



A RESEARCH REVIEW™
PRODUCT REVIEW

Meloxicam in the Management of Mastitis in Dairy Cows



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About the Reviewer



David Hawkins, BVSc.

Graduating from Massey University in 1992, David has spent the bulk of his career servicing dairy clients in the South Auckland and North Waikato regions. He has served on the DCV, NMAC, and tutors on the Advanced Mastitis Course. David's time is spent predominantly servicing dairy clients as a consultant and managing projects for various industry and private clients. He has published several studies in NZ veterinary publications including the New Zealand Veterinary Journal and has spoken in a wide range of local and international conference settings. Outside of the office, David is a keen musician involved in the local church and likes to get out on the water in his sailing boat whenever possible.

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This product review summarises relevant pharmacological and clinical properties of meloxicam (Metacam 20) when used for management of mastitis in dairy cows. This article is supported by an educational grant from Boehringer Ingelheim. A companion Product Review summarising the pharmacological properties of meloxicam (Metacam 20) used for management of disbudding in dairy calves is available on request.

Mastitis is inflammation of the udder, which is usually caused by a bacterial infection.^{1,2} Cows with clinical, and even subclinical, mastitis experience discomfort, pain, and reduced welfare.³⁻⁵ Mastitis can also have a negative impact on factors of production and reproductive performance in dairy cows.

Economic costs of mastitis

Despite the use of control strategies over many years, bovine mastitis continues to be one of the most prevalent production diseases affecting the dairy industry worldwide.⁶ In NZ, estimates of disease put the prevalence of cows with one or more cases of clinical mastitis during a single lactation at between 13–15%.^{7,8}

As an indicator of the potential effects of mastitis on production, US dairy industry losses due to bovine mastitis were estimated to be \$US2 billion in 1993.⁹ Most of the economic loss results from reduced milk production but there is also the cost of altered milk composition.^{9,10} In the NZ dairy industry, estimates of loss in 2005/06 were \$NZ180 million.⁸ Bulk milk somatic cell counts (SCC) elevated above 150,000 cells/mL accounted for most of the loss, with treatment of clinical mastitis and culling of cows also accounting for significant components. In addition, mastitis impairs reproductive performance in dairy herds.¹⁰⁻¹² The combined economic losses associated with lower production and reproductive performance due to mastitis are likely to be significant.¹⁰ These may be exacerbated in seasonal production systems.

Mastitis and the role of NSAIDs

Many species of bacteria can invade the mammary gland where they multiply and produce substances that stimulate an inflammatory response.¹⁰ Mastitis is difficult to control in part because of the range of bacteria that can infect the udder, and in part because of the range of environments these bacteria inhabit are in close proximity to the udder even in well-managed dairy herds. Even cows from well-managed dairy herds using effective control strategies can experience a high rate of clinical mastitis at certain times.

Bacterial infections of the udder result in increased levels of interleukin-1, tumour necrosis factor-alpha, and lipopolysaccharide, which induce production of cyclooxygenase (COX).^{13,14} COX converts arachidonic acid into eicosanoids, including prostaglandins, which act as inflammatory and pain mediators.^{5,13,14} During an intramammary infection, levels of pro-inflammatory and pain-sensitising eicosanoids are elevated in milk. The increase in these eicosanoids during mastitis provides the rationale for use of anti-inflammatory therapy to relieve the local and systemic clinical signs of inflammation, which facilitates the return to normal physiological function of the udder.

Non-steroidal anti-inflammatory drugs (NSAIDs) act by inhibiting COX and hence preventing prostaglandin synthesis.⁵ The benefits of NSAIDs on temperature, rumen function, SCC, milk production, behaviour, and pain sensitivity in animals with mastitis indicate that NSAIDs have a role to play in the dairy industry.⁴ Alleviation of any perceived pain or discomfort associated with mastitis is consistent with measures to address the animal welfare concerns of consumer groups.

Meloxicam

Meloxicam (Metacam 20) belongs to the oxicam class of NSAIDs, which exerts anti-inflammatory, anti-endotoxic, anti-exudative, analgesic, and antipyretic activity via the inhibition of prostaglandin synthesis.¹⁵ It is indicated for treatment of acute mastitis in lactating cows, in combination with appropriate antibiotic therapy. For full prescribing details refer to the Metacam 20 Product Leaflet.

Dosage and administration

The recommended dosage in cattle is Metacam 20 0.5 mg/kg bodyweight (i.e. 2.5 mL/100 kg bodyweight) as a single subcutaneous (SC) or intravenous (IV) injection.¹⁵ For young calves weighing <50 kg, the appropriate dose rate of Metacam 20 is 0.5 mL/20 kg. The withholding period for cattle is 84 hours for milk and 10 days for meat from the last treatment.

These dosage and withholding period recommendations pertain specifically to Metacam 20. They may differ for other registered meloxicam products.

Precautions and contraindications

Cattle with impaired hepatic, cardiac, or renal function; haemorrhagic disorders; or evidence of gastrointestinal ulceration should not receive meloxicam.¹⁵

Concurrent administration of meloxicam with glucocorticosteroids, other NSAIDs, or anticoagulants is contraindicated.¹⁵ Because oxicams bind extensively to plasma proteins,¹⁶ caution is recommended when administering meloxicam in conjunction with other highly protein bound drugs.¹⁵



Effects on pain and inflammation

Although pain is heterogeneous and difficult to quantify in dairy cattle, there is obvious benefit to the use of NSAIDs for relieving pain and reducing inflammation.⁴

In an *in vitro* study that investigated the effects of meloxicam on the immune response of bovine mammary epithelial cells challenged with endotoxin derived from common mastitis pathogens, meloxicam dose-dependently moderated the immune response of the epithelial cells by preventing increased expression of factors involved in inflammation.¹⁷

In an *in vivo* study, the administration of SC Metacam 20 0.5 mg/kg relieved udder pain (including a significant reduction [$p=0.004$] at 6 hours post-administration) and reduced udder oedema compared with control in endotoxin-induced clinical mastitis in lactating dairy cows.³

Clinical efficacy

The clinical efficacy of a single IV dose of Metacam 20 0.5 mg/kg as adjunctive therapy in dairy cows with acute mastitis was investigated in a double-blind positive-controlled field trial.¹⁸ The composite clinical score (general condition, severity of inflammation, and milk appearance) was significantly ($p\leq 0.05$) improved on days 2 and 3 post-administration in cows that received Metacam 20 compared with those that received an established reference NSAID.

Effects on reproduction and production

A meta-analysis demonstrating an association between the incidence of mastitis and reproductive performance outcomes in dairy cattle emphasises the importance of controlling mastitis to maximising cow performance and economic benefit.¹⁹ There is also evidence that subclinical mastitis is equivalent to clinical mastitis in reducing reproductive performance of lactating cows.¹⁰ Increased numbers of days open following calving is a consistent finding in studies considering the impact of mastitis on reproduction. Where there are limited numbers of days to conceive, as in seasonal calving systems, the impact of mastitis on cow survivability in the herd may be more severe than in non-seasonal herds.

In a randomised placebo-controlled study, the addition of SC Metacam 20 0.5 mg/kg to antimicrobial therapy, for treatment of mild-to-moderate clinical mastitis, resulted in a higher probability of bacteriological cure and improved fertility in terms of higher conception to first service, higher probability of pregnancy within 120 days of calving, and fewer inseminations required to achieve pregnancy.¹³

The results of a simulation modelling study suggest that improvements in conception rate achieved by the addition of Metacam 20 to antimicrobial therapy for treatment of mild-to-moderate clinical mastitis (in the first 120 days in milk) result in a net economic benefit.²⁰ This outcome remained true over a range of technical and economic inputs suggesting that use of meloxicam is likely to be cost effective across different types of production systems.

Regarding aspects of dairy production in seasonal calving dairy herds, in a randomised placebo-controlled study, treatment of clinical mastitis cases with SC Metacam 20 250 mg in combination with antibiotic therapy resulted in significantly lower SCC ($p=0.001$) and fewer cows culled from herds ($p<0.001$) compared with antibiotic therapy alone (Figure 1), with significantly ($p=0.02$) fewer cows being culled from herds for failing to conceive.¹⁴

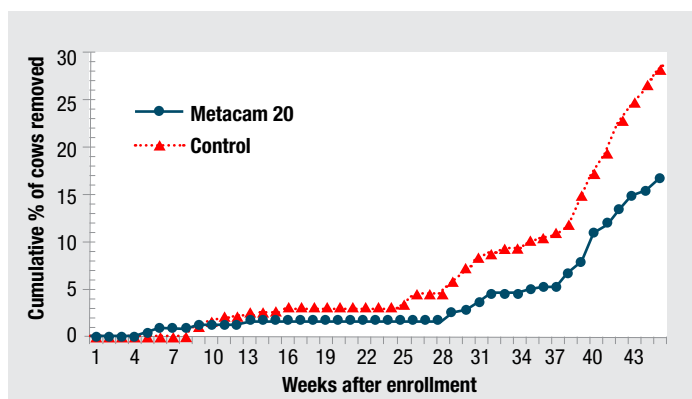


Figure 1. Cumulative percentage of lactating cows with clinical mastitis treated with antibiotic plus SC Metacam 20 250 mg (●) or antibiotic plus control (▲) for 3 days that were culled during the following 45 weeks.¹⁴

EXPERT'S CONCLUDING COMMENTS

Mastitis has been with us for as long as we have farmed cows. Given the difficulties of eliminating normal but pathogenic bacteria from the proximity of the cow, mastitis will be with us for the foreseeable future. Mastitis control strategies will continue to play an important part of reducing disease, improving productivity, and improving welfare for cows under our care. However, we will continue to see cases of clinical and sub-clinical mastitis. Consequently, improving treatment outcomes for animals affected with mastitis will continue to be a priority.

As our understanding grows, a more complete picture of the negative impacts of mastitis is emerging. Alongside this, we are learning more about how to limit these impacts. The use of NSAIDs in conjunction with more specific treatments has long been a part of the armoury of our colleagues in the field of companion animal and human medicine. Production animal veterinarians and farmers have been late to include NSAIDs into their routine treatment protocols for a variety of reasons. Over the past decade however, there has been increased uptake of tools to manage inflammation and pain from production animal communities. Many of us recognize improvements in our own case outcomes as a result. As a veterinarian assisting farmers to farm sustainably, it is particularly gratifying to see the inclusion of meloxicam in treatment protocols in these studies providing better outcomes for the farm business, assurance for consumers and improved welfare for the animals concerned. We should have confidence that by prescribing to manage pain and inflammation alongside specific treatments, we are creating "win-win situations" where the farmer, community, and the cow all benefit.

TAKE-HOME MESSAGES:

- Bovine mastitis is a common disease that has detrimental effects on animal wellbeing and negative economic consequences for dairy producers; hence,
 - there is a role for NSAIDs in the management of pain and discomfort associated with mastitis.
- In experimental studies of endotoxin-induced mastitis, meloxicam has been shown to mitigate inflammatory processes *in vitro* and to reduce pain in dairy cows.
- In clinical studies of dairy cows with mastitis, adding Metacam 20 to antibiotic therapy:
 - was associated with superior clinical efficacy versus a reference NSAID.
 - was associated with improvements in cure rates and fertility.
 - resulted in a reduction in SCC and in the risk of removal from the herd.

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