Off-label Drug Use Options in Exotic Species

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Background on registration

Veterinary chemical products (known by various names in different jurisdictions but which I will call veterinary medicines in this paper) are required to be registered by national legislation which covers the supply of all agricultural and veterinary chemical products.

This legislation is administered by the Australian Pesticides and Veterinary Medicines Authority (APVMA) which is based in Canberra. Part of the charter of the APVMA is to ensure that those products marketed for use in Australia are effective for the purpose claimed on the label. This provides security and confidence to users that the products will in fact work as they are claimed to work and that they will not cause harm to those animals on which the use is approved.

Of course registration does not come cheaply and, even for products not requiring assessment for use for human consumption, can cost many tens of thousands of dollars just to get them through the registration process. This cost is borne by the registrant who has to decide whether or not the likely return on the product registration fees is sufficient to justify registration.

It is at this point that products required for minor uses, and for minor species such is exotic ones, get into trouble. A company which may in fact wish to register such a product is faced with the problem that its likely sales revenue will not recoup the registration costs, or not recoup them sufficiently, to justify the outlay.

As most veterinarians working with exotic species would know there are few, if any, products registered for those species. This is a reflection of the above considerations, namely that the costs of registration, and in many cases the cost of obtaining the data required for registration, far outweigh the anticipated returns in sales.

What is the user to do?

The possible directions that veterinarians can take are largely regulated by legislation controlling the supply and use of agricultural and veterinary chemicals in Australia.

As indicated above the legislation administered by the APVMA, the *Agricultural and Veterinary Chemicals Code Act 1994* (the Agvet Code), regulates the supply of products onto the market in Australia. But additional controls are imposed in relation to both the use of products, registered and unregistered, and to some extent the supply of products by veterinarians, by each State and Territory under their relevant control of use legislation.

APVMA controls

The Agvet Code deals with the assessment and registration of veterinary medicines for the purposes of supply. This legislation regulates what can be sold to you as practising veterinarians.

The following restrictions apply:

- You are not permitted to import a veterinary medicine without the approval of the APVMA. This is covered under the *Agricultural and Veterinary Chemicals Administration Act 1992*. In this case the legislation refers to formulated products. I will deal later with raw ingredients.
- You are not permitted to supply veterinary medicines unless they are registered or you are allowed to under a provision of the control of use legislation in your State or Territory.

The supply restrictions mean that veterinarians cannot make up and market their own products unless State or Territory law permits it and I am not aware that this is permitted in any jurisdiction. If you want to go into the business of marketing veterinary medicines then you have to go through the process of registering them to provide the same assurances that major manufacturers have to.

You are permitted to supply directly to individual clients unregistered products of certain types. This can vary from state to state although the agreed national controls recommended that only registered human products or products compounded by a veterinarian (or on their prescription) should be permitted.

Compounding on prescription again refers to the preparation of a compounded product for a specific client. It does not extend to getting a pharmacist, or a compounding pharmacist, to prepare large quantities in advance for you to supply to clients. It certainly does not extend to getting products compounded and selling them to other practices for their use.

Does the Agvet Code restrict what you can buy? The answer is that no it does not restrict this, it only restricts what you can supply. In fact the Agvet Code allows wholesalers, general importers and chemical specialists (e.g. Sigma) to legally import, and supply you with, any "approved active". An approved active is one which meets a compendial standard, a compendium being a pharmacopoeia such as the British Pharmacopoeia (BP) or the US Pharmacopoeia (USP). In other words the majority of chemicals which you might want to formulate and use to treat exotic species are available to you as raw materials, though not as formulated products.

Restrictions on use

There are effectively no restrictions on the use of unregistered veterinary medicines for exotic species. Most products which you can lawfully obtain can be lawfully used. And once you manipulate such a product in some way (i.e. compound it) you are complying with the compounding requirement above. What you do need to remember is that you cannot put such a product on the shelf and sell its over-the-counter to anyone who comes through the door.

Obtaining formulated products

The only real way to obtain formulated products is to do so using a Permit issued by the APVMA under the Agvet Code.

Such permits can be personal ones for you to import and use a particular product, or they can be general ones, issued to all veterinarians. It really depends on who is applying for the permit and who they think should have access to the product.

For example The New Children's Hospital in western Sydney has a permit which allows them to obtain and use thiobutabarbital as an anaesthetic in their laboratory rats. This permit does not apply to anyone else. On the other hand Bristol-Myers Squibb has obtained a permit (8263) which allows them to supply Lysodren (mitotane) to registered veterinarians in all States for the treatment of hyperadrenocorticism.

State and Territory Control of Use Legislation

As indicated above if you are able to purchase the product – particularly human pharmaceuticals or raw materials for your own compounding – then you are permitted to use them on non-food producing species.

- **Record Keeping**

  States and Territories do not require records of such uses. They are, of course, required by you to comply with your professional obligations both to registration bodies and clients.

- **Advice to Clients**

  The AVA normally recommends that when unregistered products are being used to treat companion animals that informed client consent should be obtained on the basis that you do not have the protection of a registration and a company if any adverse reactions occur. In the case of exotic species most clients are probably aware of the scarcity of approved products and understand from previous interactions with you that the treatments are not approved for their particular species. This should not prevent you from advising them of the situation, particularly with treatments for which you have little or no experience, but you can also advise them that such treatments are widely recommended within the profession, within relevant literature or wherever you have obtained your advice.

Choosing products to use

This is an area in which you have to rely on your own contacts, the literature, your own SIG and other professional forums for advice. Some of you may be experimenting with drugs and treatment regimens and this is clearly acceptable provided your clients understand the situation. Appropriate pharmacological principles should be applied.

Undoubtedly your own knowledge of treating relevant species would help you in determining appropriate dose rates on the basis of issues such as metabolic pathways, relative body size, warm or cold-bloodedness, relative absorption rates and excretion rates.

Conclusion

The primary issue then in off-label treatment for exotic species is not so much what can I use, but how can I legally obtain what I need or want to use?

The regulatory system provides few impediments to your obtaining and using necessary veterinary medicines for use on non-food producing species. Problems will only occur if you step outside your own practice and seek to market products over-the-counter or to other practices without appropriate registration.

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