European Medicines Agency – role and experience on antimicrobial resistance

Regional Training Workshop on Antimicrobial Resistance (AMR)
Responding to the global challenge of AMR threats: toward a one health approach
15 - 18 November 2016, Bangkok, Thailand

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Overview

• Overview on use of antibiotics for use in animals in the European Union (EU).

• Short background European Medicines Agency (EMA).

• EMA approach to threat of antimicrobial resistance (AMR).

• Speed up development of new treatments.

• Promote responsible use.

• Collect data to guide policy and research.

• Main conclusions.
Overview on use of antibiotics for use in animals in the EU

- Antimicrobial veterinary medicinal products are prescription only.
- Significant differences in use of antibiotics between different EU regions.
- Many Member States are taking action to reduce antibiotic consumption.
- New intended regulation of veterinary medicinal products will provide tools to tackle AMR.
Short background EMA

EMA:

- Decentralised agency of EU;
- Responsible for scientific evaluation, supervision and safety monitoring of medicines developed by pharmaceutical companies for use in EU;
  → Ensures that all medicines available on EU market are safe, effective and of high quality.

EMA does not develop laws concerning medicines:

- European Commission (EC) develops EU legislation concerning medicines and European Parliament together with Council of European Union adopt it;
- EC also develops EU policies in field of human or veterinary medicines and public health.
EMA approach to AMR

- Support ‘One Health’ approach.
  → Close and integrated cooperation between human and veterinary field.
- Support global approach.
- Three main areas.
Speed up development

Examples

- Provide a faster route to develop new treatments against multi-drug resistant bacteria
- Encourage new approaches like use of bacteriophages (viruses that kill bacteria)
- Bring experts together to explore new and better treatments
Speed up development of new treatments

Provide a faster route to develop new treatments against multidrug resistant bacteria

EMA stimulates and facilitates development of new antibiotics for use in humans, e.g.:

• Workshop with EC to discuss regulatory options for approval of new antibiotics (2013);

• Guidelines, e.g. Addendum\(^1\) to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections\(^2\) (2013) which addresses e.g.:
  • Clinical development programme for antibacterial agents with potential to address unmet need;
    • Especially multidrug resistant pathogens when there are few therapeutic options.
  • In certain cases limited clinical development accepted;
    • E.g. new drug in new class; new drug of existing class with novel spectrum.

Speed up development of new treatments (cont.)

Encourage new approaches like use of bacteriophages (viruses that kill bacteria)

EMA supports exploration of new therapeutic options for difficult-to-treat infections due to multidrug resistant bacteria, e.g.:

• Workshop on therapeutic potential of bacteriophages (2015);
  • Videos and presentations available on EMA website¹.
• Taking steps to enable development of such products;
• Ad Hoc Expert Group on Veterinary Novel Therapies (ADVENT) was set up to provide guidance on requirements for authorisation of novel veterinary medicines².

¹http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2015/05/event_detail_001155.jsp&mid=WC0b01ac058004d5c3
²http://www.ema.europa.eu/ema/index.jsp?curl=pages/contacts/CVMP/people_listing_000125.jsp&mid=WC0b01ac05808625e1
Speed up development of new treatments (cont.)

**Bring experts together** to explore new and better treatments

- In partnership with European Centre for Disease Prevention and Control (ECDC) and international network ReAct – Action on Antibiotic Resistance:
  - Joint report on gap between infections due to resistant bacteria and development of new antibiotics (2009)\(^1\).

Promote responsible use

Examples
Promoting responsible use

**Shape strategies** for prudent use of available antibiotics, e.g.

- Committee for Medicinal Products for Veterinary Use (CVMP): updated strategy on antimicrobials adopted\(^1\) → strong emphasis on supporting main areas of EMA approach.

- Antibiotics strongly regulated; > 50 “referrals” on antibiotics in last 10 years:
  - Regulatory procedures used to resolve concerns regarding the safety or efficacy of medicines or benefit-risk balance of a medicine/class of medicines and to harmonize Summaries of Product Characteristics (SmPCs/SPCs) where necessary;
    - E.g. most old antimicrobials nationally approved → different interpretations leading to different (wordings of) indications, contraindications, posology.
    - E.g. Art. 35 referral for systemically administered 3\(^{rd}\)- and 4\(^{th}\)-generation cephalosporins intended for use in food-producing animals (2012), e.g.:
      - Delete poultry as target species and any indication referring to poultry;
      - Add “‘X’ is intended for treatment of individual animals (…)”.

Promoting responsible use (cont.)

Inform doctors, pharmacies, vets, patients and farmers

- Information in SmPC/SPC and product leaflet.
- Active involvement of national competent authorities in EU Member States (through e.g. CVMP and Committee for Medicinal Products for Human Use (CHMP)).
- Twitter (@EMA_News).

Use of “product name (to be completed nationally)” may constitute a risk to public health due to spread of antimicrobial resistance.

*Product name (to be completed nationally)” should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly to first line treatment. Official, national and regional antimicrobial policies should be taken into account when the product is used. Increased use, including use of the product deviating from the instructions given, may increase the prevalence of resistance. Whenever possible, “product name (to be completed nationally)” should only be used based on susceptibility testing.*
Promoting responsible use (cont.)

Advise policymakers on antibiotic use and resistance

- EMA supports EC action plan against rising threats from AMR, by providing scientific input and recommendations on use of antimicrobials in animals.
- Antimicrobial Advice ad hoc Expert Group (AMEG):
  - Impact of use of antibiotics in animals on public and animal health and measures to manage possible risk to humans;
  - In response to requests by EC;
  - Composed of experts from CHMP and CVMP, as well as European Food Safety Authority (EFSA), ECDC and Joint Interagency Antimicrobial Consumption and Resistance Analysis Report (JIACRA);
  - One Health approach.
Advise policymakers on antibiotic use and resistance (cont.)

AMEG e.g. requested by EC to rank

“...classes or groups of antibiotics according to their relative importance for their use in human medicine, in particular considering whether these antibiotics are essential to treat multidrug resistant infections in humans in the EU...”

Outcome¹:

1. Antimicrobials used in veterinary medicine where risk for public health is currently estimated as low or limited (e.g. certain penicillins, macrolides, tetracyclines);

2. Antimicrobials used in veterinary medicine where risk for public health is currently estimated as higher (e.g. fluoroquinolones, 3rd- and 4th-generation cephalosporins, aminoglycosides, polymyxins (moved from category 1 to 2 in June 2016));

3. Antimicrobials not approved for use in veterinary medicine (e.g. carbapenems, glycopeptides).

Advise policymakers on antibiotic use and resistance (cont.)

AMEG:

• “Updated advice on use of colistin products in animals within the EU: development of resistance and possible impact on human and animal health” (July 2016):
  • Reduction in use of colistin should be achieved without increase in use (in mg/PCU) of fluoroquinolones, 3rd- and 4th-generation cephalosporins or overall consumption;
  • Targets for reduction in sales of colistin should be achieved in period of three to four years;
  • If situation regarding colistin resistance in animals or humans further deteriorates, it may be necessary to lower proposed targets.

Promoting responsible use (cont.)

Advise policymakers on antibiotic use and resistance (cont.)

RONAFA (Reduction of the Need of Antimicrobials in Food Producing Animals)¹:

- Joint EFSA/EMA opinion on measures to reduce need to use antimicrobial agents in animal husbandry in EU and resulting impacts on food safety.

Transatlantic Taskforce on Antimicrobial Resistance (TATFAR)²:

- Aims to increase levels of communication, coordination and cooperation on human and veterinary antimicrobials between members;
- Organizations from EU (EC, ECDC, EFSA, EMA), Canada, Norway and United States.

²http://www.cdc.gov/drugresistance/tatfar/index.html
Collect data

Examples
Collect data to guide policy and research

**Survey** sales of veterinary antibiotics across Europe

**ESVAC:**

To develop harmonised approach for collection and reporting of data on use of antimicrobial agents based on national sales figures, as well as estimates on consumption in at least major groups of animal species.

Three work streams:

- Collection of overall sales data (core activity);
- Systems for collection of data by species;
- Establishment of units of measurements.

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Survey sales of veterinary antibiotics across Europe (cont.)

• Data from mainly pharmaceutical industry and wholesalers.

• Data provided by each country, collected by ESVAC at package level, validated and presented as weight of antimicrobials sold.

• Population Correction Unit (PCU) is estimated animal biomass that can be exposed to antibiotics (calculated annually from official statistics).
Collect data to guide policy and research (cont.)

**Survey** sales of veterinary antibiotics across Europe (cont.)

Sales for food-producing species, including horses, in mg antibiotic /PCU, of various veterinary antimicrobial classes and pharmaceutical forms, for 29 countries, in 2014

Differences likely to be due to differences in composition of animal population in various countries and other factors
Collect data to guide policy and research (cont.)

**Survey** sales of veterinary antibiotics across Europe (cont.)

Changes in total sales and in sales of fluoroquinolones and 3rd- and 4th-generation cephalosporins, for 25 EU/EEA countries, from 2011 to 2014.
Collect data to guide policy and research

**Analyse data** on use of antibiotics in humans and animals and links to resistance

Joint Interagency Antimicrobial Consumption and Resistance Analysis report (JIACRA):

- In partnership with ECDC and EFSA;
- First joint report on integrated analysis of consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals published in January 2015;
  - Several positive associations observed between consumption (in human or animal) of specific antimicrobial classes and occurrence of resistance in specific bacteria (in human or animal).
  - Mandate for second report – to be produced in 2017.

Main conclusions

• EMA coordinates and is involved in many actions with regard to AMR:
  • Global and ‘One Health’ approach;
  • Direct and indirect involvement of all stakeholders (regulatory, industry, academia, etc.);
  • Partnered with other EU institutes (ECDC, EFSA), as well as from outside EU.
• Surveillance to follow trends in sales of antimicrobials for use in animals in EU/EEA;
  • Data on sales of antimicrobials powerful tool to encourage countries to take action on use of antimicrobials in animals.
• To improve integrated analyses (e.g. JIACRA) more detailed data needed (i.e. by species).
Thank you for your attention

Further information

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