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Importance of the prescription of antimicrobial agents and control of their distribution (with a possible e-tracking system) by the Veterinary Services for a proper implementation of the antimicrobial resistance strategy

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Summary: *Animal and human health and welfare as well as environmental and food security greatly depend on the availability, effectiveness and appropriate use of quality antimicrobial veterinary medicinal products (AVMPs). The World Organisation for Animal Health (OIE) and its Member Countries are working closely with the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the Codex Alimentarius Commission to ensure the development and implementation of global strategies and measures designed to restrict the development and spread of antimicrobial resistance (AMR). This report focuses on the issues around the prescription and distribution of AVMPs, their supervision by the Veterinary Services and control by the Competent Authorities and the implementation of the results in the form of actions to address the problem of AMR. Overuse and misuse of antimicrobials are key factors in the development of AMR.*

Prescribing an appropriate AVMP, after a veterinarian has examined an animal, identified the pathogen involved and assessed the most effective treatment, is an ideal example of rational and prudent antimicrobial use. A prescription is a document that may be used to keep records of actual AVMP use. Comparing the records of AVMP prescriptions with the records of distributors on the amounts of sales makes it possible to monitor the traceability of AVMPs distribution of AVMPs at the farm level, and should represent a close estimate of the actual use, at the farm level.

Modern advances in information technology have led to the development of e-tracking systems that can be used to monitor the entire chain of AVMP circulation: production, distribution and purchasing by or supplying to the consumer, allowing appropriate levels of protection for data access, an aspect that is the responsibility of the relevant authorities. The Competent Authorities can assess data, provide risk–benefit analysis, take appropriate decisions and make recommendations for all stakeholders, and use these data to raise their awareness on rational antimicrobial use in the context of combating AMR.

Implementation of good distribution policy and good veterinary practice with regard to AVMPs requires national legislative support, collaboration between manufacturers, distributors, veterinarians, professional associations and Veterinary Services. Such multi-sectorial work at an international level has the potential to reduce antibiotic use and minimize/control the development of AMR.

Keywords: antimicrobial veterinary medicinal product; antimicrobial resistance; prescription; distribution; monitoring/surveillance.

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The report was prepared using the data obtained from the literature, OIE standards, EU recommendations, the experience of the author in AVMPs sales collection, and data collection done through a questionnaire sent to the OIE Delegates of OIE Member Countries of OIE Regional Commission for Europe. The questionnaire was developed by the author based on a concept note provided by the Regional Core Group. Taking into account that Technical Item 2 is usually without questionnaire, the Delegates were invited to respond to it on a voluntary basis. The questionnaire was developed in a way to capture examples of best practices in the following fields: general principles of the prescription and distribution of antimicrobial agents; general principles of e-tracking systems and the importance of databases; role of Veterinary Authorities in data collection, data analysis and prudent use of antimicrobials.

Introduction

Antimicrobial agents are used to protect human health, plant health and the health and welfare of companion and food-producing animals. In the case of food-producing animals, particular care is needed in the use of antimicrobials to treat cattle, pigs and poultry, as well as fish production/aquaculture, which globally provide the main sources of protein of animal origin [8]. Overuse and misuse of antimicrobial agents in the human, animal and plant sectors have accelerated the emergence and development/spread of antimicrobial resistance (AMR), which can have harmful consequences for animal health, but also for human health and the environment. Different food items can carry antimicrobial resistant bacteria, genetic determinants of resistance, or antimicrobial drug residues, which can potentially have harmful effects to the human health. Consequently, minimising the emergence and spread of AMR requires a coordinated, focused, multi-sectorial and multinational effort [4].

This explains why, since 2010, the World Organisation for Animal Health (OIE), together with the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO), has been engaged in a Tripartite Alliance that stipulates the respective responsibilities of the three organisations in the fight against diseases and, in particular, zoonotic diseases and those with a high health and economic impact [2]. The growing threat of transboundary animal diseases, the impact of environmental changes and globalisation, as well as new societal demands related to food security, food safety, public health and animal welfare, emphasise the critical need for collaboration between the three organisations through the implementation of the 'One Health' concept [4]. The European Union (EU) is supporting and actively collaborating with international organisations, such as WHO, the OIE, FAO and the Codex Alimentarius Commission, in order to ensure the development and implementation of global strategies and measures designed to restrict the development and spread of AMR [1, 5].

Disease control management and the improvement of animal welfare at national and local level need to be encouraged in order to potentially achieve a sustainable decrease change in behaviour on antimicrobial use in animals. This is in line with the OIE Strategy on AMR and the Prudent Use of Antimicrobials [4] and the WHO Global Action Plan (GAP) adopted in 2015 [11]. The objectives of the GAP should be reflected in national plans to combat AMR, to be implemented in accordance with the requirements of legislation on the production, importation, distribution and use of antimicrobial veterinary medicinal products (AVMPs).

A leading role in these activities all over the world is given to the Veterinary Services, including veterinarians and veterinary paraprofessionals. Their responsibilities include the regulation and supervision of antimicrobial distribution and use by farmers, farm workers and animal owners. Veterinarians should also offer professional advice on antimicrobial use and, under the supervision of the Competent Authorities, take part in monitoring throughout the AVMP chain: manufacturing (in context of quality, efficacy and safety of the product), distribution and use.

The Veterinary Services can play an important role in promoting awareness of AMR, encouraging a professional culture through the establishment of good animal husbandry and supporting the responsible use of antimicrobials in animals by reducing disease prevalence and by promoting the use of antimicrobials only in accordance with veterinarians' prescriptions. Good animal husbandry, vaccination and biosecurity measures help to reduce the need for antimicrobial treatment and consequently decrease antibiotic use. Developing the capacity for joint risk assessments on priority zoonotic and other high-impact diseases should be incorporated into coordinated action plans in all countries of the world, including in Europe, with the overall goal of the reduction of antimicrobial use. The OIE provides assistance and leadership to Member Countries with regard to their policies on strengthening and harmonising their surveillance systems for the use of antimicrobial agents in animals, and it supports

their efforts to implement science-based international standards [3, 6]. This explains why the Codex Alimentarius Commission and its parent organisations, FAO and WHO, are key partners of the OIE in terms of recommendations for veterinarians and livestock producers.

1. General principles of the prescription of antimicrobial agents

Antimicrobial agents are essential for the medical care of animals and livestock populations. They are used for the purpose of prophylaxis, metaphylaxis and treatment of infectious diseases. This wide range of purposes for which antibiotics are used to protect animal health may accelerate the development and spread of AMR. Considering the risk of the development of resistant microorganisms, professional supervision of the use is AVMPs is required. When intended for prophylaxis or metaphylaxis, AVMPs should only be used when the risk of infection is very high and if no appropriate alternatives are available. In order to strengthen OIE Members' national policies on prudent use of antimicrobials, it may be necessary to restrict the use of antimicrobials that are critically important in human medicine (3-rd and 4-th generation of Cephalosporins, Quinolones) for the use in veterinary medicine without available microbiological tests or relevant epidemiological data [12]. In veterinary practice, OIE members should follow the recommendations on the OIE List [5].

The results of the monitoring of manufacture, prescription, distribution and use of antimicrobials can be used to evaluate trends in their use over time and be helpful for the design of AMR awareness campaigns. Veterinarians, MAHs, wholesalers and pharmacists should collaborate on implementing measures to monitor and control the supply and use of antimicrobials. Their activity at all levels should be under the supervision of the Veterinary Services and their activity reports should be available for assessment by the Competent Authorities.

The prescription (written on paper or in an electronic format) is the document recommending the use of an AVMP in the target animal species according to the indication and in the prescribed dose. The prescription format (e.g. electronic *vs* on paper) must be clearly specified in national legislation. According to national requirements, prescriptions for veterinary medicinal products (VMPs) should be written or in an electronic format, and for medicated premixes or for VMPs that are used for a flock or herd, may be in the electronic format (in Belgium), when there is the electronic database especially for the particular animal group (as in Austria for poultry). For the preparation of medicated premixes or when group treatment is to be used, the prescription is sent to the special establishment (feed mill) where the AVMP is mixed with the feed to obtain the required level of homogeneity.

The prescription makes it possible to receive the following information: disease or infection treated or prevented, amount of antimicrobial recommended to be used, animal group, species, class of antimicrobial agent, indication (treatment, prophylaxis, metaphylaxis), route of administration, type of pharmaceutical form, dosage regimen, and treatment duration. This information is collected under monitoring of AVMP consumption, which can be reported to the national Competent Authorities, the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project (in the case of European Union Member States), and to the OIE (as part of the data collection for the Annual report on antimicrobial agents intended for use in animals). These data can support the implementation of prudent and responsible AVMP use programmes.

Veterinarians should always issue a prescription when supplying an AVMP even if they do not administer it themselves. Then, to follow-up the treatment, if needed, the veterinarian can write a prescription for the farmer to buy a specific drug. The important thing is to keep records of AVMP use, and the actual source of the product [9].

Another important point is that veterinarians should ensure that they are not in situation of conflict of interests when prescribing antimicrobials for animal treatment.

General information that should be indicated on the prescription form:

- name of the farm (code number) or animal owner, address, phone, e-mail;
- name of veterinarian, phone, e-mail;
- issue date of AVMP prescription;

- identification of animal or groups of animals to be treated (species, breed, age);
- name of AVMP;
- dose, package amount, strength;
- type of pharmaceutical form;
- indication for administration (disease code, dosage regimen, course of treatment);
- warnings necessary to ensure the proper use including, where relevant, to ensure prudent use of antimicrobials;
- for food producing species, withdrawal period even if zero day [9, 10].

The aforementioned details are essential for the annual reports that the national Competent Authorities collect and assess for the purposes of official inspection and control of traceability and use of AVMPs.

When authorised AVMPs comply with quality, effectiveness and safety requirements, this maximizes the probability that the results of therapy will be positive. Evaluation by the appropriate means of the cost – benefit (risk) balance of an AVMP is important before making a decision on the treatment.

Considering their professional knowledge and practical experience, veterinarians are the ones in better position to be the ones responsible for prescribing AVMPs. Many important clinical and pharmacological factors can influence the therapeutic success of an AVMP and limit the development of AMR. These include the following factors, influencing rational and prudent antimicrobial use:

- antimicrobial susceptibility;
- physical and chemical characteristics of active substance and excipients;
- pharmacokinetic parameters of the product;
- pharmacodynamics characteristics;
- route of administration/type of pharmaceutical form;
- dosing schedule and duration of treatment;
- effectiveness/lack of or reduced efficacy;
- safety (adverse effects);
- administration to a group of animals or an individual;
- immunocompetence and physiological status;
- withdrawal period (for food-producing animals).

First of all, the prescribing veterinarian should be familiar with the history of the herd, flock or animal being treated, and the activity level, age and stage of growth of the animal(s). In the case of a herd or flock, the veterinarian thus has a good understanding of its overall health status. Before prescribing an AVMP, the veterinarian should personally ascertain by means of a clinical examination that the symptoms indicate a probable bacterial infection. Whenever possible, an attempt should be made to identify the pathogen and measure its antimicrobial susceptibility. In acute cases, the treatment needs to be started immediately to avoid animal suffering and limit the spread of infection and then the results of pathogen identification can subsequently be taken into account. Templates (examples) of treatment protocols for forecasting animal disease outbreaks should also be developed.

In accordance with the relevant treatment guidelines, the veterinarian selects the appropriate AVMP and determines a suitable dosing regimen and route of administration. The prescriber should ensure that the most appropriate AVMP among the different classes of antimicrobials is selected, based on up-to-date

information about its pharmacodynamics and the pharmacokinetic characteristics of the pharmaceutical form (powder, granule, oral or injection solution, etc.).

Among the antimicrobial agents in worldwide use there are various antibacterial classes used in animals, most of which are also used in humans and some of these antimicrobials are critical for the prevention or treatment of life-threatening diseases in humans.

Due to concerns about the selection of antimicrobials and the dissemination of AMR between animals and humans, the OIE and WHO developed the concept of 'critically important antimicrobial agents', allowing an appropriate balance between animal health needs and human health considerations. Antimicrobial agents used for food-producing animals are classified as 'important (VIA)', 'highly important (VHIA)', or 'critically important (VCIA)', depending on the number of criteria they meet [5]. The list of Critically Important Antimicrobials developed by the OIE and WHO (for human medicine) with several adoptions is the reference to help formulate and prioritise risk assessment and risk management strategies for containing AMR [5, 12]. Regarding animal health, the OIE list has a specific section on recommendations that should be the main document to have in mind when developing animal health related policies and surveillance programmes, among others. [5]

Use of antimicrobials, and especially those that are important for the treatment of infections in humans and also necessary for use in the veterinary medicine should be based on the scientific opinion of the OIE, WHO, the European Food Safety Authority (EFSA) (Especially for EU Member States), and the Codex Alimentarius Commission. First of all, these recommendations concern fluoroquinolones and third- and fourth-generation Cephalosporins, which should never be used for food-producing animals as a preventive treatment applied with feed or water, nor should they be used as a first line treatment unless justified; extra-label or off-label use should be limited and reserved for instances where no alternatives are available.

Therefore, OIE Members should follow the recommendations stated on the OIE List of Antimicrobial Agents of Veterinary Importance in order to define restrictive conditions for the use of medically important antimicrobials in food-producing animals, e.g. conditioning their prescription on the realisation of antimicrobial susceptibility testing to ensure that there are no other antimicrobials available that are sufficiently effective or appropriate to treat the diagnosed disease [13]. Some countries, including Germany, France, The Netherlands, Italy, Denmark, Belgium and others, have undertaken major reductions in antimicrobial consumption and have placed further restrictions on the use of 'critically important' antimicrobials. Such steps provide the incentive to improve non-antimicrobial disease control strategies and focus efforts on appropriate management programmes, vaccination, genetic selection and animal nutrition, while avoiding compensatory increases in antimicrobial use for disease prevention or treatment purposes.

2. General principles of the distribution of veterinary medicines

Persons administering AVMPs should purchase them from authorised sources, whether wholesale or retail distributors, based on a veterinary prescription. The supply of AVMPs by veterinarians should be strictly limited to the amount required to treat the animals under their care.

In EU Member States, VMPs are distributed by wholesalers with a dealer's licence, or dispensed by official veterinarians, veterinarians responsible for treating animals or pharmacists. Wholesale distribution is subject to the holding of an authorisation with a licence issued by the Competent Authorities. In order to obtain the authorisation for distribution, wholesalers must have technically competent staff. In EU Member States, pharmacists, or veterinarians competent in veterinary pharmacy, may be authorised to act as wholesalers. Suitable and sufficient premises complying with the requirements laid down in national legislation as regards the storage and handling of VMPs are important for wholesalers' professional activity. In some countries in the Europe Region, VMPs may also be obtained in retail, from veterinary pharmacies (e.g. in Finland, Ukraine and Kazakhstan) or from authorised veterinarians. Authorised distributors are required to keep detailed records. In many countries in the Europe Region (e.g. Austria, Belgium, Finland, Italy and Portugal) the records have to be submitted in accordance with EU requirements for VMPs or, as for example in Denmark and Slovenia, in accordance with the requirements for medicinal products. Each incoming or outgoing transaction is documented.

Distributors should be required to record [9]:

- date of transaction;
- name of VMP and name of active substance;
- name of the pharmaceutical form;
- batch number and expiry date;
- received or supplied quantity;
- marketing authorisation number of the veterinary medicinal product(s) in the Member State from where it is sourced;
- marketing authorisation number of the veterinary medicinal product(s) in the Member State of destination;
- name and address of the supplier and the recipient.

These data should be entered manually in registers with numbered pages or electronically in dedicated accounting spreadsheets.

In current practice in EU Member States VMPs are allowed to be sold at a distance by online pharmacies when they are not subject to a veterinary prescription [9]. In such cases, national legislation should include appropriate measures to avoid the unintended consequences of such supply and establish rules on appropriate penalties. In order to ensure high standards and safety of the VMPs offered for sale at a distance, the public should be assisted in identifying only the legal websites which are offering such VMPs.

The distribution chain for VMPs should be subject to supervision and control by the Veterinary Authority. The retail activity of veterinarians, pharmacists and distributors should be in accordance with national law and not be influenced by economic incentives. Implementation of good distribution practice in supplying AVMPs can allow the traceability of antimicrobials and contribute to the development of campaigns focusing on rational therapy for infectious diseases, especially in food-producing animals such as cattle, pigs and poultry.

All of the stakeholders involved (e.g. distributors, pharmacists, veterinarians) should work together to promote prudent use of antimicrobials.

2.1. Electronic database and principles of an e-tracking system for monitoring and surveillance of AMR

A detailed database on antibiotic use and possible risk factors which can lead to the development of AMR is highly important, particularly with regard to food-producing animals. For example, in Ukraine and France, the Veterinary Authorities collect antibiogrammes on clinically sick animals and annually make reports on these risk factors. The purpose of the e-tracking system is to enable the online exchange of all data on AVMPs between stakeholders and the Competent Authorities. The development and functioning of such system should be specified in the national legislation, written, as much as possible, in a harmonized way with the relevant related international policies. The management and operation of the system require specialised equipment, software programmes and suitably qualified personnel. A standardised approach and a specific template facilitate data collection as this allows the data to be analysed and assessed when investigations are being conducted on the relationship between AVMP use and AMR. In order to introduce harmonised standards within OIE Member Countries on the methods of gathering data on the use of antimicrobials and the methods of transferring these data, appropriate technical rules should be laid down. A VMP database is important to ensure traceability of the product throughout the chain, including product authorisation, placing on the market, distribution, prescription and use.

What information should be recorded to allow a complete analysis of the sales and use data? The information required will depend on the level of data collection.

When the information comes from the MAHs or distributors the following points should be recorded:

– date of transaction;

– name of VMP and its pharmaceutical form;

– name of active substance and its strength;

– manufacturer's batch number, expiry date;

– quantity received or supplied;

– name and address of the supplier and the recipient;

– pack size and number of packs;

– where relevant, name and address of the prescribing veterinarian and a copy of the prescription.

Veterinarians should always keep records of the VMPs they have prescribed, and farmers should also keep a copy of them:

– prescription date;

– name of VMP;

– name of active substance and its strength;

– pharmaceutical form;

– manufacturer's batch number;

– quantity received and administered/supplied;

– name and address of the recipient;

– animal species, breed, age, number of animals treated;

– indication for use for each target species, code of the disease;

– doses, duration of treatment.

For the monitoring of sale and use of AVMP, an on-line application is desirable. It may contain information concerning one animal species or all AVMP sold and used for food-producing and companion animals during established period (e.g.one year).

When the Veterinary Authority considers that it is not feasible to keep all the information on AVMP use in each animal species in one database, then it is advisable to maintain several (e.g. three databases) for the main categories of food-producing animals, namely cattle, pigs and poultry, as is in Austria. For instance, in Austria the Poultry Health Data (PHD) database serves as an official register of poultry holdings, with links covering poultry farms, hatcheries, poultry slaughterhouses, egg packing centres, assigned private veterinarians, laboratories and the competent district, provincial and national authorities. The database contains all records on VMP use, vaccine use, sampling (both official and own checks), laboratory results and the results of ante-mortem and post-mortem inspections related to flocks. Levels of access to the database are well defined. For instance, food business operators (FBOs) have access to their own data only, and Competent Authorities have access according to their territorial responsibilities.

Other examples are in Denmark (VetStat) and Belgium (Sanitel-Med).

Since 2000, the Danish Veterinary and Food Administration (DVFA) have been using a central database called VetStat. The data collected include the identification numbers of the veterinarian, the farm and the product, the amount of the product sold, the code for animal species, the age group, the disease code category and the product purchase date. Two other databases, the official database of all veterinary practitioners (VetReg) and the database of all herds in Denmark (CHR), are linked to VetStat. This permits age-group-dependent benchmarking on the use of antimicrobials for pigs and cattle. VetStat delivers data to the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), which is considered to provide baseline data on AMR, record trends in AMR, monitor the use of AVMPs and the resistance level and serve as a tool to assess the impact of interventions at a national level. The data are published in the annual DANMAP report.

Harmonised and comparable data on the use of antimicrobials in each animal species, including companion animals, are necessary for carrying out risk assessments and for research purposes and evaluating the effectiveness of measures and policies taken to tackle AMR. The Competent Authorities must develop and implement policies, adopt the necessary measures and practical arrangements needed to support the e-tracking system. The e-tracking system should be supplied with the technical specifications of the VMP database and the practical arrangements for its functioning including the electronic data exchange mechanism for interconnection with existing national systems and the format for electronic submission of data. In particular, information submitted by the e-tracking system must ensure the protection of commercially confidential information. The information from MAHs or veterinarians should be submitted in accordance with the rules and methods relating to the gathering of data and within the time limits laid down in the relevant acts.

Strengths of e-tracking system	Weaknesses of e-tracking system
One framework agreement with manufacturers, distributors, prescribers, farmers (animal owners) and Competent Authorities	Product aimed at interconnectivity, which is composed of a set of specifications
Allowing to set up different levels of access: national Competent Authorities have full access to the database; regional Competent Authorities have access according to their territorial responsibilities; the general public have limited access, and without changing therein	Expensive in terms of resources required to implement the mechanism and meet the technical specifications
Advantages in management of AVMP consumption, due to the possibility collect information on outcomes over long term periods and assess the data	Requires regulatory protection of confidential information and security of information exchange
Potentially possible to instantly generate a report for an operational response to negative consequences	Requires collaboration between professionals in various sectors
Opportunities for monitoring AVMP by wholesale and retail distribution, prescription conditions, overuse	The amount of data can be massive which means the analytical time/cost is high and results are hard to extract
When the database contains all records on use of VMP, vaccines, samplings (both official and own-checks), laboratory results and results of *ante-mortem* and *post-mortem* inspections related to (e.g. poultry), safeguarding of flocks/herds through prompt detection of infections and prevention of massive losses in the event of epidemics.	

The data/results of an e-tracking system may also be used for training programmes on promoting awareness of AMR in the form of webinars, workshops or other online training programmes and tests.

One of the main advantages of an e-tracking system is that it makes it possible for the Competent Authorities to carry out surveillance in the veterinary sector. Stakeholders can quickly and easily look up any available information about antimicrobials entered in the database, access it and take the appropriate decisions on improving AVMP in accordance with international standards.

3. Responsibilities of veterinarians and veterinary paraprofessionals

Veterinarians should prescribe or dispense AVMPs in quantities suited to the size of the production package units and the expected needs, so as to avoid an excessive presence of antibiotics on the farm which might subsequently be used by farmers for animals other than those targeted or cause harm to the environment.

AVMPs to be administered through liquid or solid feed cannot be kept as stocks. However, such products may be kept in small quantities, proportionate to the farm's requirements and sufficient for a maximum period of 5 to 7 days (depending on national legislation), to be used when rapid treatment is needed.

Most frequently, AVMPs are administered by enteral route with feed or drinking water (e.g. for poultry or pigs) [8].

When water medication is selected, it is necessary to know average water consumption in order to determine the inclusion rate of the antimicrobial agent. Factors affecting water consumption of poultry, pigs and beef cattle include age and stage of growth, activity level, environmental temperature, humidity, water temperature, water quality (including hardness, mineral content, sulphate content), water palatability, feed composition and, particularly for poultry, the lighting programme [8]. Failure to ensure these factors are optimised can lead to ineffective AVMP delivery.

Administration of antimicrobial agents in feed is one of the most widely adopted practices and should be undertaken in accordance with good animal feeding practices [8].

The production of medicated feed for a herd or flock must be undertaken in accordance with the veterinarian's prescription delivered to the feed mill. During production, highly skilled workers ensure the correct inclusion level, stability, homogeneity and lack of segregation of the active constituents so that each of the animals to be treated will receive a prescribed dose of the AVMP, thereby avoiding over- or under-dosage [8]. Hence, only the professional competence of the veterinarian as the prescriber and, when applicable, the supervisor of AVMP administration can prevent ineffective antimicrobial use.

In the case of food-producing aquaculture animals and animals bred for fur, the people administering VMPs are often the farmers or farmworkers. These people are strictly responsible for following the veterinarians' instructions on administering antimicrobial products.

Veterinarians should focus their efforts on providing assistance to other persons responsible for oral administration of the product to animals in feed or drinking water, especially in the case of group treatment, to ensure they are aware of the importance of the warnings described in the summary of product characteristics (SPC) regarding the correct administration and appropriate dosing of certain AVMPs. Additional instructions should be given on proper cleaning of the equipment used for administration of AVMPs, to avoid cross-contamination and reduce the risk of development and spread of AMR.

It is advisable to draw up specific operational protocols on the methods to be used when carrying out pharmacological treatments and how to implement them, so as to avoid incorrect administration.

Veterinary paraprofessionals must strictly follow the veterinarians' recommendations. When antimicrobials are given with feed or drinking water, their quantities should be monitored and documented on a continuous basis, especially in intensive food production systems. On-farm records are usually kept in special registers, supervised by the veterinarian and controlled by an official of the Veterinary Services.

Veterinarians and veterinary paraprofessionals must observe and monitor sick animals. Sometimes during treatment, an animal may present unfavourable and unintended reactions to an AVMP. Without delay, the veterinarian should then assess whether to modify the treatment and must in all cases inform the authorities of such events by filling in the appropriate report form, which should be done within the existing pharmacovigilance system. Also within the pharmacovigilance system, the veterinarian should send a report about the lack of or reduced efficacy of the AVMP, because it may be related to poor product quality (substandard, degraded and/or counterfeit medicinal product). Substandard, falsified or counterfeit AVMPs can play a potentially significant role in global development and dissemination of AMR.

In accordance with the updated recommendations of the Regulation of the European Parliament and the Council on veterinary medicinal products [9], detailed information on VMP use should be presented in the product information provided by the manufacturer when additional investigation is required.

It is very important to raise awareness of AMR and the health risks involved by developing communication materials and organising sub-regional, regional and international events. Training workshops for veterinarians and veterinary paraprofessionals on AMR surveillance are easy to organise. Including information on the results of scientific investigations and practical experience in addressing the AMR problem in the educational curricula for all relevant professions, from initial levels to degree programmes, will lead to greater awareness of AMR among professionals. The implementation of the Global Action Plan [11] and the OIE Strategy on AMR and Prudent Use of Antimicrobials [4], have led to an increased AMR awareness in the veterinary sector, and a more prudent use of antimicrobials.

Recommendations

AMR is a serious threat to human and animal health and also to environmental and food security throughout the world. Despite the extensive efforts of international organisations, namely the OIE, FAO and WHO, to promote responsible and prudent use of antimicrobials, AMR poses a threat throughout the world and requires multi-sectorial and multinational cooperation to achieve progress and success.

OIE Member Countries need to share their experience and work together to address the problem of combating AMR and promote the prudent use of antimicrobials in human and veterinary medicine.

Taking into consideration the importance of this problem and the achievements that countries have already made in this respect, the following recommendations can be made:

a) Strengthen national legislation with the aim of implementing the OIE strategy on AMR and the prudent use of antimicrobials, adopted in the form of Resolution No. 36 by the OIE World Assembly of Delegates at the 84th General Session of the OIE in 2016, this strategy being aligned with the Global Action Plan endorsed at the WHO 68th World Health Assembly in 2015.

   – Develop or approve national action plans for AMR in human and veterinary medicine under the 'One Health' approach, taking into account multi-sectorial and multinational experience.

   – Prescribe AVMPs in accordance with national regulations governing the prescription of VMPs; a prescription for an AVMP has the status of a document confirming the actual use of the said AVMP.

   – Develop or approve national legislation for implementation of the principles of an e-tracking system and maintenance of a VMP database ensuring different levels of access for organisations and authorities commensurate with their different responsibilities.

b) Implement the principles of good veterinary practice and take steps to ensure prudent use of antimicrobials in accordance with international standards.

   – Throughout the world, it should be mandatory for antimicrobial agents, and in particular those intended for use in food-producing animals, to be available only on prescription. Electronic prescriptions should be in PDF format. Paper prescriptions must be archived for five years.

- Monotherapy with narrow-spectrum antimicrobials should be the preferred method, except in certain cases where evidence-based combinations may be available.

- All veterinarians should strictly follow OIE recommendations on antimicrobials use on the list of critically important antimicrobials (CIA) [5]. Derogations may be granted when based of the results of susceptibility testing or a negative response to the therapy justified on previous data on the susceptibility of causative agents on the farm.

c) Implement the principles of good distribution practice to improve the monitoring of amounts of AVMPs sold at national level using an e-tracking system or other forms of data collection in accordance with the requirements of the ESVAC and the OIE data collection for the Annual report on antimicrobial agents intended for use in animals.

- The usefulness of AVMP monitoring based on sales, prescription and distribution data collection should be emphasised in cost-benefit assessment initiatives and in the promotion of prudent and rational use of antimicrobials.

- Marketing authorisation holders must ensure that the data in their reports are valid and correct and that the results of reports assessment adheres to the principles of rational antimicrobial use and reflects trends in their use in veterinary medicine.

- Good quality data with a high level of detail are needed to inform political discussions regarding antimicrobial use and to detect increases in antimicrobial use and resistance.

d) Foster awareness and understanding of the problem of AMR, strengthen knowledge and ensure surveillance of all steps of antimicrobial use: manufacture, distribution, storage, application, utilisation of residues and waste materials.

- For a better understanding of the problem of AMR and to strengthen knowledge among all stakeholders, training on AMR may be organised using contemporary communication tools (websites, internet or media resources).

- Disseminate information on the results of scientific investigations and practical experience in addressing the AMR problem and include this information in the educational curricula for all relevant professions, from initial levels to degree programmes.

- Collaborative work with professional associations based on mutual trust and aimed at improving animal and human health will motivate veterinarians to become involved in the process of monitoring AVMP use. Reducing the administrative burden for veterinarians responsible for notifications will also be a motivating factor.

e) Introduce an e-tracking system to compile databases of AVMP consumption.

- Use e-tracking to record details of sales volumes and the delivered amounts of authorised AVMPs, vaccines, etc. by MAHs and wholesalers to farms, and AVMPs prescribed by veterinarians.

- Use the databases of records of AVMP consumption in animals to assess results and make recommendations to improve the practice of prudent use of antimicrobials.

- Use e-tracking for inspections of farms or veterinarians by the Competent Authority and organise meetings with veterinarian associations and farmer organisations, to raise general awareness of the importance of prudent use of antimicrobials and to ensure that the regulations of the Competent Authorities are being respected.

Conclusions

Good practices relating to the prescription and distribution of antimicrobials to treat animal infectious diseases should be developed and implemented in all Member Countries of the Europe Region, and should include cooperation between veterinarians, wholesalers, farmers and para-professionals.

All Member Countries need to improve their national legislation with a view to developing the practice of rational use of antimicrobials, implementing an e-tracking system to create AVMP databases, monitoring antibiotic consumption in the veterinary sector and assessing risk factors for the development of AMR.

Antimicrobial traceability monitoring results are an essential tool to promote awareness among all stakeholders of the threats to public health, animal health and welfare and the environment posed by AMR.

The implementation of the practice of rational and prudent use of antimicrobial agents, based on a coordinated implementation of international standards, global strategies, and collective experience will have positive influence to tackle antimicrobial resistance and increase the overall animal and public health.

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