



**An Roinn Talmhaíochta,
Bia agus Mara**
Department of Agriculture,
Food and the Marine

Policy on Highest Priority Critically Important Antimicrobials



20 November 2018

Introduction:

Ireland's National Action Plan on Antimicrobial Resistance 2017-2020 (iNAP) aims to implement policies and actions to prevent, monitor and combat AMR across the health, agricultural and environmental sectors. A key commitment for DAFM under strategic objective 4 of *iNAP*, namely, to optimise the use of antibiotics in human and animal health, is to produce a policy on the use of critically important antimicrobials (CIAs).

The World Health Organisation (WHO) categorises antimicrobials used in human health as 'critically important', 'highly important' and 'important' to human health¹. The critically important antimicrobials (CIAs) are therefore the most important to human health. The CIAs are further categorised into **Highest Priority CIAs (HP-CIAs)** and **High Priority CIAs**.

Given the importance of HP-CIAs in human health, these antimicrobials should NOT be used prophylactically or as first line of treatment in animals. They should only be used when there are no effective alternative antimicrobials available for the treatment of respective target species and indication.

- The WHO HP-CIA group contains antimicrobials licensed for use in veterinary medicine including, 3rd and 4th generation cephalosporins, fluoroquinolones, macrolides, and polymyxins. The European medicines regulator – the European Medicines Agency (EMA) - has, on request from the European Commission, assessed the WHO CIAs based on their degree of risk to human health due to antimicrobial resistance development following use in animals. The work, carried out by the EMA's Antimicrobial Advice Ad Hoc Expert Group (AMEG), has resulted in the further categorisation of CIAs into risk categories, as shown below^{2,3}. Category 1 should not be used prophylactically, and includes macrolides. Category 2 includes antimicrobials for which the risk to public health from veterinary use is only acceptable provided that specific restrictions are placed on their use. This category includes fluoroquinolones, 3rd and 4th generation cephalosporins and colistin⁴. Category 3 includes carbapenems and other penems, which are not approved for use in animals and should not be prescribed for or administered to animals.

The WHO highly important and important antibiotics must also be used with care. Uses of these antibiotics are addressed by the prudent use guidelines developed by the Veterinary Council of Ireland.

Scope

This policy paper sets out those antimicrobials which come under Highest Priority CIAs (HP-CIA), and the parameters under which they can be used in veterinary medicine. Appendix 1 sets out the HP-CIA antimicrobials licensed and sold in Ireland for use in animals, including their CIA classification, their active substance and examples of the trade names of the products.

DAFM CIA Policy:

The DAFM list of highest priority CIAs reflects the recommendations of the EMA’s Antimicrobial Expert Group (AMEG). The reasons for this include;

- I. This group, comprising a wide range of specialist European organisations, has made its recommendations after examining the impact that the use of antibiotics in animals has on public and animal health in the EU, and measures to manage the possible risk to humans.
- II. The EMA’s recommendations are reassessed as new science emerges. Any changes in classifications on the AMEG list of CIAs will be reflected in DAFM’s policy on CIAs
- III. AMEG includes public health, veterinary and food safety experts.

CIA Category	Antimicrobials Included	Advice on use
HP-CIA Category 1	<ul style="list-style-type: none">• Macrolides	<ul style="list-style-type: none">• <u>Should not be used prophylactically.</u>• <u>Should not be used as first line of treatment.</u>• Should not be prescribed by a veterinarian and / or administered more than once in a 3 month period to the same animal or animals. The animal(s) must be under the direct care of the prescribing vet.• Where, however, a second treatment within three months for the same animal(s) is considered clinically necessary,<ul style="list-style-type: none">➤ Culture and / or¹ susceptibility testing should be obtained and these results indicate that there is no effective alternative to using a HP-CIA.➤ Treatment should NOT commence until <u>after</u> culture and susceptibility test results are received from the laboratory.• In <u>exceptional cases</u> involving individual animals, an exemption to the above point can be made if the veterinary practitioner’s clinical judgement is that an acute, immediately life-threatening clinical disease is present;<ul style="list-style-type: none">○ In these circumstances, treatment can be commenced <u>before</u> culture and / or susceptibility tests results are received from the laboratory. Records must be kept of laboratory test and results.

<p>HP-CIA Category 2</p>	<ul style="list-style-type: none"> • Fluoroquinolones • Systemic 3rd /4th generation Cephalosporins • Colistin 	<ul style="list-style-type: none"> • <u>Should not be used prophylactically.</u> • <u>Should not be used as first line of treatment.</u> • 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 Category 2 HP-CIA. • Treatment should NOT commence until <u>after</u> culture and susceptibility test results are received from the laboratory. • In <u>exceptional cases</u> involving individual animals, an exemption to the above point can be made if the veterinary practitioner’s clinical judgement is that an acute, immediately life-threatening clinical disease is present; 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 Category 2 HP-CIAs.
<p>High Priority CIA Category 3</p>	<ul style="list-style-type: none"> • Carbapenems and other penems 	<ul style="list-style-type: none"> • Antimicrobials currently not approved for use in veterinary medicine. Should not be prescribed by a veterinarian and/ or administered for off label use.

ⁱ In the case of Macrolides, *in vitro* susceptibility testing is not always indicative of clinical *in vivo* susceptibility. Therefore a culture result that indicates a diagnosis of a condition requiring treatment with Macrolides is acceptable.

REFERENCES

1) WHO 5th Revision Critically Important Antibiotics 2016

<http://apps.who.int/iris/bitstream/handle/10665/255027/9789241512220-eng.pdf;jsessionid=2B9CF57C656BB101036C54112EB90F66?sequence=1>

2) EMA recommendations on the use of antibiotics in animals:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp&mid=WC0b01ac058080a585

3) EMA answers to the requests for scientific advice on the impact on public health and animal health of the use of antibiotics in animals:

www.ema.europa.eu/docs/en_GB/document_library/Other/2014/07/WC500170253.pdf

4) EMA updated advice on colistin, updated May 2016:

www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/05/WC500207233.pdf

5) The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2016:

<https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2018.5182>

HIGHEST PRIORITY CRITICALLY IMPORTANT ANTIMICROBIALS LICENSED AND SOLD IN 2016 IN IRELAND FOR USE IN ANIMALS

<u>ANTIMICROBIAL CLASS</u>	<u>HP-CIA CATEGORY</u>	<u>ACTIVE SUBSTANCE</u>	<u>EXAMPLES OF PRODUCTS</u>
3rd & 4th generation cephalosporins	Category 2	cefovecin ceftiofur cefquinome	Convenia Alfacef, Cefavex, Cefinil, Cefokel, Ceftiocyl, Cemay, Cevaxel, Curacef, Eficur, Excenel, Naxcel Ceffect, Cefimam, Cefquinome, Cephaguard, Cobactan, Plenix, Qivitan
Fluoroquinolones	Category 2	enrofloxacin marbofloxacin pradofloxacin	Baytril, Doraflox, Enrobactin, Enrocare, Enrodexil, Enrofloxacin Krka, Enro-K Aurizon, Boflox, Efex, Forcyl, Kelacyl, Marbim, Marbocare, Marbocyl Veraflox
Polymyxin	Category 2	colistin	Colfive, Coliscour, Colistin APSA, Hydrocol, Sogecoli
Macrolides	Category 1	erythromycin gamithromycin tildipirosin tilmicosin tulathromycin tylosin tylvalosin	Erythrocin Zactran Zuprevo Hymatil, Micotil, Milbotyl, Pulmotil, Pulmovet, Tilmodil, Tilmovet Draxxin Bilosin, Bilovet, Pharmasin, Tylan, Tylo, Tylosin, Tylovet, Tylucyl Aivlosin

List updated June 2018, based on 2016 sales

List due for review annually

Product names sourced from Health Products Regulatory Authority website

