



Frequently Asked Questions about

Extralabel Drug Use and AMDUCA

Q: What is extralabel drug use (ELDU)?

A: ELDU describes the use of an approved drug in a manner that is not in accordance with the approved labeling, yet meets the conditions set forth by the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) and U.S. Food and Drug Administration (FDA) regulations. Deviations from FDA-approved labeling include use in another species, use for a different indication, use at a different dose or frequency, and use via a different route of administration.

Q: What is the purpose of the Animal Medicinal Drug Use Clarification Act (AMDUCA)?

A: The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) made ELDU an FDA-regulated veterinary medical activity, allowing veterinarians to prescribe extra-label uses of approved animal and human drugs when the health of an animal is threatened, or when suffering or death may result from failure to treat animals. Prior to the passage of the AMDUCA, ELDU of animal drugs was illegal. AMDUCA amended the Federal Food, Drug, and Cosmetic Act to legalize ELDU under a valid VCPR as well as certain other conditions describing requirements for use, record requirements, and label requirements according to FDA regulations.

Q: Isn't ELDU only for food-producing animals? If not, to which species do ELDU regulations apply?

A: ELDU regulations apply to all animal species, not only food-producing animals.

Q: What does AMDUCA mean to the everyday veterinary practice?

A: Keep in mind that AMDUCA does not give veterinarians "carte blanche" for extralabel use of medications. There are certain guidelines to follow. To the everyday veterinary practice, this means that the veterinarian should do the following when considering ELDU:

- Make a careful diagnosis and evaluation of the conditions for which the drug is to be used;
- First make certain there is no approved animal drug that is labeled for such use in that species, or that contains the same active ingredient in the required dosage form and concentration;
 - Alternatively, if an approved animal drug exists but a veterinarian finds, within the context of a veterinarian-client-patient relationship, that the approved drug is clinically ineffective for its intended use, extralabel use of an alternative medication is permissible.
- Assure that the identity of the treated animal(s) is carefully maintained;
- Establish a substantially extended withdrawal period supported by appropriate scientific information prior to marketing milk, meat, eggs, or other edible products from the treated animal(s);

- In non-food-producing animals, a drug labeled for use in humans can be administered even if an animal-label drug for that species and medical condition exists.

Q: How did ELDU regulation come about and why is it necessary in veterinary medicine?

A: Prior to enactment of the AMDUCA, the Federal Food, Drug, and Cosmetic Act had provided that a new animal drug was deemed unsafe unless it was subject to the FDA's stringent approval process – for exactly what was on the label – specific species, disease indication, dose, duration, frequency, and route of administration. One of the main reasons why fewer drugs exist in veterinary medicine is that FDA's new drug approval process is very costly and time consuming for pharmaceutical companies, with little return on investment for animal drug products when compared to the return on investment associated with human drug products, creating a relative disincentive for companies to put resources toward creating new veterinary drugs.

Given the relatively few numbers of drugs available to veterinarians, AMDUCA created the professional flexibility that veterinarians need in order to adequately treat animals when their health is threatened. Additionally, many of the minor species have few to no drugs approved for various indications, making it very difficult for a veterinarian to provide the best care for their minor species patient. With ELDU regulation, many of these issues can be resolved and animals may be more readily relieved of suffering.

Q: Who regulates ELDU and enforces the regulations?

A: The FDA Center for Veterinary Medicine regulates ELDU and enforces the regulations. In cases of AMDUCA violations, FDA regulatory actions may include warning letters, seizure of product, misdemeanor fines, injunction or criminal prosecution.

Q: Is “off-label” use the same as ELDU?

A: "Off-label" is a term commonly used in foreign countries, and by physicians in the United States. It is also sometimes used in veterinary medicine in the U.S., but the term has no legal or regulatory definition. In the United States, extralabel drug use is the appropriate term.

Q: How do I know what qualifies as ELDU?

A: Specific criteria must be followed:

- A valid VCPR is a prerequisite for all ELDU;
- Only a veterinarian can determine that ELDU is needed and can administer, prescribe or dispense a medication extralabelly. The veterinarian must direct or supervise ELDU in an animal;
- ELDU rules only apply to FDA-approved [animal](#) and [human](#) drugs;
- ELDU is intended for prevention, treatment, and control purposes only when an animal's health is threatened. ELDU of drugs for production use and/or in feed is not approved;
- ELDU is not permitted if it results in an illegal food residue, or any residue which may present a risk to public health;
- A veterinarian must not pursue use of certain FDA-prohibited drugs in food-producing animals (see the [list of prohibited drugs](#) below in this document)

ELDU of an FDA approved drug may be used if:

- There is no approved animal drug that is labeled for such use, or that contains the same active ingredient in the required dosage form and concentration.

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- Alternatively, an approved animal drug for that species and condition exists, but a veterinarian finds, within the context of a VCPR, that the approved drug is clinically ineffective for its labeled use.

There are few restrictions on extralabel use in non-food-producing animals compared to food-producing animals. If the intended use is in a non-food-producing animal, then an approved human drug may be considered for extralabel use even when an approved animal drug for that species and condition exists. Economic reasons for ELDU of a human drug over the approved drug for that species are valid to treat the medical condition. Veterinarians should recognize, however, that human-labeled drugs are approved based on studies in people and their use in animals could vary. In addition, minor differences in the formulation may produce alterations in the pharmacokinetics and biological availability in the animal species compared to humans. Also keep in mind that consistent use of human-labeled drugs when approved animal-labeled drugs are available could create relative disincentives for animal health industry to pursue new animal drug approvals and could further limit the availability of veterinary drugs.

The following additional conditions must be met for ELDU in food-producing animals:

- Such use must be accomplished in accordance with an appropriate medical rationale; and
- If scientific information on the human food safety aspect of the use of the drug in food producing animals is not available, the veterinarian must take appropriate measures to assure that the animal and its food products will not enter the human food supply.

If the veterinarian determines the food-producing animal needs a drug administered in an extralabel fashion, an approved animal drug must be considered for the particular use before a drug labeled for humans is considered. The prescribed or dispensed extralabel drug (prescription legend or over-the-counter) must bear labeling information which is adequate to assure the safe and proper use of the product.

Q: What drugs qualify for ELDU?

A: Any drug approved by the FDA qualifies for ELDU in a non-food-producing animal given that a valid VCPR exists and FDA-delineated criteria are met. For food-producing animals, the extralabel use of certain drugs is prohibited.

Q: When is ELDU used/necessary?

A: Extralabel use is limited to circumstances when the health of an animal is threatened, or suffering or death may result from failure to treat. As we've already stated, extralabel use to enhance production is prohibited.

Examples of clinical circumstances in which ELDU might be employed/necessary are listed below:

1. A horse needs to be treated with enrofloxacin based on the culture/sensitivity results of a tendon sheath infection. No horse-labeled enrofloxacin products are available, so the veterinarian could consider treating with the small animal- or bovine-labeled enrofloxacin product.
2. A horse needs penicillin but the veterinarian determines the horse needs a larger dose than the labeled dose. This qualifies as an ELDU because the dose prescribed is not in accordance with the labeled dosage.

3. A dog with a skin infection needs cephalexin, according to its veterinarian. There is no animal-labeled product, thus ELDU of the human product is acceptable.
4. A dog is diagnosed with congestive heart failure by its veterinarian, and furosemide administration is part of the therapeutic plan. There are FDA-approved products labeled for use in dogs, including brand name and generic products, but the veterinarian recommends the human product from the local pharmacy for economic reasons. A prescription for ELDU of the human product is acceptable in this circumstance.

Q: What drugs are currently restricted from ELDU?

A: FDA may prohibit the extralabel use of an approved new animal or human drug or class of drugs in animals if FDA determines that:

1. An acceptable analytical method for residue detection needs to be established and such method has not been established or cannot be established, or
2. The extralabel use of the drug or class of drugs presents a risk to public health.

A prohibition may be a general ban on the extralabel use of the drug or class of drugs or may be limited to a specific species, indication, dosage form, route of administration, or combination of factors. To date, the ELDU of the following drugs has been prohibited in food-producing animals, regardless of whether or not the criteria for ELDU are met:

1. Chloramphenicol;
2. Clenbuterol;
3. Diethylstilbestrol (DES);
4. Dimetridazole;
5. Ipronidazole;
6. Other nitroimidazoles;
7. Furazolidone;
8. Nitrofurazone;
9. Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxyridazine);
10. Fluoroquinolones;
11. Glycopeptides;
12. Phenylbutazone in female dairy cattle 20 months of age or older.
13. Cephalosporin (excluding cephalirin) use in cattle, swine, chickens and turkeys:
 - Using cephalosporin drugs at unapproved dose levels, frequencies, durations or routes of administration is prohibited
 - Using cephalosporin drugs in cattle, swine, chickens or turkeys that are not approved for use in that species (e.g., cephalosporin drugs intended for humans or companion animals);
 - Using cephalosporin drugs for disease prevention

The following drugs, or classes of drugs, approved for treating or preventing influenza A in humans, are prohibited from ELDU in chickens, turkeys, and ducks regardless of whether or not ELDU criteria are met:

1. Adamantanes;
2. Neuraminidase inhibitors.

Extralabel use of drugs in treating food-producing animals for improving rate of weight gain, feed efficiency, or other production purposes is prohibited under AMDUCA.
No extralabel uses in animal feed are allowed.

Q: Some ELDU documentation requires listing a withdrawal time. What is that and why is it necessary?

A: If the animals treated with an extralabel drug are food-producing animals, it is required that the veterinarian's specified withdrawal/discard time(s) for meat, milk, eggs, or any food which might be derived from the treated animals be listed on the label.

Q: Where do I find information about withdrawal period information for ELDU in food-producing animals?

A: Withdrawal interval information can be found on the Food Animal Residue Avoidance Databank (FARAD). FARAD is a National Food Safety Project of the U.S. Department of Agriculture National Institute of Food and Agriculture (NIFA). To obtain scientific information to determine withdrawal intervals, visit the FARAD website at www.farad.org or call (888) USFARAD. Other sources that may be used to determine a scientifically-based withdrawal interval may include scientific literature or other academic sources.

Q: How do I make sure that my records for ELDU are accurate?

A: Specific guidelines describe what should be included in the record, on the label, and how to maintain records involving ELDU. These are listed below:

Record Requirements:

- Identify the animals, either as individuals or a group;
- Species of animal(s) treated;
- Numbers of animals treated;
- Medical conditions being treated;
- The established name of the drug and active ingredient;
- Dosage prescribed or used;
- Duration of treatment;
- Specified withdrawal, withholding, or discard time(s), if applicable, for meat, milk, eggs, or animal-derived food products;
- Records must be kept for a minimum of 2 years after treatment;
- The FDA must be allowed access to these records to estimate risk to public health.

Label Requirements:

- Name and address of the prescribing veterinarian;
- Established name of the drug;
- Any specified directions for use including the class/species or identification of the animal or herd, flock, pen, lot, or other group; the dosage frequency, and route of administration; and the duration of therapy;
- Any cautionary statements restricting use to a licensed veterinarian ("CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian");
- Your specified withdrawal, withholding, or discard time for meat, milk, eggs, or any other food product originating from the treated animal(s).

Q: Do generic drugs qualify for ELDU or are they subject to ELDU regulation?

A: Yes. Whether a drug is a brand-name or generic drug does not affect how a veterinarian may contemplate ELDU of that drug. The same rules apply to both brand-name and generic drugs.

Q: What if I want to deviate from ELDU regulations?

A: Deviation from ELDU regulations is an illegal action subject to prosecution by the FDA. The spirit of AMDUCA is to allow veterinarians flexibility in administering drugs that will help relieve animal pain and suffering. The overarching premise of the law is that extralabel use is acceptable when filling a medical need for an animal when its health is threatened.

For example, equine practitioners have inquired about the legality of treating horses with Previcox®(firocoxib), a nonsteroidal anti-inflammatory drug labeled for use in dogs, instead of Equioxx®, which contains the same ingredient but is labeled for use in horses. There can be a significant cost difference between the two products, which is the cause of the debate. According to AMDUCA, however, because Equioxx® is labeled for use in horses, the canine product cannot legally be used in an extralabel fashion in horses. Selecting a canine product over an equine product for any nonmedical reason, including economics, is not acceptable. Some clients or veterinarians asked if economic concerns are a valid reason to use or prescribe a drug in an extralabel manner—this is true only in that a veterinarian can select an approved human drug to relieve pain and suffering in a non-food producing animal even when an identical approved animal drug is available.

Q: Can clients themselves decide to administer drugs in an extralabel fashion to their animals?

A: No, clients cannot decide to administer drugs in an extralabel fashion. However, according to AMDUCA, if a VCPR exists, and the veterinarian decides that ELDU is a valid option, the client may administer the drug in an extralabel fashion as long as it is under the supervision of the veterinarian.

Q: Do I need to list a withdrawal time if the ELDU is for a non food-producing animal?

A: The withdrawal time of a drug prescribed for ELDU for a non-food-producing animal is not necessary according to AMDUCA.

Q: Can I treat my patient with a drug labeled for another animal species?

A: For a non-food-producing animal, ELDU of a drug labeled for another animal species can be used if there is no approved, appropriate drug that is labeled for use in the patient's species or if an approved drug exists for the patient's species but is found by the veterinarian to be clinically ineffective.

If the patient is a food-producing animal, ELDU of a drug labeled for use in another food-producing animal species is acceptable only if:

- There is no approved drug labeled for such use (or is the same drug labeled for a different use) in that species; or
- The approved drug exists for that species but is found by the veterinarian to be clinically ineffective.

However, the veterinarian must establish a substantially extended withdrawal period, maintain identity of the animal, and take measures to ensure that no illegal drug residues in food result from the use of that drug.

If the patient is a food-producing animal and the drug being considered for ELDU is a human drug or drug approved for non-food-producing animals, the above conditions must be met and in addition, there must be adequate scientific information available to determine a withdrawal time, or else the veterinarian must take measures to ensure that animal never enters the human food supply.

Labeling and record maintenance is of utmost importance when an extralabel use of a drug is prescribed. AMDUCA does not permit extralabel use of drugs in feed, nor does it permit extralabel use of any drug if public health is threatened.

Q: Can I treat my patient with a drug labeled for use in people?

A: If the patient is a non-food-producing animal, a human drug may be considered if there is no approved, appropriate animal drug that is labeled for use in that species or if the approved drug exists but is found by a veterinarian to be clinically ineffective. Alternatively, a veterinarian can still choose to prescribe an equivalent human-labeled drug for the non-food-producing animals, even if an appropriate drug exists for that species and medical condition.

If the patient is a food-producing animal, a human drug may be considered if the same criteria listed above apply, if the drug is not prohibited from use in food-producing animals, and if there is adequate scientific information available to determine a withdrawal time.

Q: Can I treat my patient with a drug labeled for use in people if it is less expensive than an approved drug for animals?

A: ELDU of human drugs is acceptable in non-food-producing animals when the animal's health is threatened, even when an animal drug exists, for economic reasons. Note, however, that minor differences in the human product's formulation may produce alterations in the pharmacokinetics and biological availability in the animal species compared to humans. Also keep in mind that consistent use of human-labeled drugs when approved animal-labeled drugs are available could create relative disincentives for animal health industry to pursue new animal drug approvals and could ultimately further limit the availability of veterinary drugs.

Q: Do I need to tell my client when I've prescribed an extralabel treatment?

A: You should always discuss the available treatment options with your clients, especially when extralabel use of a drug is indicated. It is important for the client to understand that you are prescribing a drug in a manner that is uncommon and there may be risks associated with this use.

Your state veterinary practice act may include regulations regarding client consent in ELDU; for example, in 2001, the state of Texas implemented a law requiring veterinarians to obtain client consent (<http://www.avma.org/onlnews/javma/feb03/030215k.asp>) when ELDU of a drug is prescribed or administered. However, the AMDUCA is generally sufficient to protect patients and the public from inappropriate ELDU.

Q: What is my liability if I prescribe or administer a drug in an extralabel fashion and there's a problem?

A: When you administer or prescribe a drug extralabelly, doing so within the confines of the law will help you minimize your risk of liability in the case of an adverse event. The overarching premise of the AMDUCA is that extralabel use is acceptable when filling a medical need for an animal whose health is threatened. Veterinarians who deviate from extralabel use guidelines set out in AMDUCA risk becoming the target of unfavorable actions by the Food and Drug Administration; such actions range from warning letters and regulatory meetings to product seizures, injunctions, and prosecution. Failure to follow the AMDUCA/ELDU regulations could potentially make you liable if an adverse event occurs, opening you up to the risk of a lawsuit and/or potential disciplinary action by your state's veterinary medical board. If you have questions regarding coverage for liability associated with specific extralabel uses of drugs, check with your liability insurance carrier for terms of your coverage.

Q: How does ELDU differ from compounding?

A: The FDA defines compounding as the manipulation of drugs to obtain products that differ from the starting materials in an approved dosage form drug. Under AMDUCA, compounding is considered extralabel drug use, and must be done from approved, finished dosage form human or animal drugs only. Like any extralabel use, compounded drugs must not be used if an approved drug can be used at its approved dose and dosage form and can adequately treat the patient. AMDUCA does not permit veterinarians or pharmacists, to compound preparations from bulk (ie, raw active ingredient) drugs. Unless the following criteria are met, the compounding of a new animal drug from an approved human or animal drug results in what is considered an adulterated new animal drug, not a compounded preparation, and is a violation of AMDUCA and compounding regulations:

1. The veterinarian is following ELDU regulations (as previously described in this document);
2. For non-food-producing animals: there is no approved animal or human drug that, when used as labeled or in the available dosage form and concentration, will adequately treat the diagnosed condition;
3. For food-producing animals: there is no approved animal drug (or secondarily, human drug) that, when used as labeled or in the available dosage form and concentration, will adequately treat the diagnosed condition. Compounding from a human drug for use in food-producing animals is not permitted if an approved animal drug can be used for compounding;
4. The compounding is performed by a licensed pharmacist upon the order of a veterinarian or by a veterinarian within the scope of their professional practice;
5. Proper compounding practices are followed to ensure the preparation is safe and effective;
6. Only the amount needed for treating individual patient adequately should be compounded at that time; and
7. All relevant state laws relating to the compounding of drugs for use in animals are followed.

Q: Are vaccines subject to ELDU?

A: Vaccines are considered "veterinary biologics" and fall under regulation by the USDA Center for Veterinary Biologics (USDA CVB). Veterinarians are allowed discretionary use of vaccines. For example, if a minor species requires a vaccine not labeled for that species, the veterinarian can employ discretionary use of a particular vaccine as he or she sees best fit. Veterinarians should check

state rules to discern whether it is acceptable to vaccinate animals with vaccines labeled for another animal species.

Q: Are pesticides subject to ELDU?

A: The use of pesticides by a veterinarian is not subject to ELDU regulations as these are subject to the primary jurisdiction of the Environmental Protection Agency (EPA). Pesticides must always be used according to the instructions on the label.

Q: Whom should I contact if I have specific questions about ELDU?

A: For further information, the AVMA (www.avma.org), FDA (www.fda.gov), and FARAD (www.farad.org) are valuable resources.

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