



**Australian Pesticides &
Veterinary Medicines Authority**

ADVICE SUMMARY

APPLICATION FOR REGISTRATION OF A CHEMICAL PRODUCT

Product name: METACAM 0.5 MG/ML ORAL SUSPENSION FOR CATS
Applicant: BOEHRINGER INGELHEIM PTY LIMITED, VETMEDICA DIVISION
Product number: 61575
Application number: 41164

Purpose of Application and Description of Use: Registration of 0.5mg/mL Meloxicam non-steroidal anti-inflammatory drug in oral suspension for the alleviation of inflammation and pain in both acute and chronic musculoskeletal disorders in cats.

Active Constituent(s): MELOXICAM

Regulatory Decision:

To grant the application subject to the following conditions:

Standard Conditions of Registration/Approval

For full conditions, refer to http://www.apvma.gov.au/advice_summaries/adv_summaries.shtml.

External Efficacy Reviewer

This submission included 2 dose confirmation trials, 3 European field studies 2 safety studies and 4 pharmacological studies. Study design, experimental conditions, data analysis and validation were adequate for the study of the product when used to treat cats with locomotor disorders.

The trials demonstrated adequate efficacy when the product was used to treat acute and chronic locomotor disorders in cats. The product was well tolerated by healthy research cats under laboratory conditions at 1X and 3X the proposed label dose for 90 days (0.1mg/kg for the first day of treatment, followed by a maintenance dose of 0.05mg/kg once daily), but at 5X the proposed label dose for 90 days, there was some evidence of haematological, gastric, renal and thymic side-effects. No testing of the product was performed in animals likely to be sensitive to the side-effects of non-steroidal anti-inflammatory drugs (NSAIDS) i.e. cats with renal, hepatic or gastrointestinal disorders; serum creatinine >2.5mg/dl or 212 µmol/L; hypovolaemia; pre-treatment with steroidal or non-steroidal anti-inflammatory drugs; pregnancy or lactation. This is an important point, since NSAIDS as a drug class are known to have a relatively low safety margin in cats, due to a relative lack of hepatic glucuronidation enzymes. Further, cats with chronic locomotor disorders (the most likely animals for which this product will be prescribed) are likely to be older, with possible age-related sub-clinical organ insufficiency, especially chronic renal insufficiency.

In the opinion of the reviewer, the data presented in the efficacy studies are adequate to support the registration of METACAM 0.5MG/ML ORAL SUSPENSION FOR CATS as detailed in the proposed product label (*For the alleviation of inflammation and pain in both acute and chronic musculoskeletal disorders*).

The reviewers recommendations for inclusions on the product label for METACAM 0.5MG/ML ORAL SUSPENSION FOR CATS were as follows –

- The existing warning on the proposed label regarding the use of the product in cats with pre-existing renal, hepatic or gastrointestinal disorders or hypovolaemia should be extended as follows - *WARNING - Cats should be screened for pre-existing renal, hepatic or gastrointestinal disorders or hypovolaemia (using haematology, serum biochemical analysis and urinalysis as necessary), before administration of Metacam 0.5mg/mL Oral Suspension For Cats. Use of Metacam 0.5mg/mL Oral Suspension For Cats is contraindicated in these animals.*
- Clear instructions limiting course duration and dose rate should also be shown on the label e.g. *For Acute Locomotor Conditions – Give 0.3mg/kg on the first day, followed by 0.1mg/kg daily for a maximum of 4 days, always dosing immediately after a meal. For Chronic Locomotor Conditions – Give an initial single dose of 0.1mg/kg followed by 0.05mg/kg once daily for a maximum of 28 days, always dosing immediately after a meal. Allow at least 14 days between courses of Metacam 0.5mg/mL Oral Suspension For Cats.*

The applicant responded to the recommendations with scientific argument and further data. The reviewer provided comment and the APVMA proposed changes to address the issues raised. The applicant accepted the proposed new changes. Specifically: the new dosing regimen for both acute and chronic locomotor conditions are agreed at a single initial dose of 0.1mg/kg followed by 0.05mg/kg daily; a recommendation has been placed on the label that “*Response to long term therapy should be monitored at three monthly intervals or more frequently as advised by the veterinarian.*”; the dosing recommendation is amended to dosing around mealtimes; and the label is amended to contain “*especially older cats considered for chronic treatment should be screened for pre-existing renal, hepatic or gastrointestinal disorders*”. These changes have been made to the label as approved for the new product.

Data relied on to provide the advice

Data No	Data Source*	Author(s)	Title	Date	Data Type	Data Sub-type	Authorising Party	Inherited Application No.
13998	S	Lehr Thorsten	Population Pharmacokinetic modelling and simulation of Metacam 0.5 mg/mL oral suspension in cats	2005	Efficacy and Safety	Efficacy	Applicant	
10449	S	S.P.Clarke, et al	Prevalence of radiographic signs of degenerative joint disease in a hospital population of cats	2005	Efficacy and Safety	Efficacy	Public	
10439	S	K.Okuda, et al	Dose range Arthritis induced in cat by sodium urate: a possible animal model for tonic pain	1984	Efficacy and Safety	Other Information	Public	
10454	S	B Hansen	Through a glass darkly: using behaviour to assess pain	1997	Efficacy and Safety	Other Information	Public	
10434	S	I.Bjarnason	Forthcoming non-steroidal anti-inflammatory drugs: are they really devoid of side effects?	1999	Efficacy and Safety	Other Information	Public	
10453	S	P.M.Taylor, et al	Pain management in cats - the past, present and future	2004	Efficacy and Safety	Other Information	Public	
10436	S	J.M.Giraudel, et al	Development of in vitro assays for the evaluation of cyclooxygenase inhibitors and predicting selectivity of non-steroidal anti-inflammatory drugs in cats	2005	Efficacy and Safety	Other Information	Public	
10452	S	E.M.Hardie, et al	Radiological evidence of degenerative joint disease in geriatric cats: 100 cases	2002	Efficacy and Safety	Other Information	Public	
10431	S	S Noble, et al	Meloxicam	1996	Efficacy and Safety	Other Information	Public	
10451	S	B.S.Beale	Orthopedic problems in geriatric dogs and cats	2005	Efficacy and Safety	Other Information	Public	
10437	S	G.Carroll, et al	Paw pressure assessment with a pressure mat of the efficacy of Meloxicam in cats with a sodium urate-induced arthritis	2004	Efficacy and Safety	Other Information	Public	
10433	S	M.T.Donnely, et al	Cox II inhibitors - a new generation of safer NSAIDs	1997	Efficacy and Safety	Other Information	Public	
10435	S	J.L.Wallace	Distribution and expression of cyclooxygenase (COX) isoenzymes, their physiological roles and the categorisation of non-steroidal anti-inflammatory drugs (NSAIDs)	1999	Efficacy and Safety	Other Information	Public	
10450	S	D.R.Godfrey	Osteoarthritis in cats: a retrospective radiological study	2005	Efficacy and Safety	Other Information	Public	
10432	S	E.V.Hersh, et al	Update on cyclooxygenase inhibitors: has a third	2005	Efficacy and Safety	Other Information	Public	

			COX isoform entered the fray?					
10443	S	J.Leuschner	Pharmacokinetics study of Metacam oral suspension 0.5mg/mL after oral administration to cats in three consecutive phases	2005	Efficacy and Safety	Pharmacological Data/Studies	Applicant	
10442	S	M.J.McIntosh, et al	Meloxicam - validation of an analytical method for the determination of Meloxicam in cat plasma by HPLC	2004	Efficacy and Safety	Pharmacological Data/Studies	Applicant	
10444	S	J.Leuschner	Pharmacokinetics of Metacam 0.5mg/mL oral suspension after administration to fed and fasted cats	2005	Efficacy and Safety	Pharmacological Data/Studies	Applicant	
10445	S	J.M.Giraudel, et al	Pharmacokinetics/pharmacodynamic modelling of NSAIDs in a model of reversible inflammation of the cat	2005	Efficacy and Safety	Pharmacological Data/Studies	Public	
10441	S	B.D.Lascelles, et al	Evaluation of the clinical efficacy of Meloxicam in cats with painful locomotor disorders	2001	Efficacy and Safety	Target Animal Safety Studies	Public	
10440	S	C.Justus, et al	Multicentre study on the clinical efficacy and tolerance of Meloxicam (Metacam) in cats with acute locomotor disorders	1994	Efficacy and Safety	Target Animal Safety Studies	Public	
10447	S	J.Leuschner	14-day oral tolerance of Metacam (Meloxicam) at dose levels of 0.025, 0.05 and 0.1mg/kg bw in cats	2002	Efficacy and Safety	Target Animal Safety Studies	Applicant	
10448	S	R.Narbe, et al	Clinical efficacy of Meloxicam (Metacam 0.5mg/mL oral suspension) in cats with painful chronic locomotor disorders	25-04-2006	Efficacy and Safety	Target Animal Safety Studies	Applicant	
10446	S	P.Doherty	Target animal safety study of Metacam oral Suspension when administered orally to adult cats at 1x, 3x and 5x the normal recommended dose once daily for 90 days	2005	Efficacy and Safety	Target Animal Safety Studies	Applicant	
13997	S	Ingrid Letellier et al	Clinical efficacy of melsociam (metacam oral suspension 0.5 mg/mL) in cats suffering from painful acute locomotor disorders in comparison ketoprofen	2006	Efficacy and Safety	Target Animal Safety Studies	Applicant	
10438	S	G.Carroll, et al	Dose range-finding study for the efficacy of Meloxicam suspension in cats utilizing a sodium urate-induced arthritis	2004	Efficacy and Safety	Target Animal Safety Studies	Public	

* S = Data submitted with the application