Joint informational document on the use of ponazuril, diclazuril, and toltrazuril in swine and cattle in the United States.

American Association of Swine Veterinarians (AASV) Pharmaceutical Issues Committee

American Association of Bovine Practitioners (AABP) Committee on Pharmaceutical and Biologic Issues

Questions have been raised regarding the use of compounded ponazuril, diclazuril, and toltrazuril medications being offered by compounding pharmacies. In some cases, these products are being offered directly to the public.

Ponazuril, diclazuril, and toltrazuril are not approved for food animal use in the United States. Information on drug labels approved by the Food and Drug Administration Center for Veterinary Medicine (FDA CVM) may be found at Animal Drugs @ FDA.[1] On that site, drugs may be searched by proprietary name, established drug name, or by FDA New Animal Drug Application (NADA) approval number or Abbreviated New Animal Drug Application (ANADA) approval number.

The law permits compounding of an animal drug when the source(s) of the active ingredient(s) for compounding is/are the finished FDA-approved drug(s) and not a bulk drug substance. The FDA CVM defines "Bulk Drug Substance" and "Active Pharmaceutical Ingredient" (API) in a footnote in Guidance for Industry #256.[2]

FDA regulationsdefine "bulkdrugsubstance" and"active pharmaceutical ingredient" as"any substance that isintended for incorporation into a finisheddrug product and isintended tofurnishpharmacological activity or otherdirect effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or anyfunction of the body."

Bulk API may be legally used for production of the FDA-approved product by the approved manufacturer. In this case, the source of the bulk API has been approved and is inspected by the FDA.

The extralabel use provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) permit the compounding of animal drugs made from FDA-approved animal or human drugs, provided the conditions for legal extralabel use described in the FD&C Act and FDA's extralabel use regulations are met.[3,4]The use of a drug compounded from bulk API is not permitted in any food animal under the AMDUCA regulations, except in the case of specific antidotes as noted in FDA CVM Guidance for Industry (GFI) #256 and listed on FDA's website.[2,5]**Therefore, whencompounded from bulk API, ponazuril, diclazuril, and toltrazuril products are specifically prohibited for use in food animals.**

Compound specific discussions:

Ponazuril

- There is anFDA approved equine ponazuril paste labeled for the treatment of equine protozoal myeloencephalitis (NADA #141-188). This drug is not prohibited for food animal use in the United States and is therefore able to be considered for extralabel drug use (ELDU) within a valid Veterinary-Client-Patient relationship (VCPR)under the Animal Medicinal Drug Use Clarification Act (AMDUCA) regulations.[6]

- Compounding using the FDA-approved ponazuril product may be considered under the AMDUCA regulations by a veterinarian within aVCPR. The use of compounded ponazuril originating from bulk API in food animals is illegal under any circumstances.

- **Diclazuril**
  - There is an equine diclazuril oral pellet approved for the treatment of equine protozoal myeloencephalitis (NADA #141-268)and a medicated feed for broiler chickens and growing turkeys approved for prevention of coccidiosis (NADA #140-951). The equine oral pellet is an alfalfa-based pellet designed for administration by adding to the feed of horses.Under 21CFR part 530.11, the extralabel use of an approved new animal drug or human drug in or on an animal feed is an extralabel use that is not permitted and results in the drug being deemed unsafe.[7] Similarly, any ELDU of the chicken and turkey medicated feed is strictly prohibited in food animals.
  - The use of compounded diclazuril originating from a bulk API in food animals is illegal under any circumstances.
- **Toltrazuril**
  - There is no FDA approved toltrazuril product in the United States. Therefore, toltrazuril is illegal to use in food animals in the United States in any form.

These drugs may be approved for food animal use in other countries. However, drugs approved in other jurisdictions may not be legally imported and used in food animals in the United States, regardless of their labels in other countries.

Guidance on compounding from bulk drugs should be sought from Food and Drug Administration Center for Veterinary Medicine (FDA CVM) Guidance for Industry (GFI) #256.[2]The FDA CVM may be contacted with questions at AskCVM@fda.hhs.gov.

References

1. FDA/CVM. Animal Drugs @ FDA, FDA Approved Animal Drug Products. http://www.accessdata.fda.gov/scripts/animaldrugsatfda/: Food and Drug Administration Center for Veterinary Medicine, 2022.
2. FDA/CVM. Guidance for Industry #256 Compounding Animal Drugs from Bulk Drug Substances In: Medicine FaDACfV, ed. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-256-compounding-animal-drugs-bulk-drug-substances, April, 2022.
3. Federal Food, Drug, and Cosmetics Act Section 512 [21 U.S.C. 360b]. https://www.govinfo.gov/content/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapV-partA-sec360b.htm.
4. FDA. 21 CFR part 530 Food and Drug Administration, Department of Health and Human Services, Subchapter E - Animal Drugs, Feeds and Related Products, Part 530 - Extralabel Drug Use in Animals. .
5. FDA/CVM. List of Bulk Drug Substances for Compounding Drugs for Use in Food-Producing Animals or Free-Ranging Wildlife Species. https://www.fda.gov/animal-veterinary/animal-drug-compounding/list-bulk-drug-substances-compounding-drugs-use-food-producing-animals-or-free-ranging-wildlife, 2022.
6. FDA/CVM. Food and Drug Administration Center for Veterinary Medicine Final Rule - Extralabel Drug Use in Animals. Federal Register, 1996;57731 - 57746.

7. FDA. 21 CFR part 530.11 Food and Drug Administration, Department of Health and Human Services, Subchapter E - Animal Drugs, Feeds and Related Products, Part 530 - Extralabel Drug Use in Animals. Subpart B - Rules and Provisions for Extralabel Uses of Drugs in Animals. Sec. 530.11 Limitations. . https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=530.11