Veterinary Medical Affairs, American Regent, Inc

It's not a question of if DJD will occur, but when.

Throughout a horse's lifetime, joints bend, flex, bear weight and absorb shock in varying degrees. Every movement, ride or event puts "wear and tear" on the joints, reflected by the high prevalence of Degenerative Joint Disease (DJD) across the equine population. DJD is defined as "A group of disorders characterized by a common end stage in which progressive deterioration of the articular cartilage is accompanied by changes in bone and soft tissues of the joint. Regardless of age or discipline, DJD can occur within any joint that consistently undergoes wear and tear, known as "use trauma". This is an important reminder that joint disease can affect horses of every age and lifestyle – from top competitors and weekend warriors to backyard companions. Or, as one leading equine veterinarian so aptly put it, "If you have a horse, you have an athlete."

Extend the patient's "mobility span" not just life span.

Through every life stage of horses, different management strategies may be necessary to maintain soundness. As horses are living longer, veterinarians are tasked with helping maintain quality of life.4 Since mobility is a vital component to quality of life for every equine patient, detecting problems early and prescribing prompt treatment when disease or injury occurs is key to maximizing and maintaining healthy joints over the horse's life span or career. Put another way, a proactive approach to diagnosis and treatment can help extend a horse's mobility span.

DJD RISKS THROUGH THE YEARS

EARLY RISKS MATURE RISKS SENIOR RISKS Young horses may develop lameness · In healthy aging horses, lameness is · A common cause of DJD in aged horses prematurely from conformational the #1 concern identified by owners is osteoarthritis, or end-stage DJD abnormalities which can greatly influence and veterinarians.3 the degree of wear and tear that a Older hunters or dressage horses maturing joint undergoes. · Lameness is the #1 reason for loss will commonly develop front limb of use and death.3 lameness from DJD, such as in the · These abnormalities can greatly alter coffin or fetlock joints. forces applied to joints - and can • DJD is a common problem that affects potentially lead to joint instability, the career longevity of performance · Several factors likely contribute to the injury, and DJD. horses. loss of tendon and ligament resiliency in aged horses, such as impaired In young foals and growing horses, Mature performance horses may regenerative capacity, decreased conformation abnormalities should be experience physical changes resulting metabolic efficiency and accumulation addressed as early as possible. in increased risk of injury or of products of lifelong wear and tear.3 exacerbation of chronic injury. The mature equine athlete that is > A 2018 study found an association performing well has likely adapted · Clients and trainers should between suspensory ligament to any conformational issues that exist. proactively manage joint health degeneration and the agein anticipation of senior years. related disease Pituitary pars · Cutting, reining and gaited horses put intermediate dysfunction (PPID) in significant stress on hocks and stifles aged horses.5 early in life - locations where DJD first develops. Focus on nutrition, balanced farriery, adequate Focus on avoiding injury, preserving joint health Focus on preserving mobility, detection training and muscle development. under 'wear and tear.' of underlying medical problems.

INDICATIONS

Adequan® i.m. (polysulfated glycosaminoglycan) is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

Technical Bulletin



Mobility is longevity:

Start early. Stay vigilant.

The onset and progression of Degenerative Joint Disease results in the loss of cartilage components, so early intervention is important. Once diagnosis is made, develop a treatment plan focused on inhibiting the destructive processes of DJD in the beginning stages before mobility is compromised.

Adequan® i.m. (polysulfated glycosaminoglycan) is the only FDA-Approved equine PSGAG recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.⁶

Please see accompanying Full Prescribing Information on back cover.

Adequan has been proven to work in multiple ways to maintain joint function: 67

Adequan® i.m. works in multiple ways to keep joints moving: 6,7



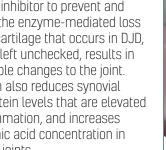
- REDUCES inflammation.
- **RESTORES** joint lubrication
- REPAIRS cartilage
- REVERSES the disease process

Inhibits enzymes that attack cartilage and synovial fluid.^{6,7}



Healthy Cartilage

Only Adequan i.m. acts as a potent enzyme inhibitor to prevent and reverse the enzyme-mediated loss of joint cartilage that occurs in DJD, which if left unchecked, results in irreversible changes to the joint. Adequan also reduces synovial fluid protein levels that are elevated in inflammation, and increases hyaluronic acid concentration in affected joints.





SELECTED IMPORTANT SAFETY INFORMATION

There are no known contraindications to the use of Adequan® i.m. and no age or breed restrictions. The safe use of Adequan® i.m. in horses used for breeding, during pregnancy or in lactating mares has not been evaluated.



Mobility is longevity:

How Adequan can help extend a horse's mobility span:







Assess mobility routinely.

Make mobility a "vital sign" at every wellness examination

- · Look for clinical signs of DJD
- Ask the owner about any changes that may indicate onset of a joint problem

Treat the disease.

- Owners work with the veterinarian to discover if Adequan® i.m. is the right choice for their horse.
- At early signs of DJD veterinarians may use or prescribe Adequan® i.m. at the approved 500 mg dose;
- 1 injection, every 4 days, 7 treatments (Total of 28 days)

Stay proactive.

- Veterinarians educate owners and trainers on early signs of joint problems reoccurring.
- Trainers and owners continue monitoring the horse's joint health and mobility and alert their veterinarian of any changes.

Repeat treatment.

Repeat the 1.4.7 series as needed upon recurrence of signs to help keep joints working and the horse performing.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.









Start with collaboration. Stay with it.

Whether managing a two-year old in training or a geriatric companion, proactive collaboration at all life stages between veterinarians, owners, and trainers in identifying and managing DJD is pivotal to healthy longevity. When you start with and stay with Adequan i.m., horses may enjoy greater mobility over a lifetime.^{1,2,6}

Discover if Adequan is the right choice for your patients.

INDICATIONS

Adequan® i.m. is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

IMPORTANT SAFETY INFORMATION

There are no known contraindications to the use of intramuscular Polysulfated Glycosaminoglycan (PSGAG). Studies have not been conducted to establish safety in breeding horses. **WARNING:** Do not use in horses intended for human consumption. Not for use in humans. Keep this and all medications out of the reach of children. **CAUTION:** Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Please see accompanying Full Prescribing Information or visit adequan.com



polysulfated glycosaminoglycan

SINGLE DOSE

Solution 500 mg/5 mL For Intramuscular Use In Horses



CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Each 5 milliliters of Adequan® i.m. contains 500 mg of Polysulfated Glycosaminoglycan (PSGAG) and Water for Injection q.s. Sodium Hydroxide and/or Hydrochloric Acid added when necessary to adjust pH. Sodium Chloride may be added to adjust tonicity.

PHARMACOLOGY: Polysulfated Glycosaminoglycan is chemically similar to the glycosaminoglycans in articular cartilage matrix. PSGAG is a potent proteolytic enzyme inhibitor and diminishes or reverses the pathologic processes of traumatic or degenerative joint disease which result in a net loss of cartilage matrix components. PSGAG improves joint function by reducing synovial fluid protein levels and increasing synovial fluid hyaluronic acid concentration in traumatized equine carpal and hock joints.

INDICATIONS: Adequan® i.m. is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

DOSAGE AND ADMINISTRATION: The recommended dose of Adequan® i.m. in horses is 500 mg every 4 days for 28 days intramuscularly. The injection site must be thoroughly cleansed prior to injection. Do not mix Adequan® i.m. with other drugs or solvents.

CONTRAINDICATIONS: There are no known contraindications to the use of intramuscular Polysulfated Glycosaminoglycan.

WARNINGS: Do not use in horses intended for human consumption. Not for use in humans. Keep this and all medications out of the reach of children.

PRECAUTIONS: The safe use of Adequan® i.m. in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated.

ANIMAL SAFETY: Toxicity studies were conducted in horses. Doses as high as 2,500 mg were administered intramuscularly to 6 horses twice a week for 12 weeks. This dosage is 5 times the recommended dosage and 3 times the recommended therapeutic regimen. Clinical observations revealed no soreness or swelling at the injection site or in the affected joint. No animal had any clinical or laboratory evidence of toxicity.

STORAGE CONDITIONS: Store at 20°-25°C (68°-77°F); (See USP Controlled Room Temperature). Discard unused portion.

Dispose of spent needles in accordance with all federal, state and local environmental laws.

HOW SUPPLIED: Adequan $^{\tiny\textcircled{\tiny 0}}$ i.m. solution, 500 mg/5 mL (100 mg/mL) in a 5 mL single dose glass vial.

NDC 10797-995-70 5 mL Single Dose Vials

Packaged 7 vials per box

AMERICAN REGENT, INC. ANIMAL HEALTH Shirley, NY 11967 (1-888-354-4857) Made in U.S.A. IN99501 Rev. 9/2021 MG #44455

Approved by FDA under NADA # 140-901



MULTI-DOSE

Solution 100 mg/mL in a 50 mL Preserved Multi-Dose Vial For Intramuscular Use In Horses Only. Not for Intra-Articular Use



CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Each mL contains Polysulfated Glycosaminoglycan (PSGAG) 100 mg, Benzyl Alcohol 0.9% v/v as a preservative, and Water for Injection q.s. Sodium Hydroxide and/or Hydrochloric Acid added when necessary to adjust pH. The solution is clear, colorless to slightly yellow.

PHARMACOLOGY: Polysulfated Glycosaminoglycan is chemically similar to the glycosaminoglycans in articular cartilage matrix. PSGAG is a potent proteolytic enzyme inhibitor and diminishes or reverses the pathologic processes of traumatic or degenerative joint disease which result in a net loss of cartilage matrix components. PSGAG improves joint function by reducing synovial fluid protein levels and increasing synovial fluid hyaluronic acid concentration in traumatized equine carpal and hock joints.

INDICATIONS: Adequan® i.m. Multi-Dose is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

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

The recommended dose of Adequan® i.m. Multi-Dose in horses is 500 mg every 4 days for 28 days intramuscularly. The injection site must be thoroughly cleansed prior to injection. Do not mix Adequan® i.m. Multi-Dose with other drugs or solvents.

CONTRAINDICATIONS: There are no known contraindications to the use of intramuscular Polysulfated Glycosaminoglycan.

WARNINGS: Do not use in horses intended for human consumption. Not for use in humans. Keep this and all medications out of the reach of children.

PRECAUTIONS: The safe use of Adequan® i.m. Multi-Dose in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated.

SAFETY AND EFFICACY: Safety and efficacy studies utilizing Adequan® i.m. Multi-Dose were not performed. Adequan® i.m. Multi-Dose was approved based on the conclusion that the safety and effectiveness of Adequan® i.m. Multi-Dose will not differ from that demonstrated for the original formulation of Adequan® i.m.

ANIMAL SAFETY: Animal Safety studies utilizing Adequan® i.m. Multi-Dose were not performed. Safety studies were conducted in horses using the single dose formulation. Doses as high as 2,500 mg were administered intramuscularly to 6 horses twice a week for 12 weeks. This dosage is 5 times the recommended dosage and 3 times the recommended therapeutic regimen. Clinical observations revealed no soreness or swelling at the injection site or in the affected joint. No animal had any clinical or laboratory evidence of toxicity.

STORAGE CONDITIONS: Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F) (See USP Controlled Room Temperature). Avoid prolonged exposure to temperatures \geq 40°C (104°F).

Use 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® i.m. Multi-Dose solution, 5,000 mg/50 mL (100 mg/mL) in 50 mL multi-dose glass vials.

NDC 10797-959-01 50 mL Multi-Dose Vials Packaged 1 vial per box

NDC 10797-959-01 AMERICAN REGENT, INC. ANIMAL HEALTH Shirley, NY 11967 (1-888-354-4857) Packaged 1 vial per box Made in U.S.A. IN959 Rev. 9/2021

MG #44453

Approved by FDA under NADA # 140-901

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