Pharmacokinetics of oral firocoxib in un-weaned calves

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Introduction

The non-steroidal anti-inflammatory drug (NSAID) firocoxib is approved by the U.S. FDA for oral administration to horses and dogs for the control of pain and inflammation. Because of its COX-2 selectivity, firocoxib is expected to have an improved safety profile compared to other NSAIDS that are not COX-2-selective. The objective of this study was to determine the pharmacokinetics of orally administered firocoxib at a target dose of 5 mg/kg in milk-fed dairy calves. The rationale for the study was to determine if a single 227 mg oral dose of firocoxib in calves would produce similar pharmacokinetic parameters to the FDA-approved dosages for horses and dogs.

Materials and methods

Clinically normal Holstein calves were enrolled when they were between 4 and 8 weeks of age. Immediately prior to drug administration, each calf was weighed and then had an intravenous catheter placed in one jugular vein and a baseline blood sample was obtained. Each calf was then dosed orally with a single 227 mg firocoxib tablet (Previcox® chewable tablets, Merial, Inc. Duluth, GA) administered using a calf balling gun. Blood samples were collected at 2, 4, 6, 8, 24, and 48, 72, and 96 hours after drug administration. Plasma drug levels at each timepoint were measured using liquid chromatography and tandem mass spectrometry. Noncompartmental and compartmental pharmacokinetic analyses were performed using software designed for such use.

Results

The weights of enrolled calves ranged from 45 to 65 kg, so the dosage after administration of a single 227 mg tablet of firocoxib ranged from 3.5 to 5 mg/kg, with a mean of 4.2 ± 0.53 (mean ± SD) mg/kg. A one-compartment pharmacokinetic model with first-order input, no lag time, and first-order elimination was the best fit for all calves. The mean dosage of 4.2 mg/kg produced a median Tmax (time of maximum plasma concentration) of 7 hours, AUC0-24 (area under the plasma concentration-time curve in the first 24 hours after dosing) of 16 µg*h/mL, and T ½ (elimination half-life) of 15.3 ± 4.8 hours. The mean Cmax (maximum plasma drug concentration) was 0.9 ± 0.25 µg/mL.

Significance

When compared to the FDA-approved 5.0 mg/kg oral dosage in non-fasted dogs, the mean oral dosage of 4.2 mg/kg in the calves in our study produced the same mean Cmax (0.9 µg/mL) and a similar Tmax (5 hours vs 7 hours, respectively). The mean T1/2 of firocoxib in the calves in our study was 15.3 hours, which is approximately twice the T1/2 of 7.8 hours in dogs. The similarity in pharmacokinetics between a single oral 227 mg dose of firocoxib in unweaned calves and the label dosage of 5.0 mg/kg in dogs provides support for the hypothesis that a single 227 mg tablet of firocoxib could provide analgesia in calves, with a good duration of effect due to the relatively long T1/2.

