Steps for banning veterinary drugs in India: Where we are

SAVE accords a very high priority to achieving bans on veterinary use of NSAIDs that have been proven to be toxic to vultures (see India policy summary). The bans on veterinary use of diclofenac in 2006 in India, Nepal and Pakistan and in 2010 in Bangladesh were important steps and were enacted by the governments with commendable speed. However, we know that further such steps are urgently needed to ban veterinary use of other NSAIDs toxic to vultures. Achieving such bans in the near future is vital. Some progress with this is being made in India, but Bangladesh has taken an important lead with its national ketoprofen ban.

Here we list the steps for achieving such a ban with the intention of making information on how to do it readily available. We welcome feedback on this document in case our list of steps is incorrect, incomplete or works differently in other SAVE member states.

Process of Banning Veterinary Drugs in India

Step 1: An organisation (or individual) writes to the Drug Controller General of India (DCGI) formally requesting a ban of a specific drug, sent together with copies of relevant publications and other documents directly relevant to this request (these become the file or dossier).

a. Although this request can theoretically come from anywhere, it is likely to be taken more seriously if submitted by a reputable organisation or, even better, by a government body. The file should contain robust, quantitative and clearly presented supporting information. Ideally, peer-reviewed scientific papers should be included. Given that the effects of NSAIDs have been shown to be similar for all Gyps vulture species tested in Eurasia and Africa, properly conducted studies based upon research done in any country should be included.

Step 2: At the discretion of DCGI, he/she agrees to review the request and passes the request and file to the 'Technical Drugs Regulation Review Committee' (TDRRC) which consists of 4-5 highly qualified and appointed experts. The TDRRC meets 4 times/year and reviews the validity of such requests and will put such requests on their meeting agenda assuming the file is considered adequately prepared.

a. DCGI meanwhile consults the Animal Husbandry Commissioner (AHC) and includes feedback from the AHC within the file for review.

Step 3: The Technical Committee (TDRRC) may require repeated discussion at successive meetings and gathering of further information before reaching a conclusion. When it has done so, a recommendation for approval or rejection of the requested ban is returned, together with the file of supporting data, to the DCGI.

Step 4: If the recommendation is for the approval of a ban, then the DCGI normally endorses this and passes the file to the Secretary of Ministry of Health.

Step 5: Secretary of Health normally signs approval and passes the file for the final legal approval of the Law Ministry for passage into legislation.

Step 6: The Law Ministry publishes the signed decision into law.

Step 7: Final Gazettement of the decision may take a further year or two, but legally the ban is binding before this stage. This step may not be necessary if the ban is considered to already be part of earlier legislation

The ban on veterinary **diclofenac** of 2006 passed through these steps and was gazetted in 2008. The restriction of **vial size of human formulations of diclofenac** was passed in 2015, and was immediately gazetted due to the clear link with the 2008 ban. In both cases, the Bombay Natural History Society (BNHS), filed the original case with help and support from numerous parties at various stages. Note the contents of the file (dossier) are an important resource for upholding any subsequent challenges to the ban, and such challenges have been handled mainly by the DGCI's office, but have also resulted in court cases.

Subsequent requests for veterinary drug bans in India:

2008: **Ketoprofen** was demonstrated to be toxic to vultures and a peer-reviewed scientific paper giving the experimental evidence for this was published was published online in 2009 (print publication: Naidoo et al (2009) Biology Letters (2010) 6, 339–341. https://doi.org/10.1098/rsbl.2009.0818). Additional experimental evidence of toxic effects on vultures was published in a further peer-reviewed scientific paper in 2010 (Naidoo et al. Archives of Toxicology (2010) 84:761–766. DOI 10.1007/s00204-010-0521-0). A peer-reviewed scientific paper reporting the prevalence and concentrations of nine NSAIDs in the carcasses of cattle available to vultures in India in 2006 was published in 2009 (Taggart et al. Environmental Science & Technology (2009), 43: 4561–4566.). This study showed that ketoprofen was a contaminant of cattle carcasses in India and that tissues of some cattle contained enough of the drug to cause the death of vultures. The supporting file was submitted by BNHS in 2009 but was not progressed by the DCGI. Hence, this application is still at Step 1 after 12 years.

2019: **Aceclofenac** was confirmed to be a pro-drug of diclofenac, and to pose a very significant threat to vultures as it is effectively the same as diclofenac. A peer-reviewed scientific paper giving the experimental evidence that aceclofenac is rapidly converted to toxic diclofenac in cattle dosed with the drug was published in 2016 (Galligan et al. (2016) Conservation Biology, 30: 1122–1127. DOI: 10.1111/cobi.12711). A study showing the same result in domestic water buffaloes was conducted by the Indian Veterinary Research Institute in 2020. BNHS submitted a request to ban veterinary use of aceclofenac with a supporting file in March 2019. It remains under review of the TDRRC. Hence, this application is at Step 2 after two years.

2021: **Nimesulide** has been confirmed to be a toxic drug to vultures, with peer-reviewed publications confirming wild birds found dead in India with gout symptoms and nimesulide in the tissues (Nambirajan et al. 2021) , and safety trials demonstrating toxicity (Galligan et al. in press). There has been no submission (Step 1) so far so this is currently at Step 0.

2021: **Flunixin** has also been found both in dead wild vultures and treated captive vultures showing gout symptoms in Europe (Zorrilla et al. 2014, Eleni et al. 2019). But no clinical trials have been carried out so far, and is still at Step 0.

2021: **Carprofen** has demonstrated toxicity to vultures, although it appears to remain at high concentrations only close to the injection site of cattle tissues (Fouri et al. 2015).

2021: **Paracetamol, ibuprofen, piroxicam** and all other veterinary NSAIDs remain untested on vultures and therefore have unknown toxicity.

Note: For the current status and references relating to each toxic NSAID, refer to the Policy Summary for India which can be downloaded from the SAVE website here:

https://save-vultures.org/2020/02/february-2020-indias-vultures-policy-summary/