Bundesministerium
für Ernährung
und Landwirtschaft

Oral administration of veterinary medicines in the livestock sector through feed or drinking water

Manual by the BMELV Working Group dated 19.06.2009

General remarks

1. The oral administration of medicines is performed via orally administered finished medicinal products (OAF) in feed and drinking water or by using medicated feedingstuffs (MF). OAF and MF are indispensable forms of the medicinal treatment of animals. However, if not applied properly, this form of therapy involves increased risks that may impair the efficacy of medicinal products, increase the danger of adverse drug reactions, jeopardise user safety, promote the spread of antimicrobial resistance or reduce the quality of animal-based foods, especially where animals are treated in groups. The input of veterinary medicines into the environment, especially via medicated drinking water, should also be borne in mind. These risks can be minimised by observing certain principles. This manual is designed to compile these principles. It thus serves animal welfare, consumer protection, food safety and the efficiency of animal production.

2. The manual is intended for veterinarians and animal keepers. It fleshes out the requirement under Section 12 (a) of the Veterinary House Dispensary Ordinance (TÄHAV), according to which veterinarians, when dispensing drugs, must make sure that the animal keeper is able to use the drugs properly. The obligations of animal keepers result from Section 58 of the German Medicinal Products Act (AMG)1. Other medicinal drug regulations are also relevant, such as the requirements for proper veterinary treatment. In addition, the keepers of food-producing animals in their role as food operators must comply with the provisions of food hygiene law (inter alia the Regulation (EC) No 178/20022 and Regulation (EC) No 852/20043 and in their role as feed manufacturers with the provisions of Regulation (EC) No 183/20054 laying down requirements for feed hygiene. In this regard, particular note should be made of

Annex I, Part A, II, No 4 point (j) of Reg. (EC) No 852/2004.

3. OAF and MF must always be applied in accordance with the labelling and package leaflet (in the case of medicated feedingstuffs that are delivered in tankers, this information may be found in the relevant accompanying documents).

Any derogation from this is only possible if required in order to achieve the treatment goal and if this does not run counter to legal requirements (see in particular Sections 56, 56(a) AMG)1 . Such derogations may only be ordered by the veterinary surgeon who is attending the animals and must be justifiable by that person. They must also be in accordance with the rules of veterinary science (e.g. the guidelines for prudent use of veterinary antimicrobial drugs5). Before using or ordering the use of medicinal products in a way that differs from the conditions for approval, the veterinarian weighs up the pros and cons.

4. Whenever food-producing animals are being treated, factors such as the efficacy of the administration of medicinal products, prevention of undesirable side effects, user safety, food safety, consumer protection, animal welfare and the prevention of the spread of antimicrobial resistance must be borne in mind when making decisions. The attending veterinarian decides on a case-by-case basis whether parenteral or oral treatment or a combination of both is necessary. Likewise, he or she decides which options of oral therapy (MF, OAF via feed or drinking water) should be used in the present case on the basis of the characteristics of the respective drug, its conditions for approval and the circumstances on the holding. Account should be taken of the fact that MF and OAF differ in their characteristics (see table on number 10) and are not interchangeable in many fields. They must be selected by the veterinarian based on the specific circumstances on the holding with regard to storage, conveying equipment, mixing and dosing devices and feed supply equipment. In doing so, the animal keeper's specific risk management concept should be taken into account.

Definitions

For the purpose of this manual,

5. Medicated feedingstuffs (MF) are: medicinal products in the form of ready-to-use feedingstuffs, manufactured from medicated premixtures and compound feed that are intended to be placed on the market for administration to animals. (Section 4 (10) AMG)1. They are produced in establishments with a manufacturing authorisation pursuant to Section 13 AMG.

6. Orally administered finished medicinal products (OAF) are: medicinal products which are manufactured beforehand and placed on the market in packaging intended for distribution to the consumer (Section 4 (1) AMG). They are intended for oral administration via feed, including milk replacers, or via drinking water [6] and they are not MF.

Conditions of use

7. When applied in accordance with the conditions of use, the medicinal product can generally be assumed to be safe and effective and to have a positive benefit/risk ratio based on having been examined by the approval authority. Any derogation from the conditions for approval may undermine the efficacy, safety or positive benefit/risk ratio of the medicinal product. The veterinarian must take this into account when weighing up the pros and cons and must assume responsibility for this. When deviating from the conditions for approval, the veterinarian must inform the animal keeper of any risks that may arise as a result.

Selection of medicinal product

8. With regard to a combination of several antimicrobial substances, please see the explanations in the guidelines for the prudent use of veterinary antimicrobial drugs [5] and for MF please also see Section 56 (2) of the AMG[1].

9. The veterinarian must make sure that the oral administration of the required dose to each animal can be ensured by observing the following test points.

   The following factors need to be considered in this examination:

   → the properties of the OAF and the feed / drinking water (e.g. mixing capacity, compatible particle sizes, solubility, possible inactivation of medicinal product),

   → the needed quantity of OAF and feed/drinking water

   → the particular circumstances and existing facilities / equipment (dosing and mixing devices) on site,

   → individual or group treatment of animals,

   → the relevant expertise and skills of the staff on the holding.

10. The typical characteristics of MF and OAF that shouldbe taken into account in the selection and examination are:

	MF	OAF (mixed with feedingstuffs or dissolved in drinking water)
Responsibility for production (MF) or admixture/additio	MF manufacturer	Veterinarian/animal keeper
Quantity	Required quantity produced in advance after the veterinarian has issued current prescription for the	Admixture/addition, if possible directly prior to administration in the respective quantity needed for single-dose dispensing
Time frame for availability	Available upon delivery	Usually immediately available upon veterinary diagnosis
Storability	Storable	Storability of the mixture has not been examined during the approval procedure
Mixing capacity	Homogeneous mixing capacity of AMV has been examined during the approval	Mixing capacity has not been examined within approval procedure
Suitability for transport	Suitability for transport has been examined under normal conditions during the	Suitability for transport of the mixture has not been examined during the approval procedure
Change of feed	May be necessary (if MF manufacturer does not offer previously used feed)	May be necessary (if feed is unsuitable for administration of OAF)
Change of active ingredient	Possible without delay, may entail residues of MF.	Possible at short notice
Change of dose	Possible without delay, may entail residues of MF.	Possible at short notice
Requirement of homogeneous admixture	MF manufacturer guarantees the homogeneous active-ingredient level in the daily ration or in a specified percentage of the daily ration	Individual animals must be provided with required daily dose. Incorporation into feed is not required if individual animals are provided with the required quantity of OAF.
Transport routes on the agricultural holding	Depending on the farm in question, there may be long transport routes to	If required, transportation via feeding pipes depending on the distance, mixture/addition and place of administration
Quality	MF has the quality of medicinal products	OAF has the quality of medicinal products, feed/drinking water medicated with OAF does not have the quality of medicinal products

These characteristics should also provide guidance as to how the required dose can be administered to each animal (see number 9).

Dosing and dispensing

11. The veterinarian informs the animal keeper about the required dose, dose interval and the duration of treatment. If the medicinal product is to be mixed with or dissolved in feed/drinking water prior to administration, the veterinarian determines the needed quantity of OAF and feed/drinking water, taking into account the expected feed/drinking water intake of the animals.

    The animal keeper shall ensure strict compliance with these requirements.

    In veterinary science, the active ingredient dose is indicated in mg per kg KGW and day. The veterinarian calculates the required daily dosage of active ingredient for the animals to be treated via the formula (mg active ingredient/kg KGW) x kg KGW x number of animals. In a further step, the veterinarian calculates the resulting amount of medicine to be administered from the amount of active ingredient.

Administration of medicinal products

12. The therapeutic objective is to ensure that each animal receives a dose that produces a therapeutic effect. Thus in the treatment of animals it is necessary to ensure that the intended dose is administered to each individual animal. This applies both to OAF and MF. The incorporation of OAF into feed is not necessary in the treatment of animals that are fed individually if the animal is individually supplied with the required amount of OAF. In contrast, when treating animals that are not fed individually, the active pharmaceutical ingredient has to be incorporated into/dissolved in the feed/ in the drinking water7 in such a way as to ensure that each animal can absorb the required dose. The criteria and characteristics mentioned in number 9 and 10 and the rules for application on the package leaflet of OAF (e.g. administration prior to actual feeding, withdrawal of drinking water beforehand) must be borne in mind. Individual animals that do not ingest the required daily dose must receive additional individual treatment.

13. As part of the approval of MF, it is checked that the medicinal premixture can be homogeneously incorporated into feed. The manufacturer is responsible for the production of the homogeneous mixture for MF. The approval of OAF does not involve any examination of the possibility of homogeneous incorporation into feed/drinking water. The veterinarian must therefore estimate in advance, taking into account the criteria and characteristics in number 9 and 10, whether an effective dose can be achieved in all animals to be treated in a particular case and must advise the animal keeper accordingly. Please see the explanations of the guidelines on antibiotics5 .

14. The veterinarian gives the animal keeper written instructions (fact sheet, see enclosures) for the use of oral medications. Attention must also be paid here to aspects of user safety e.g. preventing the unintended intake of the active pharmaceutical ingredient by the animal keeper. In conformity with Section 58 (1) AMG, the animal keeper shall not derogate from this guidance without consulting the veterinarian. The first administration is carried out jointly by the veterinarian and animal keeper.

15. If necessary (e.g. if the therapy is not successful), the causal analysis also includes an examination of the daily amount of feed/drinking water for the content of the prescribed dose. Please see the guidelines on antibiotics on this point if antibiotics are to be administered.[5]

Storage of medicated feed on the holding

16. The conditions for approval do not provide for the storage of feed with incorporated OAF. This should therefore be refrained from. Where the storage of medicated feed is desired, the use of MF is to be recommended instead. MF must be stored separately from animal feed in order to avoid any confusion or contaminations.

Transportation of medicated feed on the holding

17. Transportation of animal feed with incorporated OAF or MF can result in segregation/demixing. The approval procedure of MF includes an examination to ensure that the mixture remains sufficiently stable

under normal conditions. This is not examined as part of the approval procedure of OAF. Therefore, OAF should be incorporated or added as close as possible to the place of administration. The risk of segregation during transport must be taken into account.

Prevention of spread on the holding

18. Afterwards, all facilities and equipment that have come into contact with MF or feed/drinking water with incorporated OAF (shovels, pipes, troughs etc.) are contaminated with the active pharmaceutical ingredient. This can cause a spread of the active ingredient and may result in uninvolved animals absorbing the active ingredient. Apart from the risk of development of antimicrobial resistance, this can also result in positive residue findings in foodstuffs and give rise to complaints under feed law (see requirements of Regulation (EC) No 183/2005[4]). Facilities and equipment that have come into contact with medicated feed/drinking water must therefore be cleaned by the animal keeper. The animal keeper must take appropriate measures to prevent any spread on his holding.

Specifics of drinking water application

19. Only those medicines that are approved for this application are used for administration via drinking water. The chemical-physical properties of water must be taken into consideration (e.g. water hardness, pH value, content of iron and calcium). Furthermore, possible interactions with other components (e.g. added disinfectants) and water pipe hygiene (biofilm) must also be taken into account. The input of unused medicated drinking water into the environment has to be prevented in order to avoid the risk of resistance.

Checking of therapeutic results

20. The veterinarian has to check the level of therapeutic success in a timely manner. If the therapy proves unsuccessful, the technical equipment such as dosing devices, conveying routes etc. must also be re-examined (possibly by a specialised firm), alongside a review of the diagnosis and testing of the pathogens for resistance.

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1 German Medicinal Products Act in the version promulgated on 12 December 2005 (Federal Law Gazette p. 3394), last amended by Article 1 of the Act of 17 July 2009 (Federal Law Gazette I p. 1990).

2 Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority (EFSA) and laying down procedures in matters of food safety (EC) No 178/2002 (OJ No L 31, of 01.02.2002, p. 1), last amended by Regulation (EC) No. 202/2008 (OJ No L 60 of 05.03.2008, p. 17).

3 Regulation of the European Parliament and the Council of 29 April 2004 on food hygiene (EC) No 852/2004 (OJ No. L 139 of 30.04.2004, p. 1, No L 58 of 3.3.2009, p.3), last amended by Regulation (EC) No 1019/2008 (OJ No L 277 of 18.10.2008, p. 7).

4 Regulation of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene (EC) No 183/2005 (OJ No. L 35 of 8.2.2005, p. 1, L 50 of 23.2.2008, p. 71)

5 Published by: Bundestierärztekammer und Arbeitsgemeinschaft der Leitenden Veterinärbeamten, Deutsches Tierärzteblatt November 2000

6 including water of drinking water quality

7 with regard to drinking water this means a solution of OAF in drinking water