UNIVERSITY OF MELBOURNE

GUIDE FOR ANTIMICROBIAL USE IN DOGS AND CATS

For more information and further resources visit
www.fvas.unimelb.edu.au/vetantibiotics

Version 1

NCAS National Centre for Antimicrobial Stewardship

APCAH ASIA-PACIFIC CENTRE FOR ANIMAL HEALTH

THE UNIVERSITY OF MELBOURNE

AGRICULTURE VICTORIA

NOT ALL
BUGS
NEED
DRUGS

AGRICULTURE VICTORIA

Play your part in preventing antibiotic resistant infections.

For more information visit
agriculture.vic.gov.au/amr

AGRICULTURE VICTORIA

We all have an important role to play in the fight against antimicrobial resistance.

As part of our commitment to the implementation of the National Antimicrobial Resistance Strategy 2015-2019, AgVic and The University of Melbourne have created education materials about antimicrobial resistance (AMR) and antimicrobial stewardship (AMS).

The resources aim to provide a practical guide for the prescribing of antimicrobials that can help start the conversation about AMR with clients.

FREE RESOURCES

- A5 antibiotic category cards for cattle, horses, sheep, chickens and pigs
- Pocket guide for antimicrobial use in horses
- A3 waiting room posters
- A5 prescribing tearaway pads
- A4 fact sheet on MRSP
- A6 sticker sheets
- DL Double-sided prescribing leaflets
- A4 S4 medicated feed order posters
- A2 Australian Prescribing Guidelines for horses
- Antibiotic Guardian lapel pins

You can order our resources by emailing
animal.biosecurity@agriculture.vic.gov.au

Antibiotic Pharmacokinetics & Pharmacodynamics

Dogs & Cats

Bacteriostatic Vs Bactericidal

Bacteriostatic

"ECSTaTiC for bacteriostatic"

Erythromycin (macrolides)
Clindamycin
Sulphonamides
Trimethoprim
Tetracyclines
Chloramphenicol

Bactericidal

"Very **P**roficient **F**or **C**omplete **C**ell **M**urder"

Vancomycin
Penicillin
Fluoroquinolones
Cephalosporins
Carbapenems
Metronidazole

Intrinsic resistance Vs Acquired resistance

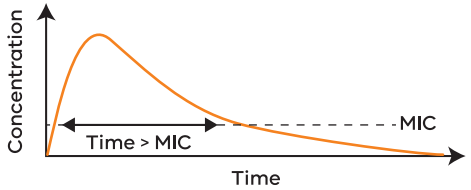
Intrinsic resistance
All members of a bacterial genus or species have properties that make them naturally resistant to certain antimicrobials.

Acquired resistance
Previously susceptible bacteria acquire new genes or a mutation occurs conferring resistance.

Time-Dependent Vs Concentration Dependent

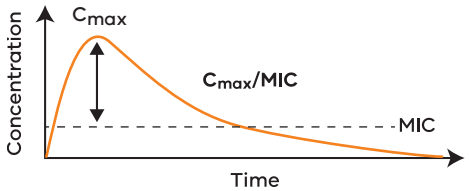
Time-Dependent

- Optimise killing by maximising **time above MIC.**
- **More frequent administration** or extended infusion increases efficacy by extending T>MIC.
- Goal **exceed MIC by 1-5 times for 50-80% of dosage interval.**
- E.g. penicillin, cephalexin, TMS, tetracyclines, clindamycin.



Concentration Dependent

- Optimise killing by maximising **peak concentration.**
- **Higher doses** at less frequent intervals (ie. once daily) increases efficacy by maximising C_{max}:MIC ratio.
- Goal **C_{max}:MIC >8.**
- E.g. aminoglycosides, fluoroquinolones, metronidazole.



Spectrum of Activity Against Common Bacteria

A guide to empirical therapy while awaiting susceptibility results.

Dogs & Cats

	Bug \ Drug	Penicillin	Ampicillin / amoxycillin	Doxycycline	Trimethoprim sulpha	Chloramphenicol	Amoxycillin clavulanate	Cefazolin / cephalexin	Gentamicin	Metronidazole	Clindamycin	Cefovecin	Enrofloxacin
Gram +ve	***Staphylococcus pseudintermedius*** **(CoP)** §			±	±	+	±	±	+		±		±
	Staphylococcus aureus **(CoP)** ‡			+	+	+	±	+			+	+	+
	Staphylococcus felis **(CoN)**	+	+	+	+	+	+	+	+		+	+	+
	β-haemolytic Streptococci (eg *S. canis*)	✔	✔	±	+		+	+	IR		+	+	±
	Enterococcus faecalis §		✔	±	IR		+	IR	IR		IR	IR	±
	Enterococcus faecium §			±	IR			IR	IR		IR	IR	
	Actinomyces **spp.**	✔	✔	+							+		
Gram -ve	***Escherichia coli***	IR	±	+	±		+	+	+		IR	+	+
	Enterobacter **spp.** §	IR	IR	+	±		IR	IR			IR		+
	Klebsiella **spp.** §	IR	IR	+	±		+*	+*			IR	+	+
	Proteus **spp.**	IR	+**	IR			+	+	+		IR	+	+
	Pseudomonas **spp.** §	IR	IR	IR	IR	IR	IR	IR	✔		IR	IR	±
	Pasteurella **spp.**		✔	+	+		+	+				+	+
	Bordetella bronchiseptica		±	✔	+		+						+
	Mycoplasma **spp.**	IR	IR	✔	IR		IR	IR				IR	±
	Anaerobes	+	+	±		+	+		IR	✔	+	±	
Urinary isolates	***Staphylococcus pseudintermedius***		✔	±	✔		+	+	+			+	+
	Enterococcus faecalis		✔	+	IR		+	IR	IR		IR	IR	
	Escherichia coli		✔	+	✔		+	+	+			+	+
	Proteus mirabilis	IR	+	IR	+		+	+				+	+
	Proteus **spp.** (excluding *P. mirabilis*)	IR	IR	IR	+		+	+				+	+

Traffic-light system is based on the ASTAG antimicrobial importance rating system.

- ✔ Drug of choice.
- \+ Good susceptibility.
- ± Variable susceptibility.
- IR Intrinsically resistant.
- CoP Coagulase positive.
- CoN Coagulase negative.
- § Susceptibility poorly predictable, multidrug resistance increasing in frequency, culture and susceptibility testing is strongly recommended.
- ‡ Multidrug resistant Staphylococcus aureus likely to be of human origin. Review aseptic technique.
- * *Klebsiella aerogenes* intrinsically resistant.
- ** *Proteus vulgaris* intrinsically resistant.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Beta-lactams	Low	Amoxycillin	IV IM PO	11-22mg/kg q8-12h	Anaphylaxis rare, other mild hypersensitivity reactions more common (urticaria, fever, angioneurotic oedema). Anorexia, vomiting, diarrhoea.	Anaerobic activity useful for cat-bite infections, periodontal disease, tooth abscesses, wound infections. Drug of choice for streptococci, clostridia, actinomycosis and *Pasteurella multocida*. Greater activity against Gram-negative bacteria than penicillin, including *E. coli* and *Proteus mirabilis*. Very high urinary concentrations, useful for UTIs, even penicillinase-producing *S. aureus*. Not recommended for pyelonephritis or prostatitis. Excreted in bile, therefore good for cholestatic infections.
	Low	Ampicillin	IV IM SC	10-20mg/kg q6-8h	Hypersensitivity reactions and gastrointestinal disturbance possible.	Slow IV (over 3 mins). Spectrum of activity equivalent to amoxycillin.
	Low	Penicillin	IM	20-40,000 IU/kg q12h	Hypersensitivity reactions.	Indicated for Gram-positive aerobic and anaerobic bacteria (streptococci, clostridia) and for infections caused by susceptible Gram-negative bacteria eg. *P. multocida*.
	Medium	Amoxycillin clavulanic acid	PO IM SC IV	12.5-25mg/kg q8-12h	Pain on injection. Anorexia, vomiting, diarrhoea. Hypersensitivity reactions. Anaphylaxis after intravenous administration during general anaesthesia.	Clavulanic acid extends the range of amoxycillin against β-lacatamase producing pathogens, such as methicillin-susceptible staphylococci. Higher dose recommended for Gram-negative infections.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Beta-lactams	Medium	Cefazolin	IV IM	20-35mg/kg q8h for therapy, 22 mg/kg surgical prophylaxis	Hypersensitivity reactions, pain on IM injection.	1st generation cephalosporin active against methicillin-susceptible staphylococci, streptococci, some Gram-negative aerobes, unpredictable against anaerobes. Greater Gram-negative activity than cephalexin and cephalothin. Good bone penetration. For surgical prophylaxis administer IV 30-60 mins before first incision. Repeat intra-operative dosing interval q4hrs for common skin flora (staphylococci, streptococci), q2hrs for *E. coli*.
	Medium	Cephalexin	PO	22-30mg/kg q12h	Vomiting and diarrhoea common when administered without food. Hypersensitivity reactions possible.	1st generation cephalosporin, similar activity to cefazolin except less Gram-negative activity. Give with food to reduce GIT side effects, can also lower dose if side effects occur. Only use for skin disease when topical therapy insufficient to control pyoderma.
	High	Cefovecin	SC	8mg/kg	Vomiting, diarrhoea, hypersensitivity.	3rd generation cephalosporin. Similar spectrum of activity to amoxycillin clavulanate. **Reserve**** for infections where no effective alternative. Label restraint FOR USE ONLY in dogs and cats where indicated by antibiotic sensitivity testing according to principles of prudent use.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Beta-lactams	High	Ceftazidime	IV	25-50mg/kg q8-12h To exceed *P. aeruginosa* MIC 30mg/kg q4h or constant IV infusion of 4.1mg/kg/h	Gastrointestinal disturbance.	3rd generation cephalosporin with 10 times greater activity against *P. aeruginosa*. Slightly less active against all other organisms than other cephalosporins. **Reserve**** for *P. aeruginosa* infections with confirmed susceptibility.
	High	Cefotaxime	IM	20-40mg/kg q8h	Pain on IM injection, gastrointestinal disturbances common due to broad antibacterial action. Superinfection with resistant microorganisms, including yeasts, may be anticipated.	3rd generation cephalosporin. Due to expense and potential to select for resistant infections, these drugs should be **reserved**** for life-threatening infections, such as bacterial meningitis caused by Gram-negative bacteria (especially *Enterobacteriaceae*). May be used in combination with an aminoglycoside for MDR infections in compromised animals (neutropaenic).
Tetracyclines	Low	Doxycycline	PO	5mg/kg q12h or 10mg/kg q24h	Administration to growing puppies and pregnant bitches results in yellow discolouration of teeth.	Excellent penetration into most tissues (including prostate). Broad spectrum acitivity, including many intracellular pathogens such as *Chlamydia, Coxiella, Nocardia* and some *Mycoplasma* species.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Sulphonamides	Low	Trimethoprim sulphonamide	PO IV	15-30mg/kg q12h	Chronic use (>2 weeks) can lead to crystalluria, haematuria, urinary obstruction, haematopoietic disorders (anaemia, leukopaenia, thrombocytopaenia) and dermatological reactions. Do not use in Doberman Pinschers. ~0.25% of dogs may suffer idiosyncratic drug reactions 10-21 days after exposure, including fever, arthropathy, blood dyscrasia, epistaxis, hepatopathy, skin eruptions, uveitis, KCS. In dogs <12kg, 1 week TMS decreases tear production by 15%, overdose can lead to KCS. Can cause hypothyroidism and/or lowered T4 in dogs. Cats salivate if tablet protective coating broken.	Broad spectrum activity, including *Nocardia* spp., *Toxoplasma* spp. and other protozoa. Well absorbed from gastrointestinal tract, excellent penetration into many tissues including meninges, prostate and urinary tract. ISCAID recommended first line empirical treatment option for sporadic bacterial cysitis (simple uncomplicated UTI) for 3-5 days (low risk of adverse effects with short course). For therapy >7 days baseline Schirmer's tear testing recommended with periodic re-evaluation.
Aminoglycosides	Medium	Gentamicin	IV IM	Dogs: 9-14mg/kg q24h Cats: 5-8mg/kg q24h	Ototoxicity possible. Nephrotoxic especially if hypovolaemia, hypokalaemia, hyponatraemia, elevated trough concentrations, pre-existing renal disease, concurrent nephrotoxic drug administration, prolonged therapy (>7-10 days), age (neonates, geriatrics). Pain on IM injection.	Excellent activity against Gram-negative bacteria and some staphylococci. No anaerobic activity. Synergistic in combination with β-lactam. Inactivated by purulent debris. Ensure adequate fluid and electrolyte balance during treatment. Clinical monitoring for toxicosis may include monitoring trough levels, daily monitoring of urine for epithelial casts and daily serum creatinine.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Nitroimidazoles	Medium	Metronidazole	PO IV	Dogs: 10-15mg/kg PO q12h (10mg/kg SLOW IV) Cats: 10-15mg/kg q24h	Care in liver disease, can predispose to CNS toxicity - reduce dose to 7.5 mg/kg. Gastrointestinal disturbance, hepatotoxicity, CNS signs, haematuria, neutropenia. Potentially teratogenic in first third of pregnancy. Can impact faecal microbiome long-term.	Not indicated in acute gastrointestinal disease unless evidence of sepsis. Excellent anaerobic activity. Critical drug for managing human *Clostridium difficile* infections. Drug interactions: phenobarbital may enhance metabolism; cimetidine may decrease metabolism and increase dose related adverse effects.
Nitrofurans	High	Nitrofurantoin	PO	4.4-5mg/kg q8h	Gastrointestinal disturbances, hepatopathy, male infertility in dogs.	Lower urinary tract infections only. **Reserve**** for exceptional cases. Do not use for pyelonephritis or other conditions where tissue (vs. urine) levels are needed. Avoid in cases with renal impairment. No activity against *Pseudomonas, Proteus, Serratia, Acinetobacter* spp. Probenecid inhibits renal excretion. Antagonistic to fluoroquinolones.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Lincosamides	Medium	Clindamycin	IV IM	11mg/kg q12h For IV: dilute 1:10 in 0.9% saline, administer over 60mins 11mg/kg q12-24h Toxoplasmosis: 25mg/kg q12h	Oesophagitis and oesophageal stricture have been reported in cats associated with use of generic capsules - follow capsules with water or food. Diarrhoea, neuromuscular blockade. Oral suspension may be unpalatable for cats. Pain on IM injection.	Active against staphylococci, streptococci, *Actinomyces, Nocardia,* and *Mycoplasma* spp. plus anaerobes (*Bacteroides* spp., *Fusobacterium* spp., *Clostridium perfringens*). Only use for skin disease when topical therapy insufficient to control pyoderma. Cross-resistance to lincosamides in bacteria resistant to macrolides. High concentration in prostate. Use for toxoplasmosis controversial as may help clinical signs but not clear infection from CNS or eye. Erythromycin and chloramphenicol are antagonistic.
Phenicols	Low	Chloramphenicol	PO IV IM Topical	Dogs: 40-50mg/kg q6-8h Cats: 12.5-20mg/kg q12h	Anorexia, hypersalivation, vomiting with systemic use. Dose related reversible bone marrow suppression may develop with prolonged treatment - usually resolves within days. Cats more susceptible - within 2 weeks of treatment. **Wear gloves and mask** when handling medication as idiosyncratic aplastic anaemia can develop in **people** handling this drug.	Mostly used topically. May be used systemically for multidrug resistant organisms. Broad spectrum. Avoid systemic use in cases with hepatic failure, renal failure, pre-existing haematologic abnormalities, pregnancy, lactation and in young animals. Eliminated by glucuronidation mechanisms, cats excrete higher proportion unchanged in urine than dogs. Potent inhibitor of P450 enzymes - reduced hepatic clearance of phenobarbital, pentobarbital.
Polypeptides	High	Polymyxin B	Topical		Nephrotoxic if administered systemically. Potentially ototoxic. Ophthalmic formulations associated with anaphylaxis in cats.	Used topically for treatment of bacterial keratitis, otitis externa and skin infections. Active topically against *Pseudomonas* spp. and other Gram negatives (except *Proteus, Morganella* and *Serratia* spp.). Inhibited by the presence of purulent exudate.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Fluoroquinolones	High	Enrofloxacin	PO IV	Dogs: 5-20mg/kg q24h Cats: 5mg/kg q24h, SLOW IV	Blindness, due to retinal detachment, and neurological signs in cats. Not always associated with dose or route of administration, however greater risk with advancing age. Anorexia, vomiting, diarrhoea. CNS effects with high doses or rapid IV. Caution in animals prone to seizures. Canine toxic shock syndrome and necrotizing fasciitis caused by fluoroquinolone use in *Streptococcus canis* infections. Arthropathy in dogs during growth, small dogs <8 months old, or large breeds less than 12-18 months. Avoid use in cats - especially those with renal disease.	2nd generation fluoroquinolone active against *Pasteurella* spp., Gram-negative enteric bacilli, staphylococci (higher MIC). Variable activity against *Pseudomonas aeruginosa* (highest MIC). Poor activity against streptococci, enterococci and anaerobes. Not indicated in superficial pyoderma. **Reserve**** for infections where culture and susceptibility indicate no effective alternative. Use is a known risk factor for selection of methicillin-resistant staphylococci. If organism resistant to one fluoroquinolone, typically resistant to all (cross-resistance). Good distribution to bone, prostate and skin. Concentrated in urine, bile and within phagocytic cells. Enrofloxacin is partially (~20%) de-ethylated to ciprofloxacin. Oral absorption inhibited by antacids, sucralfate, supplements containing aluminium, calcium, iron and zinc. Chelation/precipitation in IV fluids with calcium or magnesium. Reduced hepatic clearance of theophylline. Antagonism with chloramphenicol, rifampicin.

Antibiotic Pharmacotherapy by Class

Dogs & Cats

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Fluoroquinolones	High	Marbofloxacin	PO	2.75-5.5mg/kg q24h	Anorexia, vomiting, diarrhoea. CNS effects with high doses or rapid IV. Caution in animals prone to seizures. Arthropathy in immature animals.	2nd generation fluoroquinolone. **Reserve**** for infections where culture and susceptibility indicate no effective alternative. Similar activity, tissue distribution, drug interactions to enrofloxacin. Concentrated in urine, may be used for confirmed pyelonephritis in cats based on susceptibility testing.
	High	Pradofloxacin	PO	Dogs: 3-5mg/kg q 24h Cats: 5-10mg/kg q24h	Higher doses in dogs associated with myelosuppression. Do not use in dogs less than 1 year of age, or in pregnant or lactating animals. Gastrointestinal disturbances. Caution in animals prone to seizures.	3rd generation fluoroquinolone. **Reserve**** for infections where culture and susceptibility indicate no effective alternative. Greater activity against Gram-positive cocci and anaerobes than other fluoroquinolones. Similar drug interactions to enrofloxacin.
	High	Ciprofloxacin	PO	25mg/kg		**Avoid.** Oral absorption in dogs highly variable (~50%), lower than humans. Only reaches therapeutic targets for bacteria with MIC ≤0.06 µg/ml (vs ≤1 µg/ml in humans). Generally not effective for staphylococci or *P. aeruginosa* in dogs and cats.

* Black shading represents high importance rated antibiotics not registered for use in animals that should be avoided or **ONLY** used in exceptional circumstances.

** Exceptional circumstances defined as use in an animal based on culture and susceptibility, where there is no effective alternative therapy and a reasonable chance of survival.

NB. Many recommendations in this guide represent **off-label use** of antimicrobials. Compliance with legal requirements in your jurisdiction is your responsibility. Recommendations **only apply to dogs and cats** and cannot be safely extrapolated to other small animal species.

NOT ALL BUGS NEED DRUGS
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MRSP dermatology fact sheet

Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP)

KEY FACTS

- ***Staphylococcus pseudintermedius*** **(SP) are normal skin/mucosal flora found on dogs and cats.**
- **Methicillin resistance = resistance to all β-lactam antimicrobials (including β-lactamase inhibitor combinations).**
- **Emerging opportunistic pathogen in Australia – 12% clinical SP infections MRSP, 8% healthy urban dogs MRSP carriers.**
- **MRSP vs Methicillin-susceptible SP**
  - **No more pathogenic**
  - **No difference in clinical disease.**
- **Many MRSP carry other resistance genes, sometimes extensive drug resistance.**

β-lactams

- ⊗ Penicillin
- ⊗ Amoxycillin
- ⊗ Cephalosporins*
- ⊗ Carbapenems
- ⊗ Amoxy/clav

*Except a few anti-MRSA cephalosporins

BIOSECURITY

PERSONAL

Routinely wash hands before & after each patient.

Use liquid soap or alcohol-based hand sanitiser.

Wear gloves when handling patients.

PATIENT

Isolate MRSP patients.

Consider in-contact pets carriers.

Pets may carry MRSP after clinical resolution.

HOSPITAL

Clean gross contamination/biofilm with detergent first then disinfect.

Routine cleaning and disinfection all that is required.

MRSP readily inactivated by commonly used disinfectants.

TREATMENT OPTIONS

Critical to identify & address underlying cause.

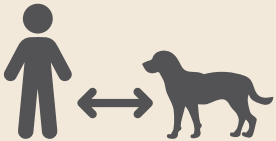
Try topical!
MRSP is not resistant to antiseptics (eg. chlorhexidine, bleach).

If needed, systemic therapy based on C&S.

No dominant susceptibility pattern, often MDR.

ZOONOTIC RISK

Dogs are the natural SP host. Infection in people is rare, but possible.



Minimise contact between infected **dogs, other animals and people.** Exposed bedding and surfaces will also be contaminated.

Avoid contact with skin, nose, mouth, perineum and faeces of infected dogs.

Warn owners of zoonotic potential, particularly those with breaches in their skin barrier or poor skin integrity (ie. **wounds, elderly** people).

Wash or alcohol-sanitise hands after handling infected dog.

For more information and further resources visit

agriculture.vic.gov.au/amr

www.fvas.unimelb.edu.au/vetantibiotics

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Version 1

NOT ALL BUGS NEED DRUGS

Play your part in preventing antibiotic resistant infections.

For more information visit

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