Banamine® Transdermal Technical Bulletin

Comparative time, behavior and economic differences associated with calves receiving a pour-on vs. an intravenous product.

Background

Banamine® Transdermal (flunixin transdermal solution) is the first and only FDA-approved product for pain control in a food producing animal. It is approved for the control of pain associated with foot rot and fever associated with bovine respiratory disease in cattle. It also is the first and only non-steroidal anti-inflammatory (NSAID) cattle product available as a pour-on. The route of administration of previous NSAIDs has been intravenous (IV) administration.

Intravenous route of drug administration requires proper animal restraint, familiarity with bovine anatomy, and it potentially increases time and costs compared to pour-on administration. In addition, intravenous drug administration requires additional appropriate restraint of the animal's neck and head, and it can be associated with increased handling stress of that animal.

The goal of this study is to evaluate the differences in time, behavior and costs associated with pour-on and injectable administration to cattle. These potential differences may prove beneficial in the adoption of a pour-on-based product versus those that require an intravenous injection.

Objectives

The objectives of this study were:

- Determine differences in time required to administer a pour-on saline solution compared to injecting saline intravenously.
- Measure behaviors of calves during and immediately post-saline administration and evaluate for potential differences.
- Determine the economic costs associated with both a pour-on saline and an injectable saline solution based on the time and supplies necessary for administration.

Materials and Methods

A total of 100 beef crossbred calves (585 ± 62 lb.) were selected for this study. These calves had been observed for 14 days prior to the study and were all considered clinically healthy. Calves were randomized to treatment based on chute order prior to the study using a random number generator in Microsoft Excel (Microsoft, Redmond, WA).

Calves were estimated to weigh 575 pounds prior to the study start. This group average value was used to calculate dosing for both pour-on and intravenous administration. Each calf was moved into a processing chute (For-Most, For-Most Livestock Equipment, Hawarden) and restrained via the use of a head gate. Calves were then administered their respective treatment based on previous randomization.

- *Pour-on (POUR)*
  Calves randomized to receive POUR treatment received 18 mL of sterile saline on their back to simulate the administration of a pour-on product.
- *Intravenous injection (IV)*
  Cattle assigned to receive IV treatment were additionally restrained using a halter to tie their head to the chute and facilitate the visualization and access to the jugular vein. Ten mL of sterile saline was intravenously injected by a veterinarian to simulate the administration of Banamine Injectable Solution (flunixin meglumine, Merck Animal Health).

Time calves were restrained in the head gate was recorded using a stopwatch (Accusplit PRO survivor 601X; Accusplit, Livermore, CA). Three scoring systems (Table 1) were used to capture potential changes in behavior associated with treatment administration. The same observer recorded scores for all calves during the trial.

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VOCALIZATION SCORE

Score	Description
Y	No vocalization while in the head gate
N	Vocalization while in the head gate

CHUTE SCORE

Score	Description
1	Calm, no movement
2	Restless, shifting
3	Squirming, occasional shaking of the chute
4	Continuous vigorous movement, and shaking of the chute
5	Rearing, twisting of the body, or violet struggling

EXIT SCORE

Score	Description
1	Walked
2	Trotted
3	Ran

Table 1. Behavior scoring systems.

Costs associated with a veterinarian, extra help and supplies necessary for intravenous administration at the stockyard in Northeast Missouri were determined and are displayed in Table 2. Total labor costs were held constant between treatment methods at one veterinarian ($135/hr) and two assistants ($27.50/hr each). Material costs associated with pour-on administration were estimated at $0, and the cost of a needle (Ideal 16G X 5/8", Ideal Instruments, Lexington, KY) and syringe (12 mL Luer Slip, Allison Medical Inc, Littleton, CO) was estimated for each IV administration (Table 2).

Description	Cost/unit
Labor	$27.50/hour
Syringe (12 cc)	$0.50 each
Needle (16ga x 5/8 inch)	$0.20 each

Table 2. Estimated costs of labor and materials associated with administration of pour-on and IV saline to 100 beef calves.

Data were imported into statistical software packages (R & JMP) for analysis. Generalized linear models were used to evaluate potential differences between treatment methods (POUR & IV) and the variables of interest. Weight of calves and the interaction of weight and treatment were offered to all models; however, both were found nonsignificant ($P > 0.05$) and were not included in final models.

Multi-category scores (chute score and exit score) were collapsed into two categories (1 = normal, > 1 = abnormal) and were coded as 1 = normal score, 0 = abnormal score. Generalized linear models with a logit link function modeled the probabilities of receiving a normal score (vocalization = N, chute score = 1, exit score = 1) by treatment method.

Results

A total of 100 crossbred beef calves were used. Data from one calf (# 32) in the IV group were not included in analysis as it was treated for corneal ulcers while in the head gate. Average ± st dev weights were 591 ± 55.7 pounds for IV-treated calves and 571 ± 66.1 pounds for POUR-treated calves.

Least squares mean total time in the head gate was lower ($P = 0.02$) for POUR calves compared to IV-treated calves (Figure 1, Table 3).

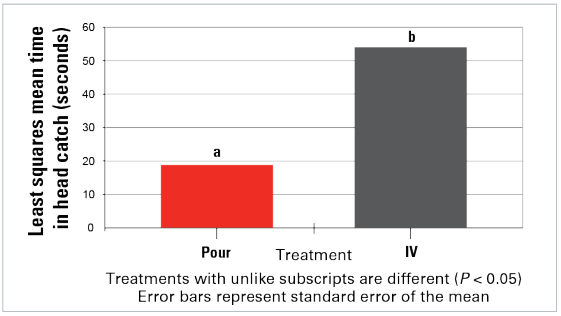

Figure 1. Least squares mean time in the head catch between calves receiving a pour-on (POUR) vs. intravenous (IV) administration of saline.

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	TREATMENT*				
	POUR (n=50)		IV (n=49)		p – value
	LSM / prob (%)¶	SE / 95% CI§	LSM / prob (%)¶	SE / 95% CI§	Treatment
Total time in head catch	17.2	1.24	53.6	1.25	0.02
Vocalization = No	0.98	0.87 to 0.99	0.86	0.73 to 0.93	0.02
Chute score = 1 (normal)	0.34	0.22 to 0.48	0.14	0.07 to 0.27	0.02
Exit score = 1 (normal)	0.44	0.31 to 0.58	0.29	0.18 to 0.43	0.11

* – POUR = pour-on, IV = intravenous

¶ – Least Squares Mean (LSM) were used for continuous variables and probabilities (prob) for all scores

§ – Standard Error (SE) of mean for total time in head catch, 95% confidence intervals for probabilities

Table 3. Statistical analysis of time in the head gate and behavior scores between beef calves administered a pour-on (POUR) or intravenous (IV) saline.

The probability of receiving a normal score (vocalization & chute) was higher ($P < 0.05$) for calves receiving POUR treatment compared to those receiving IV.

The probability of having a normal exit score was numerically higher (44 percent) in calves receiving POUR compared to those receiving IV (29 percent); however this difference was not significant ($P = 0.11$),Table 3 and Figure 2.

Costs (labor and materials) associated with administration of a saline product to 50 calves via a pour-on were estimated at $124.45 while intravenous administration of the same product to 50 calves was estimated to be $253.50

(Table 4). These calculations included time, labor and materials to administer the products.

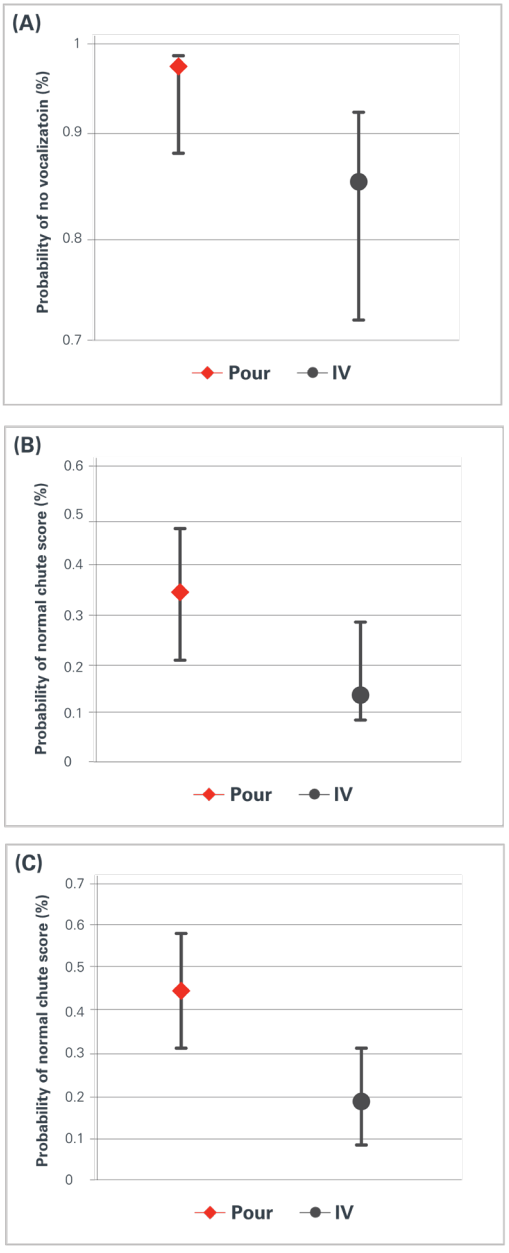

Figure 2. Probability of (A) No vocalization by treatment group, (B) Normal chute score by treatment group, (C) Normal exit score by treatment group. Error bars represent 95% CI of probability.

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TIME	Treatment POUR (n=50)	Treatment IV (n=49)	Difference POUR VS IV
Mean reload time / animal*	30.0	30.0	–
Mean time in head gate / animal§	17.2	53.6	36.5
Total mean time (seconds)	**47.2**	**83.6**	**36.5**
LABOR			
Labor wage ($/hour)¶	$55.0	$55.0	–
Cost of labor (reload time)	$0.46	$0.46	–
Cost of labor (head gate time	$0.26	$0.80	$0.54
Total labor cost	**$0.72**	**$1.26**	**$0.54**
SUPPLIES			
Needle ($/1 unit)	$0.00	$0.20	$0.20
Syringe ($/1 unit)	$0.00	$0.50	$0.50
Total supplies cost	**$0.00**	**$0.70**	**$0.70**
Total estimated cost	**$0.72**	**$1.96**	**$1.24**

* – Total time in head gate (includes time required to put on halter, position neck, and administer IV saline)
§ – Time for one calf to leave the chute and another to load into the chute and restrained in the head gate
¶ – Labor hourly rate includes two processing personnel (each at $27.50 / hour)

Table 4. Estimated costs (time, labor, and supplies) associated with administration of pour-on (POUR) or intravenous (IV) saline to beef calves.

Conclusions

The objective of the current study was to compare the time, behavior and economic differences associated with calves receiving a pour-on or intravenous saline product.

The results showed a reduction in time per animal of 36.45 seconds comparing administering an intravenous injection (53.61 seconds) versus a pour-on (17.16 seconds).

Labor cost per animal was estimated at $1.26 for cattle receiving intravenous injection and $0.72 for those receiving pour-on. This represents a difference of $0.54 in the total estimated labor cost per animal.

The cost of material needed for intravenous administration (syringe and needle) was estimated at $0.70 per animal. The total cost savings achieved by pour-on administration compared to an intravenous injection was estimated at $1.24 [$0.54 (labor) + $0.70 (material) = $1.24 (labor + material)].

Animal vocalization and excessive movement during processing has been associated with calves experiencing stressful conditions.[1,2,3] Behavior analysis in the current study showed that calves receiving a pour-on administration had a higher ($P < 0.05$) probability of not vocalizing while in the chute and having a normal chute score.

Previous studies have found exit scores to be reliable assessments of cattle temperament.[1] While no statistical differences were found, calves receiving a pour-on treatment tended ($P = 0.11$) to have a higher probability of having a normal exit score when compared to IV-treated calves. These data indicate that calves receiving a pour-on administration had a tendency of being less stressed while in the chute compared to those receiving intravenously administered saline.

[1]Vetters, M., Engle, T., Ahola, J. & Grandin, T. Comparison of flight speed and exit score as measurements of temperament in beef cattle. *Journal of Animal Science* 91, 374-381 (2012).

[2]Curley, K., Paschal, J., Welsh, T. & Randel, R. Technical note: Exit velocity as a measure of cattle temperament is repeatable and associated with serum concentration of cortisol in Brahman bulls. *Journal of Animal Science* 84, 3100-3103 (2006).

[3]Bristow, D. & Holmes, D. Cortisol levels and anxiety-related behaviors in cattle. *Physiology & Behavior* 90, 626-628 (2007).

Banamine® Transdermal

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Product Information
NADA #141-450, Approved by FDA

Banamine®
Transdermal
(flunixin transdermal solution)

Pour-On for Beef and Dairy Cattle
50 mg/mL

Non-Steroidal Anti-inflammatory Drug

Only for topical use in beef and dairy cattle. Not for use in beef bulls intended for breeding; dairy bulls; female dairy cattle 20 months of age or older, including dry dairy cows; and suckling beef calves, dairy calves, and veal calves.

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

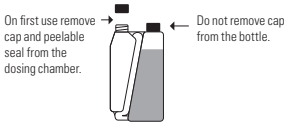
DESCRIPTION: Each milliliter of Banamine Transdermal pour-on contains 50 mg flunixin (equivalent to 83 mg flunixin meglumine), 150 mg pyrrolidone, 50 mg L-menthol, 500 mg propylene glycol dicaprylate/dicaprate NF, 0.20 mg FD&C Red No. 40, and glycerol monocaprylate NF qs.

INDICATIONS: Banamine Transdermal pour-on is indicated for the control of pyrexia associated with bovine respiratory disease and the control of pain associated with foot rot in steers, beef heifers, beef cows, beef bulls intended for slaughter, and replacement dairy heifers under 20 months of age.

DOSAGE AND ADMINISTRATION: Apply only once at a dose of 3.3 mg flunixin per kg body weight (1.5 mg/lb; 3 mL per 100 lbs) topically in a narrow strip along the dorsal midline from the withers to the tailhead. Round all doses up to the nearest weight increment on the dosing chamber. Do not treat cattle if the hide is wet or may get wet in the six hours after dosing because effectiveness has not been evaluated under wet hide conditions.

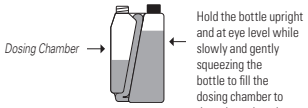
Practice the Administration and Overfill Reduction Instructions a few times to become familiar with operating the package before dosing animals.

Step 1

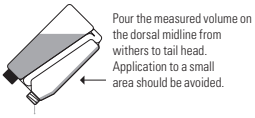


If the dosing chamber is overfilled, follow the Overfill Reduction Instructions.

Step 2



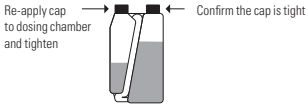
Step 3



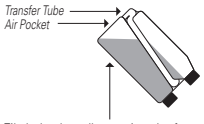
A small amount of liquid will remain on the walls of the chamber, but the chamber is calibrated to account for this.

OVERFILL REDUCTION INSTRUCTIONS

Step 1

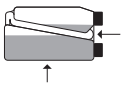


Step 2



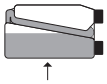
Tilt the bottle to allow an air pocket form at the beginning of the transfer tube inside the bottle.

Step 3



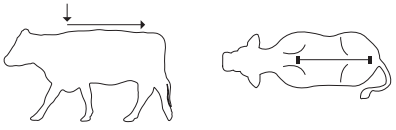
Hold the bottle horizontally to allow product to cover the end of the transfer tube inside the dosing chamber

Step 4



Squeeze and release the bottle repeatedly. Product will return to the bottle through the transfer tube.

Figure 1 – *Recommended pour-on location*



CONTRAINDICATIONS: NSAIDs inhibit production of prostaglandins which are important in signaling the initiation of parturition. The use of flunixin can delay parturition and prolong labor which may increase the risk of stillbirth. Do not use Banamine Transdermal pour-on within 48 hours of expected parturition. Do not use in animals showing hypersensitivity to flunixin meglumine.

USER SAFETY WARNINGS: Not for use in humans. Keep out of reach of children. Flunixin transdermal solution is a potent non-steroidal anti-inflammatory drug (NSAID), and ingestion may cause gastrointestinal irritation and bleeding, kidney, and central nervous system effects.

This product has been shown to cause severe and potentially irreversible eye damage (conjunctivitis, iritis, and corneal opacity) and irritation to skin in laboratory animals. Users should wear suitable eye protection (face shields, safety glasses, or goggles) to prevent eye contact; and chemical-resistant gloves and appropriate clothing (such as long-sleeve shirt and pants) to prevent skin contact and/or drug absorption. Wash hands after use.

In case of accidental eye contact, flush eyes immediately with water and seek medical attention. If wearing contact lenses, flush eyes immediately with water before removing lenses. **In case of accidental skin contact and/or clothing contamination, wash skin thoroughly with soap and water** and launder clothing with detergent. **In case of ingestion do not induce vomiting and seek medical attention immediately.** Probable mucosal damage may contraindicate the use of gastric lavage. Provide product label and/or package insert to medical personnel.

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 8 days of the last treatment. Not for use in female dairy cattle 20 months of age or older, including dry dairy cows; use in these cattle may cause drug residues in milk and/or in calves born to these cows or heifers. Not for use in suckling beef calves, dairy calves, and veal calves. A withdrawal period has not been established for this product in pre-ruminating calves.

PRECAUTIONS: As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Patients at greatest risk for adverse events are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction. Banamine transdermal should be used with caution in animals with suspected pre-existing gastric erosions or ulcerations. Concurrent administration of other NSAIDs, corticosteroids, or potentially nephrotoxic drugs should be avoided or used only with careful monitoring because of the potential increase of adverse events.

NSAIDs are known to have potential effects on both parturition (see Contraindications) and the estrous cycle. There may be a delay in the onset of estrus if flunixin is administered during the prostaglandin phase of the estrous cycle. NSAIDs are known to have the potential to delay parturition through a tocolytic effect. The use of NSAIDs in the immediate postpartum period may interfere with uterine involution and expulsion of fetal membranes. Cows should be monitored carefully for placental retention and metritis if Banamine Transdermal pour-on is used within 24 hours after parturition.

Not for use in dairy or beef bulls intended for breeding because reproductive safety has not been evaluated.

CLINICAL PHARMACOLOGY: Flunixin meglumine is a non-steroidal, anti-inflammatory drug. It is a weak acid (pKa=5.82)[1] which exhibits a high degree of plasma protein binding (approximately 99%).[2] However, free (unbound) drug appears to readily partition into body tissues (Vss predictions range from 297 to 782 mL/kg).[2,5] In cattle, elimination occurs primarily through biliary excretion.

Flunixin persists in inflammatory tissues[6] and is associated with anti-inflammatory properties which extend well beyond the period associated with detectable plasma drug concentrations.[4,6] Therefore, prediction of drug concentrations based upon the estimated plasma terminal elimination half-life will likely underestimate both the duration of drug action and the concentration of drug remaining at the site of activity.

Pharmacokinetic properties of flunixin transdermal solution in cattle administered at a dose of 2.5 mg/kg, are summarized in Table 1, comparing results between animals that were allowed to self- and allo-lick vs. animals that were prevented from licking. Animals that were allowed to self- or allo-lick had lower rate and extent of absorption when compared to the animals prevented from licking. However, no dose adjustment is needed to account for the effect of licking because the substantial evidence of effectiveness was demonstrated in animals that were allowed to lick.

Table 1. Average (+/- standard deviation [SD]) PK parameters after a single administration of flunixin transdermal solution at a dose of 2.5 mg/kg in cattle that were either allowed to lick or prevented from allo- and self-licking (n = 24/group).

PK parameter	Non-licking		Licking	
	Mean	± SD	Mean	± SD
C_{max} (ng/mL)	1496	769	N/A	N/A
Concentration at 2 h*	1282	533	1072	353
T_{max} (h)	1.29	0.464	N/A	N/A
$AUC_{2\text{-last}}$ (ng*h/mL)	7499	2131	6827	4672
$T_{1/2}$ (h)	8	2	9	6

* First blood level in the licking group was taken at 2 hours post-dose.
First blood sample in non-licking group was taken at 0.25 hours post-dose.
C_{max}: Maximum observed plasma concentration
T_{max}: Time at which C_{max} was observed
$AUC_{2\text{-last}}$: Area under the plasma concentration versus time curve measured between 2 hours and the time of the last quantifiable concentration
$T_{1/2}$: Terminal elimination half-life

Absorption of flunixin transdermal solution in cattle is dependent on environmental temperature. The effect of temperature on flunixin absorption was tested in temperatures ranging from 15.3 to 20.1 °F (average low in the coldest study) to 80 to 100 °F (average high in the warmest study). Flunixin concentrations were consistently lower when the pour-on product was administered in a cold (temperature) rather than hot (temperature) environment. However, the clinical effectiveness was demonstrated over the range of environmental conditions expected under field conditions. No dose adjustments are necessary due to environmental temperature.

References:

1. Johansson M, Anler EL. Gas chromatographic analysis of flunixin in equine urine after extractive methylation. *J Chromatogr.* 1988; 427:55-66.
2. Odensvik K, Johansson M. High-performance liquid chromatography method for determination of flunixin in bovine plasma and pharmacokinetics after single and repeated doses of the drug. *Am J Vet Res.* 1995; 56:489-495.
3. Anderson KL, Neff-Davis CA, Davis LE, Bass VD. Pharmacokinetics of flunixin meglumine in lactating cattle after single and multiple intramuscular and intravenous administrations. *Am J Vet Res.* 1990; 51:1464-1467.
4. Odensvik K. Pharmacokinetics of flunixin and its effect on prostaglandin F2∝ metabolite concentrations after oral and intravenous administration in heifers. *J Vet Pharmacol Ther.* 1995;18:254-259.
5. Hardee GE, Smith JA, Harris SJ. Pharmacokinetics of flunixin meglumine in the cow. *Res Vet Sci.* 1985; 39:110-112.
6. Lees P, Higgins AJ. Flunixin inhibits prostaglandin E2 production in equine inflammation. *Res Vet Sci.* 1984; 37:347-349.

TARGET ANIMAL SAFETY: In a target animal safety study in 32 six-month old beef cattle (16 castrated males and 16 females), flunixin transdermal solution was administered topically at 3.3, 9.9, and 16.5 mg/kg body weight (1X, 3X, and 5X the labeled dose) on Days 1, 2, and 3 (3X the labeled administration frequency). Cattle were continuously restrained to prevent licking. In addition, the study was conducted under warm environmental conditions (70 °F to 80 °F on dosing days). One animal in the 3X group and three animals in the 5X group exhibiting twisting, kicking, rubbing on the fence, and or prancing, starting 5 to 15 minutes after dosing and lasting up to an hour after dosing on both Days 2 and 3. Two 5X animals had positive fecal occult blood on one of three post-treatment days, and one 5X animal had positive fecal occult blood on Days 2 and 3 post-treatment. Trace occult blood was found in the urine of three animals: one 5X animal on Day 1, one 5X animal on Day 3, and one 3X animal on Day 3. Test article-related pathology changes included a dose-related increase in the incidence and severity of abomasal erosions and ulcerations; and inflammatory cell infiltrates, epidermal necrosis, and small areas of dermal necrosis at the application site. The abomasal lesions correlated with fecal occult blood in three 5X animals. There were no animals with any other evidence of gastrointestinal bleeding or clinical signs of abomasal ulceration during the study.

Application site reactions, including dandruff/skin flakes, hair damage (thin, broken, brittle hair), and skin thickening were observed in effectiveness and/or supportive studies. The application site reactions were first observed around three to seven days post-dosing and lasted for about 14 days. These reactions were cosmetic in nature and generally resolved without treatment.

A pharmacokinetic evaluation demonstrated that the systemic exposure of flunixin is markedly lower when administered transdermally at a dose of 3.3 mg flunixin/ kg BW than when administered intravenously at a dose of 2.2 mg flunixin/kg BW, therefore, female reproductive safety is supported by reproductive safety studies conducted for the approval of BANAMINE (flunixin meglumine injection) in cattle, NADA 101-479.

EFFECTIVENESS: Pharmacokinetic studies established that the absorption of flunixin administered transdermally to cattle is highly dependent on environmental temperature. Therefore the effectiveness of flunixin transdermal solution for the control of pyrexia associated with bovine respiratory disease was demonstrated under a range of environmental temperatures in two studies: a field study conducted at four geographic locations (California, Kansas, Nebraska, and Texas) under moderate environmental temperatures (average temperatures ranged from 42 °F to 74 °F on enrollment days) and a field study conducted at a single site (Nebraska) under cold environmental conditions (average temperatures ranged from 2 °F to 20 °F on enrollment days). In both studies, cattle were housed in groups and were not prevented from licking.

In both studies, cattle exhibiting clinical signs of BRD and having a rectal temperature of at least 104.5 °F were enrolled. A total of 235 cattle in the multi-location field study and 50 cattle at the single site field study were administered either flunixin transdermal solution (3.3 mg/kg BW) or an equivalent volume of dyed saline as a pour-on once on Day 0. Six hours after treatment, rectal temperatures were measured. The treatment success rate of the flunixin transdermal solution-treated group was compared to the treatment success rate in the dyed saline-treated group. A treatment success was defined as a drop in rectal temperature of 2 °F in an individual animal. In the multi-location study, the treatment success rate was significantly different ($p < 0.0001$) and higher for the flunixin transdermal solution-treated group (70/120, 58.3%) compared to the dyed saline-treated control group (7/115, 6.1%). In the single site study, the treatment success rate was significantly different ($p = 0.0002$) and higher for the flunixin transdermal solution-treated group (19/25, 76%) compared to the dyed saline-treated control group (4/25, 16%).

The effectiveness of flunixin transdermal solution for the control of pain associated with foot rot in beef and dairy cattle was demonstrated under a range of environmental temperatures in two studies: an induced infection model study conducted in Nebraska with temperatures ranging from 61 °F to 85 °F on the day of enrollment and treatment; and an induced infection model study conducted in Kansas with temperatures ranging from 27 °F to 53 °F on the day of enrollment and treatment. In both studies, cattle from both treatment groups were commingled in pens and were not prevented from licking.

In each study, cattle were challenged by subcutaneous injection of a culture of *Fusobacterium necrophorum* into the interdigital space of the right front foot using a method that was validated to induce pain representative of foot rot. Cattle were enrolled when they demonstrated signs of pain associated with foot rot based on lameness, interdigital lesion, and interdigital swelling criteria. Pressure mat gait parameters maximum total force (kgf) and contact area (cm^2) were also measured at enrollment. A total of 30 cattle at each site were administered either flunixin transdermal solution (3.3 mg/kg BW) or an equivalent volume of dyed saline as a pour-on once on Day 0. Six hours after treatment, lameness scores and pressure mat gait parameters maximum total force and contact area were measured.

Effectiveness was determined independently at each site based on treatment success rates at six hours after treatment; and the change in maximum total force and contact area between enrollment and six hours after treatment. A treatment success was defined as a decrease in lameness score by ≥1 (scale 1 to 5, with enrollment of animals with lameness score ≥3) from the enrollment lameness score. The treatment success rate of the flunixin transdermal solution-treated group was compared to the treatment success rate in the dyed saline-treated group at both sites.

Changes in biometric gait parameters were also compared between the treatment groups.

In the Nebraska study, the treatment success rate was significantly different and higher for the flunixin transdermal solution-treated group (15/15, 100%)compared to the dyed saline-treated group (1/15, 6.67%); and the mean change in maximum total force and mean change in contact area were statistically significantly different ($p < 0.0001$) and higher in the flunixin transdermal solution-treated group (43.08 kgf and 16.76 cm^2) compared to the dyed saline-treated control group (-4.14 kgf and -2.70 cm^2). In the Kansas study, the treatment success rate was significantly different ($p = 0.0387$) and higher for the flunixin transdermal solution-treated group (14/15, 93.33%) compared to the dyed saline-treated group (8/15, 53.33%); and the mean change in maximum total force and mean change in contact area were statistically significantly different ($p = 0.0002$ and $p < 0.0001$, respectively) and higher in the flunixin transdermal solution-treated group (34.32 kgf and 16.38 cm^2) compared to the dyed saline-treated control group (-0.54 kgf and -0.96 cm^2).

CONTACT INFORMATION: For technical assistance or to report a suspected adverse drug experience, call: 1-800-219-9286. For customer service or to request a Safety Data Sheet (SDS), call: 1-800-211-3573. For additional Banamine Transdermal pour-on information go to www.BanamineTD.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

HOW SUPPLIED: Banamine Transdermal pour-on, is available in 100-mL (NDC 0061-4363-01), 250-mL (NDC 0061-4363-02), and 1-L (NDC 0061-4363-03) bottles.

STORAGE INFORMATION: Store at or below 30°C (86°F). Use within 6 months of first opening.

For Patent information: http://www.merck.com/product/patent/home.html.

5/2017

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