

Guidelines on the Prescribing and Dispensing of Veterinary Medicinal Products and the Good Use of Antimicrobials

Legal Notice [LN179/2021](#) was published on 23.04.2021. The LN amends S.L 437.47 about Veterinary Medicinal Products (VMP). A number of provisions that are related with prescribing and dispensing have been introduced. In this document one can find a number of guidelines regarding these activities with particular emphasis of the use of antimicrobials. In addition this document provides some guidelines on specific antimicrobials, mainly cephalosporins and fluoroquinolones

RETAIL SUPPLY OF VETERINARY MEDICINAL PRODUCTS

In Regulation 58A a provision was introduced that stipulates from where the retail supply of VMPs can be conducted. Retail sale can now be carried out only from veterinary pharmacies, licensed veterinary clinics/hospitals or other establishments stipulated in the legislation according to the distribution status assigned to the VMP in question (e.g. POM, OTC and their sub-categories). Retail can also be carried out by veterinary surgeon during out call visits for animals under their care. Whoever conduct such sale in places not indicated in the legislation will be in breach of the regulations and shall be guilty of an offence.

DISPENSING REGULATIONS

In Regulation 59 important changes in the existing regulation as regard dispensing were made. It concerns all type of dispensers. Now there is legal direction to those persons who are allowed to carry out dispensing of VMPs. Dispensing can only be done by pharmacist, veterinary surgeons and suitable qualified persons.

- Veterinary surgeons can dispense all types of VMPs.
- Pharmacist can dispense all type of VMPs, except those that can be administered only by veterinary surgeons.
- Suitable Qualified Persons can only dispense VMPs that are classified as OTC when under the supervision of a pharmacist or only those on the 'General Sales List' when not under the supervision of a pharmacist.

The qualifications for the Suitably Qualified Person have not been established yet. This is work in progress and the Veterinary Surgeon Council is heavily involved in this issue.

VMPs on the 'General Sales List' can be dispensed from premises other than veterinary pharmacies, veterinary clinics and by the veterinary surgeon. These other premises can be registered pet shops, registered aquarium fish product retailers and approved feed traders where animal medicated feeds are produced, sold or



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traded. Such products on the general sales list can only be those products that do not require any veterinary diagnosis or pose a risk, e.g. flea collars made with herbal products.

Whoever dispenses a VMP not in accordance with these requirements will be in breach of the regulations shall be guilty of an offence.

In accordance with sub-regulation 59(5) whoever dispenses VMPs is bound to keep dispensing records. It is to note that these obligations are in line with those mentioned in the new Regulation (EU) 2019/6 Article. A transitory provision has been introduced here whereby record keeping obligations shall come into force on the 1st November 2021. Self-audits are to be conducted by the dispenser regarding these records.

Although veterinary surgeons may dispense veterinary medicinal products during an in-call or out-call visits their clinics are not to be considered as veterinary pharmacies, Regulation 59 (2) (3). They cannot supply animal owners with VMPs that are to be administered to animals that are not under their care. This does not mean that veterinary surgeons cannot liaise with each other should there be an unavailability issue that prevents the complete treatment of an animal. When veterinary surgeons dispense VMPs the quantities dispensed should be those required for the treatment of an urgent condition. If the condition is not urgent and the VMPs are easily obtainable they should ideally be dispensed from a veterinary pharmacy. There may be circumstances when the veterinary surgeon cannot divide a product or take only certain quantities from it to cover the immediate treatment. In these cases it is permissible for the veterinary surgeon to supply the whole quantity of VMP to the animal owner.

Furthermore, the legislation stipulates the ways in which dispensers conduct the activity diligently to ensure safe and effective use of the VMPs, Regulation 59 (6) (7) (8) (9) (10) (11) (12) (13) For example, dispensers must be satisfied that the person who will use the product is competent to do so safely, and intends to use it for a purpose for which it is authorised or indicated by the veterinary surgeon, especially in the case the cascade principle is used. For this aim dispensers should be able to ask diligent and to-the-point questions to the animal owners. Dispensers should always explain in a clear and easily understandable manner any specific warning about the VMP and advise them on the dosing of the product. Special attention should be given to antimicrobials in all aspects in order to minimise the risks of antimicrobial resistance. There should be close collaboration between dispenser and prescriber. Any misunderstandings should be resolved and any disagreements discussed on scientific grounds. This is particularly important when a dispenser is presented with a veterinary prescription containing a critical antimicrobial but without any justification. As per Regulation 59 (9) the dispenser has to be satisfied that all necessary precautions have been taken in these cases.

PRESCRIBING REGULATIONS

Regulation 59A concerns only those persons that have the right to prescribe. In Malta these persons can only be veterinary surgeons. In fact this regulation starts first by stipulating how only veterinary surgeons can prescribe veterinary medicinal products.

The legal obligations of the prescriber are laid out in this regulation under several sub-regulations.

Whoever conduct such an activity and is not a veterinary surgeon will be in breach of the regulations and subject to shall be guilty of an offence.

The official veterinary prescription on which veterinary surgeons can prescribe VMPs will be issued by the Veterinary Services. Currently this exists as a 4 colour coded carbon copy prescription. The white one is the original and kept by the dispenser the pink one retained by veterinary surgeon, the yellow one kept by the farmer in the farm and the blue copy is sent to the veterinary services. The Veterinary Services will be making the veterinary prescription available in electronic version.

Veterinary surgeons can only prescribe VMPs for animals which are under their care, Regulation 59A (4). Therefore, the extent of their responsibility lies within this sphere. A veterinary surgeon cannot take responsibility of treatment recommended by another veterinary surgeon.

Veterinary surgeons can only use one prescription for each recommended treatment, and only when a clinical examination is done by the veterinary surgeon. For example, a veterinary surgeon cannot write different VMPs for more than one diagnosed condition on the same veterinary prescription. In such cases 2 different veterinary prescriptions should be issued. It is also crucial for the veterinary surgeon to understand that the use of combination of antimicrobials should be scientifically supported as per Regulation 79A (9)

It is acknowledged that sometimes it is not possible for the veterinary surgeon to make a full diagnosis of a condition that affects an animal or a herd. The veterinary surgeon may have to wait for the results of sample or swab tests, e.g. for antimicrobial sensitivity tests or antibiograms. In these cases it is acceptable that the veterinary surgeon starts empirical treatment. However, before recommending such treatment the veterinary surgeon should be familiar with the health status of the animal or herd, especially in case of farms, Regulation 59A (4).



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Whenever there is a reason for the veterinary surgeon to prescribe VMPs for prophylaxis or metaphylaxis use he should be able to provide a justification in case this is asked for by the authorities. It is advised that the veterinary surgeon keep a note when he prescribes product for such use. As per Regulation 79A(5) metaphylactic or prophylactic antimicrobial treatment may be allowed with conditions. Preventive use of antimicrobials veterinary medicinal products or medicinal products is not allowed. The veterinary surgeon should take care of not prescribing antimicrobials for preventive use on the pretext of metaphylactic or prophylactic use.

A veterinary prescription for antimicrobial medicinal products shall be valid for five days from the date of its issue as per Article 105 (10) of Regulation EU 2019/4

As in the case of dispensing, in prescribing the veterinary surgeon should also make his best to ensure that whoever will be using the VMPs is informed properly about its proper use, including dosing information and any warnings or contra-indications. In particular, veterinary surgeons should always and at all times put in considerations factors that may adversely affect the effectiveness of antimicrobials. There are a number of antimicrobials that are classified as critically important antimicrobials. Regulation 59A (8) (d). The veterinary surgeon should put particular emphasis on these. He should keep himself updated on the latest developments in this and other regards.

When the veterinary surgeon administers to the animal the VMPs he recommends he can choose not to issue a veterinary prescription, provided this is not specifically asked for by the animal owner. However, this exemption should not be confused with the other obligation related with record keeping of retail products. As a supplier of the VMP the veterinary surgeon is not exempted from this obligation and he has to keep such records as per Regulation 59(5)

PRESCRIPTION ONLY MEDICINE AND OVER THE COUNTER MEDICINE

The regulation was changed to include provisions that stipulate the way VMP shall be prescribed and dispensed. Some VMPs need to be prescribed on a veterinary prescription to be dispensed. Such requirement should be indicated on the outer pack of the product. The way this indication shall be conveyed is also stipulated. Other VMPs whose use is considered as less risky can be obtained without a veterinary prescription. This status should also be indicated on the outer pack. Other important additions include the places from where VMPs can be dispensed. Depending on the distribution categories VMPs can be supplied from veterinary pharmacies, veterinary establishments, registered pet shops, registered aquarium fish product retailers and approved feed traders where animal medicated feeds are produced, sold, or traded.

The designated abbreviations for each distribution classification are stipulated in this regulation (i.e. POM-VP, POM-V, OTC, or GS)

(a) Prescription-Only-Medicine, Veterinary surgeon and Pharmacist- abbreviated to POM-VP.

(b) Prescription-Only-Medicine, Veterinary surgeon- abbreviated to POM-V.

(c) Over- the- Counter –Medicine, abbreviated to OTC

(d) General Sales, abbreviated to GS

(4) The supply of veterinary medicinal products for each distribution category shall be made as follows:

(a) POM-VP shall only be prescribed and/or dispensed by a veterinary surgeon or dispensed by a pharmacist according the terms of a veterinary prescription. Premises from where the products can be supplied are veterinary pharmacies, licensed veterinary establishments, and by the veterinary surgeon during an outcall.

(b) POM-V shall only be prescribed, dispensed and administered by a veterinary surgeon. Premises from where the products can be supplied are licensed veterinary establishments, and by the veterinary surgeon during an outcall.

(c) OTC, may be dispensed without a veterinary prescription. The persons who can dispense this category of veterinary medicinal products are veterinary surgeons, pharmacists and suitably qualified persons under the direction of a pharmacist or a veterinary surgeon. Premises from where the products can be supplied are veterinary pharmacies, licensed veterinary establishments, and by the veterinary surgeon during an outcall.

(d) GS, may be dispensed without a veterinary prescription. The persons who can dispense this category of veterinary medicinal products are veterinary surgeons, pharmacists and suitably qualified persons. Products that fall under this category can be supplied from veterinary pharmacies, veterinary establishments, registered pet shops, registered aquarium fish product retailers and approved feed traders where animal medicated feeds are produced, sold or traded:



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Regulation 60 (4) provides for an exemption if it is deemed important that products on the General Sales List are also supplied from premises other than those mentioned above. The persons who dispense the VMPs from these other premises may not necessary be Suitably Qualified Persons but must have at least 2 years experience in handling these kind of products.

PRESCRIBING 3RD AND 4TH GENERATION CEPHALOSPORINS

To limit the selection pressure for extended spectrum betalactamases (ESBL2) and decrease reports on the presence of AmpC-producing *Salmonella* and *E. coli* in animals and food, veterinary surgeons should keep in consideration the following factors when prescribing these classes of cephalosporins

- These antimicrobials should be restricted in cases where treatment with another antimicrobial has failed.
- These antimicrobials should never be used for disease prevention or as a part of herd health programmes.
- Treatment should be done for the individual animals. Treatment of groups of animals should be strictly limited to ongoing disease outbreaks according to the approved conditions of use.
- Since no MRL is established in poultry these antimicrobials cannot be used in this species. In fact administration to Poultry is a contraindication and if this indication is present in the Product information it is not in compliance with EU legislation.

Use in poultry (including eggs) would entail a high risk for spread of ESBL to humans via food due to dissemination in the poultry production pyramid. Treatment of eggs and/or one day-olds in grandparent and parent flocks could lead to dissemination to a large number of animals in the following generation with spread to numerous farms in different countries. There is evidence of correlation between such use of cephalosporins and resistant infections in humans.

THE PRUDENT USE OF FLUOROQUINOLONES

Fluoroquinolones represent a class of potent antimicrobials which is most important in the treatment of severe and invasive infections in both humans and animals. Both older and newer generations of quinolones have an impact on resistance to antimicrobials.

They are well distributed in the body after administration and have a therapeutic effect on most infections in different organs or tissues.

Fluoroquinolones are effective in the treatment of serious infections like septicaemia, gastroenteritis and respiratory diseases caused by susceptible gram-negative bacteria. They are also used to treat urinary tract and skin infections, and soft-tissue infections caused by Gram-negative or some gram-positive aerobic bacteria. They are effective for the treatment of Mycoplasma infections.

Fluoroquinolones are well absorbed after oral administration, have a long elimination half-life and widespread distribution throughout the body, which make them attractive to be used for herd treatment.

Emergence of Resistance

However, resistance to fluoroquinolones has emerged and is increasing among several bacterial species pathogenic for food-producing animals following the introduction of **Enrofloxacin**. No resistance was observed prior to this introduction

If fluoroquinolone resistance develops any further, this may result in therapeutic failure, including mortality.

Retention of Efficacy

Although it is rare that fluoroquinolones are the only available agent for treatment of a specific infectious disease, they are an important alternative veterinary medicinal products for a veterinarian to have as option for treatment.



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Fluoroquinolones have a unique mechanism of action not related to conventional antimicrobials, and therefore their efficacy should be retained as long as possible.

Prescribing Guidelines for Fluoroquinolones

In order to maintain the efficacy of fluoroquinolone containing veterinary medicinal products and to reduce the incidence of antimicrobial resistance veterinary surgeons should follow these guidelines when prescribing this class of antimicrobials:

1. Narrow spectrum antimicrobials which are likely to create less resistance should take preference over antimicrobials which have an expanded spectrum.
2. Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials.
3. The need of prophylactic use should always be carefully considered and preserved for specific circumstances.
4. Whenever possible, fluoroquinolones should only be used based on susceptibility testing. If this is not possible, therapy should be based on local (farm level) epidemiological information about susceptibility of the target bacteria.
5. Use of the product deviating from the instructions given in the Summary of Product Characteristics may increase the prevalence of bacteria resistant to this class of antimicrobials and may decrease the effectiveness of treatment with other fluoroquinolones due to the potential for cross resistance.
6. The dosage regimens should be carefully determined on the basis of their pharmacokinetic and pharmacodynamic properties to ensure optimal efficacy and reduce selection of resistance.

CATEGORISATION OF ANTIBIOTICS USED IN ANIMALS

Veterinary surgeons should consider the European Medicines Agency (EMA) s' scientific advice on the categorisation of antibiotics when prescribing them.



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The scientific advice ranks antibiotics by considering both the risk that their use in animals causes to public health through the development of antimicrobial resistance and their need in the veterinary practice.

The advice re-categorises Critically Important Antimicrobials (CIA) in 4 categories. CIA are antibiotics most relevance for human health as classified by the World Health Organisation (WHO). The revised categorisation considers all classes of antibiotics and includes additional criteria such as the availability of alternative antibiotics in veterinary practice. The re-classification is as follows:

- Category A (“Avoid”) antibiotics that are currently not authorised in veterinary medicinal product in the European Union (EU). These medicines may not be used in food-producing animals and may be given to individual companion animals only under exceptional circumstances.
- Category B (“Restrict”) refers to quinolones, 3rd- and 4th-generation cephalosporins and polymyxins. Antibiotics in this category are critically important in human medicine and their use in animals should be restricted.
- Category C (“Caution”) covers antibiotics for which alternatives in human medicine generally exist in the EU, but only few alternatives are available in certain veterinary indications.
- Category D (“Prudence”) includes antibiotics that should be used as first line treatments, whenever possible. These antibiotics can be used in animals in a prudent manner.

An infographic about the categorisation of antibiotics is annexed with this circular. This is also available from EMA ‘s website <https://www.ema.europa.eu/en/news/categorisation-antibiotics-used-animals-promotes-responsible-use-protect-public-animal-health>

The categorisation does not translate directly into treatment guidelines and attention should also be paid to information in the Summary of Product Characteristics for individual products and applicable legislation.