Received: 4 November 2018 | Revised: 24 January 2019 | Accepted: 22 February 2019

DOI: 10.1111/jvp.12760

PHARMACOKINETIC REPORT

WILEY JOURNAL OF Veterinary Pharmacology and Therapeutics

# Pharmacokinetics of imidocarb dipropionate in white-tailed deer (*Odocoileus virginianus*) after single intramuscular administration

Ellie L. Milnes[1,2] | Pauline Delnatte[2] | Murray Woodbury[3] | Adam Hering[3] | Sam Lee[3] | Dale A. Smith[1] | Nicole M. Nemeth[1] | Yu Gu[1] | Ronette Gehring[4] | Ron Johnson[1]

[1]Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada

[2]Toronto Zoo, Toronto, Ontario, Canada

[3]Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

[4]Veterinary Pharmacotherapeutics and Pharmacy Division, Faculty of Veterinary Medicine, Institute of Risk Assessment Science, Utrecht University, Utrecht, The Netherlands

**Correspondence**
Ellie L. Milnes, Ontario Veterinary College, University of Guelph, Guelph, ON, Canada.
Email: emilnesdvm@yahoo.co.uk

**Present address**
Nicole M. Nemeth, Southeastern Cooperative Wildlife Disease Study, University of Georgia, Athens, Georgia.

**Funding information**
American Association of Zoo Veterinarians Wild Animal Health Fund; Toronto Zoological Foundation

## Abstract

This study was designed to investigate the pharmacokinetics of imidocarb, a carbanilide derivative, in white-tailed deer (*Odocoileus virginianus*). The pharmacokinetic properties of a single intramuscular (IM) dose of imidocarb were determined in 10 deer. A single IM injection of 3.0 mg/kg imidocarb dipropionate was administered, and blood samples were collected prior to, and up to 48 hr after imidocarb administration. Plasma imidocarb concentrations were determined by high-performance liquid chromatography with ultraviolet detection. The disposition of plasma imidocarb was best characterized by a two-compartment open model. The mean ± *SE* maximal imidocarb concentration in deer was 880.78 ± 81.12 ng/ml at 38.63 ± 5.30 min postinjection. The distribution phase had a half-life ($t_{1/2\alpha}$) of 25.90 ± 10.21 min, and plasma imidocarb concentration declined with a terminal elimination half-life ($t_{1/2\beta}$) of 464.06 ± 104.08 min (7.73 ± 1.73 hr). Apparent volume of distribution based on the terminal phase ($V_Z/F$) was 9.20 ± 2.70 L/kg, and apparent total body clearance (Cl/*F*) was 15.97 ± 1.28 ml $min^{-1}$ $kg^{-1}$.

KEYWORDS

*Babesia*, cervid babesiosis, imidocarb dipropionate, *Odocoileus virginianus*, white-tailed deer

## 1 | INTRODUCTION

Imidocarb, a carbanilide derivative, is used to treat hemoprotozoan parasitic infections of the genus *Babesia* in domestic livestock (Vial & Gorenflot, 2006). Imidocarb is usually administered as the dipropionate salt by intramuscular (IM) or subcutaneous (SC) injection. Cervids, including white-tailed deer (*Odocoileus virginianus*), are well-represented in North American zoological collections and in commercial deer farms. Cervid babesiosis, caused by infection of erythrocytes with *Babesia odocoilei*, is an emerging tick-borne hemolytic disease of cervids in North America (Mathieu et al., 2018). The wildlife reservoir of *B. odocoilei* is believed to be free-ranging white-tailed deer (Milnes et al., 2019). Case reports have documented resolution of parasitemia and the clinical signs associated with acute babesiosis in zoo and farmed cervids after treatment with IM imidocarb (Gallatin et al., 2003).

Effectiveness of a drug against an intracellular parasite such as *B. odocoilei* requires adequate concentrations of the therapeutic agent within the erythrocytes. Imidocarb is lipid-soluble and, therefore, readily diffuses across cell membranes (Lai et al., 2002). Once in the erythrocyte, imidocarb may exert its antiprotozoal effect by interfering with the production or use of polyamines or

  

by blocking inositol entry into infected erythrocytes (Mosqueda, Olvera-Ramirez, Aguilar-Tipacamu, & J Canto, 2012).

Pharmacokinetic studies of imidocarb are reported in several domestic animals, but a review of the published literature failed to find reference to the pharmacokinetic behavior of imidocarb in any cervid species. This study was designed to investigate the pharmacokinetics of imidocarb in white-tailed deer at the dose commonly administered to treat *Babesia* spp. infections in domestic livestock (3.0 mg/kg; Vial & Gorenflot, 2006), for the purpose of designing a drug regimen specifically designed for the treatment and prophylaxis of *B. odocoilei*-associated hemolytic anemia in cervids.

## 2 | MATERIALS AND METHODS

All procedures were approved by the University of Saskatchewan Animal Research Ethics Board, the Toronto Zoo Animal Care Committee, and the University of Guelph Animal Care Committee, in compliance with the regulations of the Canadian Council on Animal Care. Ten healthy adult female white-tailed deer (50–68 kg) were utilized in the study. The animals were housed at the Specialized Livestock Research Facility at the University of Saskatchewan (Saskatoon, SK, Canada) and had no history of imidocarb exposure or infection with *B. odocoilei*.

Deer were manually restrained in a commercial white-tailed deer handling system (The DeerHandler™; Sturgeon County, AB, Canada) to which they had been previously trained. A single deep IM injection of imidocarb dipropionate (Imizol® Merck Animal Health, Madison, NJ, USA) was administered in the lower third region of the neck. Nine deer were dosed at 3.0 mg/kg, and one deer was dosed at 2.4 mg/kg due to a technical error. Whole blood samples (10 ml) were collected via jugular venipuncture into lithium heparin tubes immediately prior to drug administration followed by 10, 20, 30 min, and 1, 2, 3, 4, 6, 8, 12, 24, and 48 hr postadministration. Animals were released into outdoor pens with herdmates in between blood samples and were monitored for potential adverse effects by veterinary staff. Plasma was separated from the collected blood samples by centrifugation at 1,500 *g* for 10 min within 1 hr after collection, transferred to sterile cryovials, and stored at −20.0°C until collection was completed. Samples were shipped to the University of Guelph for analysis.

### 2.1 | Imidocarb analysis

Imidocarb dipropionate standard, trifluoroacetic acid, 1-pentanesulfonic acid sodium, and triethylamine were purchased from Sigma-Aldrich (St. Louis, MO, USA). Ammonium hydroxide solution was purchased from Fisher Scientific (Oakville, ON, Canada). High-performance liquid chromatography (HPLC)-grade acetonitrile and methanol were obtained from Caledon Laboratories Ltd. (Georgetown, ON, Canada). Throughout the study, water was obtained from a Milli-Q™ system (Millipore, Bedford, MA, USA). HPLC analysis was performed on a Waters Alliance 2695 separations module coupled with a Waters 2696 photodiode array detector (Milford, MA, USA), according to the procedure described by Su et al. (2007), with modifications as follows. An aliquot of 1.0 ml of each plasma sample was acidified with 1 ml of phosphoric acid (4%), added to a Waters Oasis™ WCX (Waters, Dublin, Ireland) cartridge after the cartridge was conditioned with 2 ml of methanol and then equilibrated with 3 ml of water. The cartridge was first washed with 3 ml of ammonium hydroxide solution (2%) and then washed with 3 ml of a mixture of ammonium hydroxide (5%) and acetonitrile (50%). The analyte was eluted with 3 ml acetonitrile/methanol/trifluoroacetic acid (500/490/10, v/v/v). The elute was evaporated under a constant flow of nitrogen, then reconstituted in 200 µl of the mobile phase, and 50 µl was injected onto the column. The conditions for the HPLC analysis were as follows: separation was performed on a 50 × 4.6 mm column (3.5 µm; XBridge™ C18 column; Waters) equipped with a Security Guard C18 guard column (4 × 3 mm I.D., Phenomenex™, Torrance, CA, USA). The mobile phase consisted of acetonitrile, 1-pentanesulfonic acid sodium salt (5 mM), and 0.1% trimethylamine trifluoroacetic acid, pH 3.2 (15:85 v/v). The flow rate was 1.0 ml/min, and the UV detector was set at 260 nm. Imidocarb concentrations were derived by comparing peak areas of the samples to those of a standard curve of imidocarb prepared from spiked plasma samples put through the same cleanup process as described above. Experimental samples with an imidocarb concentration greater than 200 ng/ml were diluted with blank deer plasma prior to extraction.

A stock solution of imidocarb dipropionate was prepared in methanol/water (50/50, v/v) at a concentration of 1 mg/ml and stored at −80.0°C. Calibration standards (10, 20, 40, 100, and 200 ng/ml) and quality controls (15 and 150 ng/ml) were prepared from a pool of blank white-tailed deer plasma collected from animals with no history of imidocarb exposure. Correlation coefficients ($r^2$) were >0.99 for all calibration curves. The mean percentage recovery of imidocarb from plasma was 90.0%. The observed retention time of imidocarb was 2.89 min. The limit of detection for this assay, based on three times the signal to noise ratio at the time of elution of the imidocarb, was 5 ng/ml. The limit of quantification for the assay was 10 ng/ml. The analytical method was repeatable and reproducible with average intra- and inter-day precisions of 10.6% and 9.3%, respectively.

### 2.2 | Pharmacokinetic analysis

The pharmacokinetic parameters of imidocarb were calculated using Phoenix WinNonlin software (Certara™, Princeton, NJ, USA) and standard approaches to both noncompartmental and compartmental analysis conducted on individual animal data sets. The model was fitted to measured concentrations weighted by the inverse of their value to avoid overfitting to higher concentrations 1/(Y*Y). The plasma imidocarb concentration–time profile following intramuscular administration best fit a two-compartment open model with first-order absorption and elimination (Equation 1):

$$C(t) = Ae^{-\alpha t} + Be^{-\beta t} - (A+B)e^{-k_a t} \quad (1)$$

where $C$ is the plasma drug concentration at time $t$; $A$ is the mathematical coefficient for the zero-time intercept of the distribution

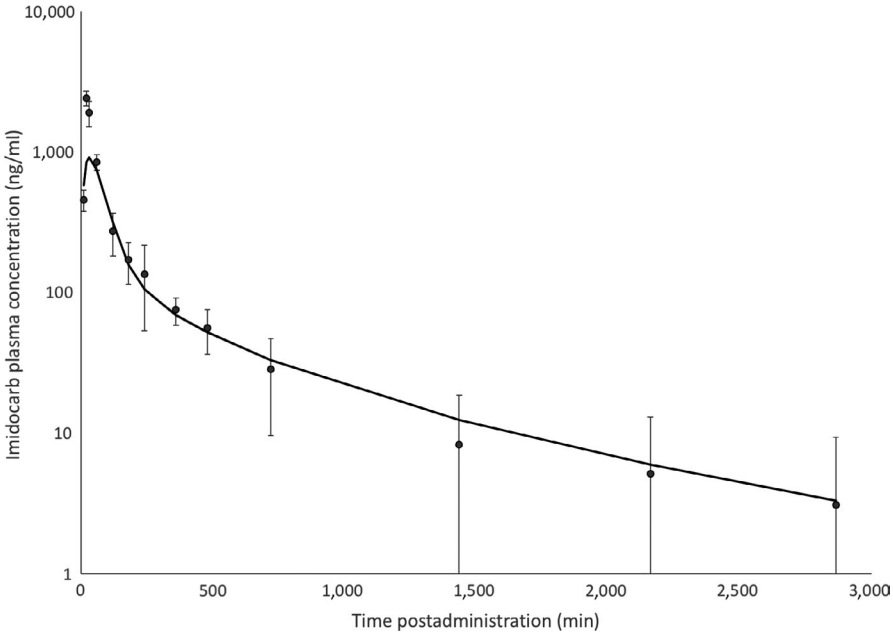


**FIGURE 1** Plasma concentrations (mean ± *SE*) of imidocarb dipropionate in plasma of white-tailed deer (*Odocoileus virginianus*) following a single intramuscular injection of 3.0 mg/kg. Superimposed on the points is a solid line representing the time–concentration profile predicted by the two-compartment open model

slope in the compartment model; *B* is the mathematical coefficient for the zero-time intercept of decline in plasma concentration of the drug; $\alpha$ is the distribution rate constant; $\beta$ is the rate constant for the terminal elimination phase; $k_\alpha$ is the first-order absorption rate constant; *e* is the natural log. The optimal model was determined based on visual inspection of goodness-of-fit plots (observed vs. predicted and residuals), and Akaike's information criterion.

The following pharmacokinetic parameters were derived from the noncompartmental analysis: the area under the curve (AUC) calculated by the trapezoidal method (linear up, log-linear down) from the time of dosing to the last measurable time point ($C_{last}$) for each deer ($AUC_{last}$) and extrapolated to infinity ($AUC_{0-\infty}$) by adding $\frac{C_{last}}{\lambda}$ (where $\lambda$ is the slope of the terminal phase of the time–concentration curve). Bioavailability (*F*) is unknown, so the absolute values of apparent volume of distribution ($V_Z/F$) and total body clearance (Cl/*F*) should be interpreted carefully. The noncompartmental analysis also provided the mean residence time (MRT) from the time of dosing to the time of the last measurable concentration ($MRT_{last}$), which is the ratio of the AUC to the area under the first moment curve (AUMC).

## 3 | RESULTS

The plasma concentration–time curve of imidocarb following IM administration is illustrated in Figure 1 with the corresponding pharmacokinetic parameters summarized in Table 1.

**TABLE 1** Pharmacokinetic parameters (mean ± *SE*) of imidocarb dipropionate in white-tailed deer (*Odocoileus virginianus*) after intramuscular administration at a dose of 3.0 mg/kg

| Parameter | Unit | Mean ± *SE* |
|---|---|---|
| *A* | ng/ml | 33094.00 ± 4154.20 |
| $\alpha$ | L/min | 0.029 ± 0.0023 |
| *B* | ng/ml | 171.97 ± 35.06 |
| $\beta$ | L/min | 0.0023 ± 0.00043 |
| $t_{1/2\alpha}$ | min | 25.90 ± 10.21 |
| $t_{1/2\beta}$ | min | 464.06 ± 104.08 |
| $k_\alpha$ | L/min | 0.03 ± 0.0024 |
| $t_{1/2Ka}$ | min | 24.09 ± 3.06 |
| $t_{max}$ | min | 38.63 ± 5.30 |
| $C_{max}$ | ng/ml | 880.78 ± 81.12 |
| $AUC_{0-\infty}$ | min ng/ml | 194.33 ± 1.36 |
| $AUC_{last}$ | min ng/ml | 184.76 ± 13.39 |
| $V_Z/F$ | L/kg | 9.20 ± 2.70 |
| $MRT_{last}$ | min | 205.52 ± 43.43 |
| Cl/*F* | ml $min^{-1}$ $kg^{-1}$ | 15.97 ± 1.28 |

*Notes*. $AUC_{0-\infty}$: total area under the concentration–time curve from zero to infinity; $AUC_{last}$: total area under the concentration–time curve from zero to the last measurable time point; *A*: zero-time intercept of the distribution slope in the compartment model; *B*: zero-time intercept of decline in plasma concentration of imidocarb; Cl/*F*: apparent total body clearance; $C_{max}$: peak drug concentration; $k_\alpha$: absorption rate constant; $MRT_{last}$: mean residence time from the time of dosing to the time of the last measurable concentration; $t_{1/2Ka}$: absorption half-life; $t_{1/2\alpha}$: half-life during distribution phase; $t_{1/2\beta}$: the half-life of elimination; $t_{max}$: time to $C_{max}$ from time zero; $V_Z/F$: apparent volume of distribution based on the terminal phase; $\alpha$: distribution rate constant; $\beta$: elimination constant.

## 4 | DISCUSSION

Imidocarb at a single dose of 3.0 mg/kg administered IM produced no adverse effects in white-tailed deer. A dose of 3.0 mg/kg was chosen based on recommendations for the treatment and prevention of babesiosis in domestic cattle, in which the typical dose is 1.0–3.0 mg/kg imidocarb administered by IM or SC injection (Vial & Gorenflot, 2006). Intravenous injection of imidocarb has been

reported to cause acute death from bronchoconstriction secondary to cholinesterase inhibition (Abdullah, Sheikh-Omar, Baggot, & Zamri, 1984). In cattle, one imidocarb treatment is usually effective, but a second treatment may be desirable after two weeks if animals are persistently parasitemic (Vial & Gorenflot, 2006). Imidocarb has been used successfully in wapiti (*Cervus canadensis*) and reindeer (*Rangifer tarandus tarandus*) to treat clinical babesiosis and to prevent the development of disease in asymptomatic parasitemic animals (Bartlett, Abou-Madi, Messick, Birkenheuer, & Kollias, 2009; Gallatin et al., 2003). The frequency of treatments reported to be effective in parasitemic cervids vary from a single IM treatment (at 2.2–3.0 mg/kg) to repeated treatments on days 1, 2, 6, 9, and 21 (Bartlett et al., 2009). No adverse effects of imidocarb have been reported in cervids. Aggressive supportive treatment, which may include blood transfusions, is indicated for cervids in acute hemolytic crisis (Pastor & Milnes, 2018).

In our study, imidocarb had a short absorption half-life ($t_{1/2Ka}$ = 24.09 ± 3.06 min) and fast distribution phase ($t_{1/2\alpha}$ = 25.90 ± 10.21 min), followed by a slower terminal elimination phase ($t_{1/2\beta}$ = 464.06 ± 104.08 min or 7.73 ± 1.73 hr). The absorption and distribution half-lives for imidocarb in the white-tailed deer of our study were comparable to published values for sheep, goats (Belloli et al., 2006), and horses (Belloli et al., 2002). As in deer, the distribution of imidocarb in these species was also best described by a two-compartment open model (Belloli et al., 2002, 2006). Rapid absorption and distribution of imidocarb is clinically valuable in the treatment of babesiosis because therapeutic levels in the biophase will be reached rapidly. The area under the curve extrapolated to infinity ($AUC_{0-\infty}$) in white-tailed deer, indicating the exposure of imidocarb to the animal, was close to the values obtained in studies of sheep and goats following a single treatment at 3.0 mg/kg IM (Belloli et al., 2006). As our study did not include an intravenous arm, the bioavailability of imidocarb in white-tailed deer could not be determined, and therefore the apparent volumes of distribution and clearance must be interpreted with caution because they are confounded by unknown bioavailability ($F$). The apparent volume of distribution ($V_Z/F$) of imidocarb in deer in our study was 9.20 ± 2.70 L/kg, which is comparable to values previously described in sheep (4.18 ± 0.44 L/kg) and goats (7.68 ± 0.57 L/kg; Belloli et al., 2006). Imidocarb is a lipid-soluble organic base. Ionic trapping of imidocarb within cells (including erythrocytes), whose intracellular pH is lower than the pH of plasma, is therefore likely to contribute to this large volume of distribution. Apparent total body clearance in our study was low (15.97 ± 1.28 ml $min^{-1}$ $kg^{-1}$) but comparable to that found in sheep and goats (Belloli et al., 2006), which, coupled with the large volume of distribution, would explain the relatively slow depletion of this drug from the plasma during the elimination phase. The elimination half-life of 7.73 ± 1.73 hr is similar to that described in horses (Belloli et al., 2002), sheep, and goats (Belloli et al., 2006). The pharmacokinetics of imidocarb are not thought to differ between males and females. Only females were used in the present study, but we expect that our results are likely to be applicable to males because studies of imidocarb in other domestic species have not noted any sex-specific PK effects (Belloli et al., 2002).

Imidocarb dipropionate (Imizol®) is approved for the treatment of babesiosis in dogs in the USA at a rate of 6.6 mg/kg by IM or SC injection, and for the treatment and prevention of babesiosis in sheep (1.0 mg/kg IM or SC), cattle (2.5 mg/kg IM or SC), and horses (2.0 mg/kg IM or SC) in other countries. An imidocarb dose of 3.0 mg/kg IM was used in cervids in the present study. All imidocarb usage in cervids worldwide constitutes extra-label use, and a conservative meat withdrawal period is recommended when considering the use of this drug in commercially farmed cervids. Imidocarb remains detectable in edible bovine tissues for several months following dosing, due to deposition in hepatocytes (Moore, Coldham, & Sauer, 1996), and thus further research is warranted to gain insight into the possible residual concentrations of imidocarb in cervid products, including velvet, intended for human consumption. Maximum Residue Levels have been established for imidocarb in cattle and sheep tissues in Europe (CVMP, 2003), and these could be extrapolated to cervid tissues for regulatory consideration.

Development of a rational dosage regimen for cervids requires knowledge of the plasma concentrations of imidocarb that may be effective for treatment and prophylaxis of babesiosis. *Babesia odocoilei* is morphologically similar to the "large" *Babesia* spp. of domestic livestock such as *B. bigemina*, *B. caballi*, and *B. divergens* (Holman et al., 2002). In cattle, an in vitro minimum inhibitory concentration of imidocarb of 27.0–34.0 ng/ml is described for *B. divergens* (Brasseur, Lecoublet, Kapel, Favennec, & Ballet, 1998). At 8 hr after treatment in our study, imidocarb was detectable in all deer, at a mean plasma concentration of 53.91 ± 6.18 ng/ml. Consequently, the imidocarb plasma concentration profile we describe in white-tailed deer following intramuscular injection at 3.0 mg/kg may be efficacious for the treatment of *B. odocoilei* in this species, and the rapid distribution and slow elimination of imidocarb in deer may result in plasma concentrations remaining at therapeutic concentrations for at least 8 hr. Clinical trials in parasitemic cervids infected with *B. odocoilei* are required in order to evaluate the efficacy of this dose of imidocarb as a treatment for cervid babesiosis.

In conclusion, results reported herein show that imidocarb injected at 3.0 mg/kg IM has a rapid distribution and relatively slow elimination rate in white-tailed deer. The apparent volume of distribution of greater than 9 L/kg was consistent with a lipophilic agent with wide distribution to tissues. These results may be used to investigate other dosage regimens that may be useful to treat *B. odocoilei* parasitemia in other cervid species under managed care. However, pharmacokinetic parameters are not necessarily comparable across different species, and caution must be used in generalizing the results of the present study to other cervid species.

## ACKNOWLEDGMENTS

Funding for this research was provided by the American Association of Zoo Veterinarians Wild Animal Health Fund and the Toronto Zoological Foundation. The license for Phoenix WinNonlin® software

was provided by Certara through their Center of Excellence program. The authors would like to thank the Lefler family, Brian Tapscott, and Jeff Miedema and the staff of Townsend Butchers for sourcing blank white-tailed deer plasma. We are grateful to Karen Gesy, Claire Janse van Rensburg, Patrick Robertson, Rob Stevens, Shannon Toy, Todd Shury, Mitch Cooper, and the staff of the University of Saskatchewan Specialized Livestock Research Facility for their assistance with the animal phase of the study.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTION

All listed authors qualify for authorship according to the criteria given in the JVPT Editorial Policies and Ethical Considerations.

## ORCID

*Ellie L. Milnes* https://orcid.org/0000-0002-7797-2217
*Ronette Gehring* https://orcid.org/0000-0002-1329-201X

## REFERENCES

Abdullah, A. S., Sheikh-Omar, A. R., Baggot, J. D., & Zamri, M. (1984). Adverse effects of imidocarb dipropionate (Imizol®) in a dog. *Veterinary Research Communications*, *8*(1), 55–59. https://doi.org/10.1007/BF02214695

Bartlett, S. L., Abou-Madi, N., Messick, J. B., Birkenheuer, A., & Kollias, G. V. (2009). Diagnosis and treatment of *Babesia odocoilei* in captive reindeer (*Rangifer tarandus tarandus*) and recognition of three novel host species. *Journal of Zoo and Wildlife Medicine*, *40*(1), 152–159. https://doi.org/10.1638/2008-0011.1

Belloli, C., Crescenzo, G., Lai, O., Carofiglio, V., Marang, O., & Ormas, P. (2002). Pharmacokinetics of imidocarb dipropionate in horses after intramuscular injection. *Equine Veterinary Journal*, *34*(6), 625–629.

Belloli, C., Lai, O. R., Ormas, P., Zizzadoro, C., Sasso, G., & Crescenzo, G. (2006). Pharmacokinetics and mammary elimination of imidocarb in sheep and goats. *Journal of Dairy Science*, *89*, 2465–2472. https://doi.org/10.3168/jds.S0022-0302(06)72320-7

Brasseur, P., Lecoublet, S., Kapel, N., Favennec, L., & Ballet, J. J. (1998). In vitro evaluation of drug susceptibilities of *Babesia divergens* isolates. *Antimicrobial Agents and Chemotherapy*, *42*(4), 818–820. https://doi.org/10.1128/AAC.42.4.818

CVMP (2003). *Imidocarb (Extension to sheep)*. Summary report. EMEA/MRL/881/03-FINAL. Committee for Medicinal Products for Veterinary Use, European Agency for the Evaluation of Medicinal Products. Retrieved from https://www.ema.europa.eu/documents/mrl-report/imidocarb-extension-sheep-summary-report-3-committee-veterinary-medicinal-products_en.pdf

Gallatin, L. L., Irizarry-Rovira, A. R., Renninger, M. L., Holman, P. J., Wagner, G. G., Sojka, J. E., & Christian, J. A. (2003). *Babesia odocoilei* infection in elk. *Journal of the American Veterinary Medical Association*, *223*(7), 1027–1032. https://doi.org/10.2460/javma.2003.223.1027

Holman, P., Swift, P., Frey, R., Bennett, J., Cruz, D., & Wagner, G. (2002). Genotypically unique *Babesia* spp. isolated from reindeer (*Rangifer tarandus tarandus*) in the United States. *Parasitology Research*, *88*(5), 405–411.

Lai, O., Belloli, C., Crescenzo, G., Carofiglio, V., Ormas, P., Marangi, O., & Cagnardi, P. (2002). Depletion and bioavailability of imidocarb residues in sheep and goat tissues. *Veterinary and Human Toxicology*, *44*(2), 79–83.

Mathieu, A., Pastor, A. R., Berkvens, C. N., Gara-Boivin, C., Hébert, M., Léveillé, A. N., … Smith, D. A. (2018). *Babesia odocoilei* as a cause of mortality in captive cervids in Canada. *The Canadian Veterinary Journal*, *59*(1), 52–58.

Milnes, E. L., Thornton, G. L., Delnatte, P., Léveillé, A. N., Barta, J. R., Smith, D. A., & Nemeth, N. M. (2019). Molecular detection of *Babesia odocoilei* in wild, farmed, and zoo cervids in Ontario, Canada. *Journal of Wildlife Diseases*, *55*(2), 335–342. https://doi.org/10.7589/2018-06-147

Moore, A. S., Coldham, N. G., & Sauer, M. J. (1996). A cellular mechanism for imidocarb retention in edible bovine tissues. *Toxicology Letters*, *87*(2–3), 61–68. https://doi.org/10.1016/0378-4274(96)03705-8

Mosqueda, J., Olvera-Ramirez, A., Aguilar-Tipacamu, G., & J Canto, G. (2012). Current advances in detection and treatment of babesiosis. *Current Medicinal Chemistry*, *19*(10), 1504–1518. https://doi.org/10.2174/092986712799828355

Pastor, A., & Milnes, E. (2018). Chapter 92 – Babesiosis in Cervidae. In R. E. Miller, N. Lamberski & P. Calle (Eds.), *Fowler's zoo and wild animal medicine current therapy, volume 9* (pp. 647–653). St. Louis, MO: W.B. Saunders.

Su, D., Li, X. B., Wang, Z. J., Wang, L., Wu, W. X., & Xu, J. Q. (2007). Pharmacokinetics and bioavailability of imidocarb dipropionate in swine. *Journal of Veterinary Pharmacology and Therapeutics*, *30*(4), 366–370. https://doi.org/10.1111/j.1365-2885.2007.00872.x

Vial, H. J., & Gorenflot, A. (2006). Chemotherapy against babesiosis. *Veterinary Parasitology*, *138*(1–2), 147–160. https://doi.org/10.1016/j.vetpar.2006.01.048

**How to cite this article:** Milnes EL, Delnatte P, Woodbury M, et al. Pharmacokinetics of imidocarb dipropionate in white-tailed deer (*Odocoileus virginianus*) after single intramuscular administration. *J vet Pharmacol Therap*. 2020;43:33–37. https://doi.org/10.1111/jvp.12760