EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

List of antimicrobials reserved for the treatment of humans

EMA/FVE info session on restrictions for use of certain antimicrobials in animals

Presented by Professor Rory Breathnach on 23 May 2024
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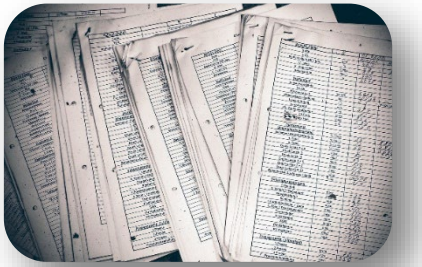
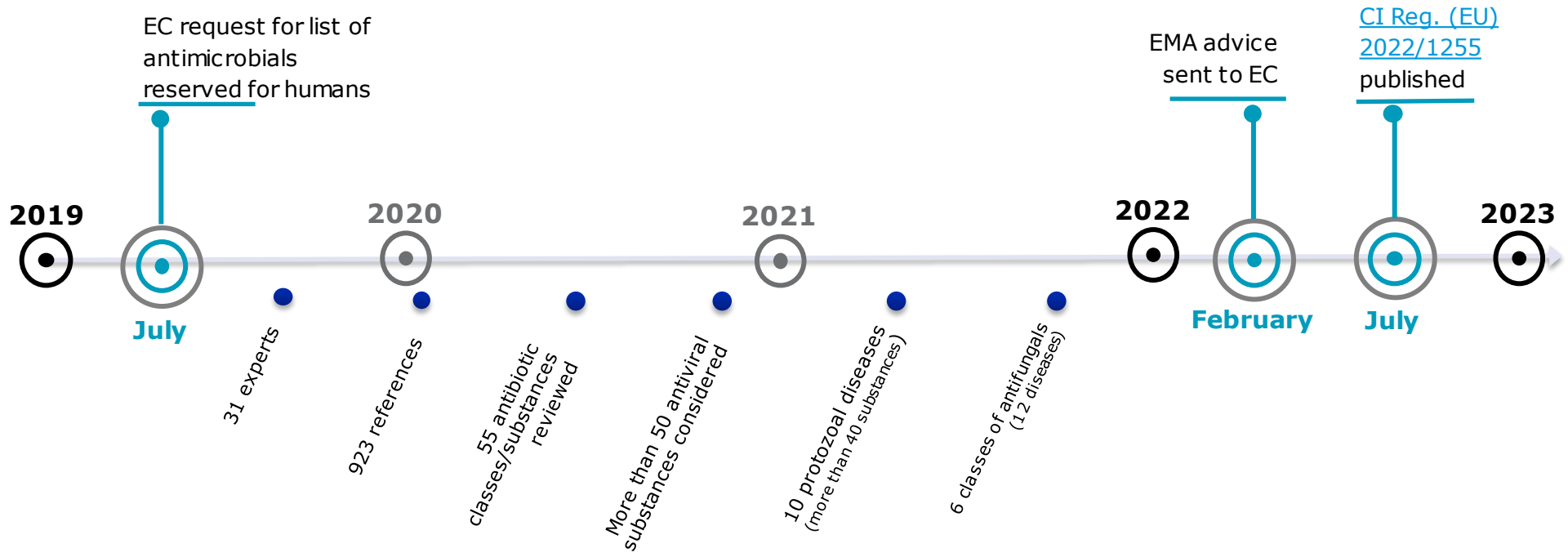
Reducing the emergence of antimicrobial resistance

- Antimicrobial use in animals can contribute to the emergence of resistant bacteria that **can be transferred** to humans through the food chain or direct contact.
- This can reduce the effectiveness of antimicrobials for treating human disease.
- Antimicrobial resistance also brings consequences for animal health and welfare and food production.
- To limit the development of resistance for the benefit of animal and public health, it is important to promote the **prudent and responsible use of antibiotics**.

Setting the scene



Timeline



Information sources used

- peer-reviewed and grey literature, textbooks;
- WHO and OIE (WOAH) categorisations;
- stewardship and prescribing guidance.

- Open call for data on antimicrobial use in animals, including uses outside labelled indications.

- Expert opinion.

Methodology used

All classes were initially assessed against **criterion A - human importance**

Only those that met 'A' were assessed against **criterion B - AMR transmission**

Only those meeting **'A' + 'B'** were assessed against **criterion C - non-essential need for animal health**

Antimicrobials reserved for the treatment of humans must meet **all three criteria**

Outcome

Antibiotics/substances not meeting all criteria

Classes NOT meeting criterion A – human importance

Narrow-spectrum penicillins, aminopenicillins, amdinopenicllins, cyclic polypeptides, pleuromutilins, ketolides, lincosamides, streptogramins, aminocyclitols, tetracyclines, minocycline, amphenicols, sulfonamides, trimethoprim deriv., quinolones (non-fluorinated), nitrofurans, steroid antibiotics, bicyclomycins, orthosomycins, quinoxalines, thiopeptides, phosphoglycolipids, elfamycins, aminocoumarins

Classes meeting criterion A but
NOT meeting criterion B – AMR transmission

Substances used solely to treat TB/mycobacteria, riminofenazines, sulfones

Classes meeting criteria A and B but
NOT meeting criterion C – non-essential for animal health

Antistaphylococcal penicillins, aminopenicillins+BLI, 1st – 4th G cephalosporins, polymyxins, macrolides, aminoglycosides, TMP-sulfonamides, fluoroquinolones, nitroimidazoles, rifamycins, pseudomonic acids

Slido code: #**Infosession_23May**

Human Reserve List - Regulation (EU) 2022/1255

Substances banned for use in animals

Antibiotics

- Carboxypenicillins
- Ureidopenicillins
- Ceftobiprole
- Ceftaroline
- Cephalosporins with beta-lactamase inhibitors
- Siderophore cephalosporins
- Carbapenems
- Penems
- Monobactams
- Phosphonic acid derivates
- Glycopeptides
- Lipopeptides
- Oxazolidinones
- Fidaxomicin
- Plazomicin
- Glycylcyclines
- Eravacycline
- Omadacycline

Antivirals

- Amantadine
- Baloxavir marboxil
- Celgosivir
- Favipiravir
- Galidesivir
- Lactimidomycin
- Laninamivir
- Methisazone/metisazone
- Molnupiravir
- Nitazoxanide
- Oseltamivir
- Peramivir
- Ribavirin
- Rimantadine
- Tizoxanide
- Triazavirin
- Umifenovir
- Zanamivir

11 antibiotic classes, 6 antibiotic substances and 18 antiviral substances

Prudent use of antimicrobials (AM)

General

1. All singing from the "same hymn sheet"
2. The 6Rs
3. Initial overview of scenario:
   - disease status on farm, stables, kennel etc.
   - susceptibility/resistance data – on site and regional labs
4. Alternative options: vaccination, topicals, etc
5. Never substitute for poor husbandry/infection control/sterility
6. Radical idea: buy a new textbook (PK/PD, concentration/time)

Prudent use of antimicrobials (AM)

Specific

1. Accurate diagnosis: clinical examination, WBCs, cytology, acute phase proteins
2. CST/molecular tests pivotal: breakpoints (MIC data)
3. AM needed? If so, **optimal AM and posology selected** (AMEG)
4. Laboratories should test/report in sequence
5. Acute emergencies (e.g. septic peritonitis)?
6. Combination therapy ethical, but **de-escalate if possible**
7. Repeat culture appropriate?

But…

- We don’t always get it right!!!!!!
- We often need to initiate treatment before CST results, but never “cover with AMs”
- Ethical issues compound our approach!
  - MDR otitis externa infections
  - chronic lobar pneumonia

However, the profession’s efforts are making definitive inroads into tackling AMR and contributing to One Health

Prudent use of antimicrobials

Categorisation of antibiotic classes for veterinary use
(with examples of substances authorised for human or veterinary use in the EU)

A

Amdinopenicillins
mecillinam
pivmecillinam

Ketolides
telithromycin

Monobactams
aztreonam

Rifamycins (except rifaximin)
rifampicin

Carboxypenicillin and ureidopenicillin, including combinations with beta lactamase inhibitors
piperacillin-tazobactam

Carbapenems
meropenem
doripenem

Lipopeptides
daptomycin

Oxazolidinones
linezolid

Riminofenazines
clofazimine

Sulfones
dapsone

Streptogramins
pristinamycin
virginiamycin

Drugs used solely to treat tuberculosis or other mycobacterial diseases
isoniazid
ethambutol
pyrazinamide
ethionamide

Other cephalosporins and penems (ATC code J01DI), including combinations of 3rd-generation cephalosporins with beta lactamase inhibitors
ceftobiprole
ceftaroline
ceftolozane-tazobactam
faropenem

Glycopeptides
vancomycin

Glycylcyclines
tigecycline

Phosphonic acid derivates
fosfomycin

Pseudomonic acids
mupirocin

Substances newly authorised in human medicine following publication of the AMEG categorisation
to be determined

AVOID

Categorisation of antibiotic classes for veterinary use

(with examples of substances authorised for human or veterinary use in the EU)

B — RESTRICT

Cephalosporins, 3rd- and 4th-generation, with the exception of combinations with β-lactamase inhibitors

- cefoperazone
- cefovecin
- cefquinome
- ceftiofur

Polymyxins

- colistin
- polymyxin B

Quinolones: fluoroquinolones and other quinolones

- cinoxacin
- danofloxacin
- difloxacin
- enrofloxacin
- flumequine
- ibafloxacin
- marbofloxacin
- norfloxacin
- orbifloxacin
- oxolinic acid
- pradofloxacin

C — CAUTION

Aminoglycosides (except spectinomycin)

- amikacin
- apramycin
- dihydrostreptomycin
- framycetin
- gentamicin
- kanamycin
- neomycin
- paromomycin
- streptomycin
- tobramycin

Aminopenicillins, in combination with beta lactamase inhibitors

- amoxicillin + clavulanic acid
- ampicillin + sulbactam

Cephalosporins, 1st- and 2nd-generation, and cephamycins

- cefacetrile
- cefadroxil
- cefalexin
- cefalonium
- cefalotin
- cefapirin
- cefazolin

Amphenicols

- chloramphenicol
- florfenicol
- thiamphenicol

Lincosamides

- clindamycin
- lincomycin
- pirlimycin

Pleuromutilins

- tiamulin
- valnemulin

Macrolides

- erythromycin
- gamithromycin
- oleandomycin
- spiramycin
- tildipirosin
- tilmicosin
- tulathromycin
- tylosin
- tylvalosin

Rifamycins: rifaximin only

- rifaximin

Categorisation of antibiotic classes for veterinary use

(with examples of substances authorised for human or veterinary use in the EU)

D — PRUDENCE

Aminopenicillins, without beta-lactamase inhibitors

amoxicillin
ampicillin
metampicillin

Tetracyclines

chlortetracycline
doxycycline
oxytetracycline
tetracycline

Aminoglycosides: spectinomycin only

spectinomycin

Anti-staphylococcal penicillins (beta-lactamase-resistant penicillins)

cloxacillin
dicloxacillin
nafcillin
oxacillin

Sulfonamides, dihydrofolate reductase inhibitors and combinations

formosulfathiazole
phthalylsulfathiazole
sulfacetamide
sulfachlorpyridazine
sulfaclozine
sulfadiazine
sulfadimethoxine
sulfadimidine
sulfadoxine
sulfafurazole
sulfaguanidine
sulfalene
sulfamerazine
sulfamethizole
sulfamethoxazole
sulfamethoxypyridazine
sulfamonomethoxine
sulfanilamide
sulfapyridine
sulfaquinoxaline
sulfathiazole
trimethoprim

Natural, narrow-spectrum penicillins (beta lactamase-sensitive penicillins)

benzathine benzylpenicillin
benzathine phenoxymethylpenicillin
benzylpenicillin
penethamate hydriodide
pheneticillin
phenoxymethylpenicillin
procaine benzylpenicillin

Cyclic polypeptides

bacitracin

Steroid antibacterials

fusidic acid

Nitroimidazoles

metronidazole

Nitrofuran derivatives

furaltadone
furazolidone

Veterinarians are encouraged to check EMA's AMEG categorisation before prescribing any antibiotic for animals in their care.