



**Federal Veterinary Surgeons'
Association (BTK =
Bundestierärztekammer)**

**Guidelines for the prudent use
of veterinary antimicrobial drugs
- with notes for guidance -**

Preamble

In recognition of the responsibility of veterinarians in the use of medicines for animals containing anti-bacterial active ingredients (summarised as antibiotics hereinafter), the Federal Veterinary Surgeons' Chamber, in cooperation with the Arbeitsgemeinschaft der Leitenden Veterinärbeamten (ArgeVet = Working Group of Leading Veterinary Officials), had first issued the "Guidelines for the prudent use of veterinary antimicrobial drugs" in 2000. The initiative and tireless engagement of Prof. Dr Fritz Rupert Ungemach (†) contributed very significantly to the success of the difficult project.

These guidelines are now available in their **third edition**. They are now up to date in terms of the current legal situation, new active substances and the latest scientific knowledge. The updates are partly editorial and partly of a veterinary nature. Clarifications are made e.g. concerning the themes of deficiencies in living conditions, metaphylaxis, initial treatment and combinations of active substances. References to prescriptions and guidelines were kept more general to simplify future adjustments. In veterinary terms, tolerability was added as a criterion for selecting a suitable antibiotic. The active substance tildipirosine was added to the list of licensed macrolide antibiotics.

The development of the **second** version of the guidelines, which was also initiated and coordinated by Fritz Rupert Ungemach to a significant degree, was overshadowed by his severe illness and his death in December 2009. Prof. Ungemach worked on the project until a few days before his premature death. Prof. Dr Manfred Kietzmann, Hanover, declared his willingness to continue the work without hesitation.

Regarding the application of the guidelines in the various fields of veterinary practice, there was a need for updates and modifications, as the authors had intended. Due to its demanding expansions, the second, expanded and revised edition developed in detailed discussions in various working groups.

Since there are major differences between the species when using antibiotics, it made sense to include specific information about individual animal species within the guidelines. Treatment of individual animals predominates for small animals and horses, while group and population treatments are in the majority for livestock (are the majority for farm animals?). The working group took these special circumstances into account with specific additions for fish, poultry, small animals, horses, pigs and ruminants. Naturally, such guidelines cannot describe all details of a specific treatment; therefore the texts only contain the additional information for the individual animal species which is regarded as particularly relevant.

The guidelines neither directly nor indirectly constitute a legal regulation; they are a veterinary description of optimal procedures in the use of antibiotics, from which one should only deviate in well founded cases. Herein, it is necessary to comply with medicinal products regulations. These guidelines are intended to serve practising veterinarians as a summarising recommendation for the responsible use of antibiotics in animals. At the same time, they are naturally also an important source of information for the supervisory authorities in assessing matters of medication use based on veterinary medical science. The use of antibiotics in animal medicine in accordance with the guidelines contributes to preserving antibiotics as safe and effective medications for humans and animals. With the now updated guidelines, veterinarians also document their determination to the public to use antibiotics, which are so valuable for humans and animals, in a conscientious and responsible manner.

The guidelines will be continuously updated. All colleagues are asked to inform the BTK business office about **suggestions for changes and additions**; these will be discussed in the BTK committees and added to the next edition if applicable.

Guidelines for the prudent use of veterinary antimicrobial drugs

- with notes for guidance -

Revised version (version of January 2015)

Guidelines

General information

Antibiotics¹ should only be used in bacterial infections.

Any use of antibiotics, e. g. in human and veterinary medicine, may result in the development of resistance. The risk rises with non-specific use, sub-therapeutic dosages, extended, repeated and routine use of antibiotics.

Antibiotics are essential for treating and preserving the health of animals and animal herds. Currently, alternatives are not sufficient.

The use of antibiotics is only justified in the cases in which they are actually required, and the active substance is carefully selected while taking the individual case and the requirements into account.

Antibiotics are not intended to compensate for deficiencies in the implementation of "good veterinary medical practice", as well as poor husbandry conditions, management errors or insufficient hygiene standards.

The guidelines specify requirements which must always be noted when using antibiotics in animals. They are rules of veterinary medical science concerning the use of antibiotics, and must be taken into account in any appropriate treatment in accordance with existing legal principles.

Explanations

Anti-bacterials are almost solely effective against bacteria. They are not active against viruses and fungi.

These guidelines describe the prerequisites for the use of antibiotics in animals. Herein, it must be taken into account that whenever antibiotics are used, it is not only the bacterial microbe which we seek to fight, but also the corresponding physiological bacterial flora which is exposed to selection pressure, so that resistance can also be acquired and passed on, even when selection pressure is not directly applied. The guidelines are valid for any use of antibiotics within the scope of "good veterinary medical practice". They must therefore be taken into account not only when treating bacterial disorders in agricultural livestock, but also when treating individual animals, small animals and pets.

Prior to treating any organ system, it must be specifically verified whether other treatment measures may be suitable for replacing or minimising the use of antibiotics.

If the repeated occurrence of a bacterial disorder is due to husbandry deficiencies or insufficient hygiene standards, diseased animals can be treated, particularly to avoid unnecessary pain, suffering and damages. At the same time, however, one must persistently work towards correcting existing deficiencies to avoid the further use of antibiotics.

When the guidelines are taken into account, it can be assumed that the use of antibiotics in the respective individual case is, in accordance with the state of veterinary medical science, suited to attaining the treatment goal.

¹ The term "antibiotics" which is used in the text for reasons of simplification covers all anti-microbial substances.

Guidelines

1. Antibiotics must only be used when it is proven or can be assumed with certainty that the target bacterial pathogen in the animals being treated or in the herd is sensitive to the utilised antibiotic. Their use is therefore justifiable only in therapeutic and metaphylactic terms. Prevention in healthy (uninfected) animals must be avoided, apart from well founded exceptions.

The use of antibiotics is only justified if it is proven based on the diagnostic procedures described under no. 3 of this guideline or if it can be assumed with certainty that the disease was caused by a microbe which is sensitive to the utilised antibiotic. If only individual animals in a herd show signs of illness, it must at least be proven for metaphylactic use of antibiotics that a corresponding infectious microbe is expected in those animals of the herd which do not yet show symptoms, and that these animals will soon fall ill. Treatments which are not due to a diagnosed bacterial disease do not constitute metaphylaxis in the sense of this guideline, and must therefore be avoided.

Prevention is only justifiable in particularly well founded cases, e. g. in association with surgery or in immune suppressed patients (as a consequence of the underlying illness or in therapy with immunosuppressant medications or cytostatics, or in long-term use of glucocorticoids, etc.).

2. The selection and decision to use antibiotics is the responsibility of the treating veterinarian after a proper diagnosis. Based on his knowledge and the current state of science, the veterinarian must weigh the *benefits and risks* to animals, humans and the environment.

Antibiotics are prescription medications. Only the veterinarian is allowed to make decisions regarding their use.

They may only be used in accordance with drug regulations and only with reference to the concrete individual case for which the veterinarian has determined the indication for the antibiotic and the animals requiring treatment after a corresponding diagnosis.

According to the legal regulations, antibiotics must only be issued by the treating veterinarian or based on a veterinarian's prescription, and applied in accordance with the veterinarian's instructions and under a veterinarian's supervision.

Use under a veterinarian's supervision does not mean that the veterinarian must be personally present when the antibiotic is administered. However, he must - with the use of written directions if possible - ensure correct use by the animal owner regarding the dosage schedule and animals to be treated, and verify this by monitoring the treatment success at suitable intervals.

It is not permissible to supply an antibiotic for an indication which is not yet determined since the decision about the time of use and animals to be treated must never be left to the animal owner.

3. The use of antibiotics always requires a diagnosis based on appropriate clinical examinations and further laboratory diagnostic tests if required, including the immune status of the animals, herd-specific aspects, as well as other experience and knowledge.

Appropriate diagnostics must be performed in each individual case to constitute the basis for a selection of which antibiotic to use. The guidelines leave sufficient room to veterinarians to choose the required diagnostic measures in accordance with the individual case.

If a bacterial infectious disease is found, but the microbe is not yet definitively identified and immediate treatment is required due to the severity or spreading tendency of the disease, the veterinarian may initiate treatment in the absence of microbiological findings (microbe identification, antibiotigram). Even in this event, however, traceable clinical veterinary findings and diagnostic measures are required. They must be documented in accordance with the duties of documentation specified in no. 7.

The need for the use of an antibiotic must be proven by suitable, traceable diagnostic measures.

If the symptoms permit a definitive conclusion as to a specific microbe or indicate a probable microbe which, in accordance with past experiences, can be fought with a narrow-spectrum antibiotic, random microbiological testing is sufficient to confirm the diagnosis and resistance situation.

If the symptoms indicate a bacterial infection but do not permit a conclusion regarding a specific microbe and a broad-spectrum antibiotic is therefore used, microbiological diagnostics are generally required to clarify the involved microbes and their resistance patterns.

In a severe bacterial disorder in which conclusions regarding a specific microbe are not possible, microbiological testing should absolutely be done (if feasible).

Insofar as possible and justifiable, microbiological diagnostics with microbe identification and antibiotigram should be initiated to an appropriate extent in accordance with good veterinary medical practice when treatment with an antibiotic is initiated. This permits specific further treatment in accordance with the guidelines when therapy changes are made, if the initially selected antibiotic does not obtain the desired treatment success.

Prior to generating an antibiotigram, it is always necessary to isolate the microbe, since this is the only way to determine possible resistances. It does not make sense to generate an antibiotigram for mixed bacterial flora, since the resistance properties cannot be precisely allocated to the individual microbes in this case.

Detection of microbes and an antibiotigram after microbes are isolated are fundamentally necessary:

- when an antibiotic is changed during therapy due to insufficient treatment success,
- at regular intervals for repeated or long-term use in animal groups or herds,
- in combined use of antibiotics for a disease,
- in deviations from the license conditions (cascade or off-label use)

In acute infectious disorders whose treatment cannot be delayed, the veterinarian must select the antibiotic with which to initiate treatment based on clinical findings and his experience regarding the herd-specific conditions of the particular case, as well as any other applicable knowledge (including the pharmacokinetic properties and tolerability).

Antibiotics must generally be changed on the basis of microbiological diagnostic findings which were initiated before any kind of treatment has been started (also see no. 7, last dash).

Repeated use of antibiotics in an animal herd - e. g. in specific age and production segments or when they are moved into barns - must be fundamentally verified by regularly checking the resistance situation. Microbiological diagnostics are not needed for every treatment. The appropriate scope of such tests can be determined based on the individual case. Possibly promising alternatives to the use of antibiotics should also be verified (e. g. vaccination programmes).

If several antibiotics which are not licensed as a fixed combination are to be administered in combination for the same underlying illness, it must be diagnostically confirmed that the involved microbes cannot be fought with a single active substance. In particularly severe acute illness cases with an unknown microbial spectrum, combination treatment may already be necessary at the outset of treatment, before microbiological test results become available.

If a further pathogen is identified, administering an additional antibiotic may be justified if the new microbe is not sensitive to the initially applied antibiotic.

The cascade use of an antibiotic - that is, its use in another route of administration or animal species than those intended by the license - can generally take place only based on an antibiotigram or other knowledge on resistance which proves that the prerequisites of a so called "therapy emergency" apply (no corresponding medication licensed for the animal species or indication, and welfare of the animals otherwise seriously placed at risk). The need for an increased dosage must be proven with suitable findings on the resistance situation. Here as well, the veterinarian must immediately initiate treatment in acute infections whose treatment cannot be delayed, and will select the antibiotic based on clinical findings and his own experience.

4. The suitable antibiotic must be selected based on the following criteria:

- by the best possible match to the selection criteria (see the annex);
- deviations from the selection criteria must be well founded;

In most cases, it can be assumed that several antibiotics will be effective in a bacterial infectious disorder.

The annex shows selection criteria for antibiotics and allocates them to the respective active substances. Preference should be given to the active substance which shows the best match to the selection criteria. If several antibiotics can be used to treat a bacterial infection, the antibiotic with the narrowest spectrum, a wide therapeutic range and if required, a bactericidal acting mechanism and good tissue penetration should be selected insofar as possible.

If an active substance is selected contrary to the criteria stated in the annex, objective reasons and documentation must be provided.

If, for instance, a broad spectrum antibiotic is used even though the microbe can normally be fought with an antibiotic which has a narrower spectrum, the need for this measure must be founded and documented with suitable findings, an antibiotigram or on the basis of known data on the applicable resistance situation. However, necessary initial treatment for severe bacterial infectious diseases with an unknown microbial situation often requires the use of a broad spectrum antibiotic. This must be justified on the documentation of the diagnosis, including the most important findings.

- so called "reserve antibiotics" (particularly fluoroquinolones and cephalosporins of the third and fourth generation) must only be used with a strict indication to treat individual animals and diseased groups of animals;

Certain antibiotics constitute an important therapeutic reserve against multi-resistant microbes. The availability of these antibiotics is of life-saving importance for patients with life-threatening infections (e. g. MRSA infections due to methicillin/oxacillin resistant staphylococci). Therefore, those antibacterials which, based on their acting spectrum and good resistance situation, are available for the treatment of life-threatening infections in humans and animals for which other sufficiently effective antibiotics are no longer available must be used with extreme restrictions. These active substances are therefore the "products of last choice" and are, for this reason, also referred to as "reserve antibiotics". The use of such "reserve antibiotics" is permissible if e. g. successful therapy with other antibiotics is most likely not expected based on preceding sensitivity tests or other knowledge on the resistance situation, or if therapy success was insufficient after treatment with other antibiotics was initiated.

Since resistances which are significant in human medicine can be selected both when treating agricultural livestock and in small animals and pets which are in close contact with humans, the use of such antibiotics in animals must be handled restrictively.

The antibiotics licensed for animals also include modern active substances which are indispensable for treating severe infections in both animals and humans. Strict determination of the indication and a special duty of due care apply to the use of these active substances - especially if groups of animals are to be treated. Strict compliance with the licensing conditions is required, particularly concerning the dosage, therapy duration and the criteria for selecting the antibiotic. Their use is only justified if sensitivity tests, knowledge of the resistance situation or a lack of therapy success lead to the conclusion that there are no treatment alternatives in the applicable case of illness.

- for the initial treatment, particularly in the event of acute illness, the antibiotic can be selected based on clinical experience;

In acute infectious disorders whose treatment cannot be delayed, the veterinarian can select the suitable antibiotic with which to initiate treatment based on clinical findings and his experience regarding the herd-specific conditions of the particular case, as well as any other applicable knowledge (including the pharmacokinetic properties and tolerability). In such cases, deviations from the recommendations regarding the selection criteria may become necessary.

Results of regular resistance monitoring in the treated herd or, if such data are unavailable, supra-regional resistance assessments provide an important decision-making aid.

- Immune status of the animal being treated, wherein bactericidal antibiotics must be given preference in immunosuppressed patients;

If immune defences are impaired, e.g. in septicemic processes or due to treatment with immunosuppressant pharmaceuticals, care must be taken to ensure the use of bactericidal antibiotics when selecting the therapy. Bacteriostatic antibiotics cannot ensure sufficient microbe reduction in this event.

- pharmacokinetic properties of the antibiotic and pharmaceutical properties of the utilised medication to obtain sufficiently high and sufficiently long acting levels at the infection site;

The level and duration of effective antibacterial acting levels at the infection site - depend on the dosage and on the pharmacokinetic properties of the antibiotic. Tissue penetration and therefore, attainable tissue levels may vary considerably; e. g. active substances from the groups of aminoglycoside and polypeptide antibiotics have a low apparent distribution volume (V_d), so that they only pass into tissues and intracellular spaces to a limited degree, and may not be able to reach sufficiently high active substance concentrations. Antibiotics with a high V_d can reach tissue levels exceeding blood levels (e. g. fluoroquinolones, macrolide antibiotics, phenicols).

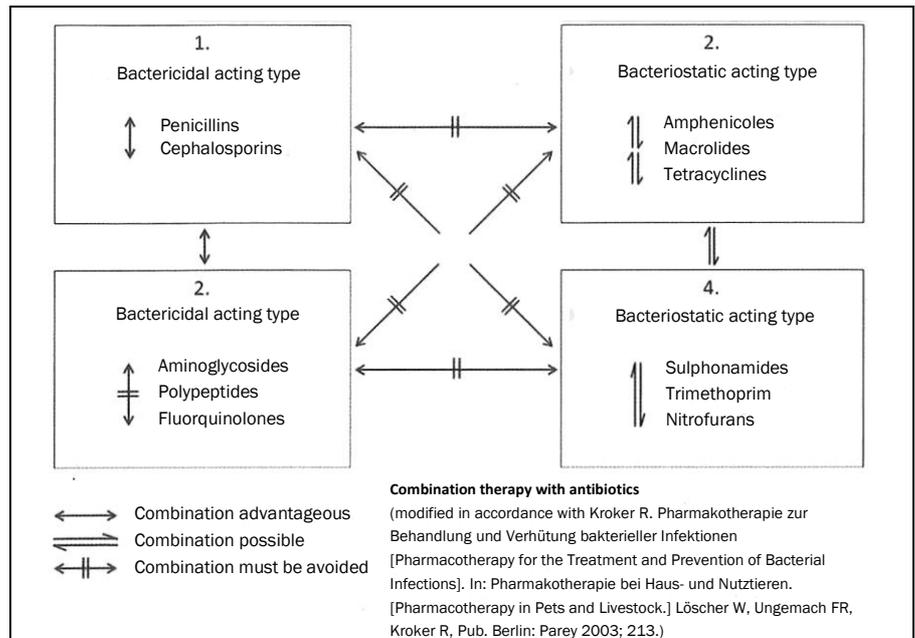
Other pharmacokinetic properties which are relevant to the dosage level and interval are taken into account in the dosage schedule as set out in the package leaflet for the applicable product. For instance, these properties include bioavailability, excretion behaviour, any occurring post-antibiotic effects, and influences of the pharmaceutical formulation (e. g. extended release or depot products).

- when combined administration of antibiotics is required, care must be taken to comply with the rules on combinations of antibacterial active substances.

Combinations of antibiotics with bactericidal and bacteriostatic effects must be avoided, due to possible antagonistic effects.

However, specific combinations may also be unfavourable within the groups of bactericidal and bacteriostatic substances, since they may result in possibly intensified side effects, trigger cross-resistance, or mutually hinder each other at the same site of action within the bacterium.

,The combination of sulphonamides with trimethoprim is regarded as suitable.



5. Antibiotics should be used in accordance with the license conditions. Any deviation (indication, animal species, dosage, route of administration, duration of use) must be well founded:

If an antibiotic is to be used off-label, this can only take place based on a diagnosis which is confirmed, e. g. with microbe confirmation, an antibiotigram or epidemiological knowledge on resistance, traceable clinical findings, or pathological-anatomical tests. Products can only be used off-label when there is a so called therapy emergency; that is, no suitable licensed medication is available (i.e. commercially available) for the field of application or the animal species, and the necessary animal welfare would otherwise be placed at serious risk.

In all deviations from license conditions, the veterinarian is responsible for efficacy as well as the safety of the treated animals, and for ensuring consumer safety. The veterinarian must ensure with sufficiently long withdrawal periods that residue in foods obtained from treated animals is safe. In any deviation from license conditions, the veterinarian must set the withdrawal periods for the individual case so that specified maximum residue levels are not exceeded.

If an antibiotic is used under the cascade but in the registered target species, the withdrawal periods stated on the medication for the treated animal species applies unless there are other deviations from the license conditions.

If an antibiotic is used under the cascade in a species not included on the registration, (whose active substances are included in table 1 in the annex to regulation (EU) no. 37/2010), the withdrawal period must be at least 28 days for edible tissues, 7 days for milk, 7 days for eggs, or 500 days divided by the average water temperature in degrees Celsius for fish.

Changing the route of administration or increasing the dosage may also alter the formation of residue (e. g. lengthen it). Since the stated withdrawal periods are only tested for the administration routes and dosages listed in the package leaflet, the veterinarian must specify and state a withdrawal period of sufficient length for the respective case in any deviation, which may also be shorter than the aforementioned minimum withdrawal periods in this case if the target species is unchanged.

Lastly, a withdrawal period recommendation can only be confirmed based on a specific residue test when deviating from license conditions.

a sufficiently high dosage must be selected (at least in accordance with the package leaflet),

Antibiotics must always be administered in the dosage stated in the package leaflet.

If, based on the resistance situation of the involved microbes, a higher dosage than that stated in the package leaflet is required, this must be documented with corresponding findings on the respective resistance situation.

atment intervals must be sufficiently short to avoid sub-therapeutic active substance levels,

In order to effectively fight the microbes, the treatment interval must be selected so that sufficiently high concentrations of the antibiotic are maintained at the infection site for the entire duration of treatment.

In bacteriostatics, sub-therapeutic active substance levels in the target tissues must absolutely be avoided.

- for oral administration to a herd (population), the intended dosage must be ensured for the animals requiring treatment, active substance carry-over must be avoided, and this must be monitored with suitable methods at appropriate intervals,
- dosage information must be communicated to the animal owner in writing.

6. The therapy duration must be kept as short as possible, but sufficiently long to fight the infection in the individual case. It depends on the target organ and microbe specific requirements.

7. Documentation is maintained about

- diagnostic measures,
- reasons for deviations from recommendations,

The dosage interval depends on various substance-specific factors (e. g. distribution and excretory behaviour; if applicable, also on post-antibiotic effects, the mechanism of action, the route of administration and the product-specific pharmaceutical preparation (e. g. as an extended release formulation). In order to ensure sufficient active levels during treatment, the product-specific dosage intervals stated in the package leaflet must never be exceeded.

Administration of medications via the feed is associated with the risk of an imprecise dosage and carry-over. Therefore the veterinarian must ensure that when antibiotics are administered in the animal husbandry operation via the feed, sufficient knowledge and technical prerequisites exist to guarantee a precise dosage for the treated animals, while simultaneously avoiding medication of animals not requiring treatment. Oral treatment should take place in compliance with the Federal Ministry of Food and Agriculture (BMEL) guideline concerning "Oral administration of veterinary drugs in the livestock sector via feed or drinking water".

When administering antibiotics through the drinking water, it must be guaranteed that a sufficient therapeutic concentration is reached as quickly as possible in all areas of the drinking water. It must be ensured that the recommended dosage per kilogram of bodyweight can be completely ingested by the individual animal throughout the recommended treatment period. Sufficient water intake must be assured, particularly in diseased animals.

Once treatment is completed, the watering systems and equipment which have come into contact with the medication or medicated feed must be cleaned in a suitable manner to avoid active substance carry-over which may result in the ingestion of sub-therapeutic residual quantities of the antibiotic, which may encourage resistance.

When issuing medications for animals used in food production, the dosage must be stated with the written and, if applicable, electronic supply documentation, which the veterinarian immediately gives or transmits to the animal owner. In small animals and pets, animal owners should also be given written dosage instructions stating the length of therapy, route of administration, individual dosage amount and treatment intervals, ensuring careful handling of the antibiotic as well as compliance.

Any therapy with antibiotics must be implemented consistently.

Single administration of an antibiotic is only sufficient in rare exceptions, e. g. in uncomplicated infections of the lower urinary tract or when using a long-acting formulation.

Several days of treatment are generally required. For example in bacterial infections with fever, for instance, treatment should be continued at least until the second day after the fever subsides. In order to keep selection pressure on bacteria and therefore the risk of developing resistance as low as possible, the treatment duration must be limited to the therapeutically required minimum. Any unnecessary exposure of the animals to antibiotics must be avoided. This applies particularly to treating herds or populations. In most cases, administering antibiotics for three to seven days is sufficient for the therapy or metaphylaxis of bacterial infections.

In some indications, however, individual animals may also require longer-lasting antibiotic therapy, e. g. in osteomyelitis, deep pyodermy, infections of the upper urinary tract, or infections with a high tendency to recur.

For every use of antibiotics, the reasons must also be traceable in controls carried out by the supervisory authorities.

When using or supplying antibiotics, the following documentation should be produced and stored in a clearly ordered manner (e. g. sorted by animal owners):

- All findings which serve as a basis for the diagnosis concerning the use of the antibiotic in accordance with no. 3 of these guidelines (e. g. results of the clinical examination, pathological-anatomical tests, microbiological diagnostics or epidemiological surveys);
- findings (particularly results of microbiological diagnostics) which can prove the need for cascade use, deviations from the dosage schedule in the package leaflet, or selection criteria for antibiotics;

- measures of treatment success,

- findings on the microbial and resistance situation in the population,

- time and results of follow-up examinations of the treated animals or animal population. According to the rules of veterinary medical science, measures of treatment success are required for every proper treatment at time intervals which are appropriate for the respective case.

Regularly obtained findings of microbiological diagnostics in animal populations in which antibiotics are used repeatedly (e. g. in specific age and production segments, when they are moved into barns and adverse medication effects) provide important indicators of population-specific problems.

8. Loss of efficacy due to decreasing sensitivity and/or development of resistance of target microbes must be reported to the responsible agencies in the adverse medication effects reporting system.

According to the professional regulations, every veterinarian is obligated to report adverse medication effects to the federal veterinary chamber or Federal Agency for Consumer Protection and Food Safety including suspected cases as well. This also includes lack of efficacy of an antibiotic, e. g. due to decreasing sensitivity and/or development of resistance by target microbes. Reporting sheets which are available online (www.vet-uaw.de) and also published at regular intervals in the German Veterinary Gazette are available for the reports.

Annex

Criteria for selecting a suitable antibiotic

1. Acting spectrum

The acting spectrum of an antibiotic states which microbe types suffer growth inhibition or are killed by the substance. If both gram positive and gram negative bacteria are covered by an antibiotic, it is referred to as a broad spectrum antibiotic.

When selecting the active substance class, it must be ensured that the selected active substance inhibits the growth of the microbes involved in the infection or kills them.

Active substances with a narrow spectrum are fundamentally preferable to broad spectrum antibiotics, since they have less influence on the physiological microbial flora and exercise a lower selection pressure on commensal microbes.

2. Resistance situation

In addition to the substance-specific acting spectrum, the current resistance of the bacteria which are being treated must be taken into account for every antibiotic. This must include both information which is specific to the husbandry operation and further (regional) information. It must also be taken into account that resistance may develop rapidly for some active substances, or more slowly for others.

3. Tolerability and therapeutic range

Sufficient local and systemic tolerability must be assured for medications. The treating veterinarian must particularly take this into account in cases of cascade use, when medications are not used in accordance with their license conditions.

The therapeutic range describes the safety of the product in its therapeutic application. The dosage effect of desired and adverse effects is compared.

It is important for safety in clinical use to know the ratio of overdose/dose at which one could begin to expect severe side effects. The greater this quotient, the greater the therapeutic range, and with it, the interval between the therapeutic dosage and the dosage at which one could begin to expect such side effects. In antibiotics with a narrow therapeutic range (≤ 2), severe side effects may already occur in small overdoses up to twice the amount of the therapeutic dosage. A dosage increase is generally not possible. Antibiotics with an average to wide therapeutic range (> 3) have a sufficient safety range.

The therapeutic range is determined in safety studies in the target animal species, in which the product is tested in multiples of the licensed dosage and in treatment periods longer than the licensed treatment period to determine possible side effects. Aside from the active substance characteristics, formulation-specific or product-specific attributes (particularly local tolerability) as well as hypersensitivities and contraindications in certain animals are also important.

4. Acting type

Antibiotics have specific points of attack within the bacteria, where they either inhibit the growth of the bacteria, or kill them by damaging essential structures, e. g. the bacterial cell wall. The inhibitory effect is termed bacteriostasis; the bacteria whose growth is disturbed in this manner must then be eliminated via the body's own defence mechanisms. Bactericidally-acting substances kill the bacteria at sufficient concentrations in the target tissues and with a sufficient duration of acting.

The use of bactericidally acting substance groups is generally indicated if the immune status is unclear or the patients are immunosuppressed.

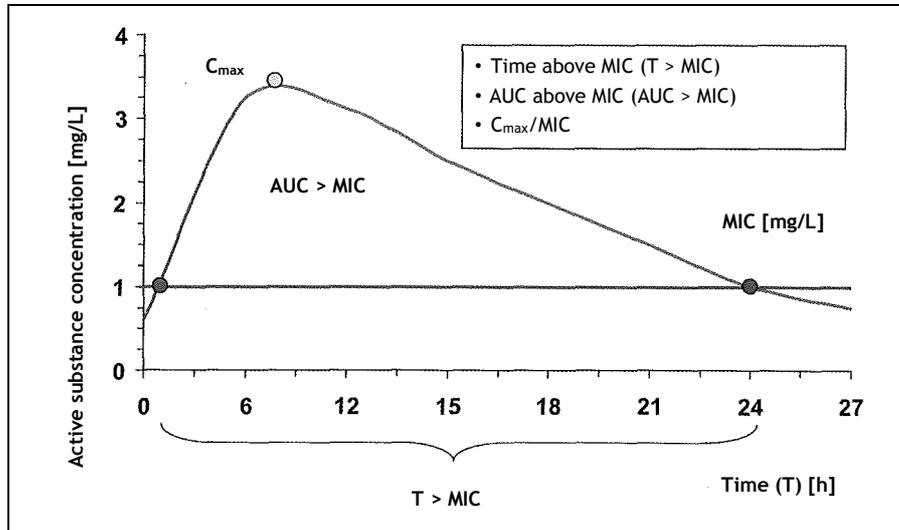
5. Pharmacokinetics

Information about the pharmacokinetics of the active substances and products is significant in assessing their efficacy. Blood/plasma levels, distribution volume as well as the active substance concentrations attained in body fluids or target organs and tissues are specific to the claimed dosage and the product.

Regarding tissue distribution, there are clear differences between the active substance groups. These differences must be taken into account when selecting an antibiotic to ensure that sufficiently high active substance levels are reached in the target tissues.

Active substances with a low apparent distribution volume ($V_d \leq 0,25$ l/kg) only pass into organs and tissues to a very limited degree, and mainly distribute into the extracellular regions. Such substances are therefore not suited to treating disorders with definite organ manifestations or for advanced, subacute-chronic infectious processes, since sufficiently high active substance levels are not reached in the tissues. Their use is primarily indicated in acute infections in the bacteraemia phase, and in septicaemically progressing infections.

Active substances with a distribution volume of $V_d > 0.25$ l/kg and ≤ 0.6 l/kg show tissue levels whose maximum equals the blood or serum concentrations. Here, tissue levels can be concluded based on blood levels. When the dosage is sufficiently high, effective tissue levels can be reached even with a $V_d < 0.6$ l/kg. In a high distribution volume ($V_d > 0.6$ l/kg), the active substances accumulate in the organs / tissues as compared to active substance levels measured in the blood or serum.



The efficacy of an antibiotic substance is determined by its pharmacokinetic (PK) and pharmacodynamic (PD) properties. The pharmacokinetic processes of absorption, distribution and metabolism of the active substance in the animal as well as excretion determine the blood level progression curve of the active substance and its concentration in the target tissues. The Minimum Inhibitory Concentration (MIC) is the key pharmacodynamic parameter. The MIC is a property which is specific to each bacterial strain, and is based on the presence and expression of non-specific and specific resistance mechanisms. The PK-PD analysis and PK-PD models place the pharmacokinetics and pharmacodynamics in relation to each other, and are an important instrument to determine the dosage schedule of an antibiotic. PK-PD calculations serve to optimise the dosage in terms of its maximum therapeutic efficacy, with simultaneously minimal selection of resistant bacteria. The PK-PD analysis utilises the indicators of $T > MIC$, AUC/MIC and C_{max}/MIC .

T>MIC states the period in which the plasma concentration of the antibiotic is higher than the MIC parameter of the bacterium, and is stated as a percentage of the dosage interval. The Plasma-AUC (Area Under the Curve) is a measure for the systemic availability of an antibiotic over time. The PK-PD analysis generally utilises the AUC of the first 24 hours after the active substance is administered (AUC₀₋₂₄). C_{max} is the maximum plasma concentration of an antibiotic.

Depending on their acting mechanism, antibiotics can be classified into time dependent (PK/PD-Index: T>MIC), concentration dependent (PK/PD-Index: C_{max}/MIC or AUC/MIC) and both time and concentration dependent (PK/PD-Index: AUC/MIC) substance classes.

Most time dependent antibiotics must be given several times daily, unless they are long-acting formulations. Concentration dependent antibiotics which have post-antibiotic effects permit comparatively longer dosage intervals. The PK/PD model can be used to adjust the dosage schedule to a changed resistance situation in the individual case. This requires a sufficient database of clinical breakpoints for important pathogens in veterinary medicine, which should be uniformly specified in accordance with internationally recognised specifications, e. g. by the CLSI (Clinical and Laboratory Standards Institute).

Summary

If various antibiotics can be used to treat a bacterial infection, the license conditions must be used to select an active substance from the active substance group in the following table which best matches the aforementioned five selection criteria.

In principle, an ideal antibiotic should possess

- a narrow acting spectrum,
- a wide therapeutic range, and
- if required, good tissue penetration.

If the microbial situation and resistance are unknown, a broad spectrum active substance will generally be required.

A bactericidally-acting antibiotic should be used for severe infections, particularly in the presence of septicaemic processes or impaired immune defences.

Members of the working group:

The third edition was written under the direction of Prof. Dr Manfred Kietzmann (Hanover) by the members of the BTK Committee for Medication and Feed Laws: Dr Ilka Emmerich (Leipzig), Dr Ulrich Bettin (Neumünster), Dr Michael Drees (Worpswede), Dr Alfred Mennekens (Legden), Dr Rainer Schneichel (Mayen), Dr Hans-Joachim Selbitz (Dessau-Roßlau), Dr Sabine Schüller (Bonn), Dr Luc Goossens (Greifswald), Dr Cornelia Ibrahim (Berlin), Dr Jürgen Sommerhäuser (Potsdam)

The second edition was written by the "Antibiotics Guidelines" working group of the Federal Veterinary Surgeons' Chamber: Prof. Dr F. R. Ungemach † (Leipzig) - Chair, Prof. Dr M. Kietzmann (Hanover) - Chair, Dr U. Buettner-Peter (Bonn), Dr T. große Beilage [sic] (Essen), Dr A. Böttner (Wiesbaden), Dr L. Goossens (Hoyerhagen), Prof. Dr A. Grabner (Berlin), Prof. Dr H. Greife (Leverkusen), Dr P. Hajek (Leipzig), Prof. Dr K. Hartmann (Munich), Dr H. P. Heckert (Berlin), Prof. Dr K. Heinritzi (Munich), R. Hensel (Bonn), Dr C. Höfer (Munich), Prof. Dr R. Hoffmann (Munich), Dr W. Klawonn (Hungenroth), Prof. Dr W. Klee (Munich), Dr K. Kluge (Bonn), Prof. Dr E. M. Krautwald-Junghans (Leipzig), Prof. Dr L. Kreienbrock (Hanover), Prof. Dr R. Kroker (Berlin), Dr W. Luft (Blaubach), Dr J. Nilz (Hohenahr), Prof. Dr I. Nolte (Hanover), Dr M. Pöppel (Delbrück-Anreppen), Dr R. Schneichel (Mayen), Dr E. Schüle (Dortmund), Dr g. Schulz (Munich), Dr C. Schwarz (Berlin), Prof. Dr S. Schwarz (Neustadt- Mariensee), Dr C. Sigge (Bonn), Dr T. Steidl (Tübingen), Prof. Dr K. H. Waldmann (Hanover), Prof. Dr L. H. Wieler (Berlin)

Table: Properties of antibiotics licensed for use in animals

Active substance groups / active substances (examples)	Spectrum	Tolerability and therapeutic range	Possible side effects	Acting type	Pharmacokinetics: Tissue penetration (V _d) PK/PD classification
Aminoglycosides/Aminocyclitoles Apramycin Gentamycin Kanamycin Neomycin Spectinomycin Streptomycin Dihydrostreptomycin	gram negative partly gram positive	low (system. use) average (oral/local application)	Neurotoxicity Ototoxicity Nephrotoxicity	bactericidal	V _d : low postantibiotic effects: concentration dependent antibiotics
Phenicole Chloramphenicol Florfenicol	gram positive + gram negative	average high		bacteriostatic Florfenicol: bactericidal effects proven for <i>Mannheimia haemolytica</i> , <i>Pasteurella multocida</i> and <i>Histophilus somni</i>	V _d : high time dependent antibiotics
β-lactams Penicillins: Aminopenicillins Ampicillin Amoxicillin Amoxicillin + clavulanic acid Benzyl penicillin Cloxacillin Oxacillin Cephalosporins: early generation: e. g. Cefacetril Cefalexin Cefazolin newer generations: e. g. Cefoperazon Ceftiofur Cefquinom Cefovecin	gram positive + gram negative gram positive + gram negative β-lactamase former gram positive + Pasteurella gram positive gram positive (+ gram negative) gram positive + gram negative + β-lactamase formers.	high	Hypersensitivity potential, esp. penicillin Cross-hypersensitivity possible between β-lactams	bactericidal	V _d : average time dependent antibiotics
Fluoroquinolones Danofloxacin Difloxacin Enrofloxacin Ibafloxacin Marbofloxacin Orbifloxacin	gram positive + gram negative + mycoplasma	high	joint damaging in young animals	bactericidal	V _d : high postantibiotic effects: concentration dependent antibiotics
Fusidinic acid	gram positive	high		bacteriostatic	V _d : high time dependent antibiotics
Lincosamide Clindamycin Lincomycin Pirlimycin	gram positive + mycoplasma	average	gastrointestinal disorders	bacteriostatic	V _d : high time-dependent antibiotics

Active substance groups / active substances (examples)	Spectrum	Tolerability and therapeutic range	Possible side effects	Acting type	Pharmacokinetics: Tissue penetration (V_d) PK/PD classification
<u>Macrolides</u> Tulathromycin- Erythromycin Spiramycin Tylosin Tilmicosin Aivlosin Gamithromycin Tildipirosin	gram positive + Pasteurella + Mycoplasma	average average (low in i.m. or i.v. injection)	local irritation possible (parenteral)	bacteriostatic	V_d : high time-dependent antibiotics
<u>Pleuromutilines</u> Tiamulin Valnemulin	gram positive + gram negative + mycoplasma	high	incompatibility with ionophores	bacteriostatic	V_d : high
<u>Polypeptide antibiotics</u> Colistin Polymixin B	gram negative (systemic use) gram positive + gram negative (local use)	low (system. use) average (oral/local application)	local irritation possible Neurotoxicity	bactericidal	V_d : low concentration dependent antibiotics
<u>Sulphonamides</u> Sulfadiazin Sulfadoxin Sulfadimidine and others Combination with Trimethoprim	gram positive + gram negative	average	potentially nephrotoxic Risk of shock in i.v. use	bacteriostatic bactericidal	V_d : average time dependent antibiotics
<u>Tetracyclines</u> Tetracycline Chlortetracycline Oxytetracycline Doxycycline	gram positive + gram negative + mycoplasma + Chlamydia	average	local irritation possible (parenteral)	bacteriostatic	V_d : high time and concentration dependent antibiotics

Therapeutic range: Classification into high (> 3) - average ($\leq 3 - > 2$) - low (< 2)

Acting spectrum: gram negative = including gram negative staff cells

Pharmacokinetics: Classification in accordance with the "apparent" distribution volume V_d [l/kg]

low	$V_d < 0.25$	no/low tissue distribution
average	$V_d < 0.6$	Tissue levels max. as in blood or serum levels, good
high	$V_d \geq 0.6$	tissue penetration with accumulation

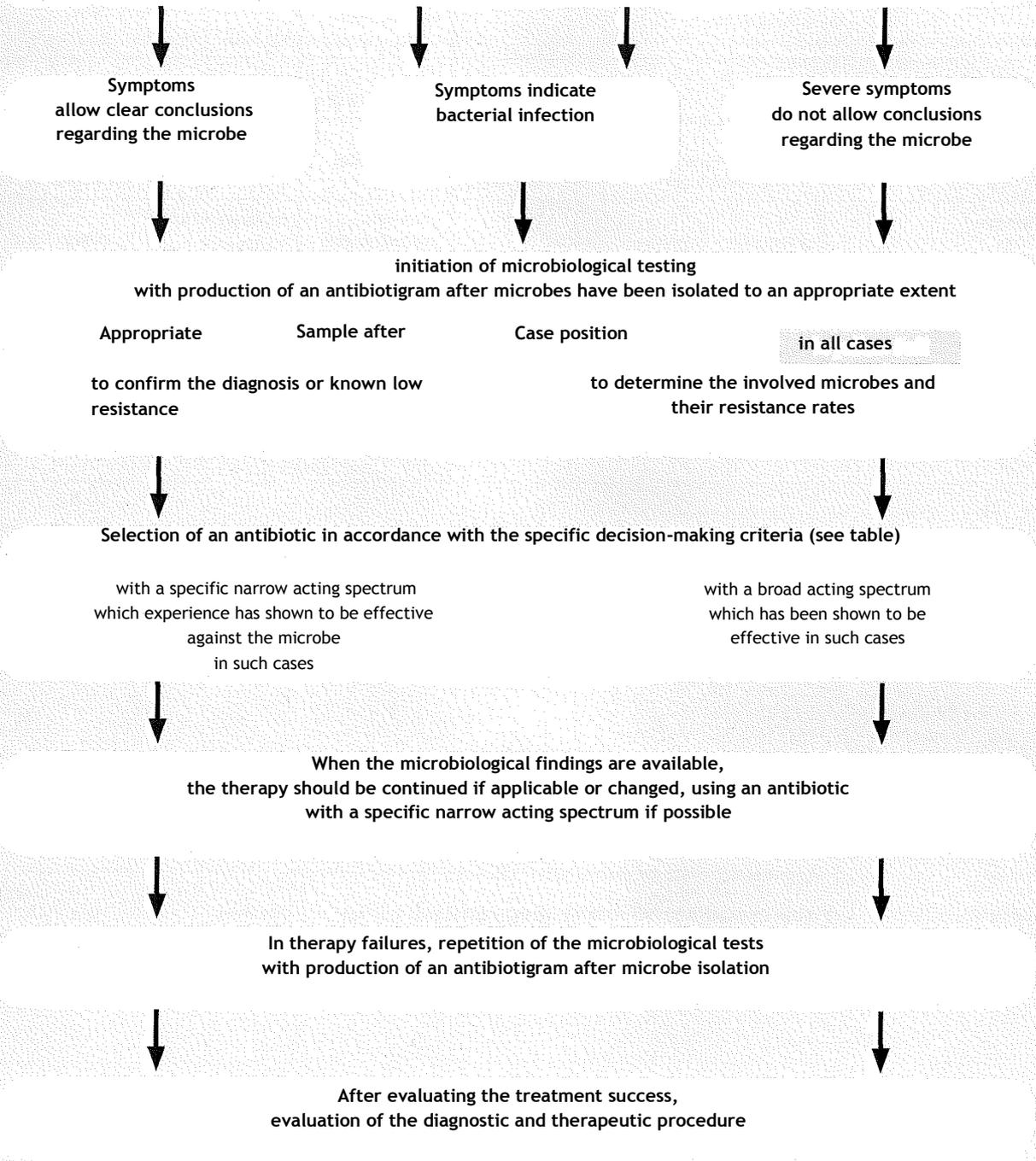
Good veterinary medical practice in therapy of bacterial infectious diseases

Veterinary expertise

(expert knowledge, clinical experience, use of laboratory diagnostic options, continued education)

Disease diagnosis

„Precise examination constitutes the basis of veterinary action“ (Götze)



Animal species specific additions

Fish

1. General section

Treating fish raised for food or feed as well as ornamental fish requires profound specialised knowledge in aquaculture and aquaristics.

When administering medications, group and population treatments are the primary methods. Antibiotics should be applied via the feed insofar as possible. In individual cases, bath treatments are also performed, e.g. in young fish. To avoid carrying active substances into the environment, such treatments should take place only in containers with the least possible volume. Due to the low number of veterinary medications licensed for fish, it is generally necessary to use off-label medications licensed for other animal species. It is necessary to observe a withdrawal period of 500 degree days.

Population management plays a significant role to avoid infectious diseases and thereby, to reduce the quantity of antibiotics which are used. This includes largely optimising living conditions (e. g. water quality, feeding regimen) and a sensible vaccination strategy.

The use of antibiotics requires a careful examination of individual animals or the group. Group-specific factors, which are obtained during regular visits by the veterinarian who is treating the group, are also important. Care must be taken to ensure the precise implementation of the veterinarian's treatment instructions by the livestock owner.

In-vitro sensitivity testing for bacterial microbes in fish differs from sensitivity testing of bacterial microbes in other animal species. It is necessary to comply with the implementation regulations which are recognised for this purpose. In particular, care must be taken to comply with the reference temperatures which apply to the relevant fish species.

If no definitive aetiological diagnosis can be determined, the antibiotics which are used can be selected based on population-specific experience if corresponding knowledge about the health status of the population and results of previous antibiotigrams is available. We refer to:

Internet pharmacokinetics database for fish

Database of the U.S. Food and Drug Administration,
Phish-Pharm Listing at: www.fda.gov/AnimalVeterinary/Science-Research/ToolsResources/Phish-Pharm/default.htm
(Link: Phish-Pharm Database on the lower third of the page)

We point out the need for strictly determining an indication due to the special significance of so called "antibiotic reserve products". Also see the antibiotic guidelines no. 4, third dash.

Antibiotic combinations must be restrictively handled, and the need for them must be proven in the individual case. In this regard, we refer to the antibiotic guidelines, no. 3, third dash and no. 4, last dash.

2. Specialised section:

For oral medication, it is necessary to comply with the guideline of the Federal Ministry of Food and Agriculture (BMELV) working group of 19 6. 2009 "Oral administration of veterinary drugs in the livestock sector via feed or drinking water" (addendum to the German Veterinary Gazette 4/2010).

Aside from therapeutic use in clinically ill animals, metaphylactic use in animals which are regarded as infected but show no clinical symptoms is a primary method. In this regard, we refer to the antibiotic guidelines, no. 3, second dash:

"Detection of microbes and an antibiotigram after microbes are isolated are fundamentally necessary at regular intervals for repeated or long-term use in animal groups."

Explanation: Repeated use of antibiotics in an animal herd - e. g. in specific age and production segments or when restocking fish - must be fundamentally verified by regularly checking the resistance situation, noting the conditions to be met for microbes which are pathogenic in fish (see above). Microbiological diagnostics are not needed for every treatment. The appropriate scope of such tests can be determined based on the individual case.

By minimising factors which favour disease, veterinarians can contribute to avoiding repeated and long-term use of antibiotics. This also includes an appropriate vaccination regimen (e. g. against furunculosis and Enteric Redmouth Disease).

The documents named in the references can be found at www.bundestieraerztekammer.de and www.vetidata.de

Animal species specific additions

Poultry

1. General section

When administering medications, group and flock treatments are the primary methods, especially in poultry husbandry. Flock management plays a significant role to avoid infectious diseases and thereby, to reduce the quantity of antibiotics which are used. This includes largely optimising living conditions (e. g. barn climate, feeding regimen) and a sensible vaccination strategy.

Avoiding infections within a poultry group and between poultry groups which are kept separately, as well as avoiding the introduction or spread of microbes via living and non-living vectors, are important factors in keeping flocks healthy.

The use of antibiotics requires a careful examination of individual animals or the flock. Monocausal disorders play a subordinate role in poultry. This results in specific requirements for the diagnostics, selection of antibacterial acting substances, and design of the therapy plan.

Flock-specific and epidemiological factors, which are obtained during regular visits by the veterinarian who is treating the flock, are also significant. Care must be taken to ensure the precise implementation of the veterinarian's treatment instructions by the livestock owner.

Regarding flock examinations, we refer to:

- Federal association of practising veterinarians (bpt) guidelines for the implementation of veterinary flock care in poultry flocks
- Zrenner/Paintner/Bert: Medicinal product regulations for veterinarians and current regulations from other legal fields, herein: BTK sample contracts on care of animal herds

If no definitive aetiological diagnosis can be determined, the antibiotics which are used can be selected based on flock-specific experience if corresponding knowledge about the health status of the flock and results of previous antibiotigrams is available.

We point out the need for strictly determining an indication due to the special significance of so called "antibiotic reserve products". Also see the antibiotic guidelines no. 4, third dash.

Antibiotic combinations must be restrictively handled, and the need for them must be proven in the individual case. We refer to the antibiotic guidelines no. 3 sentence 3, third dash and no. 4, last dash in this regard.

Many poultry species are among the "minor species" for which only a few licensed veterinary medications are available in Germany, so that many veterinary medications can only be applied by means of the cascade (see the special section).

2. Specialised section:

Specific recommendations for infectious diseases in poultry

The vast majority of treatments for bacterial infectious disorders with antibiotics take place orally via the drinking water.

The goal of therapy is to administer a therapeutically effective dosage to each animal. When treating animals, the water intake must therefore be checked daily to ensure that the animals receive the intended dosage.

We refer to:

- Guideline of the Federal Ministry of Food and Agriculture (BMELV) working group of 19/06/2009 "Oral administration of veterinary drugs in the livestock sector via feed or drinking water" (addendum to the German Veterinary Gazette 4/2010)
- „Recommendations on sample collection for bacteriological diagnostics in pigs, cattle and poultry" of the working group on "Antibiotic Resistance" of the DVG (German Veterinary Gazette 5/2008 P. 596-609).
- Richter, A. et al. (2009): Verabreichung von Antibiotika in Geflügelbeständen. [Administration of antibiotics in poultry flocks.] Tierärztliche Praxis [Veterinary Medical Practice] (G). 37, 321-329

Regarding the antibiotic guidelines no. 3, sentence 3:

There are currently no recognised, standardised examination procedures and evaluation criteria for some of the relevant microbes in poultry. This must be taken into account when deciding to perform an antibiotigram. In this regard, we refer to the antibiotic guidelines, no. 7, second dash.

Aside from therapeutic use in clinically ill animals, metaphylactic use in animals which are regarded as infected but show no clinical symptoms is a primary method. In this regard, we refer to the antibiotic guidelines, no. 3 sentence 3, second dash: "Detection of microbes and an antibiotigram after microbes are isolated are fundamentally necessary: - at regular intervals for repeated or long-term use in animal groups."

Explanation: Repeated use of antibiotics in an animal - e. g. in specific age and production segments or when they are moved into barns - must be fundamentally verified by regularly checking the resistance situation. Microbiological diagnostics are not needed for every treatment. The appropriate scope of such tests can be determined based on the individual case."

Since many veterinary medications, particularly in "minor species", can only be used off-label, this results in barely solvable problems in determining the withdrawal period if a very short lifespan is not compatible with the applicable minimum withdrawal period. This may render clinically feasible treatment impossible, e. g. in broiler chickens and waterfowl. One should aim at a solution which meets the needs of animal protection and economy as long as no licensed products are available for these animal species.

The documents named in the references can be found at www.bundestieraerztekammer.de and www.vetidata.de

Animal species specific additions

Small animals (dogs, cats)

1. General section:

Successful, responsible antibiotic therapy also includes the veterinarian's duty to avoid bacterial resistance. Within this context, the particularly close contact between humans and small animals must be taken into account.

The use of antibiotics requires a careful examination of the individual animal. Care must be taken to ensure the precise implementation of the veterinarian's treatment instructions by the animal owner.

If no definitive aetiological diagnosis can be determined, the initial selection of antibiotics to be used can take place based on clinical experience if the animal's health status necessitates their use and there is a well founded suspicion that it is a bacterial disease (also see the guidelines no. 4, fourth dash).

We point out the need for strictly determining an indication due to the special significance of so called "antibiotic reserve products". Also see the antibiotic guidelines no. 4, third dash.

Antibiotic combinations must be restrictively handled, and the need for them must be verified in the individual case. In this regard, we refer to the antibiotic guidelines, no. 3, third dash and no. 4, last dash.

It must be specifically verified for every organ system whether other treatment measures may be suitable for minimising the use of antibiotics.

It may be necessary to apply human medications in small animal medicine in individual cases. Herein, it is necessary to comply with medicinal products regulations.

2. Specialised section:

2.1 Respiratory tract infections

Most respiratory tract infections are not primarily bacterial. Secondary bacterial pneumonia is more common. It must therefore be verified whether therapy with an antibiotic is necessary. In chronic or therapy resistant disorders, further diagnostics (e. g. bronchoalveolar lavage (BAL) with subsequent cytological and bacteriological testing) are needed.

2.2 Gastrointestinal tract infections

Primary bacterial infections of the gastrointestinal tract are very rare. Non-specific use of antibiotics is not indicated in diarrhoea disorders.

2.3 Urogenital tract infections

Bacterial infections of the lower urinary tract are common in dogs, but rare in cats. The clinical testing must include a urine test to obtain indicators of bacterial infection.

Chronic, therapy resistant or recurring bacterial diseases mandatorily require further clinical (e. g. ultrasound) and bacteriological tests. Urine samples must be collected by means of cystocentesis. The pH of the urine influences antimicrobial activity. This must be considered when planning the therapy.

If the prostate or uterus is involved, the tissue penetrability of the antibiotic must be taken into account aside from other measures (hormonal, surgical).

2.4 Infections of the central nervous system

Bacterial CNS infections are very rare. An aetiological diagnosis should be attempted (e. g. cerebrospinal fluid puncture). It is necessary to ensure that the selected antibiotic will obtain sufficient concentrations in the target tissues (blood-brain barrier).

2.5 Skin infections

Only in deep pyodermy, pathogenic microbes can be confirmed by collecting a sample under sterile conditions (pustule contents). Systemic therapy is preferable to the topical application of antibiotics. For instance, antiseptics are suitable for topical use. Long treatment times which may amount to several weeks are often necessary. The success of the therapy should be confirmed with clinical and cytological skin tests. In chronic, therapy resistant skin disorders (e. g. otitis - often a mixed infection with the involvement of yeasts, lip eczema, intertrigo), specific diagnostic and therapeutic measures (e. g. ventilating the auditory canal, plastic surgery) must be taken into account. In particular, whether the eardrum is intact must be verified prior to the topical application of ototoxic substances into the ear.

2.6 Systemic infections

When the involvement of intracellular microbes is suspected or confirmed (e. g. *Ehrlichia*, *Chlamydomphila felis*), it must be ensured that the utilised antibiotic accumulates within cells.

Specific infectious diseases (e. g. leptospirosis, tetanus, Ehrlichiosis) are treated with antibiotics without routinely performing a resistance test. If sepsis is present, bactericidal antibiotics must be applied in correspondingly high dosages and at optimal therapy intervals; microbial sensitivity is verified using blood cultures.

2.7 Side effects, interactions, contraindications and multi-resistant microbes

In chronic and therapy resistant infections, it is always necessary to test for the presence of multi-resistant microbes (e. g. methicillin resistant *Staphylococcus pseudintermedius* (MRSP), methicillin resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii*, *E. coli*) and apply corresponding additional hygiene measures (e. g. hand disinfection, hygiene management). An extensive antibiotigram must be initiated for these multi-resistant microbes. The tolerability of antibiotics should be considered and monitored, particularly in longer-term use.

Animal species specific additions

Horses

1. General section:

When using antibiotics in horses, it must fundamentally be taken into account from a medicinal products law perspective that horses are deemed to constitute animals raised for food purposes, unless the horse has been permanently excluded from the food chain. When making a declaration in the horse passport that the horse is not intended for food production, the veterinarian has informational duties regarding the legal consequences. Aside from the therapeutic intention of the use of antibiotics, it is the veterinarian's responsibility to keep the development of bacterial resistance as low as possible on the one hand, and on the other hand ensure that safe foods are obtained in the sense of consumer protection. Apart from this, most horses in leisure or sports are in especially close contact with humans, which is an additional reason for careful use of antibiotics in horses in view of the resistance problem.

It must also be taken into account that horses, which ferment their feed in the caecum, are fundamentally sensitive to the gastrointestinal side effects of antibiotics.

The use of antibiotics in foals should take place with specific dosage regimens based on the pharmaceutical manufacturer's specifications, due to the juvenile organism. The behaviour (temperament) of the horse and appropriate injection volumes must also be taken into account when selecting antibiotics and in deciding the application mode.

The use of antibiotics presumes a careful examination of individual animals or the herd. Herd-specific factors, which are obtained during regular visits by the veterinarian who is treating the herd, are also significant. If no definitive aetiological diagnosis can be determined, the antibiotics which are used can be selected based on herd-specific experience if corresponding knowledge about the health status of the herd and results of previous antibiotigrams is available.

We point out the need for strictly determining an indication due to the special significance of so called "antibiotic reserve products". Also see the antibiotic guidelines no. 4, third dash.

Antibiotic combinations must be restrictively handled, and the need for them must be proven in the individual case. We refer to the antibiotic guidelines no. 3 sentence 3, third dash and no. 4, last dash in this regard.

Antibiotic preventive treatment is only indicated perioperatively (in long and complicated interventions). It does not replace good surgical practice. Routine antibacterial treatment of newborn foals does not make sense (see the antibiotic guidelines, no. 1).

By minimising factors which favour disease, veterinarians can contribute to avoiding repeated and long-term use of antibiotics. This also includes an appropriate vaccination regimen.

2. Specialised section:

2.1 Respiratory tract infections

Respiratory tract diseases are often treated in horses. Most respiratory tract infections are viral. Secondary bacterial pneumonia are very rare. It must therefore be thoroughly clarified whether therapy with an antibiotic is necessary. Microbes which are more common in bacterial infections include β -haemolysing *streptococci*, *Pasteurella spp.* and intracellular living bacteria (*Rhodococcus equi*). Diagnostic techniques permit the safe collection of sample material, which can then be used to cultivate and generate an antibiotigram. Aside from blood count and fibrinogen tests, this includes the collection of tracheobronchial secretions (TBS) with endoscopic monitoring, as well as bronchoalveolar lavage (BAL).

Therapy with a broad spectrum antibiotic which is based solely on a clinically suspected diagnosis must be avoided. A therapy duration of up to twelve weeks may be necessary to treat rhodococcosis in foals.

Strangles: Antibiotic treatment of strangles requires a specific course of action. Even with a feverish progression, antibiotic treatment only makes sense after the retropharyngeal and mandibular abscesses have been completely opened.

Adequate stable management is very important for recovery. Stress during the illness delays recovery. In bacterial infections of the lower respiratory tract, the animal should rest in the stable for approx. three weeks. Inhalative application of antibiotics is to be rejected based on current knowledge.

2.2 Gastrointestinal tract infections

An imbalance of the intestinal flora due to becoming overgrown with pathogenic microbes is a main gastrointestinal problem which may lead to colitis, and must be treated. Colitis can also be a consequence of antibiotic treatment (e. g. macrolides and tetracyclines).

Infections by clostridia and salmonella require treatment. Clostridia induced colitis can be treated with metronidazole in horses not intended for use in food production. The administration of "broad spectrum antibiotics" is contraindicated.

2.3 Infections of the muscular and skeletal system

The difficulty in infections of the muscular and skeletal system consists of obtaining sufficiently high active levels, particularly in the bones, tendons and joints. No licensed antibiotic formulations are currently available for local application (intra-articular, intra-ossary).

Antibiotic therapy is particularly indicated in the case of septic arthritis. This requires immediate treatment; nonetheless, a sample should be collected for bacteriological diagnostics prior to initiating therapy. Antibiotic treatment is initially provided based on the clinical diagnosis and the veterinarian's experience. Local application is described in the literature. However, there are currently no licensed medications in Germany for this purpose. Therapy should be continued for at least 14 days. The generation of an antibiotigram using synovial fluids generally takes a week; however the results are unsatisfactory in the individual case, since the sample often shows only few bacteria, even though contamination has occurred.

A gram tint of the synovial fluids is well suited for obtaining an initial overview of possibly involved bacteria.

2.4 Urogenital tract infections

Urogenital tract infections are less common than in other animal species. Cystitis often plays a role. Therapy should initially last seven to ten days. Therapy success should then be confirmed by microbiological testing of a urine sample collected with a catheter, since there is often a risk of recurrence. When selecting an antibiotic, care must be taken to ensure good accumulation in the urogenital tract. The pH of the urine influences antimicrobial activity. If pyelonephritis is present, therapy should be applied for at least two weeks.

2.5 Infections of the central nervous system

Bacterial CNS infections are very rare. When applying antibiotics, care must be taken to ensure that they pass into the cerebrospinal fluids.

2.6 Skin infections

Differentiating pathogenic microbes from the normal flora is a problem in skin infections. Pathogenic microbes must be confirmed by collecting a sample biopsy under sterile conditions. Systemic therapy is preferable to the topical application of antibiotics. Antiseptics can be topically applied as an additional measure. In superficial infections, therapy should last for at least 7-10 days, and should not be interrupted after the symptoms initially subside. In deep infections, therapy should last for at least 14-21 days.

When treating wound infections, antibiotics should only be applied systemically. Additional local use of antiseptics may be indicated.

2.7 Side effects, interactions and contraindications

Dysbacteria triggered by antibiotics represents a special problem in horses. Therefore, for instance, antibiotics from the macrolide group should not be used in horses, since horses may react with severe gastrointestinal disorders (dysbacteria).

Animal species specific additions

Pigs

1. General section

When administering medication, group and herd treatments are the primary methods for treating pigs. Aside from this, there are also treatments for individual animals - usually by injection. Herd management plays a significant role to avoid infectious diseases and thereby, to reduce the quantity of antibiotics which are used. This includes largely optimising living conditions (e. g. barn climate, feeding regimen) and a sensible vaccination strategy.

Avoiding infections within an animal group and between animal groups which are kept separately, as well as avoiding the introduction or spread of microbes via living and non-living vectors, are important factors in keeping herds healthy.

The use of antibiotics requires a careful examination of individual animals or the herd. Herd-specific factors, which are obtained during regular visits by the veterinarian who is treating the herd, are also significant. Care must be taken to ensure the precise implementation of the veterinarian's treatment instructions by the livestock owner.

Regarding herd examinations, we refer to:

- Federal Association of Practising Veterinarians (bpt) guidelines for the implementation of veterinary herd care in pig herds,
- Zrenner/Paintner/Bert: Medicinal product regulations for veterinarians and current regulations from other legal fields, herein: BTK sample contracts on care of animal herds,
- Federal Association of Practising Veterinarians (bpt) sample contracts on care for farms which are members of the QS Qualität und Sicherheit GmbH.

If no definitive aetiological diagnosis can be determined, the antibiotics which are used can be selected based on herd-specific experience if corresponding knowledge about the health status of the herd and results of previous antibiotigrams is available.

We point out the need for strictly determining an indication due to the special significance of so called "antibiotic reserve products". Also see the antibiotic guidelines no. 4, third dash.

Antibiotic combinations must be restrictively handled, and the need for them must be proven in the individual case. We refer to the antibiotic guidelines no. 3 sentence 3, third dash and no. 4, last dash in this regard.

2. Specialised section:

The vast majority of treatments for infectious disorders with antibiotics take place orally via feed or drinking water.

The goal of therapy is to administer a therapeutically effective dosage to each animal. When treating animals, it must therefore be ensured that each individual animal receives the intended dosage. Animals which do not ingest the required daily dose due to insufficient feed or water intake require additional individual treatment.

We refer to:

- Guideline of the Federal Ministry of Food and Agriculture (BMELV) working group of 19.6.2009 "Oral administration of veterinary drugs in the livestock sector via feed or drinking water" (addendum to the German Veterinary Gazette 4/2010),
- "Recommendations on sample collection for bacteriological diagnostics in pigs, cattle and poultry" of the working group on "Antibiotic Resistance" of the DVG (German Veterinary Gazette 5/2008 P. 596-609).

Aside from therapeutic use in clinically ill animals, metaphylactic use in animals which are regarded as infected but show no clinical symptoms (e. g. in specific age and production segments or when they are moved into barns) is a focal point. In this regard, we refer to the antibiotic guidelines, no. 3 sentence 3, second dash:

"Detection of microbes and an antibiotigram after microbes are isolated are fundamentally necessary:

- at regular intervals for repeated or long-term use in animal groups."

Explanation: Repeated use of antibiotics in an animal herd - e. g. in specific age and production segments or when they are moved into barns - must be fundamentally verified by regularly checking the resistance situation. Microbiological diagnostics are not needed for every treatment. The appropriate scope of such tests can be determined based on the individual case."

By minimising factors which favour disease, veterinarians can contribute to avoiding repeated and long-term use of antibiotics. This also includes an appropriate vaccination regimen.

The documents named in the references can be found at www.bundestierärztekammer.de and www.vetidata.de

Animal species specific additions

Ruminants

1. General section

When administering medications, there are treatments for individual animals - usually by injection or as local treatments (e. g. udder or uterus) - as well as group and herd treatments (e. g. calves and lambs). Herd management plays a significant role to avoid infectious diseases and thereby, to reduce the quantity of antibiotics which are used. This includes largely optimising living conditions (e. g. barn climate, feeding regimen) and a sensible vaccination strategy. The oral use of antibiotics is generally contraindicated in adult cattle and small ruminants.

Only few licensed veterinary medications are available for small ruminants in Germany, so that many veterinary medications can only be used under the cascade (particularly for goats and fallow deer).

Avoiding infections within an animal group and between animal groups which are kept separately, as well as avoiding the introduction or spread of microbes via living and non-living vectors, are important factors in keeping herds healthy.

The use of antibiotics requires a careful examination of individual animals or the herd. Herd-specific factors, which are obtained during regular visits by the veterinarian who is treating the herd, are also significant. Care must be taken to ensure the precise implementation of the veterinarian's treatment instructions by the livestock owner.

Regarding herd examinations, we refer to:

- Federal Association of Practising Veterinarians (bpt) guidelines for carrying out veterinary herd care in cattle or small ruminant herds,
- Zrenner/Paintner/Bert: Medicinal product regulations for veterinarians and current regulations from other legal fields, herein: BTK sample contracts on care of animal herds,
- Federal Association of Practising Veterinarians (bpt) sample contracts on care for farms which are members of the QS Qualität und Sicherheit GmbH.

If no definitive aetiological diagnosis can be determined, the antibiotics which are used can be selected based on herd-specific experience if corresponding knowledge about the health status of the herd and results of previous antibiotigrams is available.

We point out the need for strictly determining an indication due to the special significance of so called "antibiotic reserve products". Also see the antibiotic guidelines no. 4, third dash.

Antibiotic combinations must be restrictively handled, and the need for them must be proven in the individual case. We refer to the antibiotic guidelines no. 3 sentence 3, third dash and no. 4, last dash in this regard.

2. Specialised section:

The goal of therapy is to administer a therapeutically effective dosage to each animal requiring treatment. Animals which do not ingest the required daily dose due to insufficient feed or water intake require additional individual treatment. This is common in small ruminants.

We refer to:

- Guideline of the Federal Ministry of Food and Agriculture (BMELV) working group of 19.6.2009 "Oral administration of veterinary drugs in the livestock sector via feed or drinking water" (addendum to the German Veterinary Gazette 4/2010),
- "Recommendations on sample collection for bacteriological diagnostics in pigs, cattle and poultry" of the working group on "Antibiotic Resistance" of the DVG (German Veterinary Gazette 5/2008 P. 596-609).

Aside from therapeutic application in clinically ill animals, metaphylactic use in animals which must be regarded as infected but do not yet show clinical symptoms applies in cattle. In this regard, we refer to the antibiotic guidelines, no. 3 sentence 3, second dash:

"Detection of microbes and an antibiotigram after microbes are isolated are fundamentally necessary at regular intervals for repeated or long-term use in animal groups."

For instance, repeated use of antibiotics in an animal herd - e. g. in specific age (e. g. when animals are moved into barns) and production segments (e. g. mastitis as a herd problem) must be verified by regularly checking the resistance situation.

By minimising factors which favour disease, veterinarians can contribute to avoiding repeated and long-term use of antibiotics. This also includes an appropriate vaccination regimen.

The documents named in the references can be found at www.bundestieraerztekammer.de and www.vetidata.de

2.1 Respiratory tract infections

Since immediate treatment is generally required when infectious respiratory tract disorders appear, this is provided on the basis of definite clinical symptoms (e. g. dyspnoea and fever) and the veterinarian's experience. Here, moving animals of different origins into barns (calves) is a particularly critical phase. It is difficult to collect sample materials for bacteriological testing. Suitable methods include bronchoalveolar lavage (BAL) or examinations (pathological, microbiological) of dead stock. Bacteriological test results from dead stock must be assessed with caution, since the animals were most likely previously treated and the microbes responsible for the underlying disorder are no longer present. They are often unsatisfactory as it is often difficult to interpret test results.

2.2 Gastrointestinal tract infections

Uncomplicated calf diarrhoea is not an indication for the use of antibiotics. On the other hand, such use is indicated if there are signs of a lack of passive immunity and if general well-being is definitely disturbed.

Immediate antibiotic therapy is required in necrobacillosis of fallow deer, which can occur as a herd problem, and in diarrhoea in lambs which is most likely triggered by clostridia and *E. coli*, since these can result in high mortality rates.

2.3 Infections of the claws

In the case of foot rot (panaritium), systemic treatment with antibiotics is indicated. Local treatment is generally applied for digital dermatitis.

Local antibiotic treatment is often insufficient for foot rot. This requires parenteral treatment. Attempting to detect microbes is difficult and of questionable value.

2.4 Metritis

The indication for systemic or local use of antibiotics applies if there are corresponding clinical symptoms and fever. In small ruminants, this applies only in the event that miscarriages occur due to an infection, e. g. caused by *chlamydia*, *salmonella* or *coxiella* (Q-fever).

2.5 Mastitis

Antibiotics are locally or systemically applied when treating mastitis in dairy animals. It is recommended to dry up cattle with antibiotic protection when there is a milk somatic cell count of more than 200,000 cells and in problem operations. We refer to:

- Ehinger, A.M., Kietzmann, M. (1998): Pharmakokinetische Aspekte der Mastitistherapie. Berl. Münch. Tierärztl. Wschr. 111, 337- 343

2.6 Zoonoses

The use of antibiotics against secondary infections is indicated in the severe form of orf.

Using antibiotics in animals which have latent infections of *coxiella burnetti* or show positive serology results does not make sense. One should work towards preventive measures and vaccination.

In terms of listeriosis, there is an urgent need for action in small ruminants. If a clinical examination result in suspicion, antibiotic treatment as an immediate measure and intensive advice are mandatory.

No vaccines are currently (July 2010) available for the three stated zoonoses. The use of antibiotics can only be regarded as an emergency solution, but is currently the treatment of choice.

schlütersche
Verlagsgesellschaft mbH & Co. KG

Business field Summary of Product Characteristics
Postal address: 30130 Hanover • Hans-Böckler-Allee 7 • 30173 Hanover
Telephone 0511 8550-2422 • Fax 0511 8550-2405
vertrieb@schluetersche.de • www.schluetersche.de