Table 29.2. Specific therapeutic antimicrobial application suggestions.

	Label applications are U.S. labels except for those in bold print, which are E.U. labels.				
Category	Disease/Pathogen(s)	Drugs for which this disease is a label application (therapy and/or prevention)	Extra-label antimicrobials that are a reasonable choice	Unreasonable extra-label antimicrobal selections for this disease	Comments
Respiratory disease	Pneumonia—*Mannheimia haemolytica., Pasteurella multocida, Histophilus somni*	Ampicillin trihydrate, *ceftiofur (sodium, hydrochloride, and crystalline free acid salts),* chlortetracycline, *danofloxacin, enrofloxacin, florfenicol, gamithromycin,* oxytetracycline, procaine penicillin G, spectinomycin sulfate, sulfadimethoxine, sulfamethazine, *tildipirosin, tilmicosin, tulathromycin,* tylosin, **cefquinome, trimethoprim/ sulfadiazine. trimethoprim/ sulfadoxine, procaine penicillin/ dihydrostreptomycin, amoxicillin trihydrate, amoxicillin/clavulanic acid**		Gentamicin due to potential toxicity in dehydrated animals and prolonged renal residues in cattle.	Antimicrobials with bovine respiratory disease on the label may be indicated for one or all of these pathogens. The italicized antimicrobials are the author's primary U.S. choices for cattle in advanced stages of the disease or which have experienced extensive stress. Not all of the antimicrobials are labeled for all respiratory pathogens. The labels should be consulted for complete indications.
Respiratory disease	Pneumonia—*Mycoplasma bovis*	Enrofloxacin, gamithromycin, florfenicol, tulathromycin, **tylosin (*Mycoplasma* on label)**	Oxytetracycline, spectinomycin, fluoroquinolones*	Any beta-lactam (penicillins, cephalosporins) due to lack of a cell wall.	See text for comments. *In the USA, fluoroquinolones would only be legal when used for the purpose of respiratory disease due to the primary label pathogens.
Respiratory disease	Diphtheria (necrotic laryngitis)—*Fusobacterium necrophorum*	Oxytetracycline	Ampicillin, ceftiofur, florfenicol, penicillin G, sulfadimethoxine, tylosin and other macrolides such as tulathromycin		Extra-label recommendations are made based on published MIC values that are in the range of other pathogens succesfully treated by these antimicrobials and/or label inclusion of foot rot due to *Fusobacterium necrophorum.* (Baba, 1989; Berg, 1982;

					Druan, 1991; Jousimies-Somer, 1996; Jang, 1994; Lechtenberg, 1998; Mateos, 1997; Piriz, 1990; Samitz, 1996) . All of these isolates were from other sites than necrotic laryngitis. The nature of the site of necrotic laryngitis may make therapy with less lipid soluble antimicrobials more of a challenge.
Infectious enteric disease	Scours, neonatal diarrhea due to *E. coli*	Chlortetracycline, neomycin, oxytetracycline, sulfachlorpyridazine, sulfamethazine, tetracycline (all of these antimicrobials display consistently high MICs that suggest the drugs would be ineffective), A**moxicillin/clavulanic acid bolus, cefquinome (septicemia), danofloxacin, enrofloxacin (septicemia and colibacillosis), marbofloxacin bolus, trimethiprim/ sulfadiazine, trimethiprim/ sulfadoxine**	Ceftiofur, potentiated sulfonamides (all only after susceptibility testing)	(These extra-label indications demonstrated very high MICs to most isolates.) Erythromycin, tylosin, tilmicosin, lincomycin, penicillin, ampicillin, florfenicol.	Recommended extra-label antimicrobials are based on susceptibility data and serum pharmacokinetics and should therefore be interpreted as relating to septicemia associated with enteric disease. See text for additional discussion.
Infectious enteric disease	Scours, neonatal diarrhea due to *Salmonella* spp.	Chlortetracycline, oxytetracycline (these antimicrobials display consistently high MICs that suggest the drugs would be ineffective), E**nrofloxacin, trimethoprim/ sulfadiazine, trimethoprim/ sulfadoxine, procaine penicillin/ dihydrostreptomycin**	Ceftiofur, potentiated sulfonamides (all only after susceptibility testing)	Gentamicin will cause extended withdrawal times that will compromise the ability to slaughter an animal that recovers from the acute disease but does not return to satisfactory production.	Recommended extra-label antimicrobials are based on susceptibility data and serum pharmacokinetics and should therefore be interpreted as relating to septicemia associated with enteric disease. See text for additional discussion.

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Table 29.2. Specific therapeutic antimicrobial application suggestions. (*continued*)

	Label applications are U.S. labels except for those in bold print, which are E.U. labels.				
Category	Disease/Pathogen(s)	Drugs for which this disease is a label application (therapy and/or prevention)	Extra-label antimicrobials that are a reasonable choice	Unreasonable extra-label antimicrobal selections for this disease	Comments
Infectious enteric disease	Enterotoxemia, overeating disease—*Clostridium perfringens* type C,D		Amoxicillin, ampicillin, penicillin G		Antiserum therapy is more likely related to therapeutic success. Septicemia resulting from enterotoxemia may involve multiple gut-related bacteria. Antimicrobial selection should reflect this possibility (see septicemia related to neonatal diarrhea above).
Infectious enteric disease	Hemorrhagic bowel disease—*Clostridium perfringens* type A		Penicillin G, florfenicol		Prognosis of hemorrhagic bowel disease is very guarded, with surgery necessary for resolution in many cases (Dennison, 2002). There is no published evidence that antimicrobial intervention changes the clinical outcome. While there is no published data to support florfenicol efficacy in this disease, the general activity against anaerobes make it a reasonable consideration.
Infectious enteric disease	Cryptosporidiosis—*Cryptosporidium parvum*	**Halofuginone lactate (prevention, and reduction in excretion in affected calves)**	For prevention: lasalocid in calves ≥ 1 week old (toxic in neonates at effective doses!)	Amprolium, sulfas	See text for comments on clinical trial data for cryptosporidiosis. Affected calves have severe acid/base and hydration insults.
Infectious enteric disease	Giardia		Albendazole, fenbendazole, metronidazole (see comments)		The extra-label use of nitroimidazoles (e.g., metronidazole) in food animals is banned in the United States. Fenbendazole regimens of 5 mg/kg q 12H for 3 days or 5 mg/kg q 24H for 5 days, PO, have been suggested (Rings, 1996). Fenbendazole liquid is labeled for giardia in puppies and kittens in the E.U.

Infectious enteric disease	Coccidiosis—*Eimeria bovis, Eimeria zeurnii*	Prevention/control: monensin, lasalocid, amprolium, decoquinate, sulfaquinoxaline; therapy of acute disease: sulfaquinoxaline, sulfamethazine, amprolium	Sulfadimethoxine, sulfadimidine		Amprolium and sulfadimidine were found superior to halofuginone in an induced *Eimeria bareillyi* calf model (Sanyal, 1985). Toltrazuril was found effective in a dose-dependent manner against an induced *Eimeria bovis* model in calves (Mundt, 2003).
Genitourinary	Leptospirosis	Oxytetracycline, **dihydrostreptomycin, tylosin (spirochetes on label)**	Penicillin/dihydro-streptomycin, ceftiofur		Ceftiofur was effective in clearing induced leptospirosis (*hardjo*) in cows at 2.2 and 5.0 mg/kg q24h for 5 days. These regimens were not effective when administered for 3 days. Long-acting 200 mg/ml oxytetracycline (20 mg/kg) and penicillin/dihydrostreptomycin (25 mg/kg) were effective after single doses (Alt, 2001).
Genitourinary	Metritis/endometritis			Intrauterine administration of penicillins, aminoglycosides, and sulfonamides is questionable, as these may undergo enzymatic cleavage, operate poorly in an anaerobic environment, or lose activity in the presence of pus.	Chenault (2004) reported 14-day cure rates of 77%, 65%, and 62% for cows suffering from acute postpartum metritis treated with 2.2 mg/kg IM/SQ ceftiofur HCl (CE) q 24h for 5 days, 1.1 mg/kg CE q 24h for 5 days, and controls, respectively. Königsson (2000) demonstrated that cows treated with 10 mg/kg IM oxytetracycline SID for 5 days demonstrated a shorter time to eradication of intrauterine *A. pyogenes* and *F. necrophorum* than untreated controls ($p < 0.05$).
Genitourinary	Seminal vesiculitis—*Arcanobacterium pyogenes, Brucella abortus., E. coli, Pseudomonas* spp., *Actinobacillus seminis, Actinomyces bovis, Histophilus somni (Haemophilus somnus), Salmonella* spp., *Chlamydia* spp.		Antimicrobial therapy has not been shown to make a difference in clinical outcome. Oxytetracycline in the feed at various doses has been used for prevention. Tilmicosin phosphate, long-acting oxytetracycline, and florfenicol have been used in therapeutic attempts.		*Arcanobacterium pyogenes* is the most common agent in the United States. *Brucella abortus* is the most common in countries with this disease. There is debate as to the role of bacterial or viral pathogens in the pathogenesis of seminal vesiculitis (Larson, 1997).

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Category	Disease/Pathogen(s)	Drugs for which this disease is a label application (therapy and/or prevention)	Extra-label antimicrobials that are a reasonable choice	Unreasonable extra-label antimicrobal selections for this disease	Comments
Genitourinary	Nephritis/ pyelonephritis—*Corynebacterium renale*, *Arcanobacterium pyogenes, E. coli*	**Trimethoprim/ sulfadiazine, trimethoprim/ sulfadoxine**	*For C. renale, Arcanobacterium pyogenes*—penicillin G, ampicillin; *E. coli*—ceftiofur, fluoroquinolones (where legal)		
Genitourinary	Cystitis	**Amoxicillin, trimethoprim/ sulfadiazine, amoxicillin trihydrate**	Amoxicillin, ampicilllin, ceftiofur, oxytetracycline, florfenicol, fluroquinolones (where legal), penicillin G, trimethiprim/sulfa		Antimicrobials for cystitis have traditionally been chosen for their urine concentrations. However, the infection of concern is in the wall of the bladder, not the urine. Therefore, while urine concentrations may be of benefit, lack of significant urine concentrations does not necessarily preclude selection for cystitis.
Musculo/skeletal	Adult arthritis—*Histophilus somni*, *Mycoplasma bovis*		Oxytetracycline, florfenicol, fluoroquinolones (where allowed by law), tulathromycin, spectinomycin, gamithromycin, lincomycin (given due consideration to potential rumen flora alterations)	If *M. bovis* is suspected, any beta-lactam would be an unreasonable choice. If another organism is confirmed, then ceftiofur and ampicillin may be considered.	Other pathogens may be present as listed for neonatal arthritis. However, therapy of adult bovine arthritis should include consideration of these organisms unless ruled out by culture. Arthritis due to *M. bovis* is often characterized as a tenosynovitis. An extended duration of therapy (1–2 weeks) and a prolonged recovery period are necessary.
Musculo/skeletal	Neonatal arthritis—*E. coli, Arcanobacterium pyogenes, Staphylococcus spp., Streptococcus spp.*	**Amoxicillin trihydrate, amoxicilin/clavulanic acid, procaine penicillin/ dihydrostreptomycin, procaine penicillin G**	Potentiated sulfonamides, flouroquinolones (where allowed by law)		The potential presence of *E. coli* and the varied susceptibility results of ampicillin, florfenicol, and oxytetracycline suggest they are not primary considerations for this disease. The primary metabolite of ceftiofur has a greatly elevated MIC_{90} value for *Staphylococcus* spp. as compared to the parent

					compound (Salmon, 1996), indicating it is not a primary choice where *Staph.* spp. may be part of the infection.
Central nervous system disease	Listeriosis—*Listeria monocytogenes*	**Procaine penicillin/ dihydrostreptomycin, procaine penicillin G**	Penicillin G, oxytetracycline, enrofloxacin (depending on legal status). Therapy durations of 1–2 weeks may be necessary.		Varying results are reported for the recomended drugs. Five of 6 bulls in a case report survived after therapy with oxytetracycline and dexamethasone (Ayars, 1999). A sheep and goat case report indicated poor response to chloramphenicol and oxytetracycline, but 6 of 9 animals recovered when treated with penicillin and gentamicin (Braun, 2002). Enrofloxacin has been reported as effective (Tripathi, 2001) but is illegal in countries with a ban on extra-label use of fluoroquinolones in food animals (e.g., United States).
Central nervous system disease	Thromboembolic meningo-encephalitis (TEME), *Histophilus somni* (*Haemophilus somnus*)		Oxytetracycline, florfenicol		Oxytetracycline is a standard drug of choice for this application. Florfenicol is also suggested due to low MICs for *H. somni* combined with high lipid solubility.
Central nervous system disease	Meningitis—*E. coli* in neonates, multiple other pathogens possible	**Procaine penicillin/ dihydrostreptomycin**	Ceftiofur, fluoroquinolones (where legal), trimethoprim/sulfa	Due to inconsistent coverage of the potential *Enterobacteriacae* component: penicillin G, first-generation cephalosporins, macrolides, tetracyclines, florfenicol	While consideration of penetration of the blood-brain barrier is valid, it is likely that this barrier is disrupted in meningitis, allowing greater penetration of water-soluble compounds. Doxycycline is a lipid-soluble tetracycline, but the high protein binding in serum limits the amount available to the diffusionary pool, and therefore CNS penetration.

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Category	Disease/Pathogen(s)	Drugs for which this disease is a label application (therapy and/or prevention)	Extra-label antimicrobials that are a reasonable choice	Unreasonable extra-label antimicrobal selections for this disease	Comments
Central nervous system disease	Otitis media and interna—potential pathogens include respiratory (all ages) and enteric pathogens (neonates) . *Mycoplasma bovis* should be suspected in dairy calves where *M. bovis* mastitis is present in the herd.	**Trimethoprim/sulfadiazine (infections of the ear on the label), tylosin**	In cattle where respiratory pathogens are suspected: macrolides, florfenicol, fluoroquinolones (where legal). Beta-lactams might be expected to have lower concentrations in remote otic tissues.	Aminoglycosides may be expected to have extensive binding to protein debris at the site of infection and are less active in areas with lowered pH.	Without adequate trial data, extra-label recommendations are made on the basis of reported pathogen population MICs and lipid solubility of the compound. Many of the extra-label recommendations would have a hole in the spectrum for at least one possible pathogen (e.g., enrofloxacin—*Strep.* spp., ceftiofur—*Staph.* spp. and *M. bovis*, macrolides and florfenicol—inconsistent against *Enterobacteriacae*, penicillin G and ampicillin—*Enterobacteriacae* and *M. bovis*).
Tissue/integumentary disease	Infectious bovine kerato-conjunctivitis (Pinkeye)-*Moraxella bovis*	oxytetracycline, topical gentamicin, tulathromycin	penicillin G, florfenicol, tilmicosin, topical benzathine cloxacillin		Florfenicol was found to be effective against IBK at either of the label dose regimens (Angelos, 2000, Dueger, 1999). Topical benzathine cloxacillin, 250 or 375 mg/eye, has been shown to be effective in naturally occurring and induced pinkeye models (Daigneault, 1990). Tilmicosin was shown to be effective at both 5 and 10 mg/kg (Zielinski, 1999). Although local penicillin G is a standard treatment, one report indicated no difference in healing of naturally occurring IBK after subconjunctival administration (Allen, 1995).

Tissue/integumentary disease	Infectious pododermatitis (foot rot)—*Fusobacterium necrophorum, Bacteroides melaninogenicus, Porphyromonas levii*	Amoxicillin, ceftiofur (sodium, hydrochloride, crystalline free acid), erythromycin, florfenicol, oxytetracycline, sulfadimethoxine, sulfamethazine, tulathromycin, tylosin, **cefquinome, tilmicosin, sulfadiazine/ trimethoprim**	Procaine penicillin G, ampicillin trihydrate, florfenicol	Different labels will have different pathogens. Severe tissue reactions result from intramuscular use of tylosin and erythromycin.
Tissue/integumentary disease	Actinobacillosus, "wooden tongue"—*Actinobacillus lignieresii*	Long-acting oxytetracyclines (200 and 300 mg/ml), **amoxicillin trihydrate, amoxicillin/clavulanic acid, cefalexin dihydrostreptomycin, trimethoprim/ sulfadiazine (*Actinobacilli* on label)**	Streptomycin, sodium iodide combined with antimicrobial therapy for effect on granulomatous tissue	A case report indicated that cattle receiving IV sodium iodide and intralesional streptomycin regressed lesions faster than negative controls or penicillin-treated cattle (Campbell, 1975). No clinical trials are available.
Tissue/integumentary disease	Actinomycosis, "lumpy jaw"—*Actinomyces bovis*	**Amoxicillin trihydrate, amoxicilin/ clavulanic acid, dihydrostreptomycin, cefalexin, trimethoprim/ sulfadiazine (*Actinomycae* on label)**	Penicillin G, ampicillin trihydrate, oxytetracycline. Sodium iodide may be combined with antimicrobial therapy for effect on granulomatous tissue	No clinical trials are available to confirm efficacy of these antimicrobials. Prolonged therapy is recommended with surgical debridement of the lesion if possible.
Tissue/integumentary disease	Blackleg—*C. chauvoei;* malignant edema—*C. sordellii, C. septicum;* tetanus—*Clostridium tetani*; bacillary hemoglobinuria—*Clostridium hemolyticum*; Black disease—*C. novyi*	**Amoxicillin trihydrate, amoxicillin/clavulanic acid, cefalexin**, procaine penicillin G (*C. chauvoei*), procaine/benzathine penicillin G (*C. chauvoei*), **tylosin**	Penicillin G	All of the approved drugs have "clostridia" on the label without indications for specific clostridial diseases unless indicated. Japanese isolates of *C. perfringens, C. septicum*, and *C. sordellii* displayed phenotypic resistance to oxytetracycline and were confirmed to carry oxytetracycline-resistance genes (Sasaki, 2001).

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Tissue/integumentary disease	Peritonitis—*Escherichia coli*, *Arcanobacterium pyogenes*, *Clostridium perfringens*, multiple Gram-positive and Gram-negative aerobes and anaerobes. Isolate reports in other species include organisms in all 4 quadrants.		Trimethoprim/sulfa (probably the most consistent for *E. coli*), florfenicol, oxytetracycline (both inconsistent on *E. coli*), ceftiofur for short withdrawal but may not cover *Staph.* spp.	Penicillin/gentamicin is reasonable as to spectrum but gentamicin engenders an extreme withdrawal that precludes salvage slaughter attempts in recovered animals.	No clinical trials are available in cattle. Recommendations are based on wide-spectrum, lipid solubility, and duration of activity. An extended duration of therapy (≥ 1 week) is necessary. Prognosis is extremely poor in advanced cases. Note that the MIC90 of the ceftiofur metabolite against Staph. spp is approximately 8 times that of the parent compound.
Tissue/integumentary disease	Omphalophlebitis (navel ill)	**Amoxicillin trihydrate, amoxicilin/clavulanic acid, procaine penicillin/ dihydrostreptomycin, procaine penicillin G**			
Tissue/integumentary disease	Trichophytosis (ringworm)	Benzalkonium chloride (0.15% topical solution), **enilconazole, natamycin**	Topical iodine solution/scrub, systemic griseofulvin*		*Regulations and availability of extra-label slaughter withdrawal time information should be confirmed prior to using griseofulvin in countries without a label for this application. Griseofulvin is teratogenic.
Tissue/integumentary disease	Rainrot (Dermatophilosis)—*Dermatophilus congolensis*		Penicillin G, oxytetracycline		Penicillin G and oxytetracycline are often cited for therapy of dermatophilosus. A paper evaluating MIC and MBC concentrations, *in vitro* data, and unbound serum concentrations also recommended erythromycin, ampicillin, streptomycin, amoxicillin, and chloramphenicol (Hermoso-de Mendoza, 1994).

					The chloramphenicol results suggest potential for florfenicol efficacy.
Cardiovascular/systemic	Anaplasmosis	Chlortetracycline in the feed for control of active infection	Oxytetracycline, imidocarb diproprionate		Prevention or amelioration of clinical signs with oxytetraycline are well established. However, there are reports in the literature citing both successful and unsuccesful clearance of carriers with oxytetracycline. Recent work has documented unsuccessful clearance of induced anaplasmosis carrier status with the OIE regimen of 22 mg/kg oxytetracycline, IV, q 24h, for 5 days (Coetzee, 2005). Clearance of the carrier state with imidocarb has been documented (Roby, 1972).
Cardiovascular/systemic	Endocarditis—*Arcanobacterium pyogenes* and *Streptococcus* spp. are most common. *Escherichia coli*, other organisms also possible.		Penicillin G, presence of a Gram-negative on blood culture indicates ampicillin, amoxicillin, or cefiofur.		Prolonged therapy is necessary. Addition of rifampin (5 mg/kg, PO, q 12h) has been suggested to improve response. Prolonged therapy (4–6 weeks) has been suggested as an appropriate duration of therapy. (Dowling, 1994; McGuirk, 1991). Lack of clinical efficacy may be due to lack of antimicrobial penetration into vegetative lesions. Florfenicol would be appropriate for pathogens with appropriate MICs (variable on E. coli). In cases where the law and economics permit, fluoroquinolones would be appropriate if an organism other than a *Strep*. spp. was confirmed.

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Cardiovascular/systemic	Anthrax—*Bacillus anthracis*	**Amoxicillin, amoxicillin/clavulanic acid, tylosin (*Bacillus* on label)**	Penicillin G, oxytetracycline, fluoroquinolones (where legal) doxycycline, first-generation cephalosporins. Chloramphenicol results suggest florfenicol may be an option.		A study evaluating the MICs of 25 geneticially diverse *B. anthracis* isolates from multiple countries reported MIC90 values as follow: ciprofloxacin 0.09 µg/ml, penicillin 0.2 µg/ml, doxycycline 0.34 µg/ml, cefuroxime 32 µg/ml, cephalexin 0.25 µg/ml, cefachlor 1.65 µg/ml, and tobramycin 0.97 µg/ml (Coker, 2002). Except for cefuroxime, and possibly cefachlor, these MIC90 values are in a range where efficacy might be expected with typically used doses. Universally "susceptible" disk diffusion results with unvalidated interpretive criteria have been reported for tetracycline, ampicillin, streptomycin, chloramphenicol, and erythromycin in South African isolates (Odendaal, 1990).