TECHNICAL BULLETIN

The Difference is in the Details:
FDA Approved Drugs vs. Compounded Products and Veterinary Medical Devices

Dr. Marian G. Little, Technical Services Veterinarian, Luitpold Pharmaceuticals, Inc.

Equine veterinarians are increasingly challenged to provide sound medical care while operating within economic restrictions. In efforts to maintain client goodwill and minimize treatment costs, veterinarians may consider non-Food and Drug Administration (FDA) approved product alternatives, such as compounded drugs and veterinary medical devices. When veterinarians choose to administer products that have not undergone equivalent clinical testing for safety and efficacy in the horse, unforeseen risks may arise. Therefore, it is important for veterinarians to understand and, if appropriate, communicate the importance of using FDA approved drugs, such as Adequan® i.m. (polysulfated glycosaminoglycan) and BetaVet® (betamethasone sodium phosphate & betamethasone acetate).

Adequan® i.m. and BetaVet® are FDA Approved Pioneer Drugs.

FDA Pioneer Drug:¹

- A drug that has undergone the scrutiny of blinded controlled studies to demonstrate safety and efficacy in accordance with Good Laboratory Procedures (GLPs)
- The product is manufactured under FDA mandated Good Manufacturing Practices (GMPs) in regularly inspected plants

(Continued on next page)

Adequan® i.m.

INDICATIONS
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 Adequan® i.m. brand Polysulfated Glycosaminoglycan in horses. 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. Each 5 mL contains 500 mg Polysulfated Glycosaminoglycan.
BetaVet® (betamethasone sodium phosphate & betamethasone acetate)

**INDICATION:** BetaVet® is indicated for the control of pain and inflammation associated with osteoarthritis in horses.

**SELECTED SAFETY INFORMATION**
For Intra-Articular (I.A.) Use in Horses.

**CONTRAINDICATIONS:** BetaVet® is contraindicated in horses with hypersensitivity to betamethasone. Intra-articular injection of corticosteroids for local effect is contraindicated in the presence of septic arthritis.

There is NO generic Adequan® i.m. (polysulfated glycosaminoglycan) or BetaVet® (betamethasone sodium phosphate & betamethasone acetate).

**Generic Drug:**

- A generic drug is bioequivalent to a pioneer drug in dosage form, efficacy, safety and strength, route of administration, quality, and intended use
- Generic drug approvals are only considered after the pioneer drug’s patent has expired
- Generic drugs are manufactured under the same GMP requirements as pioneer drugs
- Use of a human drug in an animal constitutes off-label use

**How to identify:**

- Most generic drug labels display an Abbreviated New Animal Drug Application (ANADA) number signifying FDA approval of a generic animal drug
- Abbreviated New Drug Application (ANDA) numbers signify approval of a generic human drug

**Therapeutic consistency, product quality, accurate shelf life, and scientifically substantiated labeling are FDA mandated**

**Stringent standards for drug potency and purity must be established and stability data generated to determine expiration dating**

**Detailed records of each batch of drug produced are maintained and retained for future testing**

**The manufacturer conducts ongoing surveillance for adverse events involving lack of safety or efficacy and must regularly provide reporting data to the FDA**

**How to identify:**

- All FDA approved veterinary pharmaceutical pioneer products carry a six-digit New Animal Drug Application (NADA) number. Most drug manufacturers list the number and the statement, “Approved by FDA,” on the drug’s label

Generic Drug: 1

Generic Drug: 1

- A generic drug is bioequivalent to a pioneer drug in dosage form, efficacy, safety and strength, route of administration, quality, and intended use
- Generic drug approvals are only considered after the pioneer drug’s patent has expired
- Generic drugs are manufactured under the same GMP requirements as pioneer drugs
- Use of a human drug in an animal constitutes off-label use

**How to identify:**

- Most generic drug labels display an Abbreviated New Animal Drug Application (ANADA) number signifying FDA approval of a generic animal drug
- Abbreviated New Drug Application (ANDA) numbers signify approval of a generic human drug

(Continued on next page)
WARNINGS: Do not use in horses intended for human consumption. Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Additionally, corticosteroids administered to dogs, rabbits and rodents during pregnancy have resulted in cleft palate in offspring and in other congenital anomalies including deformed forelegs, phocomelia and anasarca. Therefore, before use of corticosteroids in pregnant animals, the possible benefits to the pregnant animal should be weighed against potential hazards to its developing embryo or fetus. Human Warnings: Not for use in humans. For use in animals only. Keep this and all medications out of the reach of children. Consult a physician in the case of accidental human exposure.

What about Compounded Veterinary Drugs?

Compounded Drug:\(^1\)

- Any drug manipulated to produce a dosage form (other than that provided for in the directions for use on labeling of the approved drug product)
- Compounded drugs are not ‘generic’ drugs
- Neither cost nor convenience is a justification for using compounded preparations. Compounding provides a customized formulation for the special needs of a particular patient, when no approved presentation is available, within the context of a Veterinarian-Client-Patient Relationship (VCPR)
- FDA-approved medications should be used to formulate compounded medications
- Some state pharmacy boards require compounded drugs to be dispensed at cost
- Every compounded drug must have a beyond-use date which should not exceed 180 days from preparation\(^3\)
- The prescribing veterinarian assumes responsibility when using compounded preparations
- **How to identify:**
  - The primary label of a compounded medication should include a statement notifying the client that the medication has been compounded. When a branded drug product has been used as a source of the drug, the generic name of the drug product, not the proprietary name, should be placed on the label\(^1\)
  - State regulations differ in label requirements, but the FDA recently issued a document Guidance for Industry: Compounding Animal Drugs from Bulk Drug Substances, May 2015, in which specific labeling recommendations are contained\(^4\)

(Continued Important Safety Information for BetaVet\(^\text{®}\))
Are Veterinary Medical Devices Equivalent to FDA Approved Drugs?

**Veterinary Medical Devices:**

- Medical devices as defined by the FDA in the Food Drug and Cosmetic Act, Section 210(h): “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent,...which does not achieve any of its principal intended purposes through chemical action... and is not dependent upon being metabolized for the achievement of any of its principal intended purposes”

- Although under FDA oversight for promotion and marketing, devices manufactured solely for use in veterinary medicine are not required to undergo a pre-marketing approval process

- The manufacturing process of veterinary devices is not required to meet uniform standards, i.e. no set standards to assure quality control for purity, potency, stability and sterility; no mandatory requirements for reporting adverse events

- “Off-label” drug use does not apply to veterinary medical devices. These devices have not undergone clinical testing for safety or efficacy as a drug, hence no approved label Indication, Dosing, or Contraindication information
  - A 2016 study evaluated the efficacy of IV administration of a combination product containing hyaluronan, sodium chondroitin sulfate, and N-acetyl-D-glucosamine for prevention or treatment of osteoarthritis in 32 healthy 2- to 5-year old horses
  - The study concluded that caution should be used when administering the product IV to horses, particularly when administering it prophylactically, as it may have no benefit or may even cause harm

---

**BetaVet®**

**SELECTED SAFETY INFORMATION**

**PRECAUTIONS:** Corticosteroids, including BetaVet®, administered intra-articularly are systemically absorbed. Do not use in horses with acute infections. Acute moderate to severe exacerbation of pain, further loss of joint motion, fever, or malaise within several days following intra-articular injection may indicate a septic process. Because of the anti-inflammatory action of corticosteroids, signs of infection in the treated joint may be masked. Due to the potential for exacerbation of clinical signs of laminitis, glucocorticoids should be used with caution in horses with a history of laminitis, or horses otherwise at a higher risk for laminitis. Use with caution in horses with chronic nephritis, equine pituitary pars intermedia dysfunction (PPID), and congestive heart failure. Concurrent use of other anti-inflammatory drugs, such as NSAIDs or other corticosteroids, should be approached with caution. Due to the potential for systemic exposure, concomitant use of NSAIDs and corticosteroids may increase the risk of gastrointestinal, renal, and other toxicity. Consider appropriate wash out times prior to administering additional NSAIDs or corticosteroids.
Veterinary device labeling and ingredients may appear very similar to FDA approved drugs

- For example, some products contain only monosulfated chondroitin sulfate, which is not chemically equivalent to polysulfated glycosaminoglycan (PSGAG) in Adequan®. Adequan® contains 3-4 sulfate esters per disaccharide molecule, differs in structure and function, and no bioequivalent product exists.⁷,⁸

- **How to identify:**
  - The labeling of medical devices used within veterinary medicine may not contain language identifying the product as a device. If the practitioner has questions regarding the status of a product, he or she should contact the manufacturer.

In summary, the significance of FDA approval is essential for both veterinarians and clients to understand. For a new drug to satisfy each stage of the FDA approval process often takes years, and veterinarians should consider the benefits of using these drugs over non-approved alternatives. Stringent FDA approval requirements provide the benchmark for veterinary drug safety and efficacy, and allow practitioners to provide optimal care to the horse.

**References:**


(Continued Important Safety Information for BetaVet®)

**ADVERSE REACTIONS:** Adverse reactions reported during a field study of 239 horses of various breeds which had been administered either BetaVet® (n=119) or a saline control (n=120) at five percent (5%) and above were: acute joint effusion and/or local injection site swelling (within 2 days of injection), 15% BetaVet® and 13% saline control; increased lameness (within the first 5 days), 6.7% BetaVet® and 8.3% saline control; loose stool, 5.9% BetaVet® and 8.3% saline control; increased heat in joint, 2.5% BetaVet® and 5% saline control; and depression, 5.9% BetaVet® and 1.6% saline control.

**DOSAGE AND ADMINISTRATION:** Shake well immediately before use. Use immediately after opening, then discard any remaining contents.

**RX ONLY**
Luitpold Animal Health is proud to provide the equine industry with the following Food and Drug Administration (FDA) approved products:

To report an adverse event for any Luitpold Animal Health product:

- **Contact Luitpold Animal Health**
  - Toll-free: (800) 734-9236
  - Email: pv@luitpold.com

- **Contact the Center for Veterinary Medicine**
  - Email: CVMAESupport@fda.hhs.gov
  - Call: (888) FDA-VETS

Please see Full Prescribing Information in pocket.