

Ms. Stella Kyriakides
EU Commissioner for Health and Food Safety
European Commission
Rue de la Loi 200
1049 Brussels

Monday, 14 March 2022

RE: Advice on the designation of antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans

Dear Commissioner Kyriakides,

We are writing to you to express our deepest concern about [EMA's recent advice to exclude colistin](#) from the upcoming list of antimicrobials to be reserved for human health mandated by Regulation 2019/6.

Last month, 150 health professionals, and 18 organisations representing human health and animal welfare, cautioned against [the dangers of using colistin in farming](#) to sustain intensive practices, such as early weaning in piglets. They called on the European Commission to preserve this life-saving antibiotic for human use.

As you know, colistin is an antibiotic from the polymyxin class first discovered in the 1940s. Whilst initially restricted in human medicine due to its toxicity, colistin is now widely used to treat infections caused by gram-negative bacteria that are resistant to carbapenems. It is notably used to treat pulmonary bacterial infections in cystic fibrosis patients.

A [recently published OECD, ECDC, EMA and EFSA joint report](#) warns that between 2011 and 2020 the consumption of colistin in European hospitals has risen by 67 %. These data suggest that colistin is increasingly crucial in healthcare in Europe, and any loss of efficacy of this medicine would lead to many infections not being able to be treated.

Despite critical importance for human health, the EMA does not recommend to reserve polymyxins for human medicine, arguing that this class of antibiotics is essential for animal health and therefore does not meet criterion C. However, we believe that the EMA fails to present a compelling argument for essential use in food-producing and companion animals.

Food producing animals

Polymyxins are used in food production to treat colibacillosis, which is, as EMA's advice states, "a major cause of morbidity and mortality in neonatal and juvenile livestock of various species, especially swine". According to the EMA, alternatives to colistin for resistant *E. coli* are limited to other AMEG Category B substances, however, the [Agreement for the Voluntary Reduction of the Colistin Use in Swine Livestock in Spain](#) programme demonstrates how the use of colistin can be almost completely reduced without it being substituted by other AMEG Category B substances.

In six years, this programme managed to reduce the use of colistin in swine from 52 mg/PCU to 0.4 mg/PCU. Colistin was successfully [substituted with apramycin and neomycin](#), which are aminoglycosides, an antimicrobial class classified as AMEG Category C.

Between 2015-2020, Spain not only saw [a decrease in colistin consumption](#), but also in apramycin and neomycin. This suggests that there has been no indiscriminate use of aminoglycosides when substituting polymyxins. If we analyse the use of other AMEG Category B substances in the same period, we observe a reduction in sales of active ingredients.

- Cephalosporins: 2.3 tonnes > 2.2 tonnes
- Quinolones: 5.9 tonnes > 0
- Fluoroquinolones: 67.4 tonnes > 28.7 tonnes

We therefore cannot conclude that the reduction of colistin use in Spain's pig farming had a major impact on the use of other AMEG Category B substances.

The EMA also argues that removing colistin from the market "could increase the selection pressure for resistance to other human Highest Priority Critically Important Antimicrobials (HPCIA)". However, the EMA also recognises in its advice that "restrictions implemented in member states have led to a reduction in colistin use of 76.5% from 2011 to 2020, currently without increased use of other HPCIA". This is confirmed by data from the six countries with the lowest use of colistin [in the latest ESVAC report](#) (Denmark, UK, Lithuania, Finland, Iceland, and Norway). The proportion of the total sales of 3rd- and 4th-generation cephalosporins, fluoroquinolones, other quinolones, and polymyxins for food-producing animals in these countries are below 2% of total antimicrobial sales (with the exception of Lithuania) - well below the 5.8% average in the 31 countries covered in the report.

Colistin is mainly used in farming to treat neonatal diarrhoea in piglets. Intensive farming systems often reduce the weaning period of piglets as much as possible to increase productivity. Longer weaning periods could substantially reduce colistin consumption. In Sweden average weaning periods are 10-12 days longer than other EU countries. Between December 2012 and December 2013, piglets raised in Sweden [consumed 20-30 times fewer antibiotics](#) than piglets raised in France, Belgium, and Germany.

Companion animals

The EMA argues that "polymyxin B is among few alternatives for topical treatment of serous otitis due to gram-negative infections". However, we refute this claim and insist that, in the

majority of cases, polymyxin B can be replaced by other topical substances such as solutions containing gentamicin or amikacin. These antibiotics belong to the same class of aminoglycosides as above. In the case of infections caused by multiresistant pseudomonas, polymyxin B is not even a suitable option, since this antibiotic is easily inactivated by purulent exudates and these infections tend to produce a vast quantity of exudates.

Considering that polymyxins can be replaced by alternatives belonging to AMEG Category C substances and the decrease in colistin use has not had a significant effect on the use of other AMEG Category B substances, we argue that polymyxins meet Criterion C, provision b of the delegated act establishing the criteria for reserving antimicrobials for human use:

Commission delegated regulation supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by establishing the criteria for the designation of antimicrobials to be reserved for the treatment of certain infections in humans. Annex - C(2021)3552 Criterion C, provision b:

The antimicrobial or group of antimicrobials is used to treat serious, life-threatening infections in animals which, if inappropriately treated, would lead to significant morbidity or significant mortality, or would have a major impact on animal welfare or public health, but adequate alternative medicinal products are available for the treatment of those infections in the animal species concerned.

We therefore call on the European Commission to add colistin to the list of antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans. We remain at your disposal should you have any questions and reiterate our offer to meet with you or a member of your staff to present our arguments in more detail.

Yours sincerely,



Erik Ruiz
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Health Care Without Harm (HCWH) Europe