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# Antimicrobial Prescribing Guidelines for Veterinary Practitioners

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UCD DUBLIN

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These guidelines were developed jointly by the Veterinary College, University College Dublin and the Department of Agriculture, Food and the Marine

## Acknowledgement

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## Foreword

Ireland's second One Health National Action Plan on Antimicrobial Resistance 2021 – 2025, (iNAP2), was published in October 2021. The development of these antimicrobial prescribing guidelines for veterinary practitioners aligns with strategic objective number four of iNAP2, which aims to optimise the use of antibiotics in human and animal health.

These guidelines have been developed by the academic staff in the veterinary teaching hospital at University College Dublin (UCD) in collaboration with the Department of Agriculture, Food and the Marine. I wish to acknowledge the time and effort of all involved and thank them for their efforts in producing this thorough and accessible document which will be a useful resource for veterinary practitioners into the future.

Antimicrobial resistance or AMR is a global One Health threat and an urgent challenge. It poses a significant risk to human health first and foremost, but also to animal health and welfare and our shared environment. The Department of Health (DOH) and the Department of Agriculture, Food and the Marine (DAFM) with support from the Environmental Protection Agency continue to adopt a 'One Health' approach to AMR, which encourages multidisciplinary collaborative efforts across the different sectors in order to achieve the best health outcomes for people, animals and the environment.

As part of the European response, in 2018, the EU Commission published the 'Farm to Fork' strategy. As part of this strategy, the EU undertook to reduce the quantities of antimicrobials sold for use in European food producing animals by 50% between 2018-2030. This is an ambitious target but thanks to the considerable efforts of veterinary practitioners and animal owners there has been a reduction of approximately 26% in sales of antimicrobials in Ireland since 2018.

Disease prevention remains a key role for veterinary practitioners and in this context an increased focus on biosecurity and vaccination practices have supported the reduction in use of antimicrobials in animals. Prudent use remains a key focus to maintain the effectiveness of the current suite of antimicrobials available in veterinary medicine. These guidelines will serve to inform practitioners with regard to best practice in terms of disease treatment options based on current scientific evidence and as a reference tool to inform responsible prescribing practices.

Dr June Fanning
Chief Veterinary Officer
14th January 2025

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## Definitions

The following terms are used throughout this document and are understood to have the following specific meanings.

| Terminology | Definition |
|---|---|
| **Antimicrobial** | Refers to any substance with a direct action on micro-organisms used for treatment or prevention of infections or infectious diseases, including antibiotics, antivirals, antifungals and anti-protozoals. Antibiotics are one type of antimicrobial that kill or inhibit the growth of bacteria. The term is sometimes used interchangeably with antimicrobial but strictly defined, antibiotic refers only to naturally produced agents and does not include synthetic compounds. Antimicrobial will be used in this document. |
| **Antimicrobial Resistance (AMR)** | Refers to a microorganism's ability to grow and reproduce or to survive exposure to an antimicrobial. AMR occurs when an antimicrobial that was previously effective is no longer effective to treat an infection or disease caused by a microorganism. AMR is exacerbated by human factors such as inappropriate use of antimicrobials in human and veterinary medicine, poor hygiene conditions and practices in healthcare settings or in the food chain facilitating the transmission of resistant microorganisms. Over time, this makes antimicrobials less effective and ultimately useless. |
| **Antimicrobial stewardship** | Refers to coordinated interventions designed to promote the optimal use of antimicrobial agents, including the decision to use them, drug choice, dosing, route, and duration of administration. |
| **Antimicrobial Susceptibility Testing (AST)** | Refers to microbiological laboratory techniques that allow a disease-causing microorganism to be identified, and that determine which antimicrobials the identified microorganism is susceptible to in vitro (which antimicrobials are effective against the microorganism). |
| **Companion animal** | Includes a domestic dog, cat, rabbit (other than a rabbit kept for human consumption), a small rodent, cage bird, homing pigeon, terrarium animal and an aquarium fish or an equid declared as not intended for use as food for human consumption. |
| **Food producing animal** | An animal of the bovine, caprine, ovine or porcine species, poultry, rabbits, deer, fish or honeybees, if such rabbits, deer or fish are intended for use as food for human consumption, or equidae intended for use as food for human consumption. |
| **Highest Priority Critically Important Antimicrobials** | Are antimicrobials of last resort for treatment of human and animal infection when the first line antimicrobials fail to work. |

| | |
|---|---|
| **Metaphylaxis** | Metaphylaxis means the administration of a medicinal product to a group of animals after a diagnosis of clinical disease in part of the group has been established, with the aim of treating the clinically sick animals and controlling the spread of the disease to animals in close contact and at risk and which may already be subclinically infected; The administration of antimicrobials for metaphylaxis is heavily restricted under Article 107(4) of EU 2019/6. |
| **"Off label"** | Use of a medicine outside the terms of the marketing authorisation as specified on the product documentation and summary of product characteristic (SPC) datasheets. |
| **Pharmacovigilance** | The science and activities relating to the detection, assessment, understanding and prevention of suspected adverse events or any other problem related to a medicinal product. |
| **Prophylaxis'** | Prophylaxis' means the administration of a medicinal product to an animal or group of animals before clinical signs of a disease, in order to prevent the occurrence of disease or infection; In accordance with Article 107(3) of 2019/6; Antimicrobial medicinal products shall not be used for prophylaxis other than in exceptional cases, for the administration to an individual animal or a restricted number of animals when the risk of an infection or of an infectious disease is very high and the consequences are likely to be severe. In such cases, the use of antibiotic medicinal products for prophylaxis shall be limited to the administration to an individual animal only, under the conditions laid down in the first subparagraph |
| **Veterinary prescription** | An electronic or physical document issued by a registered veterinary practitioner in respect of an animal under his or her care that provides for the administration of veterinary medicine to the animal. |
| | |

# 1. Introduction

The UCD Veterinary Hospital is a referral hospital with first opinion cases seen through the equine, farm and companion animal field services. Many of the animals referred to the hospital have already received antimicrobial (AM) treatment; in a 2021 study, 44% of dogs and 50% of cats had received antimicrobials prior to presentation at UCD. Thus, there is a higher risk than in first opinion practice that infections in these animals may be resistant. These guidelines have been developed to always ensure prudent use of antimicrobials in UCDVH to optimize treatment of the animals under our care and to ensure our residents, interns and undergraduate students receive the best possible training in antimicrobial stewardship.

Antimicrobial stewardship is only one element in combatting antimicrobial resistance (AMR) in a veterinary hospital setting, with good hygiene and infection control practices also playing a major part (see UCDVH Infection Control Manual).

The UCDVH is also required to abide by the provisions of EU Regulation 2019/6, which imposes restrictions on antimicrobial use in animals. Individual clinicians/clinical teams must be able to assess all the relevant factors and then design a treatment plan that is tailored to the specific circumstances and features of the case in question. Therefore, these guidelines are intended neither to be proscriptive nor prescriptive; they are intended to provide support and guidance for UCD veterinary clinicians, residents, interns and students based on the current best available evidence. More detailed guidelines giving the preferred antimicrobial choices for each disease are available for each discipline area (Small Animal Medicine and Surgery, Equine and Farm Animal).

## 1.1 Legislative and professional context of guidelines

These guidelines are informed by:

- EU Regulation 2019/6 on Veterinary Medicinal Products, which applied throughout the EU from 28th January 2022.
- European Union (Veterinary Medicinal Products and Medicated Feed) Regulations 2022 (S.I. 36/2022). These regulations transposed EU Regulation 2019/6 into Irish law.
- Veterinary Medicinal Products, Medicated Feed and Fertilisers Regulation Act 2023 (No. 21/2023). This Act deals with areas of national discretion in relation to the retail of veterinary medicines and mandates the use of the National Veterinary Prescription System (NVPS) developed and operated by the Department of Agriculture, Food and the Marine.
- The Veterinary Medicinal Products, Medicated Feed and Fertilisers Regulation Act 2023 (Section 7 Commencement) Order 2024 (S.I. 542/2024) provides the mandatory start date for the NVPS as 13th January 2025. From this date all veterinary prescriptions for food producing animals including all horses in Ireland shall be issued electronically via the NVPS.
- Veterinary Medicinal Products Regulations 2024 (S.I. 462/2024), which provide for:
    - the rules pertaining to prescribing of prescription only medicines
    - the rules pertaining to the use of the NVPS
    - the regulation of retail and internet sales of Veterinary Medicinal Products (VMPs)
    - the possession, administration and storage of VMPs and medicated feed, and
    - the licencing of the importation of certain VMPs and medicated feed.

These guidelines on prescribing practice were specifically developed for use in the University College Dublin Veterinary Hospital and may not be applicable to all situations in general practice. The guidelines are underpinned by clinical experience and research data. They compile current best practice information and may be subject to revision as the art and practice of veterinary medicine advances, so that the guidance remains current.

## 1.2 Advisory

**Please note that in a small number of instances the recommendations may not be consistent with SPC sheets in terms of dosage and duration of treatment and thus represent off-label use, with the associated requirement to adhere to off-label withdrawal periods. It is also important to bear in mind that, in order to remain within the current parameters of the law, in the event of employing treatment rates that are 'off label', then practitioners should satisfy themselves that this scope is available within the treatment regimes outlined within the SPC of the medicines involved and whether the treatment rates in the SPC are categorized as recommended rates or absolute rates (in which case, there is no scope for off label use).**

It is hoped that these guidelines will be a useful tool to assist practitioners in adhering to prudent prescribing practices. Nevertheless, it is recognised that ultimately it is the responsibility of the veterinary practitioner to exercise their clinical judgement in each specific circumstance and prescribe accordingly.

**Veterinary practitioners should also refer to the Veterinary Council of Ireland Code of Professional Conduct Chapter on Responsible Use of Medicinal Products in Animals**
See: https://www.vci.ie/Publications/Code-of-Professional-Conduct

## 1.3 Veterinary treatment of bacterial infections; consider the 6 "RIGHTs":

1. **Right** Animal: make sure the animals that need to be treated are accurately identified.
2. **Right** Diagnosis - by a vet who has the animal under their care; and can follow up for further treatment, if required, or if complications arise;
    a. Laboratory results (including Serum Amyloid A /Acute phase proteins) should be interpreted alongside a thorough clinical examination, an understanding of the history and in conjunction with any diagnostic imaging.
3. **Right** Drug – select the right drug for the likely pathogen and site of infection considering the absorption, tissue penetration, potential in-activation and potential toxicity of the medicine in the patient, and antimicrobial susceptibility testing (AST) results where available.
4. **Right** Dose: use the appropriate amount, interval and route of administration, bodyweight should be estimated as accurately as possible.
5. **Right** Duration: use the drug for as long as it is needed; as per the Summary of Product Characteristics
6. **Right** Storage/Disposal: consider how the keeper will store the medicine; encourage responsible disposal of remaining medicine/ packaging.

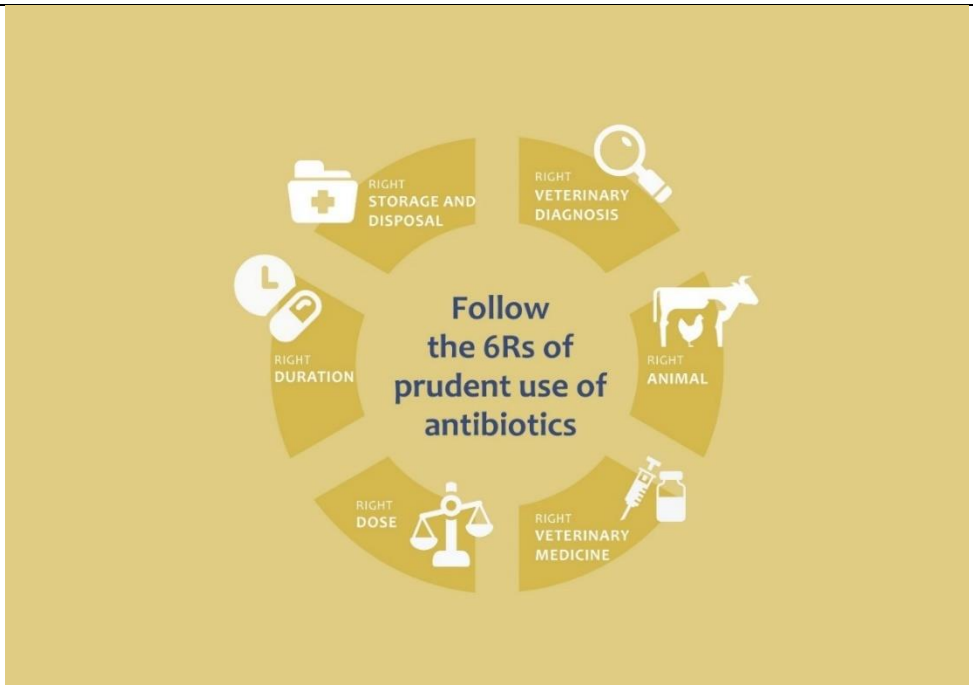



Illustration of the 6Rs, the cornerstones of reducing antimicrobial usage in animals.

## 1.4 General principles of antimicrobial treatment in animals

Throughout this document, reference is made to the European Medicines Agency's Antimicrobial Advice Ad-Hoc Expert Group (AMEG) Categorisation of Antimicrobials for use in animals. The classification comprises four categories, from A to D: Avoid, Restrict, Caution and Prudence.

The infographic is available at: https://www.ema.europa.eu/en/documents/report/infographic-categorisation-antibiotics-use-animals-prudent-responsible-use_en.pdf and additional information on these drugs is to be found in Appendix 1.

In summary:
Category A ("Avoid") includes antimicrobials that are currently not authorised in veterinary medicine in the European Union (EU). These medicines may not be used in food-producing animals and may be given to individual companion animals only under exceptional circumstances.

Category B ("Restrict") refers to quinolones, 3rd- and 4th-generation cephalosporins and polymyxins. Antimicrobials in this category are critically important in human medicine and their use in animals should be restricted to mitigate the risk to public health.

Category C ("Caution") covers antimicrobials for which alternatives in human medicine generally exist in the EU, but only few alternatives are available for certain veterinary indications. These antimicrobials should only be used when there are no antimicrobial substances in Category D that would be clinically effective.

Category D ("Prudence") includes antimicrobials that should be used as first line treatments, whenever possible. These antimicrobials can be used in animals in a prudent manner. This means that unnecessary use and long treatment periods should be avoided.

Use of antimicrobials should be based on the following principles:

- Antimicrobial treatment should be initiated only if bacterial infection is proven /strongly suspected following thorough clinical examination/ proper assessment which may include supportive tests. In addition, due consideration must be given to whether cure is expected following treatment or whether the animal's immune system is likely to be sufficient to fight infection without the requirement for antimicrobials.
- Consider whether topical antiseptic /antimicrobial treatment would be effective.
- Treat underlying conditions, thus reducing the likelihood of repeat infections as much as possible.
- The antimicrobial agent and route of administration should be chosen considering the absorption, tissue penetration, potential in-activation and potential toxicity of the medicine in the patient and to minimise effects on the host animal normal flora.
- EMA category A agents should never be used in food-producing animals.
- First choice treatments should be EMA category D agents if possible and Category C agents if there is no suitable category D agent. Narrow spectrum therapy should be used whenever possible.
- Category B agents must only be used if no other suitable agent is available based on culture and susceptibility test results or, in cases of severe disease where treatment must be initiated immediately, samples should be collected for testing before treatment is initiated. Use of Category B agents must always be in consultation with a senior clinician.
- When selecting treatment for a polymicrobial infection consider how to expose the animal patient to the least number of antimicrobials possible; if changing/adding an antimicrobial, consider if the previous choice can be stopped.
- Where appropriate, use cytology and/or other test results to determine resolution of infection and duration of treatment.
- De-escalate treatment to lower category agent whenever possible based on culture and susceptibility results.

## 1.5 Overview of the properties of antimicrobials affecting their use

Beyond compliance with legislative requirements, the issues to be considered when choosing an antimicrobial empirically include:

- The spectrum of activity
- Pharmacokinetic-Pharmacodynamic (PK-PD) factors
- The degree of penetration to the site of infection
- Local factors that might affect drug activity.
- Whether this drug is safe for this patient

Much of our understanding of antimicrobial action has been determined "*in-vitro*"- in the laboratory, providing an evidence basis for antimicrobial use. A limitation is that "*in-vitro*" results do not always match to what the clinician finds "*in-vivo*", and therefore evidence-based clinical judgement is also important.

The "Spectrum of activity" of an antimicrobial relates to the presence of accessible targets for the pharmacological action of the antimicrobial in a genre or species of bacteria. Conversely, intrinsic resistance occurs where a bacterial species is naturally resistant to the antimicrobial concerned, for example *Klebsiella spp*. are considered intrinsically resistant to beta-lactams.

A simple approach is to consider the activity of antibacterial drugs based on their activity against the four groups of bacterial pathogens: Gram-positive aerobes, Gram-positive anaerobes, Gram-negative aerobes and Gram-negative anaerobes. However, in companion animal practice, Gram-negative and Gram-positive anaerobes do not greatly differ in susceptibility patterns, and therefore it can be useful to treat “obligate anaerobes” as a single group.

The mode of action of the antimicrobial can determine whether the effect is to “kill” the bacteria (bactericidal) or stop multiplication (bacteriostatic). All antimicrobials are bacteriostatic at some (low) concentrations, but some antimicrobials are bacteriostatic at all concentrations (i.e. tetracyclines and sulfonamides).
Certain antimicrobials, i.e. aminoglycosides, can have persistent suppressive or killing effects even after all drug has been removed from the plasma; this is termed a post-antibiotic effect (PAE). Drugs with a long PAE often only require once-a-day treatment, even if the plasma half-life is short.

Modern understanding of the PK/PD effects of antimicrobials includes the concept of “concentration” and “time” dependance. Concentration-dependent antimicrobials eradicate pathogenic bacteria by achieving high concentration at the drug target. Achieving a high concentration relative to the established minimum inhibitory concentration (MIC) is key and thus dose size is critical.
With time-dependent antimicrobials, the killing response is dependent on the duration of time that the drug levels are maintained above the MIC and using higher concentration of such drugs does not necessarily result in greater effect. With these drugs, dosing interval is critical and missed doses may have a major impact on efficacy.

Tissue penetration is largely determined by chemical features of the drug concerned. Local factors, such as such as anaerobic environment, or the presence of pus or debris can have a profound impact on the efficacy of specific antimicrobial groups. Penetration into certain tissues i.e. brain, may be enhanced in inflammation.

Table 1.1 provides a general overview of the antimicrobial classes used in veterinary medicine and their properties. Note that individual members of drug groups may differ in the properties outlined.

*Table 1.1 General properties of antimicrobial classes commonly used in veterinary medicine.*

| Antimicrobial class | Example drugs | Spectrum of activity* | | | Tissue penetration | Time or concentration dependent/ Bactericidal or bacteriostatic | Additional comments |
|---|---|---|---|---|---|---|---|
| | | Gram positive | Gram negative | Anaerobes | | | |
| Penicillin | Benzyl Penicillin/ Penicillin G | ++ | - | ++ | Moderate | Time dependent /bactericidal | Sensitive to beta-lactamases |
| Aminopenicillins | Ampicillin, Amoxicillin | +++ | ++ | ++ | Moderate (not intracellular) | Time dependent /bactericidal | Sensitive to beta-lactamases |
| Aminopenicillins in combination with beta-lactamase inhibitors | Amoxicillin-clavulanate | +++ | ++ | +++ | Moderate (not intracellular) | Time dependent /bactericidal | Resistant to beta-lactamases but susceptible to AmpC producers, e.g. AmpC+ *E. coli* |
| 1st/2nd generation cephalosporins | Cefalexin, cefalonium | +++ | ++ | - | Good (not CNS) | Time dependent /bactericidal | MRSA and MRSP are resistant |
| 3rd/4th generation cephalosporins | Ceftiofur, cefovecin, cefquinome | ++ | +++ | + (ceftiofur ++) | Good (not CNS, exception cefquinome) | Time dependent /bactericidal | MRSA and MRSP are resistant |
| Aminoglycosides | Gentamicin Streptomycin, Neomycin | ++ | +++ | - | Poor | Conc. dependent/ bactericidal | Long PAE, inactive in the presence of pus or necrotic tissue; nephrotoxic, ototoxic; Some activity against mycobacteria and mycoplasmas |
| Amphenicols | Chloramphenicol Florfenicol | +++ | ++ | +++ | Good | Time dependent/ Florfenicol is bactericidal | **Chloramphenicol banned from use in food animals;** Activity against mycoplasmas and chlamydia |
| Fluoroquinolones | Enrofloxacin Marbofloxacin | +++ | +++ | - | Good | Conc. dependent /bactericidal | Activity against *Chlamydia, Borrelia, Anaplasma Mycoplasma* species and mycobacteria; caution if use in young animals, potentially retinotoxic in cats |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Lincosamides | Clindamycin<br>Lincomycin<br>Pirlimycin | +++ | - | +++ | Good | Time dependent/ bactericidal or bacteriostatic depending on conc. at site | Serious adverse effects in GIT |
| Macrolides | Erythromycin, tilmicosin, tylosin, tulathromycin | ++ | + (*Campy*. spp. ++) | ++ | Good (not CNS) | Time dependent/ bactericidal | Good activity against mycoplasmas |
| Sulphonamides and potentiated sulphonamides | Sulphamethoxazole +/- trimethoprim | ++ | ++ | ++ | Good | Time dependent/ bacteriostatic | Inactive in the presence of pus or necrotic tissue; some activity against *Anaplasma, Chlamydia* spp. Potential adverse immune responses in dogs. |
| Tetracyclines | Doxycycline, oxytetracycline | ++ | ++ | ++ | Good | Time dependent / bacteriostatic | Resistance widespread in GIT pathogens of farm animals, usually good activity against *Chlamydia, Borrelia, Anaplasma, Mycoplasma* species. Bind to $Ca^{++}$ |
| Nitroimidazoles | Metronidazole | - | - | +++ | Good | Conc. dependent/ bactericidal | **Banned from use in food animals** |

* Spectrum of activity given in very general terms

MRSA/P Methicillin Resistant Staphylcoccus aureus/pseudointermedius

\- Bacterium intrinsically resistant to antimicrobial; not suitable for use

\+ Low efficacy against and/or widespread resistance to this antimicrobial in these organisms

++ Moderate efficacy against and/or variable resistance to this antimicrobial in these organisms

+++ High efficacy against and limited resistance (reported to date) to this antimicrobial in these organisms

Category B: HP-Critically Important Antimicrobials

## 1.6 Note on Exceptional 'Off-Label' use

The current Veterinary Medicines legislation states that medicines must be used in accordance with the product datasheet or SPC. Under Article 106 of EU Regulation 2019/6, all antimicrobials must be used in accordance with the Marketing Authorisation of those products, and under article 5.17 of the Statutory Instrument no 36/2022 it is an offence to use a veterinary medicinal product other than under the terms of its marketing authorization. These details are supplied with each product in a document called the 'Summary of Product Characteristics' (SPC). These snippets of legislation have, as a result, reduced the scope available to veterinary prescribers in relation to prescribing veterinary medicines at rates other than those detailed on the summary of product characteristics (SPC). The SPC is the datasheet which outlines the conditions of use for that product and contains vital information like the dose rate, treatment regimens and potential side effects associated with use of that medicine.

'Off Label' use is the use of a veterinary medicinal product that is not in accordance with the summary of the product characteristics, including the misuse and serious abuse of the product. Retaining access to 'off label' prescribing is vital as it allows practitioners to retain access to some older, first line antimicrobials reducing the use of more critically important antimicrobials, thereby slowing the development of antimicrobial resistance (AMR).

The veterinary profession, as the custodians of antibiotics in animal health, play a key role in preventing the development and spread of antimicrobial resistance. Addressing antimicrobial resistance requires responsible prescribing and use of antimicrobials to maximise their efficacy in treating bacterial disease. Due to the development and spread of antimicrobial resistance there may be a need for off label use of antimicrobials in exceptional and limited circumstances in individual animals. It is of paramount importance, that in any scenario where a veterinary practitioner chooses to prescribe an antimicrobial at a dosage rate or treatment regimen other than that detailed in the SPC, **that it is only done in line with published peer reviewed scientific advice** and clinical experience.

Due to variations between veterinary medicinal products, the dosage rates to be administered of some are issued by the marketing authorization holder as recommendations. Where indicated treatment rates are published as recommendations, there remains scope for veterinary prescribers to prescribe these medicines at rates other than those outlined in the SPC. Critically, it must be recognized, that in writing prescriptions such as this, then prescribers should only do so in line with **published peer reviewed scientific advice** and clinical experience.

It is in each veterinary practitioner's best interests, to satisfy themselves that they have the required scope to prescribe veterinary medicinal products available to them in an 'off label' capacity. This data can be gleaned from the SPCs of each product used in clinics and assimilating the data from them.

In prescribing medicines in an 'off label' capacity, veterinarians also need to give consideration to the consequential adjustment to withdrawal periods to be observed as a result of 'off label' use. Within Regulation EU2019/6, Article 115 deals specifically with this issue (See Appendix 2).

## 1.7 Special Import Licences

In order to ensure the safety, efficacy, and quality of veterinary medicinal products (VMPs), and in so doing protect the health and welfare of treated animals, vets are required to only use veterinary medicinal products which have been assessed by the HPRA and granted a national marketing authorisation (IE authorised) or assessed by the EMA and granted a centralised EU authorisation (EU).

Medicinal products not covered by an Irish authorisation or an EU centralised authorisation may only be used under special circumstances, outlined in the Regulation, and only where a Special Import Licence has been granted by DAFM. Further detail on application procedures and legal background to SILs is available in Appendix 3.

# 2. Prudent Prescribing in equine practice

## 2.1 Introduction

Antimicrobial resistance is one of the greatest human and animal health crises in the world today. Veterinary clinicians play a critical role in preserving the efficacy of these medicines for use in both humans and animals. They do so first and foremost by promoting disease prevention (through vaccination and biosecurity measures); and thereafter by only prescribing antimicrobials for use in animals when they are fully indicated, at the appropriate dose and for the appropriate duration.

The owners/keepers of horses in Ireland also have an important role to play in addressing this crisis, by working in cooperation with their vet to ensure an environment that minimises the occurrence and spread of disease. In so doing, they may realise a significant economic benefit, whereby the use of expensive medicines is avoided unless absolutely necessary.

When prescribing antimicrobial medicines, veterinary clinicians must operate within the parameters of the current legislation. Individual practitioners must be able to assess all the relevant factors and then design a treatment plan that is tailored to the specific circumstances and features of the case in question. Therefore, these guidelines are intended neither to be proscriptive nor prescriptive; they are intended to provide support and guidance for veterinary clinicians in equine practice in Ireland based on the current best available evidence.

## 2.2 Owner/keeper and vet cooperation: focus on disease prevention to minimise the need for antimicrobial use:

1. Implement a yard vaccination and deworming programme, under veterinary advice and specific to the circumstances of the farm, to keep the health status of the herd high;
2. Be conscious of air quality; mild to severe asthma, caused by dust and other allergens in the environment, is common in horses; this can make them more susceptible to infectious respiratory disease. Aim to provide good air quality through well-ventilated housing and exercise areas and reduce exposure to dust and other allergens;
3. Provide plenty of clean, fresh water and check the water source often for contamination;
4. Check the feed sources often for mould and for contamination by birds and rodents that carry diseases that affect horses. Store feed and forage to prevent contamination;
5. Maintain appropriate stocking density to reduce stress levels and limit the ability of disease to spread through a herd;
6. Manage young stock separately to breeding stock, and separate these from competition/other stock;
7. Have a rigorous cleaning and disinfection plan for stabling, equipment, transport vehicles and high traffic areas such as walkers, stocks etc., and a plan to deal with horses that become sick;
8. Closely observe all new arrivals, and those returning to the yard from mixing with other equines, in quarantine for two weeks before introducing them to the general yard.

## 2.3 Further considerations for the equine veterinary clinician:

1. Availability of medicines: consider what antimicrobials are licensed and available for use in the horse, or are available in another EU MS for equines or another species 'off label' (either for food producing animals or for companion animals/human use, depending on the food status of the horse) The HPRA website/ Union Product Database should be consulted to inform what is available;

2. Some of the drug dosage regimes in the most up to date literature for some of the older category D antibiotics may not be consistent with manufacturer's recommendations. If a veterinary practitioner plans to treat an animal "off-label" with a medicinal product, they must inform the client and explain why "off-label" use is required.
3. Local/regional use: IVRA, intra-synovial, intra-uterine, nebulised drugs: medicines may not be granted licenses for these specific usages; consider evidence of efficacy or toxicity, whether use may contribute to resistance or residues; observe the above considerations for 'Off-label' use;
4. Owner competence: administration of injections by animal owners may result in increased incidence of complications; oral formulations may be easiest for owners to administer; but there are limited licensed oral antimicrobials available.
5. Size and temperament of the horse and its husbandry (stable or pasture, etc.);
6. Withdrawal times for competition and for meat, if the horse may end up in the food chain.

**Prescription:** Issue a veterinary prescription when administering and dispensing antimicrobials.

**Records**: Keep records of the animal, owner/keeper, drug, dose, duration and recommended withdrawal period (for competition and/or meat).

**Prophylactic Use:** Don't prescribe antimicrobials "just in case" or for preventive reasons (e.g. prior to transport; in healthy new-born foals; clean surgeries in healthy animals, after intra-synovial medication/block) except in exceptional individual cases when the risk of infection is unavoidably high, or the consequences are likely to be severe.

**Metaphylactic Use:** Antimicrobials should only be used for metaphylaxis when the risk of spread of infection in a group of animals is high and where no other appropriate alternatives are available.

**Avoid HP-CIAs:**

The European Medicines Agency's Antimicrobial Advice Ad-Hoc Expert Group (AMEG) constantly reassesses the impact on human health of using antimicrobials in animals, alongside the need to treat disease in animals for health and welfare reasons.

Given the importance of the HP-CIAs in human health, these antimicrobials should NOT be used as first line of treatment in horses. Category B agents must only be used if no other suitable agent is available based on culture and susceptibility test results or, in cases of severe disease where treatment must be initiated immediately, samples should be collected for testing before treatment is initiated. COMMISSION IMPLEMENTING REGULATION (EU) 2022/1255 designates antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with Regulation (EU) 2019/6 on veterinary medicinal products. This Implementing Regulation applies from **9th February 2023**. Medicinal products that contain any of the antimicrobials or groups of antimicrobials listed in this Regulation should not be used in animals, even under the conditions set in Articles 112, 113 and 114 ('cascade' use) of Regulation (EU) 2019/6.

**Adverse events** associated with antimicrobial use in horses are not uncommon and range from mild to fatal. These include:

1. Urticaria
2. Muscle soreness
3. Clostridial myonecrosis
4. Neurologic reaction
5. Gastrointestinal dysbiosis
6. Immune mediated haemolytic anaemia
7. Anaphylaxis

All Adverse Events should be reported to the Health Products Regulatory Authority, the details of the process can be found at Report an issue (hpra.ie). Greater detail in the procedure surrounding the reporting of adverse events can be found in Appendix 4.

## 2.4 Failure of therapy

When failure of therapy is suspected (e.g. persistent fever, persistent discharge) consideration should be given to case review in terms of causation, further culture and susceptibility testing, consideration of further diagnostic tests and/or surgical treatments as appropriate.

*Table 2.1 Antimicrobial Activity Against Some Common Equine Pathogens*

| | *Staph aureus* | Beta-haemolytic *Streptococcus* | *Rhodococcus equi* | *Escherichia coli* | *Klebsiella pneumoniae* | *Pseudomonas aeruginosa* | *Anaerobes* |
|---|---|---|---|---|---|---|---|
| Procaine penicillin | ++ | +++ | + | - | - | - | ++ |
| Sodium penicillin | ++ | +++ | + | - | - | - | ++ |
| Ceftiofur | +++ | +++ | + | +++ | +++ | + | ++ |
| Oxytetracycline | ++ | ++ | + | ++ | ++ | - | + |
| Doxycycline | ++ | ++ | ++ | ++ | ++ | - | + |
| Trimethoprim/ Sulphadiazine | ++ | ++ | ++ | ++ | ++ | - | + |
| Gentamicin | ++ | - | + | +++ | +++ | ++ | - |
| Streptomycin | ++ | - | + | ++ | ++ | + | - |
| Neomycin | ++ | - | + | ++ | ++ | - | - |
| Rifampin | +++ | +++ | +++ | - | - | - | ++ |
| Azithromycin | +++ | +++ | +++ | - | - | - | + |
| Enrofloxacin | ++ | + | ++ | +++ | +++ | ++ | - |
| Metronidazole | - | - | - | - | - | - | +++ |
| Chloramphenicol | +++ | ++ | ++ | ++ | ++ | - | ++ |

- Bacterium intrinsically resistant to antimicrobial; not suitable for use
+ Low efficacy against and/or widespread resistance to this antimicrobial in this bacterium
++ Moderate efficacy against and/or variable resistance to this antimicrobial in this bacterium
+++ High efficacy against and limited resistance (reported to date) to this antimicrobial in this bacterium

*Table 2.2 Antimicrobial dosages and indications*

| | EMA | Dosing Regime | HPRA Licencing | | | | Comments |
|---|---|---|---|---|---|---|---|
| | | Literature | Equine | HPRA Sample SPC | Other species | HPRA SPC | |
| Procaine penicillin | D | 22,000 iu/kg IM q 12 h<br>25 mg/kg q 12 h | Infections caused by bacteria sensitive to penicillin | 12 mg/kg IM q 24 h for 5 days | | | |
| Ampicillin sodium | D | 20 mg/kg IM or IV q 6-8 hours | Respiratory, GI and Urogenital infection | 6-22 mg/kg IM or IV q 12-24 h | | | |
| Oxytetracycline | D | 5-10 mg/kg IV q 12 h | Infections caused by organisms sensitive to oxytetracycline | 3-10 mg/kg IV or IM q 24 h for 5 days | | | Slow IV injection |
| Trimethoprim/<br>Sulpha | D | 15-30 mg/kg IV q 12 h<br>15-30 mg/kg PO q 12 h | Resp (Strep and Staph), Gastrointestinal (E coli), Urogenital (Strep) , Wounds (Strep, Staph) | 15 mg/kg IV q 24 h for up to 3 days<br>30 mg/kg PO q 12-24 h for up to 5 days | | | Slow IV injection |
| Gentamicin | C | Adults 6.6 mg/kg IV/IM q 24<br>Foals < 2 wk 11-15 mg/kg IV / IM q 36 h | Lower resp tract infection caused by aerobic Gm neg bacteria | 6.6 mg/kg q 24 h for 3-5 days<br>Not rx in foals/neonates | Cattle: septicaemia, GI, Urogenital and Skin infections | 2mg/kg IM BID | Narrow therapeutic safety index - nephrotoxicity |
| Sodium penicillin | D | 20,000-25,000 IU/kg IV q 6 h | | | Human only | | |
| Amikacin | C | Adult 10-15 mg/kg IV or IM q 24 h<br>Foals 20-30 mg/kg IV or IM q 24 h | | | | | |
| Doxycycline | D | 10mg/kg PO q 12 h<br>20 mg/kg PO q 24 h | | | Dogs, cats, pigs, calves, turkeys | 10 mg/kg PO q 24 hours for 5 days | |
| Metronidazole | D | Adults 25 mg/kg PO q 12 h<br>Foals < 14 days 10mg/kg PO q 12 h | | | Dogs and cats: GIT and Uro-Gen tract Giardia and Clostridia | 50mg/kg PO q 24 h | Prohibited from the food chain |
| Tulathromycin | C | 2.5 mg/kg IM q 1 week | | | Cattle, pigs, sheep | Single IM injection 2.5 mg/kg | Fatal colitis in adult horses |
| Azithromycin<br>Clarithryoycin | C | Foals 10 mg/kg PO q 24-48h<br>Foals 7.5mg/kgPO q12 h | | | Human only | | Fatal colitis in adult horses |
| Rifampin | A | 10 mg/kg PO q 12-24 h | | | Human only | | Never use alone |
| Enrofloxacin | B | 5.5 mg/kg IV q 24 h<br>7.5 mg/kg PO q 24 h | | | Cattle, pigs, sheep, dogs, cats, turkeys, chicken, rabbits…. | 5 mg/kg IV, IM or SC q 24<br>5mg/kg PO q 24 h | |
| Marbofloxacin | B | 2 mg/kg IV q 24 h<br>3.5-4mg/kg PO q 24 h | | | Cattle, pigs, cats, dogs, | 2 mg/kg IM q 24 h<br>Dog:2 mg/kg q 24 h | |
| Ceftiofur | B | Adult 2.2mg/kg IV or IM q 12-24 h<br>Foals 5-10 mg/kg IV or IM q 6-12 h | | | Pigs, cattle: resp dz; foot rot; metritis | Suspension: 3mg/kg IM SID for 3 days | |

Antimicrobials with HPRA license for use in horses

Category A: Avoid

Category B: HP-Critically Important Antimicrobials

## 2.5 Practical scenarios in general practice

*Hoof abscess:* Generally, antimicrobial treatment is not routinely indicated for simple hoof abscesses; administer Tetanus anti-toxin (TAT) if vaccination status is not up to date or is unknown.

*Wounds:* For fresh wounds that can be managed in the field (no deep/vital structures involved), antimicrobials are not routinely indicated; administer TAT if vaccination status is not up to date or is unknown; deeper wounds or those involving vital structures should be hospitalised for evaluation and treatment.

*Routine castration and other minor surgeries:* For clean surgeries in healthy animals, antimicrobials may not be indicated, alternatively 24 hours of perioperative treatment with penicillin; administer TAT if vaccination status is not up to date or is unknown.

*Joint Injections:* As these should only be performed using strict aseptic technique, the use of "prophylactic" intra-synovial antimicrobials is not routinely indicated.

*Lymphangitis:* Diffuse, non-painful swelling of one limb, (presumptive diagnosis of lymphangitis); generally, no antimicrobial treatment is necessary if the horse is well, is non-febrile and there is no evidence of a wound or tract suggesting a septic focus. The mainstay of treatment should be aimed at restoring lymphatic drainage and homeostasis (corticosteroid and/ or a diuretic, walking as appropriate, bandaging and cold hosing).

*Cellulitis:* The horse is usually lame and resents palpation of the affected limb which is often hot to touch; this may warrant antimicrobial as well as non-steroidal anti-inflammatory treatment. Involvement of synovial structures should be investigated. A draining wound or tract may yield material for AST. Doxycycline is suggested as a suitable first line antimicrobial with penicillin and gentamicin in combination as an alternative; administer TAT if vaccination status is not up to date or is unknown.

*Dermatitis/Folliculitis:* Dermatophilosis (rain scald): discrete or generalized tufted papules and crusts (paint brush lesions). Mild to moderate cases can be treated via reduced exposure to wet conditions and topical antibacterial therapy (using warm water and dilute chlorhexidine, the crusts are gently soaked and removed, and the affected area is dried with **clean** towels or disposable paper towel). In severely affected animals, systemic antimicrobial therapy may be indicated. Suitable first line options include trimethoprim and sulphadiazine, procaine penicillin or doxycycline. *Staphylococcal species* can cause superficial or deep pyoderma with alopecia and crusting. These are typically very painful and are usually found in a region where the natural barrier function of the skin has been compromised, such as those areas in contact with the saddle or other tack. Mild to moderate cases can be treated with topical antibacterial therapy. In more severe cases systemic antimicrobial therapy may be indicated. Suitable first line options include trimethoprim and sulphadiazine, procaine penicillin or doxycycline.

*Cough in a healthy horse:* A healthy horse with an occasional cough during exercise, unexplained poor performance and mucus in the trachea "dirty scope"; severe cases may also have a heave line and a thick nasal discharge; Equine asthma is far more common than bacterial pneumonia/bronchitis in horses; cytology on a bronchoalveolar lavage (BAL) or tracheal aspirate can differentiate bacterial infection from allergic inflammation; consider addressing ventilation, dust and allergens in the environment and treating the acute signs with inhaled bronchodilators and corticosteroids

*Cough with fever, nasal discharge and decreased appetite:* Horses with a respiratory tract infection are usually systemically unwell, with pyrexia, anorexia, lethargy, increased respiratory rate or effort

and/or nasal discharge; viral causes of respiratory tract infections are more common than bacterial causes particularly in young horses and after travel; recent long-distance travel in adults should raise a suspicion of bacterial pleuropneumonia; thoracic ultrasonography can allow early detection of pleuritis and highlight a need for surgical drainage of the thoracic cavity; PCR on a naso-pharyngeal swab is a rapid test that can differentiate causes of respiratory tract infection such as viruses and *Streptococcus equi* var *equi* (Strangles) infection; cytology on a tracheal aspirate can confirm bacterial infection in the lower respiratory tract and AST an direct therapy; blood work will show elevated APPs, globulins and leucopaenia or leukocytosis. Suitable first line options for bacterial respiratory tract disease include trimethoprim and sulphadiazine, procaine penicillin or doxycycline; Bacterial pleuropneumonia can be fatal and requires broad spectrum treatment (penicillin, gentamycin +/- metronidazole) and intensive supportive care pending AST on a tracheal aspirate sample.

*Acute toxic diarrhea:* Bacterial infection of the intestinal tract in adult horses will result in systemic signs of illness and toxemia – pyrexia, anorexia, lethargy, increased heart rate and respiratory rate, injected/congested mucous membranes. Bacterial enterocolitis can be fatal and requires broad spectrum treatment (pen, gent, metro) and intensive supportive care while awaiting the results of 3-5 sequential faecal *Salmonella* cultures and fecal testing for clostridial toxins.

*Chronic scour +/- weight loss in an otherwise healthy adult horse:* Weight loss and scour are most likely caused by intestinal parasites or immune mediated disease; generally, antimicrobials are not routinely indicated.

## 2.6 Practical scenarios in stud practice - foals

*High-risk newborn foals:* Foals that suffered complications during late gestation or parturition. Clinical signs consistent with the systemic inflammatory response syndrome (tachycardia, tachypnoea, fever) and consistent changes in blood work (leucopaenia, leukocytosis, left shift). Take a blood culture prior to starting broad spectrum antimicrobial therapy pending AST results. Continue treatment until clinical signs have improved and leukocyte changes have resolved. Particular consideration should be given to the potential for nephrotoxicity with aminoglycosides due to altered renal perfusion.

*Umbilical infection in a young foal:* Infection of the umbilical remnants should be treated in the same way as a high-risk newborn foal. Ultrasonography of the umbilical remnants is used to monitor response to broad spectrum antimicrobial therapy. If there is no response to medical therapy, surgery is recommended to remove the infected remnants; administer TAT if vaccination status and/or colostrum intake is unknown.

*Patent urachus:* Chlorhexidine (0.5%) is considered the most effective treatment for the external umbilical remnants for reducing bacterial numbers without tissue destruction. Foals with a patent urachus may be treated with oral broad-spectrum antimicrobials such as trimethoprim and sulphadiazine that are mainly excreted in the urine until the urachus closes.

*Septic arthritis/physitis:* Young foals with heat, pain, swelling and non-weight bearing lameness associated with joints or growth plates; treat the same as a high risk new-born foal; arthrocentesis and blood sample for AST prior to commencing broad spectrum cover; joint lavage; administer TAT if vaccination status and/or colostrum intake is unknown

*Respiratory disease in 1-5 month old foals:* Viral pneumonia is uncommon in foals from mares vaccinated against equine herpes and influenza viruses. Young foals with an increased respiratory rate or effort, fever, cough and/or nasal discharge may have bacterial pneumonia. Common causes include *Rhodococcus equi* and *Strep zooepidemicus*. Thoracic ultrasonography can assist in selecting foals that require treatment for pulmonary abscessation. Those with a combined diameter of visible abscesses > 10-20cm are likely to require antimicrobial treatment. Macrolides are considered the most effective treatment for pulmonary abscessation. Blood work (leukocytosis and neutrophilia) can assist with decision making here, and, along with sequential ultra-sonographic examinations, can guide treatment duration.

*Respiratory disease in young stock (1–3 year-old):* Young horses with nasal discharge, cough, lymphadenopathy; often caused by viruses or migrating parasites. A nasal swab can be taken for PCR testing; deworming history should be ascertained. Tracheal aspirate cytology can confirm bacterial pneumonia. Treatment for viral disease is supportive. Penicillin or trimethoprim and sulphadiazine can be used to treat bacterial respiratory tract disease while awaiting AST results.

*Diarrhoea in young foals:* Foals that are dull, not nursing, febrile and/or dehydrated with increased volume and/or decreased consistency of dung; In foals 1-4 months old, the cause of the diarrhea is likely viral and treatment should be supportive, focusing on fluid therapy and non-steroidal anti-inflammatory drugs. Foals < 1 month old with diarrhoea are considered at greater risk for bacterial translocation across the gut wall and development of sepsis. These foals can be treated with broad spectrum antimicrobial drugs.

*Diarrhoea/ill thrift in weanlings:* Diarrhoea/ill thrift are commonly caused by intestinal parasites and ulceration. *Lawsonia intracellularis* is an infectious cause; confirmation requires fecal PCR and

serologic testing. On endemic farms, vaccination may reduce the incidence. Recommended treatment includes oxytetracycline/doxycycline.

## 2.7 Practical scenarios in stud practice - mares

*Routine breeding:* The use of prophylactic antimicrobials in mares with negative swabs pre-cover is not indicated. Good hygiene (e.g. perineal cleaning/sterile lubricant) can reduce the requirement for antimicrobials. Treat inflammation (fluid) with lavage/ecbolics and ensure turnout and exercise regime is adequate.

*Endometritis:* A mare that doesn't conceive to a fertile stallion; uterine fluid may be detected post breeding or unexpectedly early return to season; consider cytology to confirm inflammation; often non-infectious inflammation; cervical swab for AST (common isolates are *Streptococcus zooepidemicus* and *E coli*): treat with lavage and ecbolics (oxytocin) until infection is confirmed (beware contamination); then use appropriate antimicrobial as a uterine infusion

*Table 2.3 Intra-uterine antimicrobial use in mares (adapted from LeBlanc EVE 2009)*

| | | |
|---|---|---|
| *Ampicillin* | *2 g* | *Only use the soluble product* |
| *Amikacin* | *2 g* | *Needs to be buffered with bicarbonate or a large volume (200mls) of saline* |
| *Gentamicin* | *1-2 g* | *Needs to be buffered with bicarbonate or a large volume (200mls) of saline* |
| *Penicillin (crystalline)* | *5 x $10^6$IU* | |
| *Ceftiofur* | *1 g* | *Resistant to many beta-lactamases; save for particularly resistant organisms* |

*Placentitis:* A mare with premature lactation, +/- vulval discharge, +/- US confirmation of thickening of the utero-placental unit; gentle swab of external cervical os for AST if vulval discharge is present (avoid excess cervical stimulation); most common isolates: *Streptococcus zooepidemicus, E.coli, Pseudomonas, Klebsiella*; broad spectrum antimicrobial cover (trimethoprim and sulphadiazine, however note that Pseudomonas is intrinsically resistant to trimethoprim and sulphadiazine).

*Post-partum metritis:* A mare that has fetid uterine discharge post-partum, lack of uterine involution and has a fever and/or systemic signs of infection with evidence of inflammation on blood work; or, a mare with retained fetal membranes for greater than 6 hours; metritis in mares is usually a mixed infection; take a uterine swab for AST; most common isolates *E.coli* and *Streptococcus zooepidemicus*; cover with broad spectrum systemic antimicrobials (pen and gent combination) pending results; administer TAT if vaccination status is not up to date or is unknown.

## 2.8 Practical scenarios with hospitalized horses

*Suspected life-threatening infection:* Initiate broad spectrum cover pending AST on the appropriate samples. A suitable first line option is a penicillin and gentamicin combination:

- Horses with arthritis, tenosynovitis, peritonitis, pleuritis/pleuropneumonia, pericarditis.
- Horses with acute colitis/enteritis: fever, colic with/without diarrhoea with toxic neutropenia and left shift.

*Non-life-threatening cases:* Submit the appropriate samples and await AST:

- Horses with chronic sinusitis, cystitis etc.

## 2.9 Antimicrobial use for surgeries in horses

### *Background*

Given the importance of reducing overall use of antimicrobial agents, careful consideration of whether any antimicrobial therapy is indicated for clean, elective procedures in healthy patients is needed. However, given the potential catastrophic consequences of certain types of infections (e.g. synovial, peritoneal) in equine patients due to the challenges and costs of treating these infections it is anticipated that perioperative antimicrobial use will continue to be indicated for many cases. The following table outlines some general guidelines for perioperative prophylactic antimicrobial use in the UCDVH. Regarding surgical treatment of established infection (e.g. synovial infection, peritonitis) samples should be taken as soon as possible for microbial culture and antimicrobial susceptibility testing and broad-spectrum antimicrobial treatment should be initiated as described below for contaminated surgeries) and maintained until the susceptibility test results are available.

*Table 2.4 Antimicrobial use in equine surgeries*

| **Category of Surgery** | **Examples** | **Antibiotic therapy** | **Notes** |
|---|---|---|---|
| Clean Surgery | • Elective castration - semi-closed approach student-led<br>• Cryptorchidectomy - inguinal or parainguinal approach +/- closed castration other side; laparoscopic<br>• Uncomplicated umbilical hernia repair<br>• Laparotomy - without enterotomy – no significant compromise of bowel<br>• Laparoscopy – ovariectomy, PGE2 gel application<br>• Elective Arthroscopy – OCD/diagnostic<br>• Neurectomy of deep branch of lateral plantar nerve and fasciotomy | Consider no antibiotic therapy *or*<br>First Line:<br>Procaine Penicillin 22,000 IU/kg (25 mg/kg) IM BID (*or* Benzylpenicillin* 22,000 IU/kg IV QID) for 24 hours Perioperatively<br>Alternative:<br>Oxytetracycline 6.6 mg/kg slow IV BID for 24 hours perioperatively | Factors that may lead to decision to give antibiotics include:<br>• Body condition and history (or lack of complete medical history) of patient<br>• Prolonged surgery and/or anaesthesia time<br>• Incisions extended in laparoscopy or arthroscopy (e.g. hand-assisted ovariectomy) |
| Clean-Contaminated Surgery | • Airway surgery - laryngotomy<br>• Laparotomy - – significant compromise of bowel<br>• Laparotomy - with pelvic flexure enterotomy<br>• Laparotomy – resection and anastomosis | First Line:<br>Procaine Penicillin 22,000 IU/kg (25 mg/kg) IM BID *(or* Benzylpenicillin* 22,000 IU/kg IV QID)<br>&<br>Gentamicin)6.6 mg/kg IV SID (adults) for 3-5 days perioperatively<br>Alternative:<br>Oxytetracycline 6.6 mg/kg slow IV BID for 3-5 days perioperatively | Dose of gentamicin in foals 11-15 mg/kg IV q 24-36 hours |

| | | | |
|---|---|---|---|
| "High Risk Surgery" | • Osteosynthesis with implant<br>• Prosthesis used – laryngoplasty, tie-forward | First Line:<br>Procaine Penicillin 22,000 IU/kg (25 mg/kg) IM BID *(or* Benzylpenicillin* 22,000 IU/kg IV QID)<br>&<br>Gentamicin)6.6 mg/kg IV SID (adults) for 3-5 days perioperatively<br>Alternative:<br>Oxytetracycline 6.6 mg/kg slow IV BID for 3-5 days perioperatively | Dose of gentamicin in foals 11-15 mg/kg IV q 24-36 hours |
| Contaminated Surgery | • Significant bowel leakage | Procaine Penicillin 22,000 IU/kg (25 mg/kg) IM BID *(or* Benzylpenicillin* 22,000 IU/kg IV QID)<br>&<br>Gentamicin)6.6 mg/kg IV SID (adults) for 3-5 days perioperatively<br>&<br>Metronidazole 25 mg/kg PO BID<br>For 5 days and reassess based on patient parameters | Metronidazole 35 mg/kg PR BID |

| | | | |
|---|---|---|---|
| Other | • Urogenital surgery (caudal reproductive tract surgeries)<br><br>• Sinus surgery<br><br>• Dental Procedures | First Line:<br><br>Procaine Penicillin 22,000 IU/kg (25 mg/kg) IM BID (*or* Benzylpenicillin* 22,000 IU/kg IV QID) for 24 hours perioperatively then<br><br>TMPS 30mg/kg PO BID for 5 days<br><br>Alternative:<br><br>Oxytetracycline 6.6 mg/kg slow IV BID for 24 hours perioperatively then<br><br>Doxycycline 10mg/kg PO BID for 5 days | |

Note: Benzylpenicillin is also known as Penicillin G, which is commonly found as crystalline Penicillin.

***Note: Many of the recommendations in this guide represent off-label use of antimicrobials and this should be made clear to owners.***

# 3. Prudent Prescribing in cattle practice

## 3.1 Introduction

The following guidelines have been developed by the UCD Herd Health Group for use by students and clinicians in the UCD VH. They are based on best available evidence and experience of the group. In all cases clinical judgement should take precedence in all prescribing decisions and the following is intended as a guide, subject to periodic review.

## 3.2 General guidelines in farmed animals

In brief, all antimicrobial prescribing should be governed by the "6 Rs".

In addition to the general principles outlined in 1.2:

- Ruminant microflora must be considered. The antimicrobial agent and route of administration should be chosen considering the absorption, tissue penetration, potential in-activation and potential toxicity of the medicine in the particular patient and to minimise effects on the host animal normal flora.
- EMA category A agents must never be used in food-producing animals.
- First choice treatments should be EMA category D agents if possible and Category C agents if there is no suitable category D agent. Narrow spectrum therapy should be used whenever possible.
- Category B agents must only be used if no other suitable agent is available based on culture and susceptibility test results or, in cases of severe disease where treatment must be initiated immediately, samples should be collected for testing before treatment is initiated. Use of Category B agents must always be in consultation with a senior clinician.
- When selecting treatment for a polymicrobial infection consider how to expose the animal patient to the least number of antimicrobials possible; if changing/adding an antimicrobial, consider if the previous choice can be stopped.
- Unless specifically justified, the posology used should accurately reflect that stated in the authorization/SPC/product literature.
- Where possible, use cytology and/or other test results to determine resolution of infection and duration of treatment.
- De-escalate treatment to lower category agent whenever possible based on AST results.

## 3.3 Neurological disease in cattle

### *Background*

- A number of bacterial-origin neurological diseases occur in cattle.
- For some such as advanced Salmonella cervical osteomyelitis, or pituitary abscess syndrome, treatment is not recommended.
- Antibacterial therapy for the most common, treatable, bacterial-origin neurological diseases are outlined below.

*Table 3.1 Antimicrobial recommendations in common neurological infections*

| **Diagnosis / pathogen** | **Clinical signs** | **Recommended antibacterial treatment regimen** |
|---|---|---|
| Listeriosis<br>(Gram +ve) | Unilateral/asymmetric cranial nerve deficits predominantly affecting Cranial Nerves V, VII and VIII | Procaine penicillin 44 000 IU/kg<br>= 440mg/10kg (please note this is an **"off label"** dose, standard dose is 22 000IU/kg)<br>Given SID (some cases BID) for 7-14 days intramuscularly (IM)<br>Oxytetracycline (standard dose 20mg/kg IM, or double dose as an alternative treatment, **"off-label"** dose) |
| Neonatal bacterial meningitis/meningoencephalitis<br><br>+/- concurrent bacteraemia/septicaemia<br><br>Generally, Gram -ve but occasionally G+ve | Lethargy progressing to depression and stupor; absent suck reflex.<br><br>*Less common*<br>Extended lowered (stiff) neck, hyperaesthesia, opisthotonos<br><br>+/- septicaemia signs e.g. hypopyon | Trimethoprim-sulphonamide 5mg/kg<br><br>Given BID/TID slow IV (or initial IV, followed by IM) for 7 days.<br><br>Alternative treatment option is Amoxicillin/Amoxicillin clavulanic acid |
| *Histophilus somni* meningoencephalitis<br><br>Gram-ve | Often preceded by resp signs; outbreaks in feedlot cattle (8-12 months); Depression (sleeping syndrome- eyes partially closed); recumbency death/sudden death | Oxytetracycline<br>10mg/kg IV twice daily until clinical resolution<br>Or 20mg/kg IM q 48 hrs until clinical resolution<br>Non-dairy: florfenicol 20mg/kg IM |

## 3.4 Antimicrobial use for surgeries in cattle

### *Background*

In other species it may be appropriate to avoid or reduce the duration of antimicrobial treatment regimens for routine surgeries. However, in bovine surgery, which is frequently carried out in less than preferable environmental conditions, even low risk surgeries do involve puncture of a viscus (e.g. LDA), therefore at present, antimicrobial therapy is still recommended for these procedures.

*Table 3.2 Suggested antimicrobial choices in bovine surgery on-farm*

| **Surgery-type** | **Examples** | **Antimicrobial therapy** |
|---|---|---|
| Laparotomy with GIT viscus or uterine puncture, entry or drainage<br><br>Low risk of bacterial translocation / no impairment to gut wall integrity | Abomasal surgery (LDA/RDA)<br><br>Caecal dilation<br><br>Caesarean section | Penicillin and streptomycin SID 4ml/100kg (equivalent to 8mg/10mg [pen/strep] per kg)<br><br>for 3-5 days. |
| Laparotomy with GIT viscus puncture or entry/drainage<br><br>Medium risk of bacterial translocation / likely impaired gut wall integrity | Complicated abomasal surgery (RVA)<br><br>Complicated caecal surgery (Caecal torsion)<br><br>Complicated caesarean section | Amoxicillin clavulanate (SID)<br><br>1ml/20 kg (equivalent to 8.75 mg/kg) for 5 days. |
| Non abdominal surgeries, not infected | Tibial neurectomy, vasectomy/epididymectomy | Penicillin and streptomycin SID 4ml/100kg (equivalent to 8mg/10mg [pen/strep] per kg) for 3 days. |
| Non abdominal surgeries, infected site | Enucleation, digit amputation due to septic pedal arthritis | Penicillin and streptomycin SID 4ml/100kg (equivalent to 8mg/10mg [pen/strep] per kg)<br><br>for 5 days. |

## 3.5 Vegetative Endocarditis and Septic Pericarditis

### *Background*

Vegetative endocarditis refers to infection of the heart valves and develops after haematogenous spread to the valves from other foci of bacterial infection such as metritis, mastitis, liver abscess or foot infection etc. Septic pericarditis refers to infection of the pericardial sac surrounding the heart, often after a sharp metal object (i.e., nail/wire) penetrates the pericardial sac after passing through the reticular wall and diaphragm. Both conditions occur sporadically and most often present with prolonged history of non-specific illness and/or chronic signs related to congestive heart failure.

Signs of non-specific illness may include decreased appetite, drop in milk yield, weight loss, pyrexia, a hunched stance, stiffness or shifting lameness with or without multiple joint effusion. Signs that may indicate cardiac compromise may include tachycardia/bradycardia, murmurs, muffled heart sounds, brisket and/or submandibular oedema and jugular pulses and/or distension. As both diseases are insidious, cattle often present in the advanced stages of heart failure and treatment carries a poor prognosis and thus treatment is rarely warranted. Early cases without cardiac signs and whereby a wire penetration of the reticulum is suspected may benefit from conservative treatment with a magnet, pain relief and antimicrobial. Surgical rumenotomy to remove a wire may be beneficial also in such early cases.

*Table 3.3 Common bacteria found in endocarditis and septic pericarditis in cattle*

| **Common Bacteria in Endocarditis and Septic Pericarditis** | **Type of Bacteria** |
|---|---|
| *Trueperella/Arcanobacterium pyogenes* | Gram positive anaerobes |
| *Streptococci* spp. | Gram positive |
| *Staphyloccus* spp. | Gram positive |
| Mixed infections typical with traumatic reticulitis/pericarditis | Gram positive and negative |

### *Criteria to treat with antimicrobials.*

Any bovine showing signs of non-specific mild systemic illness, such as inappetence, dullness, pyrexia, a sudden decrease in milk yield with signs of cranial abdominal pain may warrant conservative treatment with a magnet, pain relief and an antimicrobial if traumatic reticulitis is suspected. Additionally, cattle with other foci of bacterial infection (e.g., metritis or foot infection) should be treated with antimicrobials appropriate for these conditions. However, if a bovine presents with signs indicating severe cardiac compromise (i.e., brisket/submandibular oedema or jugular distension), it is highly unlikely that any therapy including antimicrobials will be successful and culling should be strongly considered on animal welfare grounds.

### *Class of AM to consider first line in cases of endocarditis and pericarditis.*

Parenteral penicillin and streptomycin

Parenteral ampicillin or amoxicillin (+/- clavulanic acid)

Parenteral oxytetracycline

*Prolonged administration of antimicrobials for 14-21 days may be warranted.

## 3.6 Infectious ophthalmic disease

### *Bovine Keratoconjunctivitis (Pink Eye)*

Infectious keratoconjunctivitis of cattle, also known as pink eye or infectious ophthalmia, is characterised by blepharospasm, conjunctivitis, tear staining and varying degrees of corneal opacity and ulceration. The disease can occur at any time of year but are generally seen when cattle are fed silage from a central source such as a round feeder as well as during warmer times of year.

*Moraxella bovis* (gram negative) is the most common bacterial cause of keratoconjunctivitis, but infections with infectious bovine rhinotracheitis (IBR) may also play a role in disease.

As culture of the agents involved could lead to irreversible damage to the eye if resulting in a potential delay in treatment, clinical judgement of the condition will be involved in determining the course of treatment.

#### *Criteria to treat with antimicrobials.*

Any adult bovine which is showing the clinical signs described above should be considered for treatment. As culture is not available in real time, clinical judgement is always required.

#### *Class of AM to consider first line*

Topical cloxacillin (ophthalmic antimicrobial cream formulation) twice-a-day (BID) or three-times-daily (TID).

Parenteral long-acting tetracycline combined with NSAIDs.

#### *Uveitis (Silage Eye)*

Uveitis in cattle is most commonly a sequel to infection with *Listeria monocytogenes*. Listerial uveitis is encountered most frequently in wintertime when animals are feeding on poor quality silage, often grey in appearance, due to soil contamination during the harvesting process.

*Listeria monocytogenes* is a Gram-positive organism and leads to microabscessation of the hindbrain as well as ocular listeriosis. Uveitis may also be accompanied by keratitis if facial nerve paralysis occurs. Uveitis may often be associated with the accumulation of fibrin and purulent debris in the anterior chamber of the eye. This increases the risk of blockage of the drainage angle, adhesion formation between the iris and the cornea and resultant permanent blindness.

#### *Class of AM to consider first line*

Recommended treatment involves the use of systemic antimicrobials together with systemic NSAIDs and topical atropine drops to open the drainage angle and facilitate elimination of fibrin from the anterior chamber.

Antimicrobial recommendations include oxytetracycline for a 7-day period, although longer courses of treatment may be required.

**Notes:**

Local antibiosis by means of a subconjunctival injection with penicillin or oxytetracycline may also be effective for *Moraxella.* However, it is used **"off label."**

## 3.7 Neonatal enteritis

#### *Background*

Neonatal enteritis is the most common cause of gastrointestinal disease in calves. There are numerous causes of neonatal enteritis including parasites, viruses and bacteria. The leading causes of neonatal enteritis in calves under 1 month of age include Rotavirus & *Cryptosporidium parvum (*All Island Animal Disease Report 2022) - these leading causes are non-bacterial infections and do not usually require antimicrobial treatment. Regardless of the cause, the primary treatment is fluid therapy (oral electrolytes in the first instance and possibly intravenous fluids if necessary). Biosecurity and nursing care considerations such as isolating infected calves and continuing to feed

milk if the calf is willing to drink are also important. Secondary or ancillary treatments such as antimicrobials are only warranted in some cases. Clinical judgment will be required in conjunction with diagnostic tests if available.

*Table 3.4 Common bacteria found in calf neonatal enteritis.*

| **Primary Bacteria in Neonatal Enteritis** | **Type of Bacteria** |
|---|---|
| *E.Coli K99/Enterotoxigenic E.Coli* | Gram negative |
| *Salmonella sp.* | Gram negative |

### *Criteria to treat with antimicrobials.*

Any calf with diarrhoea and showing signs of systemic illness for example such as pyrexia, lethargy, inappetence and associated dehydration or any diarrhoeic calf with blood or mucosal casts in their faeces indicating breakdown of the blood-gut barrier and possible bacteraemia. Indeed, the experience of the clinician will always be required as frequently diagnostic tests are not readily available in real time.

### *Class of AM to consider first line in cases of diarrhea in calves.*

- Parenteral potentiated sulphonamides
- Parenteral amoxicillin or ampicillin
- Parenteral amoxicillin clavulanate

**Notes:** It is view of the Farm Animal clinicians in UCD that oral antimicrobials should never be given to calves as the absorption is not always reliable, especially in sick calves. Moreover, the oral antibiotics tend to cause dysbacteriosis in the digestive tract which can lead to further deterioration of the calf.

## 3.8 Foot Lameness

Lameness is common on many Irish farms, particularly lameness due to foot lesions. These can be infectious or non-infectious in nature. It is crucial that investigation of lameness at the individual animal and herd level is carried out to differentiate between these two categories. Antimicrobial therapy is not indicated for the treatment of non-infectious lameness in cattle unless there is evidence of involvement of deep tissue, a risk of joint infection or cellulitis. Antimicrobial footbaths are no longer licensed and are not indicated for the treatment or control of infectious foot lameness.

### *Non-Infectious Foot Lameness*

Non-infectious foot lameness (sole haemorrhage; sole ulcer; white line disease) frequently requires treatment with NSAIDs at the individual animal level. However, antimicrobial therapy is not indicated for non-infectious causes of foot lameness. White line disease, often with concurrent foot abscess development, may progress to lead to septic pedal arthritis which will require a combination of NSAID and antimicrobial therapy (penicillin-streptomycin; amoxicillin), often post-claw amputation.

### *Infectious Foot Lameness*

Infectious foot lameness, caused by anaerobic (interdigital dermatitis; interdigital necrobacillosis/footrot) or treponeme bacterial infections (Mortellaro's digital dermatitis) do require a combination of NSAID and antimicrobial therapy at the individual animal level.

*Table 3.5 Therapeutic options in infectious foot lameness*

| Diagnosis | Tissue affected | Lameness severity | Clinical Appearance | Bacteria | Topical Oxytetracycline | Parenteral Antimicrobials |
|---|---|---|---|---|---|---|
| Interdigital Necrobacillosis (Footrot) | Interdigital skin and deep tissue | severe | Skin broken; foul smell; swelling and infection of deeper tissue | Anaerobes | Low efficacy | Penicillin; oxytetracycline |
| Digital Dermatitis (Mortellaro) | Skin above/between heel bulbs | severe | Skin eroded; raw ulcerated; can be wart-like | Treponemes | Good Efficacy - preferred treatment | Rarely required |
| Slurry Heel/ Heel Erosion | Heel Bulbs | mild to moderate | Erosions of the heel bulbs often with deep grooves | Anaerobes | Good Efficacy in severe cases only | Not required |
| Interdigital Dermatitis (Scald) | Interdigital skin | moderate to severe | Skin intact; red and inflamed | Anaerobes | Low efficacy | Penicillin; oxytetracycline |

### *Topical Treatment*

Topical antimicrobial treatment with oxytetracycline is sufficient for acute active digital dermatitis lesions followed by control and prevention of further cases using regular foot bathing (at least 4 times weekly to begin with). Topical antimicrobial treatment with oxytetracycline is also sufficient for cases of slurry heel/heel erosion caused by anaerobic bacteria.

### *Parenteral Treatment*

Parenteral antimicrobials are indicated in cases of footrot and interdigital dermatitis due to the involvement of deep soft tissue, the severity of pain and the risk of ascending cellulitis developing. Penicillin is effective in the treatment of footrot and interdigital dermatitis, as is oxytetracycline. Cellulitis often requires a prolonged course of treatment (1-3 weeks) with these first line antimicrobials – however, prognosis may be guarded.

## 3.9 Arthritis – Adult Cattle and Neonatal Calves

For lameness in adult cattle associated with arthritis or polyarthritis, arthrocentesis followed by targeted pathogen identification can help to inform diagnosis and treatment decisions. In the case of *Mycoplasma bovis* arthritis, the penicillin family of antimicrobials are ineffective. Oxytetracycline would be first line antimicrobial therapy for lactating cows. However, *Mycoplasma bovis* infections may frequently prove resistant to antimicrobial treatment using oxytetracycline. Florfenicol could be considered in non-dairy animals and macrolides may also be considered but not as a first line treatment. It is worth remembering that whilst macrolides are classified as AMEG group C and the WHO has classified them as Critically Important Antimicrobials (CIAs) they remain of considerable interest in animal health.

For septic arthritis/joint ill in calves, several bacteria have been implicated, including E. coli (Gram negative); *Staphylococcus aureus*, Streptococci, *Trueperella pyogenes* (all Gram positive). Arthrocentesis followed by bacterial targeted pathogen identification can aid in diagnosis and inform a treatment plan. In neonatal calves with septic arthritis in the first 5 days of life, Gram negative bacterial infection is most likely. In older calves, a Gram positive or mixed infection often occurs.

It is recommended to treat joint ill in neonatal calves using amoxicillin or amoxicillin clavulanate.

## 3.10 Mastitis

### *Background*

Mastitis is inflammation of the udder of a cow, most often caused by bacterial infection. Mastitis can occur at the individual cow level or can occur at the group or herd level with many animals affected.

Cows with mastitis can be clinically affected, where they have obvious changes in the milk such as the presence of clots or watery milk. Clinical mastitis can further be classified as mild, moderate, and severe. A mild case of clinical mastitis only involves obvious changes in the milk, without obvious changes in the udder itself and the cow is not systemically unwell. Moderate cases of clinical mastitis usually have changes in the milk, as well as changes in the udder, such as a hot, painful or swollen gland. Severe cases of clinical mastitis include changes in the milk, the gland and the cow is obviously systemically unwell such as pyrexia and off form but can also progress to being severely affected such as an animal who is seriously ill for example with toxic E. coli mastitis displaying signs of shock, recumbency and often death.

Mastitis can also be subclinical where there are no obvious changes in the milk, the gland or the cow but we know the cow is infected by using indirect measurements such as somatic cell count (SCC). If a cow does not have any clinical signs but has an SCC above 200,000 cells/ml when a sample of the milk is tested, then she is deemed as a subclinically infected cow. Subclinical infection is serious as it maintains a reservoir of infection in the herd and the cows can infect other cows. They are also affected in several ways including having reduced yield.

Clinical mastitis cases tend to occur acutely and often require a course of antimicrobial treatment, although not always. Subclinical cases tend to be infected for a long time and become chronically infected cows. Although sometimes treatment of these cases is warranted, often they respond poorly to treatment and require a dry period to allow the infected quarter a chance to clear the infection and recover.

Antimicrobial therapy for mastitis can be applied during lactation for clinically infected cows (and possibly subclinically affected cows in some cases under veterinary instruction). Alternatively, longer acting antimicrobial products can be used at the point of drying off for cows with evidence of infection to provide antimicrobial treatment for longer during the dry period before the onset of the next lactation.

Prescribing guidelines for mastitis for herds is complicated and requires a sophisticated knowledge of the farm, targeted pathogen identification of both clinical cases across the lactation and subclinically infected cows to gain a proper understanding of the pattern of infection on farm. Mastitis is primarily driven by Gram-positive or Gram-negative pathogens which can alter the treatment protocols and antimicrobial product types selected. Activity of selected antimicrobial agents against common mastitis pathogens is given in Table 3.6.

Herds should have an SOP in place for treatment of clinical mastitis cases developed in conjunction with their veterinarian. This should include criteria to treat, the product to use and when veterinary examination is required. In all cases, whether for in lactation or dry cow use, antimicrobial products should only be prescribed to cows with evidence of infection and in all cases products from EMA guidelines category D should be selected, unless testing of some clinical mastitis cases necessitate the use of a drug from category C. The use of non-steroidal anti-inflammatory drugs can also help alleviate the symptoms of mastitis and should be considered in any SOP for treatment of clinical mastitis cases. In most cases of mastitis intramammary preparations of antimicrobials are the most suitable route of administration unless specifically directed otherwise by a veterinarian.

Further detail on prudent prescribing for use in mastitis treatment can be found at:

*https://animalhealthireland.ie/assets/uploads/2022/01/CellCheck-Prudent-Prescribing-2022-FINAL.pdf?dl=1*

*Table 3.6 Antimicrobial activity against common pathogens causing mastitis in cattle in Ireland*

| | ***Staph aureus*** | ***Strep uberis*** | ***Strep dysgalactiae*** | ***Escherichia coli*** |
|---|---|---|---|---|
| Procaine penicillin | + | ++ | +++ | - |
| Ampicillin/ amoxycillin | ++ | +++ | +++ | ++ |
| Cloxacillin | +++ | ++ | +++ | _ |
| Ceftiofur | +++ | +++ | +++ | +++ |
| Oxytetracycline | ++ | + | + | ++ |
| Trimethoprim/ Sulphadiazine | +++ | ND | ND | ++ |
| Florfenicol | ND | ND | ++ | +++ |
| Gentamicin | +++ | - | - | ++ |
| Streptomycin | ++ | - | - | ++ |
| Neomycin | ++ | - | - | ++ |
| Kanamycin | ++ | - | - | ++ |
| Enrofloxacin | +++ | +++ | +++ | +++ |
| Marbofloxacin | +++ | +++ | +++ | +++ |
| Tylosin | +++ | +++ | +++ | - |
| Erythromycin | +++ | ++ | +++ | - |
| Pirlimycin | +++ | ++ | +++ | - |

| | |
|---|---|
| ND | No data; AMR data currently unavailable in Ireland |
| - | Bacterium intrinsically resistant to antimicrobial; not suitable for use |
| + | Low efficacy against and/or widespread resistance to this antimicrobial in this bacterium |
| ++ | Moderate efficacy against and/or variable resistance to this antimicrobial in this bacterium |
| +++ | High efficacy against and limited resistance (reported to date) to this antimicrobial in this bacterium |

Category B: HP-Critically Important Antimicrobials, restricted use*

### *Toxic Mastitis*

Cows that suffer an acute case of *E.coli* mastitis may present with severe systemic signs due to the toxaemia associated with release of the lipopolysaccharide (LPS) toxin as E.coli are lysed. These endotoxins cause severe systemic effects, usually of shock, dehydration, recumbency, tachycardia, cold extremities, and even death, in conjunction with watery milk with the presence of clots. E. coli mastitis usually occurs close to calving but can occur at any time.

Treatment is primarily related to appropriate fluid therapy to address the circulatory collapse, but aided using NSAID, calcium borogluconate, proper nursing care, and milking out the quarter. There is debate about how useful antimicrobial therapy is in the advanced stage of acute, toxic mastitis. Some antimicrobial therapy may be considered, and classes are listed below.

### *Class of AM to consider first line in cases of E. coli mastitis*

- Parenteral potentiated sulphonamides
- Parenteral oxytetracycline
- Parenteral amoxicillin clavulanate
- Aminoglycoside such as framycetin

**Notes:**

*As per DAFM guidelines any HP-CIA antimicrobial such as a 3$^{rd}$/4$^{th}$ generation cephalosporin or a fluroquinolone should not be used unless on foot of targeted pathogen identification deeming it the only available option.

## 3.11 Infection of the reproductive tract: cow

### *Background*

Reproductive diseases requiring antimicrobials occur in the post-partum period. The main disease processes in this period are shown in Table 3.7 below.

*Table 3.7* Infections of reproductive tract in the post-partum period: cow

| **Disease** | **Clinical symptoms** | **Timeframe** |
|---|---|---|
| Retained foetal membranes | • failure to expel foetal membranes within 24 hrs post parturition.<br>• systemic signs can be those of puerperal metritis or none | 24 hrs post parturition |
| Puerperal metritis | • abnormally enlarged uterus.<br>• foetid watery red-brown discharge<br>• signs of systemic illness and fever >39.5 C | within 21 days after parturition |
| Clinical metritis | • abnormally enlarged uterus and purulent uterine discharge detectable in the vagina<br>• no systemic signs | Within 21 days after parturition |
| Clinical endometritis | • purulent (>50% pus) uterine discharge detectable in the vagina<br>• mucopurulent (approximately 50% pus, 50% mucus) discharge detectable in the vagina<br>• no systemic signs | 21 days or more after parturition<br>26 days after parturition |
| Pyometra | • accumulation of purulent material within the uterine lumen in the presence of a persistent corpus luteum and a closed cervix<br>• *note: pyometra may be present with no visible systemic signs* | |

Common bacteria involved in uterine disease are *E. Coli* (gram negative) and *Trueperella pyogenes* (gram positive), with *E. coli* being present in the more acute phases and *Trueperella* in the more chronic phases.

### *Criteria to treat with antimicrobials*

Any cow showing signs of systemic illness for example such as pyrexia, lethargy, inappetence and associated dehydration. Clinical endometritis that persists 21 days or more after parturition.

### *Class of AM to consider first line in cases of reproductive disease in cows*

Clinically ill cows that present with RFM/puerperal metritis:

- Parenteral amoxicillin/amoxicillin clavulanic acid
- Parenteral potentiated suphonamides

Subacute and chronic endometritis cow that present with discharge as only clinical sign:

- Intrauterine cephapirin (recommended to only use in cows greater than 21 days calved)

## 3.12 Bovine respiratory disease (BRD)

### *Background*

Bovine respiratory disease (BRD) is a leading cause of death in cattle of all ages, from calves aged one month and over, weanlings and adults (All Ireland Animal Disease Report 2022). BRD is a classic multifactorial disease often without one simple viral or bacterial pathogen involved. More often it involves multiple pathogens, possibly an initial viral insult followed by secondary bacterial infection with respiratory pathogens that may or may not be commensals of the upper respiratory tract, progressing in the very chronic stages to lung abscesses with *Trueperella pyogenes.* In addition to the multiple pathogens involved the animal's immunity, age and environmental and other management factors may have a role in precipitating outbreaks of BRD.

The main viruses involved in BRD include respiratory syncytial virus (RSV), parainfluenza 3 (PI3), infectious bovine rhinotracheitis (IBR) and with the advent of molecular epidemiology other less commonly diagnosed viruses such as bovine coronavirus, influenza D, bovine rhinitis, adenovirus etc. are thought to have a role but little work is done to elucidate their role in field outbreaks of BRD. Regardless of the primary virus or viruses involved in BRD cases in calves or adults, they usually result in secondary bacterial infection necessitating antimicrobial treatment.

The pathogens involved in BRD in adult cattle and in calves are largely similar, BRD in cattle under 1 year of age is usually caused by an infectious agent, as is often the case in adult cattle BRD also. However, in adults' other causes such embolic pneumonia should be considered a possibility. Parasitic pneumonia due to patent infection with *Dictyocaulus viviparous* (lungworm) can affect calves and adult cattle, and the reinfection syndrome can present as respiratory disease in adults also. Parasitic pneumonia must be considered in any bovine exposed to pasture.

*Table 3.8 Bacteria involved in Bovine Respiratory Disease*

| **Common Bacteria involved in BRD** | **Type of Bacteria** |
|---|---|
| *Mannheima haemolytica* | Gram negative |
| *Pasteurella multocida* | Gram negative |
| *Histophilus somnus* | Gram negative |
| *Mycoplasma bovis* | Atypical bacteria (no cell wall) |
| *Trueperella pyogenes (chronic stages/abscesses)* | Gram positive |

### *Criteria to treat with antimicrobials*

Any bovine showing signs of respiratory illness for example such as pyrexia, increased respiratory rate and effort (blowing), nasal discharge, coughing, as well presenting dull and off feed. The experience of the clinician will always be required as frequently diagnostic tests are not readily available in real time. A range of diagnostic tests exist, examples include nasopharyngeal swabs of acutely affected pyrexic animals which can be tested for multiple pathogens using PCR techniques, as well as pathogen demonstration tests of the lower airways including lung washes and transtracheal washes. Careful test interpretation is required as many pathogens causing BRD can also be commensals of the upper respiratory tract. However, these tests are invasive and require a time delay for results. Although tests will often be required in the face of an outbreak, treatment should not be delayed as early, effective treatment is more likely to result in successful cures.

### *Class of AM to consider first line in cases of BRD*

- Parenteral oxytetracycline
- Parenteral florfenicol
- Parenteral cephalexin could be considered in adult cattle (short withdrawal)
- Parenteral amoxicillin clavulanic acid
- Parenteral procaine penicillin 44 000 IU/kg for chronic pneumonia where *Trueperella pyogenes* is suspected as the likely pathogen (please note this is an **"off label"** dose, standard dose is 22 000IU/kg)

Parenteral macrolides can be considered, but not first line treatment and not to be used prophylactically. It is worth remembering that whilst macrolides are AMEG classified as group C and classified by WHO as CIAs, they remain of particular concern in animal health.

Respiratory disease usually requires a minimum of 3 days, and often a 5–7 day course of antimicrobial treatment is required depending on clinical signs and chronicity

**Notes:**

The use of non-steroidal anti-inflammatory (NSAID) drugs is strongly advised in conjunction with appropriate therapy for cases of BRD.

Prophylactic or metaphylactic use of antimicrobials should not be used for the control of bovine respiratory disease.

## 3.13 Infectious skin disease

### *Background*

Bacterial infections of the skin of ruminants usually occur secondary to initial trauma, sloughing of skin (e.g. photosensitisation) or secondary to concurrent dermatitis due to parasitic infections (e.g. mites) leading to severe pruritis. In these cases, secondary infection with Staph spp. (Gram positive) is the most common finding.

Primary bacterial infection of the skin of cattle or other ruminants is less common and is often associated with exposure to extreme environmental or weather conditions or underlying immunosuppression.

### *Dermatophilus Congolensis*

Dermatophilosis, also known as rain scald or mud rash, often leads to bacterial dermatitis along the back or distal limbs of cattle, sheep or camelids exposed to excessive moisture and wet weather conditions. *Dermatophilus congolensis* is a Gram-positive bacteria and is susceptible to penicillin. However, parenteral therapy is only indicated for diffuse lesions in animals with poor body condition and suspected underlying immunosuppression. For small, localised lesions, especially on the distal limbs, repeated topical washing using chlorhexidine solution can be effective in eliminating the bacterial infection, with the addition of topical oxytetracycline spray for more severe cases.

### *Staphylococcal Infections of the Skin*

The majority of Staphylococcal bacterial infections of the skin are susceptible to penicillin. However, Staph aureus, and some other members of the family, can produce the β-lactamase enzyme necessitating the use of potentiated penicillins, e.g. amoxicillin or amoxicillin clavulanate. The use of appropriate diagnostic swabs for bacterial culture and targeted pathogen identification are

recommended for refractory lesions due to the risk of multi-resistant Staph aureus (MRSA) or mixed infections.

### *Cutaneous Actinobacillosis*

Cutaneous actinobacillosis usually occurs following trauma to the skin. Transmission of *Actinobacillus ligniersii* (Gram negative) to the skin can occur by the affected animal subsequently licking the traumatised area, as *Actinobacillus* ligniersii is a commensal of the oral cavity and also the cause of Timber/Wooden Tongue. Cutaneous actinobacillosis is usually characterised by the formation of nodular, wart-like masses on the skin, often clumped together, which are commonly located along the back, flank or limbs. Enlarged peripheral lymph nodes may also be found.

Treatment with parenteral streptomycin or oxytetracycline is indicated.

### *Criteria to Treat with Antimicrobials*

Parenteral antimicrobials are indicated where there is evidence of diffuse bacterial dermatitis and/or in animals where underlying immunosuppression is strongly suspected or confirmed.

Topical antimicrobials, usually oxytetracycline spray - are indicated for superficial infected abrasions to skin or localised bacterial infections.

## 3.14 Cystitis and Pyelonephritis

### *Background*

Cystitis refers to infection and inflammation of the bladder. When bacteria ascend through the ureters and cause infection in the kidneys, it is termed pyelonephritis. Both conditions are sporadic and most often seen after calving, typically in the first 3 months post-calving. Pyelonephritis is more commonly seen in multiparous beef cows and most often associated with a history of dystocia or other post-partum complications (i.e. retained placenta or metritis). Unhygienic urinary catheterisation has also been implicated in transmitting some bacteria (i.e., *Corynebacterium* spp) from cow to cow so veterinarians should be aware of this risk. Diagnosis is commonly based on a history of recent calving (potentially a dystocia) and clinical signs such as haematuria, stranguria, pyuria and a painful response and/or loss of lobulation when the left kidney is palpated per rectum. Additional cow-side tests might include the presence of white blood cells, proteinuria or blood cells on a dipstick evaluation of the urine and ultrasonographic changes in the kidneys or bladder. Further diagnostics might include urine bacteriology to identify the organism or blood biochemistry to determine the degree of azotemia (i.e. elevated blood urea nitrogen and creatinine). In the case of pyelonephritis, many cases may be quite advanced and even with treatment, these cases carry a guarded prognosis. Nephrectomy may be indicated in high value cows with unilateral pyelonephritis that fail to respond to treatment, although it is rarely done.

*Table 3.9 Common bacteria in bovine urinary tract infections*

| **Common Bacteria in Cystitis and Pyelonephritis** | **Type of Bacteria** |
|---|---|
| *Corynebacterium renale* | Gram positive |
| *E coli* | Gram negative |
| *Trueperella pyogenes* | Gram positive |

### *Criteria to treat with antimicrobials*

**Cystitis**

Any bovine showing signs of systemic illness, such as dullness, pyrexia, stranguria, pyuria, hematuria and pain on palpation of the bladder would warrant treatment with an antimicrobial. Cystitis has a good prognosis, however, early diagnosis with prompt and ongoing sustained treatment are needed for a successful recovery and failure to do so could lead to it progressing to pyelonephritis.

**Pyelonephritis**

Any bovine presenting with a severe dullness, signs of chronic disease (e.g., marked weight loss) and uremic fetor (breath), may indicate severe irreparable damage to the kidneys and has a poor prognosis. Thus culling instead of antimicrobial treatment may be warranted. The decision to treat will depend on the clinician's experience as to the degree of chronicity and likely response to therapy. Further diagnostic tests (*mentioned above*) will assist in this decision-making process.

### *Class of AM to consider first line in cases of cystitis and pyelonephritis*

- Parenteral procaine penicillin (particularly in cases caused by *Corynebacterium renale*)
- Parenteral potentiated sulphonamides
- Parenteral ampicillin, amoxicillin (+/- clavulanate) (in cases where *E.coli* is suspected)
- *Prolonged administration of antimicrobials for 14-21 days is often warranted in cases of pyelonephritis

# 4. Prudent prescribing in sheep practice

This document covers prescribing guidelines for the following ovine conditions:

- Watery mouth /E. coli septicaemia
- Navel ill and joint ill
- Lameness caused by scald, footrot or Contagious Ovine Digital Dermatitis (CODD), scald
- Pneumonia caused by pasteurellosis
- *Listeria monocytogenes* infection
- Mastitis
- Chlamydial abortion

## 4.1 Watery mouth

### *Background*

Watery mouth or *E.coli* septicaemia is an infectious bacterial disease with a high mortality rate in newborn lambs. It usually manifests within the first 3 days of life when lambs pick up *E. coli* from the environment and the bacteria multiply very rapidly in the gut. The infection is peracute with affected lambs succumbing to the disease within hours. Clinical signs include lethargy, failure to suck, profuse salivation, bloating, retained meconium and death.

Despite the bloat, oral electrolyte therapy at a rate of 50 ml/kg up to 3-4 times daily is important to prevent dehydration as well as warm soapy water enemas in the early stage to improve gut motility and expulsion of meconium.

Appropriate ewe pre-partum nutrition and Body condition scoring (BCS), as well as lambing pen hygiene and colostrum management in newborn lambs is fundamental to prevention. These are **essential** to remember as routine prophylactic antimicrobial administration in all lambs is no longer acceptable for the prevention of watery mouth.

### *Criteria to treat with antimicrobials*

Lambs with obvious signs of septicaemia can be treated with parenteral antimicrobials.

Oral antimicrobials can be effective during the earlier phases of the disease and/or in a disease outbreak in at risk lambs (e.g., low birthweight lambs, triplets or when infectious pressure is high).

### *Class of AM to consider first line in cases of watery mouth*

- Oral spectinomycin
- Parenteral potentiated sulphonamides
- Parenteral amoxicillin alone/amoxicillin with clavulanic acid

## 4.2 Navel ill and joint ill

### *Background*

Navel ill or umbilical infection occurs when lambs are born into unhygienic conditions and when there is inadequate navel disinfection. Receiving insufficient colostrum is also a major risk factor. It is more common in male lambs because urination delays drying of the umbilicus and can remove the umbilical disinfectant.

Umbilical infections can remain localised in the umbilical region or spread to involve the abdominal cavity, joints, meninges, lungs, kidneys and heart. When the infection spreads to one or more joints it leads to joint ill (infectious polyarthritis) which affects the long-term prognosis for the animal.

As stated above, preventative strategies focusing on ewe nutrition, hygiene and colostrum management are **essential** to remember as prophylactic antimicrobials are not appropriate to prevent navel/joint ill outbreaks.

### *Criteria to treat with antimicrobials*

Lambs with obvious signs of umbilical or joint infection (enlarged, hot and painful swelling) and/or should be treated with parenteral antimicrobials.

### *Class of AM to consider first line in cases of join and navel ill*

- Parenteral penicillin with streptomycin.
- Parenteral amoxicillin alone/amoxicillin with clavulanic acid.

## 4.3 Lameness

### *Background*

Infectious causes of lameness include scald (interdigital dermatitis), footrot and CODD. Scald is caused by *Fusobacterium necrophorum*, footrot is caused by *Dichelobacter nodosus* as the primary pathogen while Contagious Ovine Digital Dermatitis (CODD) is associated with *Treponeme* spp. bacteria, although there is growing evidence that many of these the bacteria work in synergy to cause their characteristic lesions. Isolation of infected sheep (especially those with footrot and CODD) to an area with dry and clean underfoot conditions also speeds the healing process.

### *Criteria to treat with antimicrobials*

Sheep who are clinically lame need to be examined and appropriately treated based on the clinical presentation.

### *Class of AM to consider first line for infectious causes of lameness*

- Scald: Treat individual cases with topical antimicrobial spray containing oxytetracycline.
- Footrot: Treat individual cases with isolation and topical oxytetracycline spray and long acting oxytetracycline parenterally.
- CODD: Treat individual cases by isolation, application of topical oxytetracycline and injection of long-acting amoxicillin (10 mg/kg IM) or oxytetracycline (10mg/kg) parenterally.

## 4.4 Pasteurellosis pneumonia

### *Background*

Pasteurellosis is an infectious pneumonia complex caused by a combination of *Mannheimia haemolytica, Bibersteinia trehalosi* and *Pasteurella multocida*. All these bacteria are normal residents of the tonsils and throat of healthy animals but in cases of immune suppression can multiply, invade the lungs and then cause clinical disease in the form of pneumonia or septicaemia.

### *Criteria to treat with antimicrobials*

Septicaemia is often characterised by sudden death or rapidly dying sheep with treatment rarely successful. Therefore, the criteria described here are for pneumonia caused by pasteurellosis. These include increased respiratory rate, mucopurulent nasal discharge, conjunctivitis, coughing and an increased temperature. When all these signs are present treatment with antimicrobials is warranted.

Using clinical signs, it is important to differentiate pasteurellosis from more chronic respiratory diseases such as Jaagziekte/Maedi Visna or atypical pneumonia (enzootic pneumonia) caused by *Mycoplasma ovipneumoniae*. As these are either unlikely to respond to antimicrobials in the case of the former or are of low pathogenicity in the case of the latter, neither typically require antimicrobial treatment unless secondary pneumonia is suspected.

### *Class of AM to consider first line for pasteurellosis*

- Parenteral oxytetracycline.
- Parenteral florfenicol.

## 4.5 *Listeria monocytogenes* infection

### *Background*

Listeria monocytogenes is a Gram-positive organism and, as in cattle, leads to microabscessation of the hindbrain. Clinical signs associated with listeria infection are unilateral/asymmetric cranial nerve deficits predominantly affecting the fifth, seventh and eight cranial nerves.

### *Criteria to treat with antimicrobials*

Any sheep which is showing clinical signs associated with the cranial nerves that are usually affected by *Listeria monocytogenes* should be considered for treatment.

### *Class of AM to consider first line for listeriosis*

- Oxytetracycline or amoxicillin (standard dose or double dose as an alternative treatment).

## 4.6 Mastitis

Mastitis is an inflammation of the mammary gland, usually caused by various bacteria including *Streptococcus* sp., *Staphylococcus* sp., *Mannheimia haemolytica* and coliforms. The clinical presentations can vary from acute to chronic, but also can be present in subclinical form (often goes undetected in ewes kept for meat production). Mastitis is predominately caused by bacteria, but viral causes like Maedi Visna should be considered in flocks with evidence or a history of this disease.

### *Criteria to treat with antimicrobials*

Ewes suffering from acute mastitis should be considered for treatment with antimicrobials. Clinical signs of acute mastitis in ewes are like those in cows and include heat and swelling in the udder but also a cold and hard udder, pain that can present as lameness, watery or bloody secretions or palpable intramammary masses (IMM). It should be treated symptomatically in a similar fashion to cows (i.e., NSAIDs, oral fluids, regular stripping and antimicrobials).

For chronic hard/lumpy udders, damage is likely irreversible and antimicrobial treatment (parental/intramammary) is not warranted.

Clinical mastitis with changes in milk which will typically present in milking does or ewes can be managed with culture and susceptibility testing in a similar manner to bovine mastitis. Few intramammaries are licensed for does/ewes but may be prescribed under the cascade.

### *Class of AM to consider first line for ovine mastitis.*

- Acute ovine mastitis can be treated with parental oxytetracycline or parenteral macrolides.

## 4.7 Chlamydial abortion

### *Background*

*Chlamydophila abortus* is a gram negative, obligate intracellular bacterium that can cause abortion outbreaks in sheep flocks. Abortion is usually in the last three weeks of gestation and can be preceded by the animals being off food and present with reddish vaginal discharge. Aborted foetuses are well developed with no gross anatomical abnormalities and with the occasional live but weak lamb being born. There is frequently a placentitis with yellow/pink pus-like exudate and necrosis of the cotyledons. Transmission is oro-nasal with the products of abortion and contaminated bedding, as well as the affected ewes and lambs, forming a high risk for spreading of the disease throughout the flock.

### *Criteria to treat with antimicrobials*

Confirmation of *Chlamydophila abortus* on histopathological examination of foetus and placenta and/or PCR confirmation of the presence of *Chlamydophila abortus* while there is a population of vulnerable ewes still left to lamb within the same flock

### *Class of AM to consider first line for chlamydial abortion*

- Parenteral administration of long acting oxytetracycline can be considered for all remaining pregnant ewes to suppress bacterial growth and prevent further abortions in an abortion storm scenario following laboratory confirmation.

# 5. Prudent antibacterial use in companion animal practice

## 5.1 Introduction

The following guidelines have been developed by the UCD Small Animal Clinicians for use by students and clinicians in the UCDVH. They are based on best available evidence and experience of the group. In all cases clinical judgement should take precedence in all prescribing decisions and the following is intended as a guide, subject to periodic review. General principles are outlined in this introductory section with guidelines for specific conditions given in the appropriate sections.

In line with EMA recommendations, antimicrobials in EMA category D should always be used as first choice, with Category C agents used only when nothing in Category D will suffice. For example, a macrolide may be prescribed as first choice if there is reasonable suspicion of a specific pathogen such as *Campylobacter* species.

The UCDVH is a tertiary referral hospital and cases referred to the hospital are frequently on antimicrobial treatment at time of referral.

- **If an animal is in receipt of an antibacterial drug at the time of referral and:**
    - Bacterial involvement is not suspected:
        - The drug(s) should be discontinued
    - Bacterial involvement is suspected, and continuation of therapy is not necessary:
        - The drug(s) should be discontinued
    - Bacterial involvement is suspected, and continuation of therapy is necessary:
        - There has been a response to therapy:
            - The drug(s) should be continued unless it will interfere with subsequent testing
            - De-escalation (i.e. discontinuation of some drug(s)) should be considered if a combination of drugs is being administered and is considered excessive
        - There has been no response to therapy:
            - There has been inadequate time to determine efficacy:
                - Continue if the drug choice is appropriate for the likely agents involved
                - Discontinue if the drug choice is inappropriate for the likely agents involved
            - There has been adequate time for a response to therapy
                - Discontinue the drug
                - Await results of AST testing if animal is clinically stable
                - Administer another empirical antibacterial agent if clinically unstable due to bacterial infection pending return of AST results

- **Empirical combination therapy and de-escalation:**
    - In some critical cases, empirical combination therapy is necessary to ensure coverage of all likely infectious agents. This may include use of Category B agents such as a fluoroquinolone in emergency situations (e.g. sepsis) prior to receipt of culture and susceptibility test results.
    - Appropriate sampling for AST should be performed in all cases prior to commencing therapy
    - Following return of AST results, de-escalation should be initiated:
        - If pre-treatment AST results indicate resistance to the empirical antimicrobial chosen, the drug should be changed unless there has been a good clinical response, and the response is not thought to be due to concurrent treatments (e.g. IVFT)
        - If all identified bacterial isolates are susceptible to a subset of drugs within the combination protocol, only this subset of drugs should be continued
            - If clinical deterioration occurs following this adjustment, AST should be repeated before re-escalation to the original protocol, and other causes of clinical deterioration explored
            - Care should be taken to review previously administered antibacterial drugs (including prior to referral) due to potential effects on bacterial growth

- **Zoonotic risk**
    - Owners should be made aware of zoonotic risk of multi-drug resistant bacteria, particularly in cases of infection with MRSA or *Salmonella* serotypes. However, the risk of colonization of owners with other multidrug resistant organisms such as MDR *E. coli* should also be highlighted.

## 5.2 Gastrointestinal tract

*Antibacterials are **not** indicated for:*

- Acute vomiting
- Acute diarrhoea (including acute haemorrhagic cases) in the absence of risk of sepsis. Use SIRS criteria to establish whether sepsis is present.
- Pancreatitis
- Most gastric *Helicobacter* infections
- Most *Campylobacter*, *Salmonella*, *Clostridium perfringens* or *Clostridiodes difficile* infections
- Long term management of chronic diarrhoea

*Antibacterials are indicated for:*

- **Acute diarrhoea with systemic signs indicating actual (or risk of) bacteraemia or sepsis:**
  - **Amoxicillin/clavulanate**
- **Trial treatment of "antimicrobial responsive diarrhoea":**
  - This is an infrequent diagnosis and use of antimicrobial treatment should be decided on a case-by-case basis using clinical judgement and results of diagnostic tests.
- **Cholangitis/cholangiohepatitis:**
  - Ideally base selection of antimicrobial on AST testing of bile or liver tissue
  - Treatment usually commenced pending return of AST results
  - Empirical choices:
    - **Amoxicillin/clavulanate**
    - **Cefalexin**
    - Add **metronidazole** (dogs)
  - Treat for 2–4 weeks

- **Neutrophilic enteritis (based on GI biopsies only):**
  - Investigate enteropathogenic bacteria (e.g. *Salmonella*, *Campylobacter*)
  - Choice of antimicrobial should be based on AST or (Fluorescing *in-situ* hybridization) FISH analysis of enteric biopsy.
  - **Amoxicillin/clavulanate** (first line)
  - **Fluoroquinolone** only if supported by AST/FISH results.

- **Hepatic encephalopathy:**
  - **Amoxicillin**
  - **Metronidazole**
  - Treatment should only be provided during initial control, and when clinical signs cannot be controlled with other interventions (diet and lactulose) alone.

- **Histiocytic ulcerative colitis (based on colonic biopsies only):**
  - **Fluoroquinolone** (first line) but only if supported by FISH analysis unless the animal' welfare is at risk.
  - Apparently resistant cases may require repeat biopsy for AST testing

*Other considerations:*

Neutrophilic enteritis is recognised at UCD with increasing frequency. Samples for culture should be collected during all upper and lower endoscopic procedures. These samples can be analysed immediately, or frozen to allow subsequent analysis (less ideal).

## 5.3 Urogenital tract

*Antibacterials are **not** indicated for:*

- Feline idiopathic cystitis
- Feline urolithiasis and canine non-struvite urolithiasis
- Urinary incontinence
- Subclinical bacteriuria (canine or feline) in the absence of complicating diseases
- Juvenile canine vaginitis
- Prophylactic therapy for recurrent bacterial cystitis

*Antibacterials are indicated for:*

- **Sporadic bacterial cystitis (uncomplicated, symptomatic, canine urinary tract infection):**
  - Consider use of analgesics alone in uncomplicated cases or pending culture results
  - Culture and susceptibility testing should be performed in all suspected cases
  - Ideally base selection of antimicrobial on AST testing
  - One of the following can be used as empirical treatment if not possible to delay therapy:
    - **Amoxicillin**
    - **Trimethoprim/sulphonamide**
  - Treat for 3-5 days
  - If pre-treatment culture results indicate resistance to the empirical antimicrobial chosen, the drug should be changed unless there has been a good clinical response
  - Post-treatment culture not indicated when clinical signs have resolved

- **Recurrent bacterial cystitis (Reinfection, recurrent and persistent urinary tract infections):**
  - Urine AST testing should be performed prior to treatment
  - Investigate underlying predispositions to infection
  - Consider analgesia alone while awaiting AST results
  - **Amoxicillin (± clavulanate)**
  - **Trimethoprim/sulphonamide**
  - Treatment for 3-5 days may be adequate, but a longer (7-14 day) course may be considered in persistent and potentially relapsing infections when factors inhibiting response to antimicrobials are suspected (e.g. bladder wall invasion)
  - If pre-treatment AST results indicate resistance to the empirical antimicrobial chosen, the drug should be changed unless there has been a good clinical response, and the response is not thought to be due to concurrent treatments (e.g. IVFT)
  - Antimicrobials ineffective against E. coli in tissue (e.g. amoxicillin clavulanate) should be avoided in cases with suspected bladder wall invasion.
  - If recurrent/persistent infection, modify therapy on basis of susceptibility data and review predisposing factors (e.g. urolithiasis, anatomical abnormalities)
  - Culture should be repeated during treatment and 1-2 weeks after cessation of antimicrobials in relapsing cases, but treatment may not be indicated if subclinical bacteriuria suspected.

- **Subclinical bacteriuria in some immunocompromised animals, those when infection is suspected as a trigger of secondary immune disease, or when associated with plaque-forming or urease-producing organisms:**
    - Consider antimicrobial treatment as for **Recurrent bacterial cystitis**
    - Blanket treatment of all immunocompromised animals with bacteriuria is discouraged because subclinical bacteriuria may not be harmful and may resolve following control of the underlying disease. Treatment is also more likely to be ineffective, thus promoting AMR

- **Prostatitis (entire males):**
    - Prostatic abscesses should be drained surgically or under ultrasound guidance
    - AST testing shall be performed prior to treatment
    - Empirical choice should be a drug with known activity against Enterobacteriaceae
    - **Enrofloxacin** (higher end of dose range (5-20 mg/kg q24h) in dogs). However, 20 mg/kg enrofloxacin every day may be an excessive dose for a concentration-dependent AM unless MIC data indicate such a high dose is required.
    - **Marbofloxacin** (higher end of dose range (2.7-5.5 mg/kg q24h) in dogs)
    - **Doxycycline** will reach adequate concentrations and treatment with fluoroquinolones should be de-escalated to doxycycline when supported by AST results
    - **Trimethoprim/sulphonamide** may not penetrate prostatic tissue as readily and be more likely to cause adverse effects when administered over a prolonged period
    - **Clindamycin** and **macrolides** penetrate prostatic tissue but have limited activity against Gram negative bacteria, and should therefore only be used if supported by AST results
    - Beta-lactams, aminoglycosides and tetracyclines have poor tissue penetration, and should be avoided especially in chronic prostatitis.
    - Treat for 4 weeks for acute prostatitis and 4-6 weeks for chronic prostatitis
    - Medical/surgical castration should be considered

- **Canine struvite urolithiasis (during dissolution):**
    - The decision to treat struvite urolithiasis with an antibacterial drug depends on the bacterium identified and the presence or absence of clinical signs e.g. urease-producing bacteriuria should be treated even in the absence of clinical signs of cystitis, while *Escherichia coli* without clinical signs of cystitis should not be treated, unless surgical removal is planned (see advice for cystoscopy below)
    - For struvite uroliths with clinical signs of cystitis, treat for seven days with antibacterial drugs selected by AST. If AST unavailable, use guidance for **Sporadic bacterial cystitis.** Repeat culture only if dissolution is not progressing as suspected, or if clinical signs persist/recur (see **Reinfection, recurrent and persistent urinary tract infections**)
    - Dietary modification and urine acidification should be commenced alongside antibacterial treatment in cases of struvite urolithiasis
    - For non-struvite urolithiasis without evidence of bacterial cystitis, antimicrobials should be withheld
    - For non-struvite urolithiasis with concurrent bacterial cystitis, seven days of treatment is recommended with choice of agent guided by AST
    - Consider surgical removal of uroliths in all cases

- **Suspected pyelonephritis:**
  - Treat immediately while awaiting AST results
  - Empirical choice should be drug with known activity against Enterobacteriaceae e.g. a **fluoroquinolone** at higher dose (see **Prostatitis**)
  - If pre-treatment culture results indicate resistance to the empirical antimicrobial chosen, the drug should be changed unless there has been a good clinical response, and the response is not thought to be due to concurrent treatments (e.g. Intravenous Fluid Therapy)
  - Treat for 10-14 days
  - Culture should be repeated 1-2 weeks after cessation of antimicrobials, but treatment may not be indicated if subclinical bacteriuria is suspected.

- **Cystoscopy:**
  - Cystoscopy should only be performed following a negative urine culture.
  -
- **Urinary catheters:**
  - Prophylactic antimicrobial use shall not be used.
  - Urine culture (during or after catheterisation) in the absence of clinical signs is not recommended.
  - Treatment of bacteriuria in the absence of clinical signs is not recommended.
  - Routine culture of catheter tips is not recommended.
  - Urine culture should be performed if signs of infection develop in a catheterised animal. If possible, the catheter should be removed and a urine sample collected by cystocentesis before replacement of the catheter. If cystocentesis is not possible, a urine sample should be obtained directly from a newly placed catheter, after discarding the first 3-5 mL of urine withdrawn.
  - Antimicrobials should be prescribed as for **Sporadic bacterial cystitis.**
  - Following resolution of clinical signs in catheterised animals, the catheter should be removed, or replaced with a new catheter if continued catherisation is necessary

- **Suspected leptospirosis:**
  - Treatment should be commenced prior to receipt of confirmatory test results if clinical suspicion is high.
  - Oral **doxycycline**
  - **Amoxicillin (± clavulanate)** (initially IV) if not tolerant of doxycycline, to terminate bacteraemia until doxycycline can be used.
  - Affected animals do not need to be housed in isolation but a closed urine collection system should be used.
  - Treat with doxycycline for minimum of two weeks
  -
- **Pyometra:**
  - Antibacterials not required if stable and proceeding directly to ovariohysterectomy (OHE). Antimicrobials indicated if two or more severe inflammatory response syndrome (SIRS)markers are present.
  - Surgically managed:
    - **Amoxicillin clavulanate**
    - Treatment discontinued after surgery (unless septic peritonitis)
  - Medically managed:
    - **Amoxicillin clavulanate**

## 5.4 Ophthalmic infection

*Antibacterials are indicated for:*

**Canine conjunctivitis:**

- **Fusidic acid**
- **Chlortetracycline**
- Treat for 5–7 days

**Feline conjunctivitis:**

- **Chlortetracycline**
- **Fusidic acid**
- Treat for 5–7 days
- *Chlamydia felis*:
  - Systemic **doxycycline** (amoxicillin/clavulanate in pregnant queens and kittens)
  - Treat for 21–28 days
- *Mycoplasma felis*
  - Topical **tetracycline**

**Uncomplicated corneal ulceration:**

- Topical chloramphenicol

**Complicated corneal ulceration (infectious keratitis):**

- Topical **chloramphenicol** AND
- Topical **gentamicin** Topical ciprofloxacin Topical ofloxacin
- Treat until the corneal defect has re-epithelialized q4 hours for the first 48 hours – reduced once the destructive corneal process has stopped.
- Consider systemic antibacterial if, e.g. 'melting', corneal perforation, marked uveitis.

**Orbital abscessation/bacterial cellulitis:**

- **Amoxicillin/clavulanate**
- **Cefalexin** and **metronidazole**
- **Cefalexin** and **clindamycin**
- Treat for 2 weeks
- Attempt drainage via most appropriate route.

## 5.5 Systemic infection

*Antibacterials are indicated for:*

- **Neutropenia induced by chemotherapy:**

| | Grade 1<br>1.5 – 1.99 x $10^9$/L | Grade 2<br>1.0 – 1.49 x $10^9$/L | Grade 3<br>0.5 – 0.99 x $10^9$/L | Grade 4<br>< 0.5 x $10^9$/L |
|---|---|---|---|---|
| **Managed as** | Outpatient | Outpatient if normothermic and clinically well. Inpatient if febrile. | Inpatient if febrile; outpatient if normothermic and clinically well. | Inpatient if febrile; outpatient if normothermic and clinically well. |
| **Intravenous catheter** | No | No | Yes, if in patient (aseptically and checked daily) | Yes (aseptically and checked daily) |
| **Antimicrobials** | No | Oral amoxycillin-clavulanate, if well and normothermic. Intravenous amoxicillin-clavulanate and enrofloxacin, if febrile or unwell. | Oral amoxycillin-clavulanate if normothermic. Intravenous amoxicillin-clavulanate, if febrile and if no response in 24 hours, refer to sepsis section below. | Oral amoxycillin-clavulanate if normothermic. Intravenous amoxicillin-clavulanate, if febrile and if no response in 24 hours, refer to sepsis section below. |
| **Checks** | Monitor patient. | | ● Barrier nurse<br>● Regular temperature checks (q4 hours)<br>● Treat any sign of illness (eg, vomiting, diarrhoea, anorexia) | ● Barrier nurse<br>● Regular temperature checks (q4 hours)<br>● Treat any sign of illness (eg, vomiting, diarrhoea, anorexia) |

- **Severe sepsis:**
  - Empiric combination antibacterial therapy should be initiated immediately but must be adjusted to a narrower regimen (de-escalated) in the first 72 hours, if possible, based on AST results
  - **Metronidazole**, **amoxicillin-clavulanate** and a **fluoroquinolone. Note:** IV enrofloxacin is not recommended in cats due to safety concerns**.**
  - Initially intravenously then orally when clinical signs improve.
  - Treat for 2 weeks following resolution of signs/abdominal effusion.
  - A more restricted antibacterial combination should be selected if the source of infection is known e.g. metronidazole and a fluoroquinolone may be sufficient for gastrointestinal tract leakage

## 5.6 Musculoskeletal infections

*Antibacterials are indicated for:*

- **Discospondylitis:**
  - Empirical therapy should commence immediately. Appropriate choices include:
    - **Cefalexin**
    - **Amoxicillin-clavulanate**
    - **Trimethoprim/sulfadiazine**
    - **Clindamycin**
  - Administer intravenously if severe neurological compromise or signs of sepsis.
  - AST should be performed if possible and urinary AST should always be performed.
  - If pre-treatment culture results indicate resistance to the empirical antimicrobial chosen, the drug should be changed.
  - Treat for minimum 8 weeks (based on clinical and diagnostic imaging response)

- **Infective/septic arthritis:**
  - **Amoxicillin-clavulanate**
  - AST should be performed in all cases.
  - If pre-treatment culture results indicate resistance to the empirical antimicrobial chosen, the drug should be changed.
  - Treat for 4 weeks OR until synovial fluid neutrophils <3%

- **Osteomyelitis:**
  - **Amoxicillin-clavulanate**
  - **Clindamycin**
  - Intravenously for first 2–3 days then orally
  - AST should be performed in all cases.
  - If pre-treatment culture results indicate resistance to the empirical antimicrobial chosen, the drug should be changed.
  - Treat for 6–8 weeks

## 5.7 Oral infections

*Antibacterials are indicated for:*

Severe gingivitis and periodontitis:

- **Amoxicillin-clavulanate**
- **Metronidazole**
- **Clindamycin** (if periodontal bone infections)

Ulcerative stomatitis:

- **Doxycycline**
- **Clindamycin**

*Other considerations:*

- Appropriate dental therapy should also be implemented.
- Consider chlorhexidine mouthwash.

## 5.8 Skin and ear infections

*Antibacterials are **not** indicated for:*

- *Malassezia* dermatitis
- Non-specific skin problems (e.g. pruritus)

*Antibacterials are indicated for:*

- **Bites and traumatic wounds:**
  - Debride and lavage.
  - If systemically well and not pyrexic:
    - Topical treatment with 2–4% chlorhexidine
  - If systemically unwell and pyrexic:
    - Systemic antibacterials based on cytology:
      - For cocci:
        - **Clindamycin**
        - **Cefalexin**
        - **Amoxicillin/clavulanate**
        - **Trimethoprim/sulphonamide**
      - For rods
        - **Fluoroquinolones**
  - Acute bite wound prophylaxis:
    - Thorough flushing with saline or 2–4% chlorhexidine
    - **Amoxicillin/clavulanate** (for 7 days)

- **Surface pyoderma (hot spots, intertrigo):**
  - Topical treatment ONLY
  - 2–4% chlorhexidine
  - **Fusidic acid** ± glucocorticoid
  - Silver sulphadiazine (if rods)

- **Superficial pyoderma:**
  - Topical treatment ONLY is appropriate in most cases.
    - 2–4% chlorhexidine
  - If required:
    - **Clindamycin**
    - **Cefalexin**
    - **Amoxicillin/clavulanate**
    - **Trimethoprim/sulphonamide**
  - Culture if rods are seen on cytology or there is a history of Methicillin Resistant *Staphylococcus pseudointermedius* (MRSP)/MRSA or multiple prior antibacterial courses.
  - Treat for minimum 3 weeks or 1 week beyond clinical cure
  - Repeat cytology to assess response.
  - Use doses at top end of range for better skin penetration.

- **Deep pyoderma:**
  - Whilst culture pending, systemic antibacterial therapy based on cytology as for superficial pyoderma.
  - Add topical treatment with 2–4% chlorhexidine.
  - Treat for minimum 4–6 weeks or 2 weeks beyond clinical cure

- Ideally repeat cytology.

- **Otitis externa:**
  - Topical treatment ONLY
  - No authorized products if ear drums not intact.
  - Use in-house cytology to guide drug choice and prognosis.
  - If rods:
    - **Framycetin**
    - **Gentamicin**
    - **Polymyxin B**
  - If cocci
    - **Florfenicol**
    - **Fusidic acid/framycetin**
    - **Polymyxin B/miconazole**
  - May combine with antiseptic ear cleaner.
  - Treat until cytology is negative.

- **Anal sac inflammation/engorgement without abscessation:**
  - **T**opical treatment ONLY
  - Manual evacuation
  - Flushing with chlorhexidine
  - Packing with topical polypharmacy ear product containing aminoglycoside or florfenicol

- **Anal sac abscessation:**
  - ONLY if signs of cellulitis
  - **Trimethoprim/sulphonamide**
  - **Amoxicillin/clavulanate**
  - Consider surgical treatment.

## 5.9 Respiratory infections

*Antibacterials are **not** indicated for:*

- Chronic bronchitis/allergic airway disease unless secondarily infected
- Canine sinonasal disease
- Uncomplicated canine infectious respiratory disease complex (Kennel Cough)

*Antibacterials are indicated for:*

- **Feline upper respiratory tract disease – acute bacterial upper respiratory infection**
    - Do not treat with antibacterials within the first 10 days of acute-onset infection unless fever, anorexia and pyrexia are present concurrently with mucopurulent nasal discharge
    - Empirical treatment: **doxycycline** for 7-10 days
    - **Amoxicillin (± clavulanate)** an alternative if *Chlamydophila felis* or *Mycoplasma* not suspected.
    - All cats with suspected infectious upper respiratory tract disease should be housed in the isolation ward

- **Feline upper respiratory tract disease – chronic bacterial upper respiratory infection**
    - Consider a more extensive work up for cats with clinical signs > 10 days, especially if treatment failure with empirical antibacterial treatment
    - Consider collection of samples for AST
    - **Doxycycline** or **amoxicillin (± clavulanate)** unless AST results suggest resistance
    - Third generation cephalosporins and fluoroquinolone shall not be used unless there is documented resistance to less critical antibacterial drugs
    - Azithromycin can be considered when chlamydiosis is unlikely and when doxycycline and amoxicillin (± clavulanate) are not a viable option
    - A **fluoroquinolone** should be considered if ***Pseudomonas aeruginosa*** isolated in pure or nearly pure culture. Pradofloxacin is available in Ireland (Veraflox) and is indicated for use in upper respiratory disease in cats.
    - Administer chosen antibacterial for at least seven days, and continue for as long as progressive clinical improvement and for at least one week beyond clinical resolution or any plateau in response to treatment
    - Consider adjunctive therapy e.g. flushing under general anaesthesia to remove loculated secretions
    - If signs recur, consider repeat administration of the previous empirical choice for at least 7-10 days to assess the treatment response. Another agent should only be chosen if there is no clinical response after a minimum of 48 hours, and the choice should be based on AST of a nasal swab
    - All cats with suspected infectious upper respiratory tract disease should be housed in isolation

- **Canine infectious respiratory disease complex (CIRDC; Kennel Cough)**
    - UCD Veterinary Hospital policy is to not accept cases of suspected uncomplicated CIRDC
    - All dogs with suspected CIRDC should be housed in the isolation ward
    - Do not treat with antibacterials within the first 10 days of acute-onset infection unless fever, anorexia and lethargy are present with mucopurulent discharges
    - If bacterial CIRDC is suspected in dogs with mucopurulent nasal discharge, fever, lethargy or inappetence, but WITHOUT evidence of pneumonia **doxycycline** is

recommended as an empirical choice for 7-10 days. **Amoxicillin ± clavulanate** can be used as an alternative but is less effective against *Bordetella bronchiseptica* and ineffective against *Mycoplasma* spp.
    - Further testing, including AST of bronchoalveolar lavage samples, should be performed in dogs that fail to respond to empirical therapy.
    - Treatment with nebulised **gentamicin** can be considered in animals with chronic bordetellosis in the absence of severe pneumonia.

- **Bacterial bronchitis**
    - While waiting results of AST of bronchoalveolar lavage, consider no treatment or use of **doxycycline** for 7-10 days if the clinical disease is severe.
    - Therapy should be continued, initiated or modified based on AST results.
    - Treatment should be continued until one week following resolution of clinical signs (uncomplicated bacterial bronchitis)
    - Repeat imaging or bronchoalveolar lavage cytology / AST may be necessary to guide therapy in some cases.
    - Treatment with nebulised **gentamicin** can be considered in animals with chronic bordetellosis in the absence of severe pneumonia

- **Pneumonia**
    - Choice of antimicrobial therapy should ideally be guided by AST.
    - Empirical therapy should be commenced while awaiting test results, or until the animal is adequately stable to have such tests performed.
    - Empirical choices:
        - Mild pneumonia (e.g. no fever, dehydration, lethargy, respiratory distress)
            - **Doxycycline**
        - Suspected Streptococcus equi subspecies zooepidemicus:
            - **Amoxicillin (± clavulanate)** (clavulanate not necessary but IV therapy may be required clinically)
        - Acute aspiration pneumonia:
            - **Amoxicillin (± clavulanate)**
        - Severe pneumonia with sepsis or if the animal is oxygen dependent (SpO2 <90%)
            - **Fluoroquinolone**
              AND
            - **Amoxicillin clavulanate** OR **clindamycin** parenterally
            - **Metronidazole** if *Bacteroides* spp. suspected.
    - Reassess clinical response, diagnostic imaging, haematology ± acute phase protein measurement no later than 10-14 days after commencing therapy. The decision to extend treatment is based on the response. 4-6 weeks of therapy is often necessary.

- **Pyothorax:**
    - **Fluoroquinolone (including pradofloxacin)**
      AND

    - **Clindamycin** OR **amoxycillin clavulanate**
    - Treatment may be modified based on AST results; de-escalation may be possible if all isolates are susceptible to one of the antibacterial agents. However, if the animal presented on an antimicrobial, the lack of growth on culture may allow for continuation of this antimicrobial in addition to other antimicrobials (based on AST) as long as there has been a clinical improvement.
    - Animals should be treated with antibacterial drugs for a minimum of three weeks
    - Reassess clinical response, diagnostic imaging and haematology no later than 10-14 days after commencing therapy. The decision to extend treatment is based on the response. 4-6 weeks of therapy is often necessary
    - Regular drainage via chest drains ± saline lavage should also be undertaken
    - Surgery should be considered to remove the inciting cause or to facilitate removal of inspissated material

## 5.10 Peri-and post-operative use

*Antibacterials are **not** indicated for:*

- Clean (elective surgery, no entry into hollow viscus) surgical procedures (e.g. ovariohysterectomy, castration, laparoscopic procedures such as cryptorchidectomy, ovariectomy, etc.)

*Prophylactic (perioperative) antibacterials are appropriate:*

- For prolonged clean, soft tissue surgery (>90 minutes) (some exceptions might include but not limited to portosystemic shunt surgeries with animals typically on amoxiclav/metronidazole, cutaneous/subcutaneous mast cell tumour/soft tissue sarcoma removal, surgeries involving use of polypropylene mesh [e.g. hernia repair], etc., perineal hernia repair or anal sacculectomy with incisions close to anus)
- Any orthopaedic or neurosurgery particularly that involving an implant (e.g. TPLO or total hip replacement or spinal/limb fracture repair)
- Surgery involving entry into a hollow viscus (ie, clean-contaminated, e.g. gastrointestinal tract, urinary tract)
- Where there is an obvious break in asepsis causing contamination of the wound
- For all contaminated wounds or if there is a pre-existing infection
- For debilitated or immunosuppressed patients
- Where infections would be catastrophic (e.g. CNS)

In most cases:

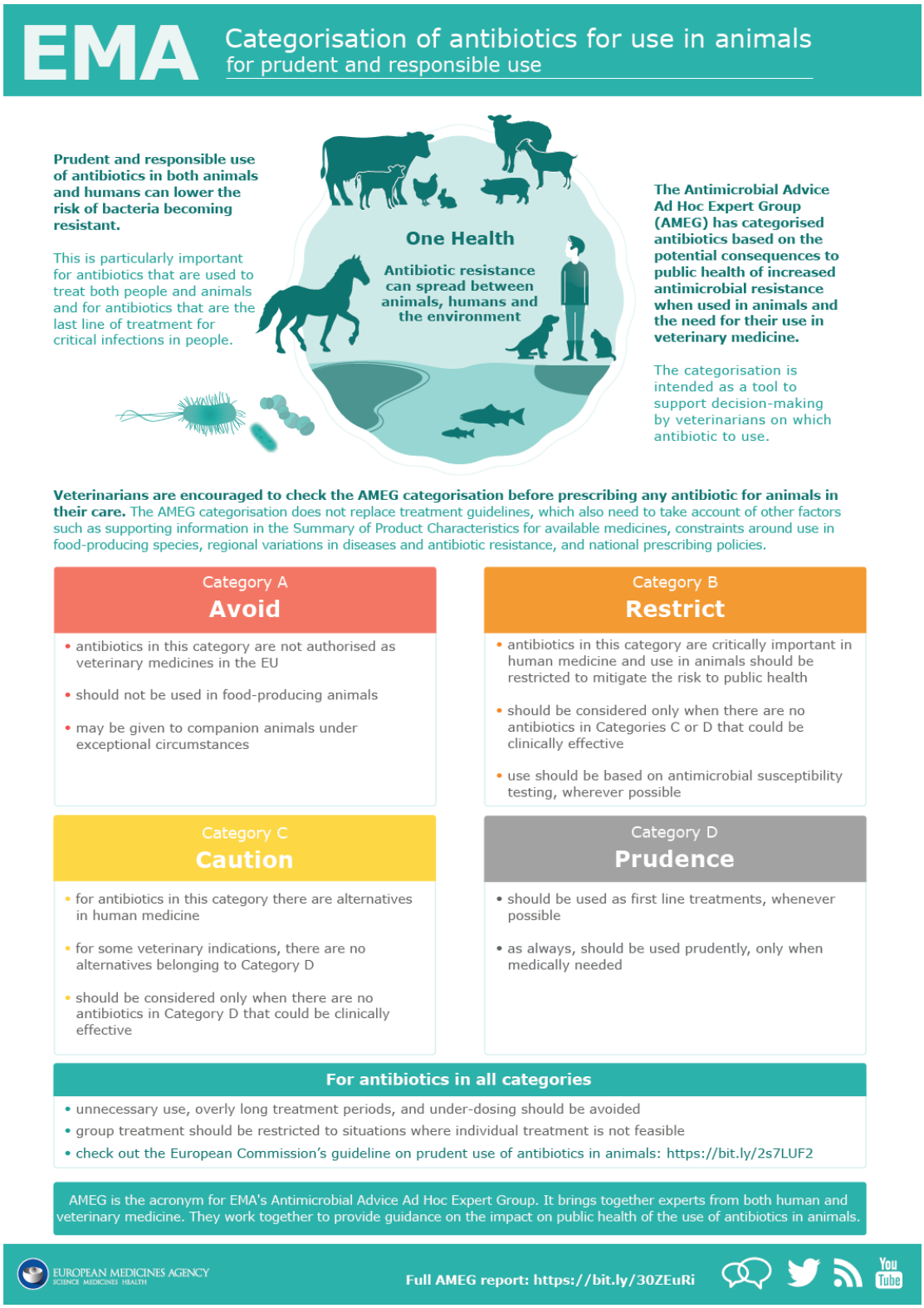
- **Amoxicillin clavulanate or Cefuroxime (AMEG Cat C)**
- Intravenously 60 minutes before the first incision, then every 90 minutes until the end of surgery
- Where anaerobic involvement is highly likely:
    - Add **metronidazole**

- Do not continue antibacterials after surgery, unless there is a therapeutic indication as this will select for resistance (some exceptions might include but not limited to TPLO, open fractures, prolonged surgery, total hip replacement, etc.)
- Therapeutic (postoperative) antibacterials are indicated:
    - To treat a known bacterial infection
    - When the risk of a postoperative infection developing is high due to contamination or major break in asepsis

# APPENDICES

## Appendix 1. EMA Categorisation of Antimicrobials for use in food producing animals

https://www.ema.europa.eu/en/documents/report/infographic-categorisation-antibiotics-use-animals-prudent-responsible-use_en.pdf



## Appendix 2. Excerpt from EU Regulation of Veterinary Medicinal Products re withdrawal periods

### Article 115 of 2019/6

**Withdrawal period for medicinal products used outside the terms of the marketing authorisation in food- producing animal species**

1. For the purpose of Articles 113 and 114, unless a medicinal product used has a withdrawal period provided in its summary of the product characteristics for the animal species in question, a withdrawal period shall be set by the veterinarian in accordance with the following criteria:

(a) for meat and offal from food-producing mammals and poultry and farmed game birds the withdrawal period shall not be less than:

(i) the longest withdrawal period provided in its summary of the product characteristics for meat and offal multiplied by factor 1.5.

(ii) 28 days if the medicinal product is not authorised for food-producing animals.

(iii) one day, if the medicinal product has a zero-withdrawal period and is used in a different taxonomic family than the target species authorised.

(b) for milk from animals producing milk for human consumption the withdrawal period shall not be less than:

(i) the longest withdrawal period for milk provided in the summary of the product characteristics for any animal species multiplied by factor 1,5.

(ii) seven days, if the medicinal product is not authorised for animals producing milk for human consumption.

(iii) one day, if the medicinal product has a zero-withdrawal period.

(c) for eggs from animals producing eggs for human consumption the withdrawal period shall not be less than:

(i) the longest withdrawal period for eggs provided in the summary of the product characteristics for any animal species multiplied by factor 1,5.

(ii) 10 days, if the product is not authorised for animals producing eggs for human consumption.

(d) for aquatic species producing meat for human consumption the withdrawal period shall not be less than:

(i) the longest withdrawal period for any of the aquatic species indicated in the summary of the product characteristics multiplied by factor of 1,5 and expressed as degree-days.

(ii) if the medicinal product is authorised for food-producing terrestrial animal species, the longest withdrawal period for any of the food-producing animal species indicated in the summary of product characteristics multiplied by a factor of 50 and expressed as degree-days, but not exceeding 500 degree-days.

(iii) 500 degree-days, if the medicinal product is not authorised for food-producing animal species.

(iv) 25 degree-days if the highest withdrawal period for any animal species is zero.

2. If the calculation of the withdrawal period according to points (a)(i), (b)(i), (c)(i), (d)(i) and (ii) of paragraph 1 results in a fraction of days, the withdrawal period shall be rounded **up** to the nearest number of days.

## Appendix 3. Background to and applying for Special Import Licences (SILs)

Provisions within Regulation 2019/6 for use of an unauthorised VMP

The Veterinary Medicines Regulation (Regulation (EU) 2019/6) provides under **Art 110 (Immunological VMPs), Art 112, 113, 114 (Cascade) and Art 116 (Health Situation)** for situations where an authorised product is not available to vets in ROI.

Under **Art 110** a Veterinary practitioner can treat animals with an immunological product not authorised within the Union.

i) in the event of an outbreak of a listed disease or emerging disease (as defined in Regulation EU 2016/429)
ii) where an immunological VMP has been authorised but is no longer available within the Union for a disease which is not a listed disease or emerging disease (as defined in Regulation EU 2016/429) but is already present in the Union
iii) where an animal is to be exported to a Third Country and thereby subject to specific binding health rules in that Third Country

Under **Art 112/113/114** (formerly known as the Cascade) a VP can treat an animal with an unauthorised medicine, exceptionally, to avoid causing unacceptable suffering. The medicinal product may be sourced from another EU Member State (Art 112 (1) (a)) or in exceptional cases (and excluding immunological veterinary medicinal products) a VMP authorised in a third country (Art 112 (2).

Under **Art 116** a veterinary practitioner can treat animals with an unauthorised VMP where the situation of animal or public health so requires and the marketing of those VMPs is authorised in another MS.

Applying for a Special Import Licence

- Queries regarding Special Import Licences may be submitted to VeterinaryMedicinesWMC@agriculture.gov.ie
- In the first instance PVPs should satisfy themselves that the criteria for use of an unauthorised product (outlined in Articles 110, 112,113,114,116 of Regulation EU 2019/6) are met.
- PVPs should determine the type of application required.
  DAFM issues three different types of Special Import Licence- Art 110 licence, Art 112/113/114 licence, Art 116 licence. Application forms for each licence type are available at Veterinary Medicines Forms
    - The Art 110 licence covers import of an Immunological Veterinary Medicinal Product in accordance with Article 110 of EU 2019/6.
    - This application only deals with immunological products from third countries**. Applications must be submitted by a holder of a Wholesale Distribution Authorisation** and must be supported with a minimum of 4 letters of veterinary justification provided by the veterinarians requesting the import and listed on the application.

- The Art 112/113/114 licence covers Import of VMPs in accordance with Articles 112, 113 & 114 i.e., for use under the Cascade and to avoid causing unacceptable suffering.
- These applications may be submitted by a PVP for products authorised in another Member State.
- Where an application relates to third country authorised VMPs **the application must be submitted by a holder of a Wholesale Distribution Authorisation** and must be supported with letters of veterinary justification (minimum 4) provided by the veterinarians requesting the import.

- The Art 116 licence covers import of VMPs in accordance with Article 116
- This licence covers VMPs from Member States only and where a situation of animal health or public health applies. Third country products are outside the scope of this Article.
- These applications are **submitted by the holder of the marketing authorisation** of the product to be imported or in exceptional circumstances a "Sponsor Co". Applications must be supported by a minimum of four letters of veterinary justification outlining the animal health situation that applies.

## Appendix 4. Reporting Adverse Events or Reduced Efficacy -Pharmacovigilance

Pharmacovigilance is defined in EU Regulation 2019/6 as "the science and activities relating to the detection, assessment, understanding and prevention of suspected adverse events or any other problem related to a medicinal product".

If a veterinary practitioner becomes aware of a suspected adverse event relating to a veterinary medicinal product or other medicinal product used in an animal, they must report it at the earliest opportunity to either the Health Products Regulatory Authority (HPRA) or the marketing authorisation holder (MAH) of the concerned product. As per Article 73 of Regulation (EU) 2019/6, adverse event reports may relate to any of the following:

a) any unfavourable and unintended reaction in any animal to a veterinary medicinal product;
b) any observation of a lack of efficacy of a veterinary medicinal product following its administration to an animal, whether or not in accordance with the summary of product characteristics;
c) any environmental incidents observed following the administration of a veterinary medicinal product to an animal;
d) any noxious reaction in humans exposed to a veterinary medicinal product;
e) any finding of a pharmacologically active substance or marker residue in a product of animal origin exceeding the maximum levels of residues established in accordance with Regulation (EC) No 470/2009 after the set withdrawal period has been respected;
f) any suspected transmission of an infectious agent via a veterinary medicinal product;
g) any unfavourable and unintended reaction in an animal to a medicinal product for human use.

The aims of pharmacovigilance are:

- To identify any previously unknown risks associated with the use of medicines
- To evaluate how the newly identified risks affect the overall benefit: risk balance of the product
- To propose suitable mitigation measures to reduce the risks to an acceptable level
- If any risk is too large to be mitigated, to eliminate it by stopping sale of the product
- To communicate the outcome of investigations.

However, none of the above is possible unless adverse events following the use of VMP are reported via the appropriate channels.

Rialtas na hÉireann
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WORKING TOGETHER TO PROTECT ANTIMICROBIALS FOR THE FUTURE