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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON THE USE OF MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS IN FOOD-PRODUCING ANIMALS IN THE EUROPEAN UNION: DEVELOPMENT OF RESISTANCE AND IMPACT ON HUMAN AND ANIMAL HEALTH

AGREED BY SAGAM (SCIENTIFIC ADVISORY GROUP ON ANTIMICROBIALS)	11 June 2009
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	17 June 2009
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 August 2009

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KEYWORDS	Macrolides, lincosamides streptogramins, antimicrobial resistance, food producing species

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1. INTRODUCTION

The 2nd WHO expert meeting (Copenhagen, 2007) "Critically important antimicrobials for human medicine: categorisation for the development of risk management strategies to contain antimicrobial resistance due to non-human antimicrobial use." defined three classes of antimicrobials as prioritized for developing risk management strategies in order to preserve their effectiveness in human medicine. These three classes are: cephalosporins (3rd and 4th generation), quinolones and macrolides.

In 2007, the CVMP released a scientific report including recommendations for action on the use of (fluoro)quinolones in food-producing animals in the European Union (EMEA/CVMP/SAGAM/184651/2005), and more recently one on 3rd and 4th generation cephalosporins (EMEA/CVMP/SAGAM/81730/2006-Rev.1).

2. PROBLEM STATEMENT

The WHO Expert panel has prioritized macrolides. As macrolides are comprehensible used in food producing animals in the EU, a critical review of information related to use of macrolides in food producing animals and potential impact on animal and public health should be prepared.

Many of the mechanisms of macrolide resistance confer cross-resistance to the classes lincosamides and to streptogramins. Any review of possible impacts of antimicrobial resistance related to the use of macrolides in food producing species should therefore also take use of and resistance to the other two classes into account.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

Resistance to macrolides can emerge in zoonotic pathogens such as *Campylobacter* spp and meticillin-resistant *Staphylococcus aureus* (MRSA). Transferable resistance genes can emerge in, e.g. *Enterococcus* spp colonising animals, and these genes can potentially be transferred to bacteria colonising or infecting humans.

Macrolides are widely used for treatment of diseases that are common in food producing animals. This class has also been categorised as critically important for veterinary medicine in the OIE list of antimicrobials of veterinary importance (http://www.oie.int/downld/Antimicrobials/OIE_list_antimicrobials.pdf). Resistance for macrolides can also emerge in important animal pathogens such as *Brachyspira hyodysenteriae*, *Staphylococcus aureus* and other staphylococci, and streptococcal species. In addition lincosamides are also widely used in animal husbandry.

4. RECOMMENDATION

The CVMP Scientific Advisory Group on Antimicrobials recommends drafting a reflection paper on macrolides, lincosamides and streptogramins.

The reflection paper will include information on:

- The classes and substances of concern.
- Use of macrolides, lincosamides and streptogramins in human medicine.
- Use of macrolides, lincosamides and streptogramins in food producing animals.
- Mechanisms of resistance in relevant bacteria.
- Occurrence of resistance in bacteria from food producing animals.
- Possible links between use of macrolides, lincosamides and streptogramins in animals and resistance in bacteria of animal origin
- Exposure of humans to bacteria resistant to macrolides, lincosamides and streptogramins in bacteria of animal origin
- Impact on human health
- Impact on animal health

5. PROPOSED TIMETABLE

The CVMP, with the scientific support of the SAGAM, will consider the comments received to this concept paper (release for consultation June 2009, deadline for comments 31 August 2009). Initial discussions will then take place in SAGAM in September 2009. Following discussions at SAGAM and CVMP, the intended date for release of a draft scientific report is end 2010.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The development of the reflection paper requires the appointment of one SAGAM rapporteur and two Co-rapporteurs.

The reflection paper will be prepared using the standard SAGAM meeting and virtual meetings as required.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is foreseen that the reflection paper will provide further clarification on the need and priority of risk management measures for the involved groups of antimicrobials.

The scientific report will enhance harmonisation and update of prudent use recommendations in the SPC as well as provide overall recommendations on the use and practices to contain antimicrobial resistance.

8. INTERESTED PARTIES

Veterinarians, antibacterial users in general, veterinary pharmaceutical industry, consumers and regulators.

9. REFERENCES TO LITERATURE, GUIDELINES ETC

- Critically Important Antimicrobials for Human Medicine: Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use Report of the Second WHO Expert Meeting Copenhagen, 29–31 May 2007 (http://www.who.int/foodborne_disease/resistance/antimicrobials_human.pdf)
- OIE list of antimicrobials of veterinary importance (http://www.oie.int/downld/Antimicrobials/OIE_list_antimicrobials.pdf)
- Public Statement on the use of (fluoro)quinolones in food-producing animals in the European Union: development of resistance and impact on human and animal health (http://www.emea.europa.eu/pdfs/vet/srwp/18465106en.pdf)
- Revised reflection paper: Use of 3rd and 4th generation cephalosporins in food-producing animals in the European Union: Development of resistance and impact on human and animal health (http://www.emea.europa.eu/pdfs/vet/sagam/8173006enfin.pdf)