

Wave Goodbye to Pain^{with} **Ketofen[®] 10%**



Ketofen® 10%

wave goodbye to pain

Ketofen 10% contains ketoprofen 100 mg/ml and, in cattle, is indicated for:

-  Reduction of the pain associated with lameness
-  Support of parturient paresis
-  Acute clinical mastitis in combination with an appropriate antibiotic
-  Udder oedema after calving
-  Reduction of pyrexia, inflammation and pain in respiratory disease (with appropriate antimicrobial)



Ketofen 10% is ideally suited for use in dairy cattle:



Zero hours milk withdrawal



1 day (IV) or 4 days (IM) meat withdrawal



Fast acting with a 24-hour duration of action



Good syringeability and non-irritant at injection site¹

Quick-acting, provides fast pain relief²

Table 1: The pharmacokinetic parameters of Ketofen 10% after IV and IM injection²

Pharmacokinetic parameters	Unit	Intravenous (Mean ± S.E)	Intramuscular (Mean ± S.E)
Cp0*	µg/ml	34.13 +/- 2.53	-
C _{max}	µg/ml	-	6.15 ± 0.24
T _{max}	h	-	0.50 ± 0.0

*Plasma concentration at T0

DOSAGE

3 ml per 100 kg once daily for up to 3 days
(IV or deep IM)

For the rapid and effective relief of pain, pyrexia and inflammation^{3,4}

Ketofen 10% delivers both peripheral and central analgesia⁴

- **Peripheral analgesia:** reduces prostaglandin synthesis at the site of inflammation
- **Central analgesia:** ketoprofen is measurable in the CSF 15 minutes post injection, leading to rapid action on central sensory receptors⁵ - reducing hyperalgesia⁶

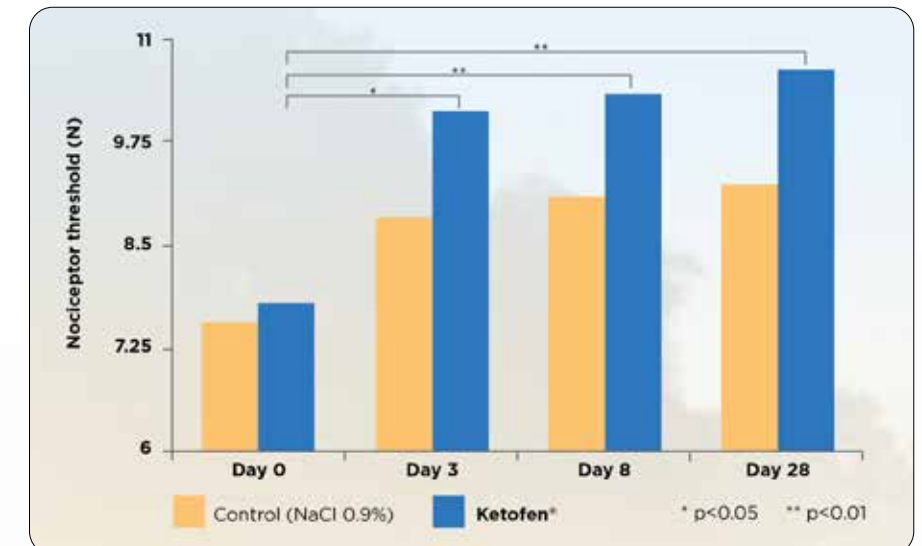


Figure 1: Decrease of central nociceptor activity for 28 days post injection⁶

Ketofen 10% concentrates in inflammatory exudate^{7,8}

- The half-life of Ketofen 10% is 23 hours in exudate, despite having a relatively short plasma half-life
- Effective concentrations can be found in exudate up to 40 hours post IV injection leading to an extended duration of action at tissue level

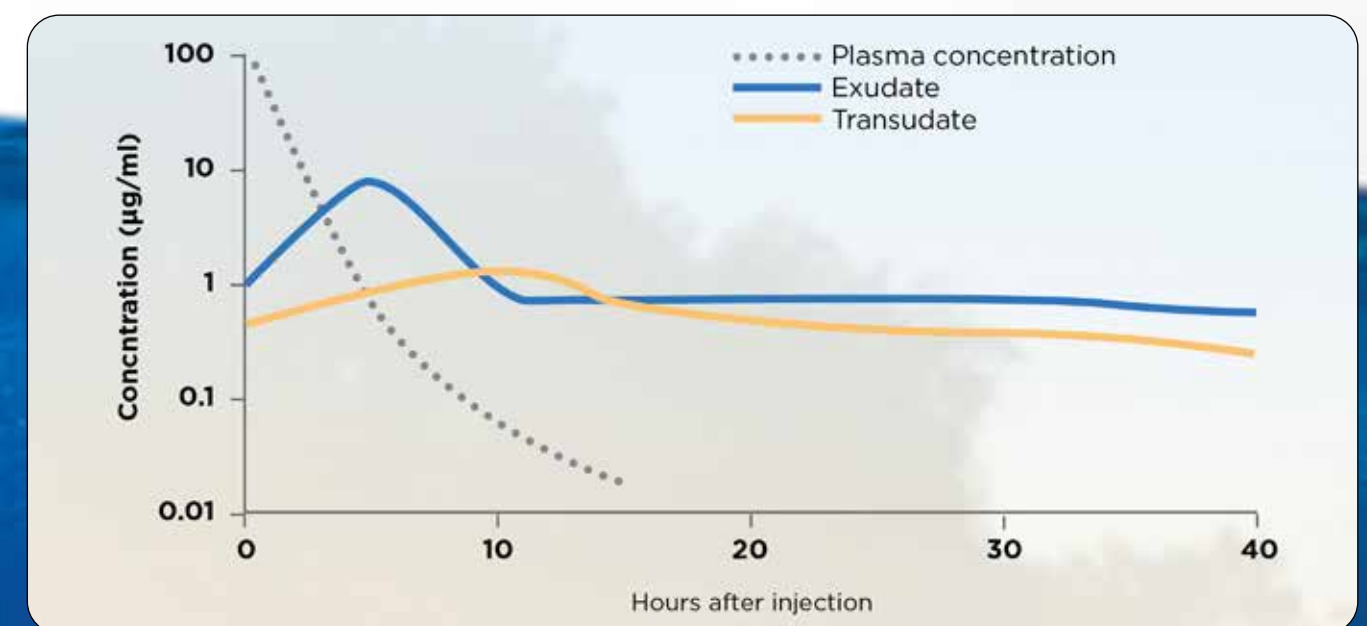


Figure 2: Concentration of ketoprofen after IV injection⁷

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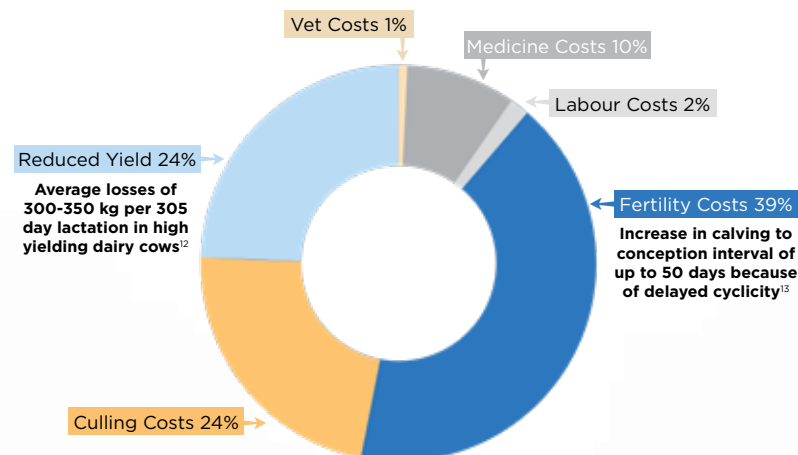
Lameness

Lameness is one of the most significant welfare issues in dairy farming and the prevalence in UK farms is still around 30%⁹.

Economically, the costs of treating lameness are significantly outweighed by production losses¹⁰. The total cost of a lameness case on dairy farms has been recently evaluated at **£196**¹¹.

Lameness management at herd level is based on 4 principles:

- > Good horn quality and hoof shape
- > Low infection pressure
- > Minimising forces on feet (decrease standing time and turning forces)
- > **Early lameness detection and prompt, effective treatment**



Breakdown of annual cost of lameness per herd¹⁰

Early treatment reduced lameness prevalence four weeks post-treatment and decreased the severity of lameness over the study period, reducing the need for repeat treatments and production losses¹⁴

A 12-month study from Nottingham University showed that regular mobility scoring enables early detection. 183 lame cows were enrolled with only one hind claw affected¹⁵. The four different treatment groups were evaluated:

- > Trim only = TRM
- > Trim + Block = TB
- > Trim + NSAID = TN
- > Trim + Block + NSAID (3 days ketoprofen) = TBN

TRM	TB	TN	TBN
69%	72%	76%	85%

Table 2: showing the cure rates in the different treatment groups (mobility score 0 or 1)



The effects of adding ketoprofen to mechanical treatment appears to be beneficial¹⁵. **Early detection and treatment can have a significant impact on the duration and severity of lameness**^{14,16}

Udder diseases

Mastitis

Ketofen 10% - anti-endotoxemic effect in acute Gram negative mastitis

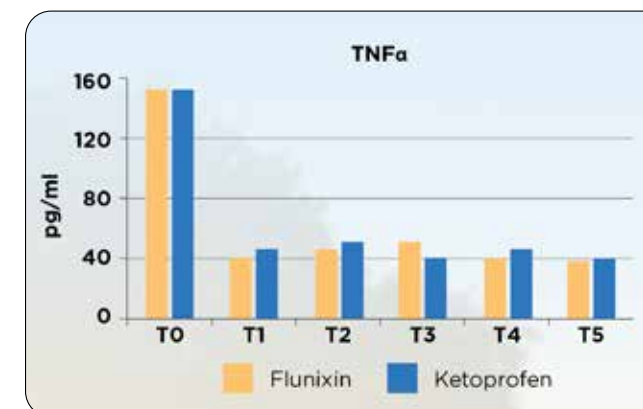


Figure 3: Ketoprofen significantly decreased the levels of TNFa (ex-vivo) in the presence of LPS from coli endotoxaemic mastitis. TNFa concentrations correlate with disease severity¹⁷

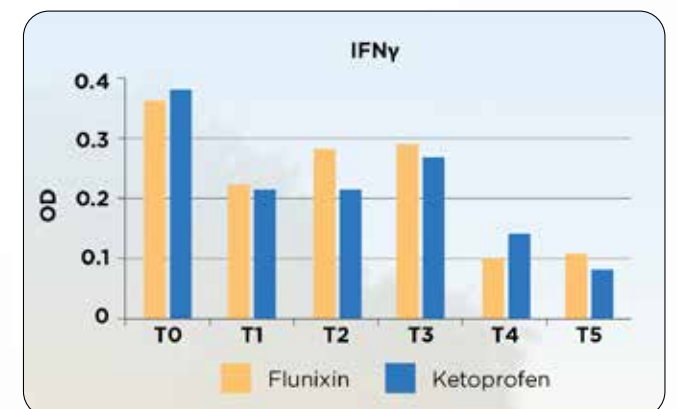


Figure 4: Ketoprofen reduced the level of the inflammatory mediator, IFNγ which is involved in the development of septic shock¹⁷

Ketofen 10% - limits production losses associated with mastitis¹⁸

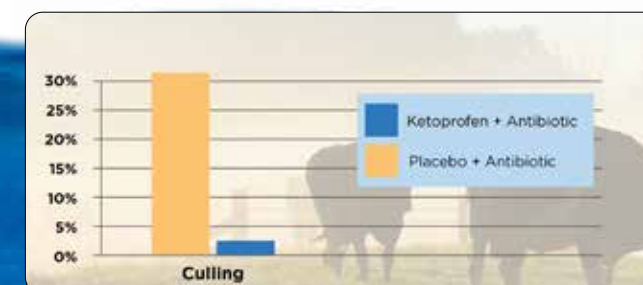


Figure 5: Reduction in culling rates vs. placebo when ketoprofen used, alongside antibiotics, in the management of mastitis¹⁸

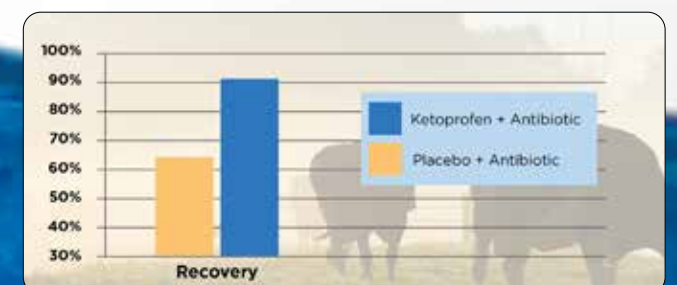


Figure 6: Improvement in recovery rates vs. placebo when ketoprofen used, alongside antibiotics, in the management of mastitis¹⁸

Other indications of Ketofen 10%



Udder oedema – reduces swelling and interstitial fluid accumulation in udder tissue, reducing pain and therefore increasing lying times



Periparturient paresis – supports cows with puerperal muscle weakness



Respiratory disease – use alongside an appropriate antibiotic in cases of viral or bacterial respiratory disease

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Ketofen 10% - treating the pain and lameness associated with digital dermatitis

Digital dermatitis (DD) is one of the most frequently recorded diseases associated with lameness in dairy cattle and has a complex, multifactorial aetiology with spirochetes from 3 families of *Treponema* spp being commonly isolated^{19,20}.

In 2021, a randomised, positively controlled study exploring the potential benefits of a single IM administration of ketoprofen when treating active DD lesions was published²¹.

STUDY SUMMARY

Design and method

158 cows with active DD lesions (score M1, 2 and 4.1) were enrolled into the study and split into two groups. Each cow was mobility scored and assessed as lame with a score of 2 or 3. Their stage of lactation was also recorded.

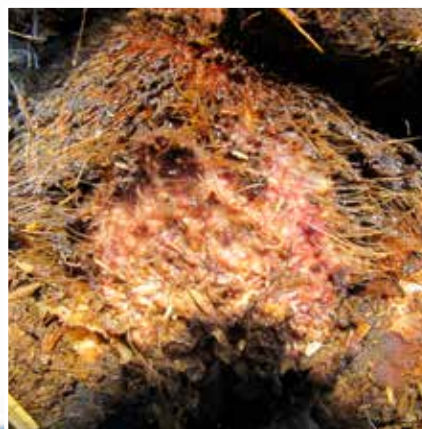
At the start of the trial, the DD lesions present in both groups were cleaned, dried and treated with an antibacterial spray.

90 cows (group 1) then received a single IM injection of Ketofen 10% (ketoprofen 100mg/ml) and 68 cows (group 2) did not. Both groups were assessed one week post-treatment for lameness score and milk yield.

Images showing classical DD lesions M1, M2 and M4.1



M1



M2



M4.1



Results overview (lameness)

Overall, cattle were **2.57 times less likely to be lame** after 1 week when Ketofen 10% was added to the treatment protocol (not statistically significant).

When data was considered only from cows that were lame (score 2 and 3) at enrolment, those receiving only topical antibiotic treatment at the first evaluation, were **20.2 times more likely to be lame** at the 2nd evaluation than those also receiving Ketofen 10% this was statistically significant ($p=0.027$)* (Figure 7).

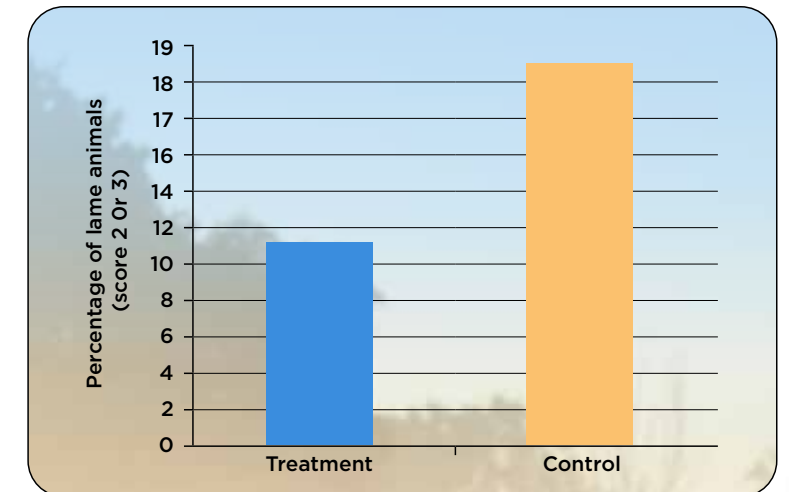


Figure 7: Graph showing the percentage of ALL animals lame after one week in the control vs. treatment groups

Results overview (milk yield)

Overall, cows in the treatment group produced 3 kg/day more milk than those in the control group for the week following enrolment ($p>0.01$).

When data was considered only from freshly calved cows that were lame at enrolment there was a statistically significant benefit in milk yield if treated with a single injection of Ketofen compared to the control animals. These cows produced 58.38 (± 1.85) kg milk per day for the week after compared to the control group that produced 47.89 (± 1.81) kg per day ($p < 0.05$) (Figure 8).

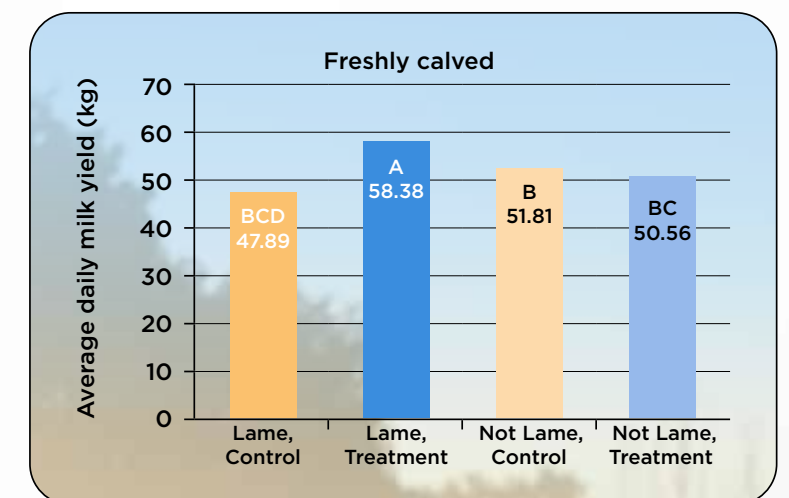


Figure 8: Graph showing the benefit in milk yield in freshly calved lame cows 1 week after treatment with Ketofen 10%

This study demonstrates that administering Ketofen 10% to cows with DD, can have beneficial effects on their mobility and milk production, especially if animals are visibly lame when treated (score 2 or 3). The study also provides the first evidence of possible welfare and production benefits associated with the use of NSAIDs when treating active DD lesions in lame cows.

Ketofen® 10%

IDEALLY SUITED TO THE TREATMENT OF PAIN
AND LAMENESS IN DAIRY COWS



Ketofen 10% is available in 50 ml, 100 ml and 250 ml shock resistant CLAS vials²¹



Zero
hours milk
withdrawal



1 day (IV) or 4
days (IM) meat
withdrawal



Fast acting with a
24-hour duration
of action



Good syringeability
and non-irritant at
injection site¹

Ceva Animal Health are committed to working with a range of industry experts to support an enhancement of the knowledge which is inextricably linked to the challenge of optimally managing lameness in dairy cattle. This has included: funding for lameness research projects, in-practice veterinary training and specific young vet initiatives, on-farm training and support of foot trimmers and vet technicians.

If you would like to find out more about how Ceva could support your practice, please contact your Ceva territory manager or call the head offices on 01494 781510.



Reduction of the pain associated with lameness



Support of parturient paresis



Acute clinical mastitis in combination with an appropriate antibiotic



Udder oedema after calving



Reduction of pyrexia, inflammation and pain in respiratory disease (with appropriate antimicrobial)

References: 1. Pyorala S. *et al.* 1999. Local tissue damage in cows after intramuscular administration of preparations containing phenylbutazone, flunixin, ketoprofen and metamizole. *Acta Vet. Scand.* 40: 145-150. • 2. Ratndee S. *et al.* 2014. Pharmacokinetics and bioavailability of ketoprofen after single dose intravenous and intramuscular administration in cattle. *Wayamba J. Animal Sci.* Vol 6: 820-823. • 3. Williams R.L. & Upton R.A. 1988. The clinical pharmacology of ketoprofen. *J. Clinical Pharmacology.* 28: S13-S22. • 4. Diaz-Reval M.I. *et al.* 2004. Evidence for a central mechanism of action of S-(+)-ketoprofen. *European J. Pharmacology.* 483: 241-248. • 5. Netter P *et al.* 1985. Diffusion of intramuscular ketoprofen into the cerebrospinal fluid. *European J. Clinical Pharmacology.* 26: 319-321. • 6. Whay H.R., Webster A.J.F., Waterman-Patterson A.E. 2005. Role of ketoprofen in the modulation of hyperalgesia associated with lameness in dairy cattle. *Vet. Record.* 157: 729-733. • 7. Landoni M. and Lees P. 1995. Pharmacokinetics and pharmacodynamics of ketoprofen enantiomers in calves. *Chirality* 7(8):586-97. • 8. Landoni M.F., Cunningham F.M., Lees P. 1995. Comparative pharmacodynamics of flunixin, ketoprofen and tolfenamic acid in calves. *Vet. Record* 137 (8): 428-431. • 9. Randall L. *et al.* 2019. Lameness prevalence in a random sample of UK dairy herds. *The Veterinary Record*, 184(11): 350. • 10. Willshire J.A. and Bell N.J. 2009. An economic review of cattle lameness. *Cattle Practice.* 17(2):136-141. • 11. Kingshay Dairy costings focus annual report 2019 • 12. Hernandez J.A. *et al.* 2005. Comparison of milk yield in dairy cows with different degrees of lameness. *J. Am. Vet. Med. Assoc.* 227:1292-1296. • 13. Huxley J.N. 2013. Impact of lameness and claw lesions in cows on health and production. *Livestock Science.* 156:64-70 • 14. Leach K.A. *et al.* 2012. The effects of early treatment for hindlimb lameness in dairy cows on four commercial UK farms. *The Vet. Journal.* 193: 626-632. • 15. Thomas H.J. *et al.* 2015. Evaluation of treatments for claw horn lesions in dairy cows in a randomized control trial. *J. Dairy Science.* 98: 4477-4486. • 16. Groeneveld M. *et al.* 2014. Measuring the response to therapeutic foot trimming in dairy cows with fortnightly lameness scoring. *The Vet Journal* 201:283-288. • 17. Donalicio C. *et al.* 2012. Effects of flunixin meglumine and ketoprofen on mediator production in ex vivo and in vitro models of inflammation in healthy dairy cows. *J. Vet. Pharmacol. Therap.* 36: 130-139. • 18. Shpigiel N.Y., Chen R. & Winckler M. 1995. Anti-inflammatory ketoprofen in the treatment of field cases of bovine mastitis. *Res. Vet. Sci.* 56: 62-68. • 19. Evans N.J., Murray R.D., Carter S.D. Bovine digital dermatitis: current concepts from laboratory to farm. *Vet J.* 2016;211:3-13. • 20. Bell N. and Vanhoudt A. 2020. Treatment and control of DD in dairy cattle. *In Practice* 42(10):554-567 • 21. Kasiora K. *et al.* 2021. Evaluation of the use of ketoprofen for the treatment of digital dermatitis in dairy cattle: A randomised, positive controlled, clinical trial. *Vet Record* Pe977

Ketofen® 10% solution for injection contains 100 mg ketoprofen per ml. **Legal Category:** UK [POM-V]
Further information is available from the SPC, data sheet, pack leaflet or from the prescriber.

Prescription decisions are for the person issuing the prescription alone. Use medicines responsibly (www.noah.co.uk/responsible)

Ceva Animal Health Ltd

Explorer House, Mercury Park, Wycombe Lane, Wooburn Green, Bucks
HP10 0HH www.ceva.co.uk www.cevolution.org/uk

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