EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Antimicrobial resistance – EMA experience with CAPs

Health care uncertainty assessment workshop

Overview of the medical regulations process, with a discussion of key uncertainties.

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Disclaimer

The views and opinions expressed in this presentation are those of the speaker and may not represent the official view of the European Medicines Agency (EMA)

Role of EMA

EMA works in collaboration with its EU and international partners in a number of initiatives aiming to limit the development of resistance.

Transatlantic Task Force on Antimicrobial Resistance (TATFAR), was established following the EU-United States summit in November 2009. The Task Force aims to increase levels of communication, coordination and co-operation between the EU and the United States on human and veterinary antimicrobials.

In September 2009, the Agency published a joint report together with the European Centre for Disease Prevention and Control (ECDC) and the international network ReAct - Action on Antibiotic Resistance. This report highlights the gap between infections due to resistant bacteria and the development of new antibiotics.

On-going harmonization efforts

- TATFAR (Trans-Atlantic Task Force on Antimicrobial Resistance);
  - provides an excellent tool to foster discussion between EMA and FDA in the area of anti-bacterials drug development.
- Pilot interaction on development plans for antibiotics:
  - new development plans (scientific advice stage) are mutually discussed between FDA and EMA experts.
- Information sharing on upcoming policies and options to foster antibacterial agents development

Support to EU funded activities for AMR

- Participation in the advisory board of:
  - IMI: COMBACTE
  - FP7: AIDA

- Participation in the stakeholders board:
  - IMI: DRIVE-AB

Guideline on the evaluation of MP indicated in the treatment of bacterial infections

Core guidance revised in 2012, addendum provided in 2013:

- simplified section 5.1 on microbiology, resistance mechanisms, pathogens treated in clinical trials, others expected to be susceptible.
- rare infections/pathogens (e.g. some MDR pathogens): efficacy data can be collected in standard RCTs and/or separate targeted studies
- minimum number of treated cases to support a specific claim for treating certain MDR pathogens to be judged on a case by case basis.
- Clinical development programme for antibacterial agents with potential to address unmet need; especially MDR pathogens when there are few therapeutic options;

Guideline on the evaluation of MP indicated in the treatment of bacterial infections – 2012-2013 update

- The type of development will depend on:
  - what ***has been*** done pre-approval;
  - what the applicant ***plans to do*** post-approval;
  - what ***can be done*** post-approval.
- Critical to conduct an extensive microbiology and PK/PD programme to fully document expectations for the product:
  - Support anticipated efficacy against "target" MDR pathogens;
  - Identify any types of infection in which it should not be used or may need a different regimen (e.g. surfactant binding, ELF penetration);

Testing the pathways

- almost 20 medicinal products for treatment of bacterial infections came for CHMP Scientific Advice since 2013
- more CHMP SA in this field in the last 2 years than in the previous 18 years
- at least one third of them possibly targeting unmet needs related to AMR
- HTA or FDA parallel advice used in few cases
- need to discuss further with HTAs, as access to patients is the ultimate goal

CAPs under J01,04 ATC Codes

J01

- 14 Medicinal products authorised centrally
- 2 orphan products (Cayston, Tobi Podhaler)
- 6 under additional monitoring (Vibativ, Zinforo, Xydalba, Orbactiv, Sivextro, Quinsair)
- 6 approved in 2015

J04

- 3 - approved in 2014 (all orphan, 2 under additional monitoring

Addendum: labels specific for MDR pathogens

Section 4.1:

For the treatment of infections due to {some types of pathogens} in patients with limited treatment options. See 4.4 and 5.1.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Section 4.2:

It is recommended that {agent name} should be used to treat patients that have limited treatment options only after consultation with a physician with appropriate experience in the management of infectious diseases.

Post-marketing surveillance for CAPs: RMP plans at approval

Safety specifications: resistance = important potential risk or important identified risk

Pharmacovigilance measures

Routine:

- Signal detection for reports of lack of efficacy (drug ineffective)
- Special reporting in the PSUR
- Cumulative analyses of spontaneous reports

Additional - PASS:

- "Multi-year in vitro susceptibility surveillance study for clinical isolates"
- "Internationl MP Surveillance protocol"
- annual reports, ~4-5 years or open ended (until further regulatory action)

Post-marketing surveillance for CAPs: RMP plans at approval

Risk minimisation plan

Routine risk minimisation – SmPC:

- ✓ 4.1. Clear indication
- ✓ 4.2. Clear posology, additional recommendations
- ✓ 4.4. Recommendation on appropriate antibiotics use: e.g. Non-susceptible organisms section
- ✓ 5.1. Mechanism of resistance

PL:

- ✓ Section 1 “What MP is and what it is used for”
- ✓ Section 3 “How you will be given MP”

Conclusions

- AMR - a major public health problem
- EMA involved in many activities aiming at improving the harmonisation of the regulatory requirements
- EU regulatory standards with respect to development of new antibiotics have recently evolved
- Discussion on alternative therapeutic approaches that could help tackle AMR
- Issue acknowleged in the RMP, post-marketing surveillance in place, routine risk minimisation activities as appropriate risk management

Thank you for your attention

Further information

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