Proposed amendment to the Poisons Standard - Meloxicam

Submission of the Australian Veterinary Association Ltd

October 2021

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The Australian Veterinary Association (AVA)

The Australian Veterinary Association (AVA) is the national organisation representing veterinarians in Australia. Our 8,500 members come from all fields within the veterinary profession. Clinical practitioners work with companion animals, horses, livestock and wildlife. Government veterinarians work with our animal health, public health and quarantine systems while other members work in industry for pharmaceutical and other commercial enterprises. We have members who work in research and teaching in a range of scientific disciplines. Veterinary students are also members of the Association.

Summary

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has submitted an application to create a new Schedule 6 entry for meloxicam that captures *injectable preparations, at up to 2% concentration, for the pre-surgical treatment of sheep undergoing husbandry procedures*. The proposed change would mean that injectable meloxicam (currently S4, and thus prescription-only) would be available over-the-counter and online without veterinary oversight.

The AVA **does NOT support** the amendment as it provides opportunity for uncontrolled use of a potentially dangerous drug in a broad number of species, including humans. We have outlined below the basis of our arguments, including the risks to animal health and welfare, and risks to public health.

Discussion

We address the relevant matters mentioned in section 52E of the *Therapeutic Goods Act 1989,* on which the TGA is likely to base their decision:

The risks and benefits of the use of a substance

Meloxicam is a potent short-acting nonsteroidal anti-inflammatory drug (NSAID) which is commonly prescribed in many species as an analgesic and anti-inflammatory. It is an excellent drug to manage inflammation and pain when given at the appropriate dose and duration to suitable patients. **However, there are known risks associated with its use in humans and in animals.** Importantly, for animal patients, veterinary knowledge and oversight are required to prescribe appropriately and mitigate these risks. These risks are further outlined below. It is critically important that meloxicam remains a Schedule 4 (prescription only) medication in all of its current forms (for both human and animal use).

The purposes for which a substance is to be used and the extent of use of a substance

Meloxicam is used to reduce pain during husbandry procedures in animals and also to manage inflammation and pain associated with disease processes or injury. It is commonly supplied by veterinarians in either injectable or oral (buccal) form to farmers to use in sheep and cattle undergoing painful husbandry procedures. Veterinarians fully support and encourage increased use for this purpose. Formulations are also available to be dispensed by a veterinarian for the control of pain in dogs, cats, pigs and horses.

The applicant has not demonstrated a persuasive need to reschedule meloxicam by injection to make the drug more accessible. When use is considered appropriate, there is no impediment to supply through veterinarians. Whenever use is indicated, veterinarians are able to supply S4 medications such as meloxicam by telemedicine or other remote means, once an initial relationship with the client and knowledge of their flock has been established. These preparations are used for routine procedures that are planned well in advance, allowing producers to obtain the correct amount of product from a veterinarian who has knowledge of the farmer's property and business. With effective transport services the rapid provision of product is possible even for the most remote properties.

The toxicity of a substance

Meloxicam dose rates vary from species to species. Administration at inappropriate doses can be associated with significant adverse effects in a range of body systems including the renal, gastrointestinal and haemopoietic systems. If meloxicam is given to diseased animals the risk of adverse effects is even higher. The literature provides copious evidence that these adverse reactions can be fatal. Given the toxicity risks, administration to animals needs to be under strict veterinary direction.

Further, there is potential for significant human toxicity, if the product is accidentally or deliberately misused. According to the ARTG, there are currently 71 human products containing meloxicam (all S4 prescription-only). The associated Consumer Medicine Information documents summarise the safety and toxicity issues and the need for cautious use. These include potential adverse cardiovascular events, risks for children, people with liver and kidney problems, gastrointestinal ulceration, interactions with other drugs including antihypertensives, immunosuppressants, diuretics and alcohol, and use in pregnancy or while lactating.

It is noted and highly relevant that in 2005 the TGA introduced stricter measures around the prescribing of Cox-2 Inhibitors including meloxicam following the findings of a review into the safety of this family of medicines: https://www.tga.gov.au/media-release/regulator-takes-tough-action-arthritis-drugs-amended

The risk of rescheduling the veterinary injectable product to S6 is that it will become a readily available and inexpensive substitute for the human prescription-only products; there is a very real likelihood of this product being taken by the oral or injectable route in humans, with serious adverse health outcomes, as has been associated recently with other veterinary products such as ivermectin.

The dosage, formulation, labelling, packaging and presentation of a substance

It is essential that this injectable veterinary meloxicam product, given its potential toxicity and potential for misuse, is only prescribed by veterinarians, as this legally requires the addition of a specific label giving directions for use. This will mitigate the risks of: accidental overdosage; use where it is contra-indicated; and misuse in other species, including humans. Furthermore, unlike the situation for use of S6 products, veterinarians must keep records of use of S4 medications, and this record can help in investigations of supply, appropriate use and adverse effects.

The applicant has not demonstrated any change in presentation, formulation or packaging that would make the drug safer and thus justify re-scheduling from S4 to S6.

The potential for abuse of a substance

Veterinarians must establish a genuine veterinary-client-patient relationship prior to supplying S4 medications. Supply of meloxicam by veterinarians requires them to have knowledge of the animals owned by the client. Supply under veterinary direction also ensures this product is not used inappropriately in other species, including humans.

Should this product be rescheduled to S6 however, any person will be able to buy this via online pharmacies or over-the-counter, for their own use, without any need to demonstrate ownership of sheep or any genuine justification for obtaining the medicine.

If rescheduled such that it is available over-the-counter, it is highly likely that it will be used in other animal species in preference to other more appropriate drugs, due to ease of access:

- It may be used without veterinary consultation to treat sick or injured companion animals, with a high likelihood of toxicity due to incorrect calculation of an appropriate dosage.
- It may be used to mask pain in racing horses and greyhounds, or to mask pain in livestock that are otherwise unfit for transport – all of these pose unacceptable animal welfare risks.

- It may also be used to mask pain in animals prior to transport to abattoirs for slaughter, **allowing the drug to enter the human food chain**. Residues in meat and other animal food products could seriously compromise Australia's food safety and impact our export industries worth billions of dollars to the economy.
- The medicine might be used to mask inflammation and clinical signs in animals suffering from **undiagnosed infections** – this poses a very real **biosecurity risk**, including the risk of serious **zoonoses** going undetected, and all the associated risks to human health.

Any other matters necessary to protect public health

1. As outlined above, if listed as a Schedule 6 substance, this product could be supplied to anyone over the age of 16 from any wholesale or retail (or online) outlet, without the need to establish actual ownership of sheep, and without any veterinary oversight and advice on the risk of harm. The risk is that it will become a readily available and inexpensive substitute for the human prescription-only meloxicam products; there is thus a very real risk of this product being taken by the oral or injectable route in humans, with serious adverse health outcomes.

2. Overdosage is possible in people unaccustomed to calculating dose rates, particularly when extrapolating from an injectable veterinary preparation in order to take in oral form. Of course, the label contains no directions to the human consumer (no CMI or PI).

3. There are public health risks if used in combination with other NSAIDs and corticosteroids, and continued use when there are potential signs of toxicity.

4. If used inappropriately in the target species, or other animal species, there is risk of masking infectious disease and thus delaying diagnosis or completely failing to identify serious biosecurity and zoonotic risks.

5. There is also risk of contamination of the human food supply through inappropriate use in the target species or other animal species.

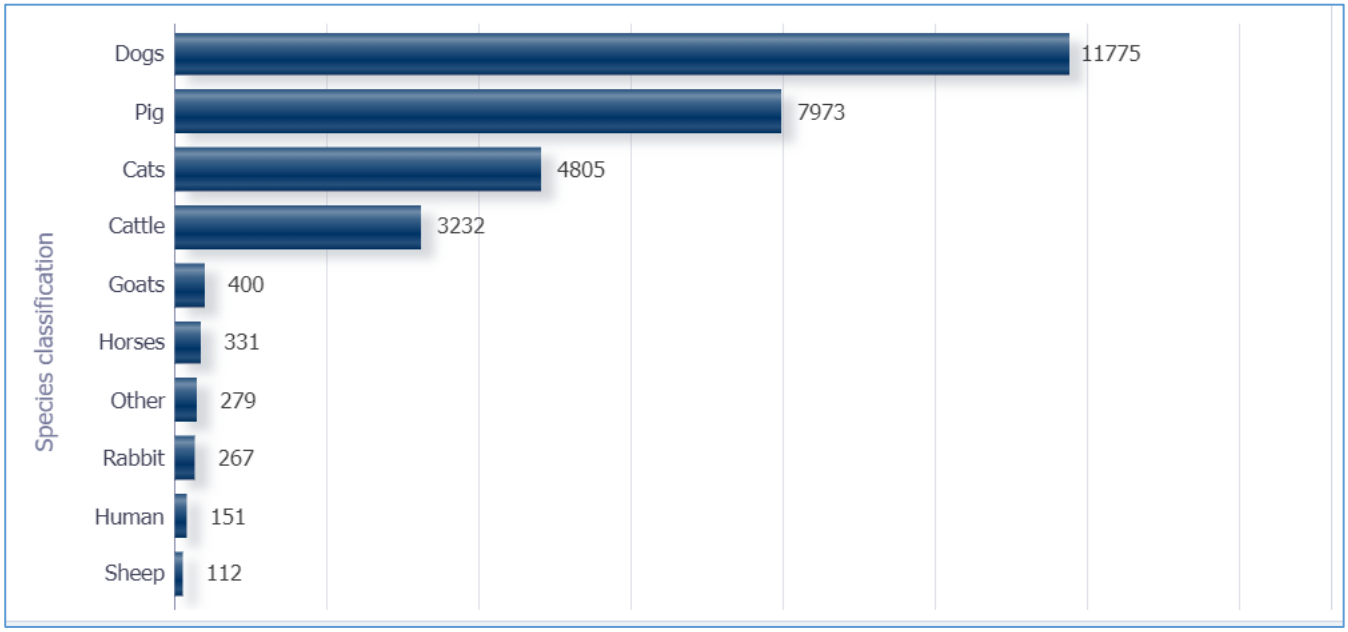
5. If misused in performance animals without appropriate diagnosis by a veterinarian, particularly in the case of lameness or gait abnormalities in horses, there exists a real risk of serious injury to the rider if the horse has a catastrophic fracture of a masked prior injury, as has been reported in the past both in Australia and overseas.

6. The AVA does not believe, given the serious toxicity and other adverse outcomes that could occur as a result of misuse, that label warnings, safety directions or even child-resistant packaging will prevent intentional misuse of this product in the ways we have described.

7. A quick search of the European Medicines Authority pharmacovigilance database shows there are numerous cases (18,410 up to 26-09-2021) of suspected meloxicam adverse events in a range of species, including humans (see next page).

European Medicines Authority pharmacovigilance database summary of reports of suspected meloxicam ADRs presented by species (including humans) as of 26-09-2021

Animal/Human	Species classification	Animals affected	% Animals affected
Animal	Dogs	11775	40.15%
Animal	Pig	7973	27.19%
Animal	Cats	4805	16.38%
Animal	Cattle	3232	11.02%
Animal	Goats	400	1.36%
Animal	Horses	331	1.13%
Animal	Other	279	0.95%
Animal	Rabbit	267	0.91%
Animal	Sheep	112	0.38%
Animal	Chicken	2	0.01%
Human	Human	151	0.51%



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Adverse drug reactions: Meloxicam

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