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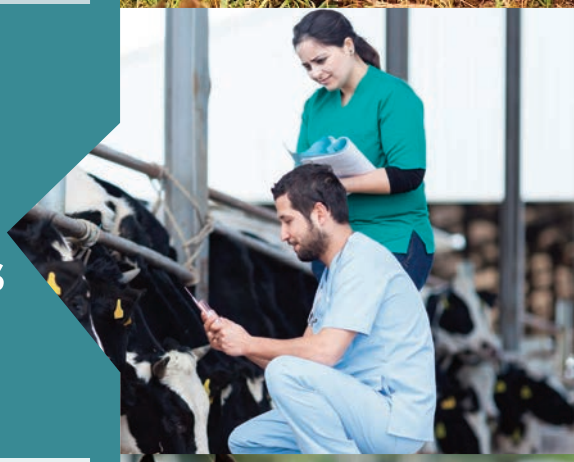
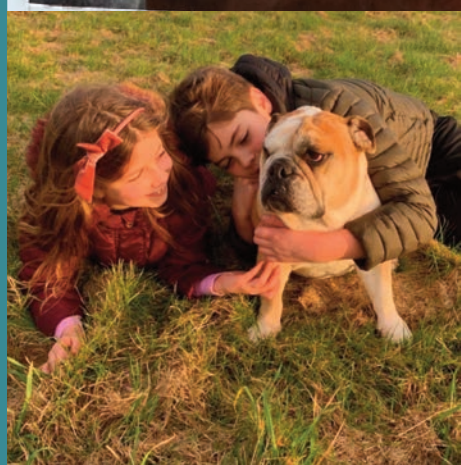
Policy on Highest Priority Critically Important Antimicrobials 1st Revision





iNAP

PROTECTING ANTIBIOTICS FOR THE FUTURE

ANTAIBHEATHAIGH A CHOSAINT DON TODHCHAÍ

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DAFM POLICY ON HIGHEST PRIORITY CRITICALLY IMPORTANT ANTIMICROBIALS- 1st Revision

Introduction:

A key action in Ireland's National Action Plan on Antimicrobial Resistance 2017-2020[1] (*i*NAP) was the development and publication of DAFM's first policy on the use of highest priority critically important antimicrobials (HP-CIAs) in human medicine for use in animals. This policy document was published in November 2018. The policy was developed in line with the first scientific advice of the European Medicine's Agency's (EMA) Antimicrobial Expert Group (AMEG) published in 2014, and in line with the World Health Organisation's (WHO) list of Highest Priority Critically Important Antimicrobials[2].

In December 2019, a new Categorisation[3] of antibiotics for use in animals was published by the AMEG. This document takes into account both the WHO list of critically important antimicrobials (CIAs) and the OIE list of antimicrobials of veterinary importance, thereby allowing an appropriate balance between human health needs, animal health needs and public health considerations. The scientific advice underpinning the new categorisation ranks antibiotics by considering both the risk that their use in animals causes to public health through the possible development of antimicrobial resistance and the need to use them in veterinary medicine. The update takes into account the experience gained since the initial AMEG categorisation of antibiotics in 2014, which proposed three categories for the antibiotics classified as CIAs in the World Health Organisation's CIA list, i.e. those of most relevance for human health.

The revised AMEG categorisation considers all classes of antibiotics (i.e. CIAs and non CIAs), and includes additional criteria such as the availability of alternative antibiotics in veterinary medicine for certain indications. The AMEG also evaluated the impact of the route of administration on the selection for antibiotic resistance, and included its conclusions in a separate list for consideration when prescribing antibiotics. The AMEG classification now comprises four categories, from A to D: Avoid, Restrict, Caution and Prudence.

Scope:

This revised policy paper sets out those antibiotics which come under the WHO HP-CIA list and the parameters under which these HP-CIAs can be used in veterinary medicine based on the 2019 AMEG updated scientific advice. Appendix 1 sets out the HP-CIA antibiotics licenced and sold in Ireland for use in animals, including their categorisation, their active substance and examples of trade names of the products.

DAFM HP-CIA Policy:

The updated DAFM HP-CIA policy reflects the latest scientific advice published by the AMEG in December 2019. During their current review, the AMEG considered additional criteria that could be taken into account for the categorisation of antibiotics. Hence in the updated categorisation more emphasis is placed on the availability of alternative antibiotics in veterinary medicine. **Antibiotics in the 'Restrict' category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health.**

Macrolides, which are HP-CIAs in human medicine are included in the 'Caution' rather than the 'Restrict' category by AMEG. The reason for this is that there are in general alternatives in human medicine in the EU but there are few alternatives in veterinary medicine for certain indications. Nonetheless any HP-CIA antibiotic should only be used when there is no available substance in a lower risk (i.e. non-HP-CIA) category that would be clinically effective.

HP-CIA Category	Antimicrobials Included	Advice on use
RESTRICT	• **Fluoroquinolones** • **3rd /4th generation Cephalosporins** • **Colistin**	• **Critically important in human medicine and use in animals should be restricted to mitigate the risk to public health.** • **Should not be used prophylactically.** • **Should not be used as first line of treatment.** • Should not be prescribed by a veterinarian and/or administered to an animal or animals before **culture and susceptibility** results are received from the laboratory and these results indicate that there is no effective alternative. to using a HP-CIA in the RESTRICT category. Treatment should NOT commence until after culture and susceptibility test results are received from the laboratory. • In exceptional cases involving individual animals, an exemption to the above point can be made if in the veterinary practitioner's clinical judgement an acute clinical disease is present which poses a serious threat to the health, welfare and economic productivity of the animal; in these cases, culture and susceptibility tests are still required, however treatment of individual animals can be commenced before culture and susceptibility tests results are received from the laboratory. • In all cases, records must be kept of all laboratory test and results to verify decisions made to treat with HP-CIA in the RESTRICT category.
Caution	• **Macrolides**	• **Should not be used prophylactically.** • Should not be used as first line of treatment where possible. • Should be considered only when there are no antibiotics in the non-HP-CIA category that could be clinically effective.

Route of administration:

There are different factors directly related to the administration of an antibiotic that affect the occurrence of AMR. These include: the type and formulation of the antibiotic agent; the dose; the total animal biomass treated, in particular the microbiota exposed to the antibiotic (i.e. individual treatment versus mass medication); the treatment interval and the treatment duration.

Oral administration of antimicrobials in livestock is of particular concern in terms of promoting the development of AMR due to the high exposure of gastrointestinal commensal bacteria to antibiotics in the lumen of the gut, and the sometimes prolonged duration of treatment or exposure, especially for products administered in feed (EMA/EFSA, 2017). Other factors such as hierarchy in the group/flock, and lower intakes by diseased animals contribute to the variability in intakes of oral group medications.

Notwithstanding that in intensively reared animals metaphylaxis may be appropriate in circumstances where there is potential for high morbidity (and sometimes mortality) due to rapidly spreading contagious disease, consideration should be given to the administration route/formulation used. Under the new Regulation (EU) 2019/6 on veterinary medicinal products, which becomes effective in January 2022, antimicrobial products for metaphylaxis and prophylaxis may be prescribed only in exceptional circumstances, and for a limited duration to cover the period of risk. In addition, when the antibiotic medicinal products are used for prophylaxis, the regulation also states that this is limited to use in individual animals only.

Best practice guidance to optimise antimicrobial drug use in both human and veterinary medicines is to give the appropriate dose for the correct duration. In order to limit the exposure of the commensal bacteria present in the animal's gut, group treatments with oral antibiotics should be restricted to situations where individual treatments are not feasible. Antibiotics must never be used to compensate for poor hygiene, inadequate animal husbandry or poor farm management.

References:

1) Ireland's National Action Plan on Antimicrobial Resistance 2017-2020:

https://www.agriculture.gov.ie/media/migration/animalhealthwelfare/amr/iNAP251017.pdf

2) The World Health Organisation list of Highest Priority Critically Important Antimicrobials in human medicine:
https://www.who.int/foodsafety/cia/en/

3) EMA AMEG categorisation of antibiotics for use in animals:
https://www.ema.europa.eu/en/documents/report/categorisation-antibiotics-european-union-answer-request-european-commission-updating-scientific_en.pdf

4) EMA/EFSA, 2017. 'Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA)', 15:1.
https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/advice-impacts-using-antimicrobials-animals/reducing-use-antimicrobial-agents-animal-husbandry

5) EMA infographic outlining the categorisation of antibiotic classes for veterinary use in the EU, with examples of active substances per class:

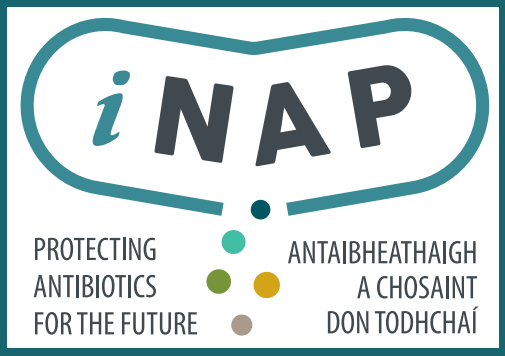
https://www.ema.europa.eu/en/documents/report/categorisation-antibiotics-use-animals-prudent-responsible-use_en.pdf

APPENDIX 1

HIGHEST PRIORITY CRITICALLY IMPORTANT ANTIMICROBIALS LICENCED IN IRELAND FOR USE IN ANIMALS

ANTIMICROBIAL CLASS	HP-CIA CATEGORY	ACTIVE SUBSTANCE	EXAMPLES OF PRODUCTS
3rd & 4th generation cephalosporins	**RESTRICT**	cefovecin ceftiofur cefquinome	Convenia Alfacef, Cefavex, Cefenil, Cefokel, Ceftiocyl, Cemay, Cevaxel, Curacef, Eficur, Excenel, Naxcel Ceffect, Cefimam, Cefquinome, Cephaguard, Cobactan, Plenix, Qivitan
Fluoroquinolones	**RESTRICT**	enrofloxacin marbofloxacin pradofloxacin	Baytril, Doraflox,Enrobactin, Enrocare, Enrodexil, Enrotril, Enrotron, Enro-K, Enroxil , Fenoflox, Floxibac, Quinoflox, Roxacin, Unisol, Valemas Aurizon, Boflox, Efex, Forcyl, Kelacyl, Marbim, Marbocare, Marbocyl, Marbonor, Marbosyva , Marbox. Marfloxin. Veraflox
Polymyxin	**RESTRICT**	colistin	Colfive, Coliscour, Colistin APSA, Hydrocol, Sogecoli
Macrolides	**CAUTION**	erythromycin gamithromycin tildipirosin tilmicosin tulathromycin tylosin tylvalosin	Erythrocin Zactran Zuprevo Hymatil, Keytil, Micotil, Milbotyl, Pulmotil, Pulmovet, Tilmodil, Tilmovet Draxxin, Tulloxxin, Tulaxa, Bilosin, Bilovet, Pharmasin, Tylan, Tylo, Tylosin, Tylovet, Tylucyl Aivlosin

Product names sourced from Health Products Regulatory Authority and European Medicines Agency websites. Correct as of August 2020.



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