REVIEW ARTICLE

European regulations on prevention use of antimicrobials from january 2022

Regulamentos europeus sobre o uso preventivo de antimicrobianos a partir de janeiro de 2022

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Abstract

Over the past several years significant progress on achieving better antibiotic stewardship in the veterinary sector has been achieved through regulatory legislations both in the USA and the European Union, including the implementation of US FDA GL 209 and 213. The EU is now taking measures to phase out the routine use of antibiotics for disease prevention, reserving prophylactic use for exceptional circumstances. This article intends to add some clarifications regarding antibiotics for disease prevention that are embedded in two EU regulations which came into force on 28th January 2022, Regulation (EU) 2019/4 on Medicated Feed and Regulation (EU) 2019/6 on Veterinary Medicinal Products.

Keywords: antibiotics, infectious disease, rational use.

Resumo

Ao longo dos últimos anos, progressos significativos na obtenção de uma melhor administração de antibióticos no setor veterinário foram alcançados por meio de legislações regulatórias nos EUA e na União Européia, incluindo a implementação do FDA GL 209 e 213 dos EUA. o uso rotineiro de antibióticos para prevenção de doenças, reservando o uso profilático para circunstâncias excepcionais. Este artigo pretende adicionar alguns esclarecimentos sobre antibióticos para prevenção de doenças que estão inseridos em dois regulamentos da UE que entraram em vigor em 28 de janeiro de 2022, Regulamento (UE) 2019/4 sobre alimentos medicamentosos para animais e Regulamento (UE) 2019/6 sobre medicamentos veterinários.

Palavras-chave: antibióticos**,** doenças infecciosas, uso racional.

Antimicrobials remain a key tool for the treatment of infectious diseases in animals. There are three different circumstances for the therapeutic use of antibiotics in food producing animals: treatment, metaphylaxis/control and prophylaxis/prevention. In all cases where administration of an antibiotic is required, this should be prescribed following appropriate diagnosis by a veterinarian preferably with a good knowledge of the disease epidemiology on the farm. Animals with clinical signs of a bacterial infection that is impacting on their health and welfare in many cases need treatment with antibiotics.

Metaphylaxis/control means the administration of a medicinal product to a group of animals after a diagnosis of clinical disease in part of the group has been established, with the aim of treating the clinically sick animals and controlling the spread of the disease to animals in close contact and at risk and which may already be subclinically infected. Prophylaxis/prevention means the administration of a medicinal product to an animal or group of animals before clinical signs of a disease, in order to prevent the occurrence of disease or infection i.e. in the absence of sub-clinical infection or detectable pathogens, there is a risk of disease outbreak.

Over the past several years significant progress on achieving better antibiotic stewardship in the veterinary sector has been achieved through regulatory legislations both in the USA and the European Union, including the implementation of US FDA GL 209 and 213. The EU is now taking measures to phase out the routine use of antibiotics for disease prevention, reserving prophylactic use for exceptional circumstances. This article intends to add some clarifications regarding antibiotics for disease prevention that are embedded in two EU regulations which will come into force on 28th January 2022, Regulation (EU) 2019/4 on Medicated Feed (European Parliament and

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the Council of the European Union, 2019a) and Regulation (EU) 2019/6 on Veterinary Medicinal Products (European Parliament and the Council of the European Union, 2019b).

In May 2020, the European Commission adopted the Farm to Fork Strategy, a tool to help shape the EU's path towards sustainable food systems. Its objective is the reduction by 50% of the overall EU sales of antibiotics for farmed animals and in aquaculture by 2030. The achievement of this objective will be supported by the implementation of the new Regulation (EU) 2019/4 on Medicated Feed (European Parliament and the Council of the European Union, 2019a) (MF, prescription required) and Regulation (EU) 2019/6 on Veterinary Medicinal Products (European Parliament and the Council of the European Union, 2019b) (VMP Regulation, prescription required). These provide for a wide range of measures to fight antimicrobial resistance (AMR) and promote a more prudent and responsible use of antibiotics in animals.

Regulation 2019/6, commonly known as the New Veterinary Regulation, legislates for the authorisation, use and monitoring of veterinary medicinal products in the European Union. The legislation came into effect on 28 January 2019 and applies in all EU Member States on 28 January 2022. The Regulation followed the adoption of a proposal in 2014 to develop fit-for-purpose veterinary legislation which would no longer be based on the equivalent human medicines authorisation system.

The legislation repeals Directive 2001/82/EC (European Parliament and the Council of the European Union, 2019b) and is intended to:

- harmonise the internal EU market for veterinary medicinal products.
- reduce the administrative burden on companies and regulatory authorities.
- enhance availability of veterinary medicinal products.
- stimulate innovation of new and existing medicines.
- strengthen the EU response to fight antimicrobial resistance.

Specifically, regarding antibiotic resistance the New Regulation strengthens the existing EU framework in fighting antimicrobial resistance. To this end, the New Regulation mandates the following in relation to medically important antibiotics that are approved as veterinary medicines:

(i) Preventive use of antibiotics in single animal and small groups is allowed following veterinary assessment.
(ii) Restricts the metaphylactic use of antibiotics.
(iii) Permits EU Member States to reserve specific antibiotics for humans only
(iv) Oblige EU Member States to collect data on the sale and use of antibiotics
(v) Prohibits, for imported animals and products from outside the EU, antimicrobial veterinary products for promoting growth and places restrictions on antibiotics reserved for human use. The EU is currently working on finalising a 'Reserved for Human Use'.

Some of the key articles and recitals from 2019/6 include the following:

1. Under recital 47 veterinarians have a key role in ensuring responsible use of antimicrobials. Prescribing should be based on antibiotic resistance, epidemiology and clinical knowledge and the amount of antibiotic prescribed should be limited to the amount required for treatment of the animal under their care. Furthermore, veterinarians should not be influenced by financial incentives when prescribing.
2. Under article 105, which relates to veterinary prescriptions, prescriptions should only be issued following a proper clinical assessment. The justification for any prescription, especially for metaphylaxis or prophylaxis should be provided. The quantity of antibiotic prescribed for treatment should only be sufficient for the disease condition present at the time. If the prescription is for disease control or prevention, then the quantity prescribed should be limited to cover the 'at risk' period.

Of particular note is article 107, which has resulted in some confusion relating to metaphylaxis and prophylaxis. Article 107 explicitly specifies that antimicrobial medicinal products shall not be applied routinely nor used to compensate for poor hygiene, inadequate animal husbandry or lack of care or to compensate for poor farm management. With respect to metaphylaxis and prophylaxis Article 107 of regulation 2019/6 specifies the following:

a. Antimicrobial medicinal products shall not be used for prophylaxis other than in exceptional cases, for the administration to an individual animal or a restricted number of animals when

the risk of an infection or of an infectious disease is very high and the consequences are likely to be severe.

b. Antimicrobial medicinal products shall be used for metaphylaxis only when the risk of spread of an infection or of an infectious disease in the group of animals is high and where no other appropriate alternatives are available. Member States shall actively support the development and application of guidelines which promote the understanding of risk factors associated with metaphylaxis and include criteria for its initiation.
c. In addition, Article 107 of 2019/6 reaffirms regulation 1831/2003 (i.e. antimicrobial medicinal products shall not be used in food animals for the purpose of promoting growth nor to increase yield.

Regulation 2019/4, commonly known as the medicated feed regulation applies in all EU Member States on 28 January 2022 and as the title suggest, relates to medicated feed. Medicated feed is a mixture of a veterinary medicinal product(s) and feed(s) which is prepared for marketing and intended to be fed to animals without additional processing. Medicated feed is mainly used to treat large groups of animals, where individual veterinary treatment would not be possible or be difficult to administer. The main advantage of medicated feed is the ease of administration and is generally used for livestock, notably pigs and poultry. The extent to which medicated feed is used depends on factors such as cost effectiveness, availability of the feed, and regulations at national level. All of these vary significantly between Member States.

The scope of the proposed medicated feed regulation is being extended to non-food producing animals and includes medicated feed for pets. To reduce the risk of antimicrobial resistance, rules on carry-over and preventive use of antibiotics are being proposed. The limits for carry-over of veterinary medicines into non-target feed will be set by delegated acts for specific active substances.

The legislation repeals Council Directive 90/167/EEC (European Parliament and the Council of the European Union, 2019a). Three points of particular interest relate to prescription, metaphylaxis and prophylaxis.

Regarding prescriptions of medicated feed, regulation 2019/4, under Article 16, requires:

1. The supply of medicated feed will be by presentation of a prescription only. The prescription will only be issued after a clinical assessment and only for diagnosed diseases.
2. Validity of prescriptions for medicated feed from the date of issue will be 6 months for non-food producing animals and three weeks for food-producing animals. However, if the medicated feed contains antibiotics, then the validity from date of issue will be limited to a maximum period of 5 days.
3. Duration of treatment and the amount of antibiotic containing feed that can be produced/supplied should be for a maximum of 2 weeks unless the summary of product characteristics (SPC) specifies differently
4. If it is not possible to confirm the presence of a diagnosed disease, a veterinary prescription for medicated feed containing an antiparasitic may be issued based on the knowledge of the parasitic infestation status in the animal or group of animals.

With regards to prescribing medicated feed containing medicinal antibiotics for prophylaxis, regulation 2019/4, under Article 17, require that:

1. Medicated feed containing antibiotic veterinary medicinal products shall not be used for prophylaxis.
2. Medicated feed containing antiparasitics may be used for prophylaxis on the basis of a prescription in accordance with Article 16 of 2019/4, as specified above.
3. Medicated feed containing immunological veterinary medicinal products can be used for prophylaxis on the basis of a prescription in accordance with Article 16 of 2019/4, as specified above.

With respect to metaphylaxis use of medicated feed, Regulation 2019/4 specifies that medicated feed containing antimicrobials for metaphylaxis should only be allowed when the risk of spread of an infection or of an infectious disease is high, in accordance with Regulation 2019/6 as assessed by a veterinarian.

In addition, it should be noted that Regulation 2019/4 Article 17 and Regulation 2019/6 Article 108 specify that the keeper of food-producing animals shall keep records of the medicinal products they use for a period of at least 5 years.

For clarity, it should be noted that anticoccidials (including ionophores) that are used in feed to kill and inhibit the coccidian parasites (these products are known as Coccidiostats in Europe) are registered as feed additives under regulation 1831/2003 (European Parliament and the Council of the European Union, 2003). Coccidiostats are approved as feed additives only for the species in which coccidias are ubiquitous in all production systems – whether free range or confined, small scale or large scale. The species for which they may be approved are chickens, turkeys, rabbits, guinea fowls, pheasants, quails, and partridges. As such they may be used as feed additives and therefore routinely in feed for these species without prescription. For all other species in which coccidiosis and the associated risk of outbreaks are not always present, antiparasitic veterinary medicines are used to prevent, control or treat infections and this must be accompanied by a veterinary prescription.

In summary, regulation 2019/4 will not allow for medicinal antibiotics to be used in medicated feed for prophylactic use, however antiparasitics and immunologics can be used for disease prevention. Medicated feed containing medicinal antibiotics can still be used for disease treatment and control. Under regulation 2019/6 antibiotics can be used for disease prevention but should be limited to single or small groups of animals where the risk of disease is deemed to be high. It is hoped that this article helps to clarify any confusions around the metaphylactic and prophylactic use of medicinal antibiotics in the EU after 28th January 2022 both as a veterinary medicinal product and in medicated feed.

Ethics statement

N/A

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All authors are employed by Elanco Animal Health.

Conflicts of interests

No conflict of interest to declare

Authors' contributions

Both authors contributed equally to the manuscript

Availability of complementary results

N/A

Place where the study was conducted

N/A. This is an review of new EU regulations

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