogs ¹	✓	✗	✗
Approved canine formula – polysulfated with a low molecular weight, allowing for diffusion into the joint and deposition into the cartilage ¹	✓	✗	✗
Shown to inhibit catabolic enzymes and promote anabolic activity in the joint ¹	✓	✗	✗
Shown to reduce inflammation	✓	✗	✓
Veterinary prescription only	✓	✗	✓
Product quality assurance, consistency and manufacturing with FDA-label requirements	✓	✗	✓
Long-standing safety profile and post-approval monitoring and reporting of adverse events with FDA	✓	✗	✓

*The specific mechanism of action of Adequan® in canine joints is not known.

**Not FDA-approved

NSAIDs – Nonsteroidal anti-inflammatory drugs

All products have the potential for adverse events that should be considered in overall management of any disease.

1. Adequan® Canine Package Insert, Rev. 1/19.

rethink OA think DMOAD

As the only DMOAD, Adequan® Canine (polysulfated glycosaminoglycan) empowers you to proactively treat the disease and not just the signs of canine osteoarthritis.¹

- Starting treatment early with Adequan® Canine can help slow the progression of osteoarthritis (OA).
- Once canine OA begins, the clock is ticking.
- Without treatment, deterioration of joint cartilage, surrounding tissue and fluid begins; eventually leading to bone-on-bone contact, chronic inflammation and loss of mobility.²

Please see the Important Safety Information on the reverse side.

Discover if Adequan® Canine is the right choice for your patients.



2. 2016 NAVC Proceedings, Osteoarthritis in Dogs and Cats: Novel Therapeutic Advances, M Epstein, DVM, DABVP C/F, CVPP; K Kirkby Shaw, DVM, MS, PhD, DACVS, DACVSM.