DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

AUG 26 2008

NADA 141-186 (L-0086, L-0088)

Randy C. Lynn, DVM
Director, Professional Services
IDEXX Pharmaceuticals, Inc.
7009 Albert Pick Road
Greensboro, NC 27409

RE: NADA 141-186 - Surpass® (1% diclofenac sodium) Topical Anti-inflammatory Cream for Use in Horses

Dear Dr. Lynn:

The U.S. Food and Drug Administration, Center for Veterinary Medicine (CVM), Division of Surveillance reviewed three advertisements and a document identified as a mail and handout ad for the product Surpass® (1% diclofenac sodium) Topical Anti-inflammatory Cream for Use in Horses, NADA 141-186. These promotional pieces are false or misleading. The advertisements misbrand the drug within the meaning of section 502(n) of the Federal Food, Drug and Cosmetic Act (the Act) [21 U.S.C. 352(n)]. The mail and handout piece misbrands the drug within the meaning of 502(a) of the Act [21 U.S.C. 352(a)].

Background
Surpass® (1% diclofenac sodium) Topical Anti-inflammatory Cream for Use in Horses, is indicated for the control of pain and inflammation associated with osteoarthritis (OA) in tarsal, carpal, metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal (hock, knee, fetlock, and pastern) joints in horses. Surpass® is approved for application of a five-inch (5") ribbon of cream twice daily over the affected joint. The cream is rubbed thoroughly into the hair covering the joint until the cream disappears.

We reviewed the advertisements identified an ad for Barrel Racer and Barrel Horse News (09-65495-04), an ad for The Horse, Equus, Chronicle of the Horse, and Practical Horseman (6819-01), and a one-page ad in Hambletonian for equine veterinarians (6926-00). We also reviewed a document identified as a mail and handout ad (6926-00), which constitutes labeling for Surpass®.

False or Misleading Statements

The mail and handout ad (6926-00) and the one-page ad in Hambletonian (6926-00) state, "And, because it's applied only where needed in very small amounts, it reduces the risk of toxicity associated with the use of systemic NSAIDs." This statement is false or misleading because Surpass® is systemically absorbed at the recommended dose, and the sponsor has not demonstrated that the risk of adverse events from use of Surpass® is lower than from use of any other NSAID in horses.

Topically applied diclofenac, and specifically the final market formulation of Surpass®, is systemically absorbed. The Target Animal Safety section of the Freedom of Information Act (FOI) Summary for Surpass® states, "Plasma concentrations of diclofenac following topical administrations: Dose dependent increases in blood levels of diclofenac were detected in horses at 1.7X (three of six horses) and 2.8X (six of six horses) the recommended dose." In a study (funded by IDEXX Pharmaceuticals, Inc.) published in the Spring 2005 issue of *Veterinary Therapeutics*, diclofenac and 4-hydroxydiclofenac (a diclofenac metabolite), was found in both the urine and the serum of all horses that had been treated with topical Surpass® for ten days at 1X, 2X, and 4X.[1] Specifically, after 10 days of topical administration of Surpass® at 1X, 2X, and 4X the recommended label dose, diclofenac and 4-hydroxydiclofenac were present in all urine samples collected from 0.25 to 72 hours after the final application of the drug. Additionally, after 10 days of topical administration of Surpass®, diclofenac was present in all serum samples collected from 0.25 to 48 hours after the final application.

Further, this statement is misleading because it suggests that Surpass® is safer than it has been shown to be by substantial evidence or substantial clinical experience. Cf. 21 CFR 202.1(e)(6)(i).

In addition, the advertisements for Barrel Racer and Barrel Horse News (09-65495-04), and The Horse, Equus, Chronicle of the Horse, and Practical Horseman (6819-01) have a diagram showing the 'distribution' of orally administered phenylbutazone (bute) in the body. This diagram shows bute absorbed in the gastrointestinal tract, then going to the liver, other organs, and then to the inflamed joint, versus the distribution of Surpass® absorbed from the skin directly into the inflamed joint. The advertisement for Barrel Racer and Barrel Horses News also states, "...because the full dosage of its potent pain reliever, diclofenac, goes right to the inflamed joint and stays there, unlike bute..." The diagram and the aforementioned statement imply Surpass® goes directly from the skin into the joint and stays in the inflamed joint after it is applied and is not systemically absorbed. Accordingly, these advertisements imply that no systemic effects will be seen in horses treated with Surpass®. Both the FOI and label for Surpass® show that your drug does produce systemic side effects, including diarrhea, gastric ulcer, and weight loss.

---

[1] Urinary and Serum Concentrations of Diclofenac after Topical Application to Horses; *Veterinary Therapeutics*, Spring 2005 (Vol 6, No 1)

Unsubstantiated Claims

The advertisements mentioned above in Barrel Racer and Barrel Horse News (09-65495-04), and The Horse, Equus, Chronicle of the Horse, and Practical Horseman (6819-01) with a diagram comparing the absorption of Surpass and bute, as well as the statement, "...because the full dosage of its potent pain reliever, diclofenac, goes right to the inflamed joint and stays there, unlike bute..." also present an unsubstantiated superiority claim over another product. The statement suggests that Surpass is more effective than bute. It also suggests that because Surpass® is not systemically absorbed, it will cause fewer and less serious side effects than other products administered by oral or parenteral routes. These advertisements contain a representation that Surpass is safer and more effective than another drug when it has not been demonstrated to be safer or more effective by substantial evidence or substantial clinical experience. See 21 CFR 202.1(e)(6)(ii)

Conclusion and Requested Action

The false and misleading statements in your promotional materials misbrand Surpass® within the meaning of sections 502(a) and 502(n) of the Act [21 U.S.C. 352(a) and 352(n)].

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to see that your promotional materials for Surpass®, as well as other IDEXX Pharmaceuticals, Inc. products, comply with the requirements of the Act and its implementing regulations.

The Division of Surveillance requests that IDEXX Pharmaceuticals, Inc. immediately cease the use of the promotional materials identified in this letter and all similar promotional items. Future promotional materials should contain truthful and non-misleading information that is consistent with the approved labeling. Please submit a written response within thirty (30) days of receipt of this letter describing your intent to comply with this request and listing all promotional materials for Surpass® containing the same or similar statements as those objected to above, and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, center for Veterinary Medicine, Division of Surveillance, HFV-210, 7519 Standish Place, Rockville, MD 20855. We remind you that only written communications are official.

Sincerely yours,

[redacted]

Lynn O. Post, DVM, PhD, DABVT
Director, Division of Surveillance
HFV-210
Center for Veterinary Medicine