Medicated feeds and the Veterinary Feed Directive (VFD) in small ruminants

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Abstract

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) amended the Food Drug & Cosmetic Act to permit extralabel use of animal drugs under certain conditions. However, AMDUCA does not permit the extralabel use of medicated feed articles. Minor species such as sheep and goats (small ruminants) have very few animal drugs approved for their use and practitioners may determine that extralabel use is justified to prevent suffering and death. *Compliance Policy Guide Sec. 615.115 Extralabel Use of Medicated Feeds for Minor Species* (CPG 615.115) provides guidance on the current thinking of the Food and Drug Administration related to exercising enforcement discretion with regard to the extralabel use of medicated feeds in minor species. This presentation will walk through the CPG 615.115 from a practitioner's perspective with goal of addressing common questions and situations where extralabel use of medicated feeds in sheep and goats may be indicated.

Key words: small ruminant, VFD, veterinary feed directive, extralabel, medicated feed

Résumé

La loi *Animal Medicinal Drug Use Clarification* de 1994 (AMDUCA) modifiait la loi *Food Drug & Cosmetic* afin de permettre l'utilisation hors norme de médicaments vétérinaires à certaines conditions. Toutefois, la loi AMDUCA ne permet pas l'utilisation hors norme d'aliments médicamenteux. Il y a peu de médicaments vétérinaires approuvés pour des espèces mineures comme le mouton et la chèvre (petits ruminants) et les praticiens peuvent juger que l'utilisation hors norme se justifie afin de prévenir la souffrance et la mort. La section *Compliance Policy Guide Sec. 615.115 Extralabel Use of Medicated Feeds for Minor Species* (CPG 615.115) comporte des lignes directrices concernant l'avis actuel de la *Food and Drug Administration* sur l'exercice d'un pouvoir discrétionnaire dans l'utilisation hors norme des aliments médicamenteux chez les espèces mineures. Cette présentation passe en revue le CPG 615.115 de la perspective d'un praticien dans le but d'aborder les questions les plus fréquentes et les situations où l'utilisation hors norme d'aliments médicamenteux pourrait être indiquée chez le mouton et la chèvre.

Introduction

Since the full implementation of the series of reports from the Food and Drug Administration (FDA) outlining changes for the use of antimicrobials in the feed and water of food production animals collectively known as the Veterinary Feed Directive (VFD) in 2017, there has been a learning curve for all involved with the use of medicated feeds. For medicated feed use in minor species such as sheep and goats (further referred to as small ruminants), FDA provided *Compliance Policy Guide Sec. 615.115 Extralabel Use of Medicated Feeds for Minor Species* (CPG 615.115). This document is an update to a previous version and provides guidance on the current thinking of the FDA related to exercising enforcement discretion with regard to the extralabel use for both VFD and over-the-counter (OTC) medicated feeds.

Approved Medicated Feeds in Small Ruminants

There are limited medicated feed options available for use in sheep and goats that have existing label indications.[1] Those products for sheep include the VFD products; chlortetracycline for the reduction of incidence of (vibrionic) abortions caused by *Campylobacter fetus*, neomycin sulfate and oxytetracycline fixed rate combination for the treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida*, and oxytetracycline for the treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida.* Over-the-counter medicated feed options with label indications in sheep are decoquinate and lasalocid with indications for prevention of coccidiosis. For goats, the only labeled medicated feeds are OTC products that include decoquinate and monensin for the prevention of coccidiosis as well as morantel tartrate for the removal and control of mature gastrointestinal nematode infections.

While the number of medicated feed options are limited for small ruminants, the number of indications and dose options are also very limited. With extralabel use of medicated feeds prohibited under AMDUCA the small ruminant producer and practitioner have limited options for treatment and control of diseases they may face on an ongoing basis. In addition, since the nature of small ruminant management often flock-based, the use of medicated feeds is a desirable

option for treatment, with other parenteral options often not practical from a feasibility perspective.

CPG 615.115 [2]

FDA has recognized that with limited approved treatment options available to minor species, and the fact that animal health may be threatened and suffering or death may result when failure to treat, that extralabel use of medicated feed may be indicated and thus considered for treatment in these cases. Subsequently FDA issued a revised Compliance Policy Guide (CPG) with the intent to provide guidance to FDA staff with respect to factors to consider when determining whether to take enforcement action against a veterinarian, animal producer, feed manufacturer, and/or feed distributor for the extralabel use of OTC and VFD medicated feeds in minor species. This CPG is titled *Compliance Policy Guide Sec. 615.115 Extralabel Use of Medicated Feeds for Minor Species* (CPG 615.115).[2] If extralabel use is consistent with considerations and guidelines within the CPG, FDA will not recommend or initiate enforcement action resulting in enforcement discretion. The remainder of this presentation will focus on those considerations as described in the CPG.

General Considerations

All of the following conditions must be present in order for enforcement discretion to be considered by FDA. These general considerations apply to all parties involved in the medicated feed use as applicable.

General Considerations (adapted from [2])

1. The medicated feed is used in an extralabel manner only with the express prior written recommendation and oversight of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship.
2. The medicated feed is used in an extralabel manner only for treatment of minor species as defined in the Code of Federal Regulations (21 CFR 516.3(b)), extralabel use under this revised CPG is limited to:
   - use in minor species not listed in the labeling,
   - use for indications (diseases or other conditions) not listed in the labeling, and
   - extension of the labeled withdrawal time
3. The Type A medicated article is approved for use in or on animal feed and such feed is manufactured and labeled according to the approved labeling.
4. Extralabel use of medicated feed in a food-producing minor species is limited to use in a minor species similar to the species for which the medicated feed is approved. Extralabel use of medicated feed for:
   - aquaculture is limited to medicated feeds approved for use in aquatic species;
   - avian species is limited to medicated feeds approved for use in avian species; and
   - mammalian species is limited to medicated feeds approved for use in mammalian species.
5. Extralabel use of medicated feed is limited to a farmed or confined minor species. Use for the treatment of unconfined wildlife is not appropriate and thus is outside the scope of this CPG;
6. Extralabel use is limited to therapeutic treatment when the health of an animal is threatened and suffering or death may result from failure to treat.
7. The person, including veterinarians, animal producers, feed mill distributors, or other distributors, as applicable, has not promoted or advertised the medicated feed for an extralabel use.

Veterinary Considerations

In addition to meeting the above general considerations, the veterinarian involved must do all of the following:

Veterinary Considerations (adapted from [2])

1. Made a careful diagnosis and evaluation of the therapeutic indication for which the drug is to be used;
2. Made a determination within the context of a valid veterinarian-client-patient relationship that there is no approved new animal drug that
   - is labeled for such use, and
   - contains the same active ingredient in the dosage form and concentration necessary for treatment; or,
   - in cases where there is an approved new animal drug, the approved drug is clinically ineffective (see #7) for the use for which the medicated feed is intended;
3. Ascertained that there is no therapeutic dosage form that can be practically used under legal extralabel use;
4. Instituted procedures to ensure that the identity of treated animals is carefully maintained;
5. Established a withdrawal period that is substantially extended beyond that of the approved use (supported by appropriate scientific information) prior to marketing of milk, meat, eggs, or other edible products derived from the treated minor species, if applicable;
6. Taken appropriate measures to ensure that assigned timeframes for withdrawal are met and no unsafe drug residues occur in any food-producing animal subjected to extralabel treatment; and
7. Has reported any adverse reactions to FDA within 10 days of occurrence. The veterinarian also should have reported treatments that were not clinically effective.

If a veterinarian is recommending the extralabel use of an OTC medicated feed, in addition to the above they must also do the following:

Additional Veterinary Consideration for extralabel OTC medicated feed (adapted from [2])

1. Made a written recommendation that includes the medical rationale (e.g., diagnosis, drug selection, dose and duration, and the required withdrawal period), dated within 6 months prior to use;
2. Provided the client with a copy of the written recommendation; and
3. Kept copies of the written recommendation and makes them available to the FDA upon request.

If a veterinarian is recommending the extralabel use of a VFD medicated feed, in addition to the above they must also do the following:

Additional Veterinary Consideration for extralabel VFD medicated feed (adapted from [2])

1. Made a written recommendation that includes the medical rationale (e.g., diagnosis, drug selection, dose and duration, and the required withdrawal period), dated within 6 months prior to use;
2. Provided the client with a copy of the written recommendation; and
3. Kept copies of the written recommendation and makes them available to the FDA upon request.
4. Completed the VFD consistent with the approved labeling for the indication. In the "Special Instructions" the veterinarian should note:
   a. "This VFD is being issued in accordance with CPG 615.115";
   b. The actual species for which the medicated feed is intended (unless that species is already reflected on the VFD because the VFD drug is approved for use in that minor species, but is being used for a different indication); and
   c. The withdrawal time associated with the extralabel use if different than the labeled withdrawal time as already reflected on the VFD

Producer Considerations

In addition to the general considerations above, the animal producer must do the following:

Producer Considerations (adapted from [2])

1. Kept complete and accurate records of medicated feeds received, including labels, invoices, and dates fed. These records are kept for at least 2 years from the date of delivery of the medicated feed;
2. Instituted procedures to ensure that the identity of treated animals is carefully maintained;
3. Taken appropriate measures to ensure that assigned timeframes for withdrawal are met and no unsafe drug residues occur in edible products derived from an animal receiving extralabel treatment;
4. Used the medicated feed in accordance with Federal, State, and local environmental and occupational laws and regulations. This is especially important for aquaculture uses;
5. Met the requirements of the Federal Clean Water Act as implemented under the National Pollutant Discharge Elimination System (NPDES), as well as any requirements applicable to ground-water pollution. The producer should contact the offices responsible for issuing NPDES permits, and other similar permits, to be certain there are no objections to the use and release of the drug; and
6. Followed user safety provisions as set forth in approved product labeling to protect individuals who may be exposed to the drug.

Feed Manufacturer or Distributor Considerations

All of the following conditions must be present in order for enforcement discretion to be considered for the feed manufacturer and/or distributor:

Feed Manufacturer or Distributor Considerations (adapted from [2])

1. Formulated the medicated feed as approved;
2. Labeled the medicated feed to reflect the approved bluebird label;
3. Maintained the manufacturing record (including capturing any nutrient modifications) for 1 year as required by 21 CFR part 225. (Note that any records that would also be required under 21 CFR part 507 relating to the manufacturing, processing, packing, or holding of animal food must be kept for at least 2 years); and
4. If applicable, met the requirements for the manufacture/distribution of a veterinary feed directive (VFD) medicated feed in 21 CFR 558.6, including maintaining the VFD for 2 years and during that time making such records available to FDA upon request.

Regulatory Action

The CPG states that priority for enforcement actions will be focused on veterinarians, producers, and manufactures or distributors who authorize, use, manufacture or distribute medicated feed for extralabel use of OTC or VFD medicated feeds in minor species in a manner that is inconsistent with the CPG.

Conclusion

There are limited medicated feeds with labeled treatment options available for small ruminants. Extralabel use of medicated feeds is prohibited under AMDUCA. CPG 615.115 provides guidance for veterinarians, producers, feed manufacturers, and distributors to facilitate the use of OTC and VFD medicated feeds for treatment options in an extralabel manner when the health of animals is threatened, and suffering or death would result from failure to treat. FDA will consider regulatory discretion when CPG 615.115 guidance is followed.

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The author has made all attempts to provide wording that is consistent with the original CPG 615.115 document for presentation purposes, and has added application discussion based on clinical experience. The author recommends accessing the original document for additional details if needed. The author does not represent FDA and all the statements made here are the author's own. The author claims no conflict of interest.

References

1. Blue Bird Labels. U.S. Food and Drug Administration – Animal and Veterinary – Products – Animal Feeds – Medicated Feeds – Blue Bird Labels. Available at: https://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/BlueBirdLabels/default.htm. Accessed December 15, 2018.

2. Compliance Policy Guides. Chapter 6 – Veterinary Medicine. Compliance Policy Guide Section 615.115 Extralabel Use of Medicated Feeds for Minor Species. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cpg-sec-615115-extralabel-use-medicated-feeds-minor-species. Accessed July 29, 2019.