

News from the EMA

The articles included in this section are a selection from the European Medicines Agency's News and Press Release archive for August 2016 – Oct 2016. More information can be found on the Agency's website: www.ema.europa.eu of medicines to treat tuberculosis.



Development of medicines to treat tuberculosis Comments on draft guidance invited until 31 January 2017

August 01, 2016 – The European Medicines Agency (EMA) has launched a public consultation on revised guidance on the development of new medicines to treat tuberculosis (TB). The guidance is an addendum to EMA's guideline on the evaluation of medicines to treat bacterial infections.

Stakeholders can send their comments to the Agency until 31 January 2017.

TB is caused by a bacterium called *Mycobacterium tuberculosis*. In Europe, approximately 340,000 new TB cases and 33,000 deaths were reported in 2014, mostly from eastern and central European countries. While TB is slowly declining worldwide, the burden of the disease is still very high with approximately 1.5 million deaths per year. Moreover, multidrug-resistant tuberculosis (MDR-TB) still poses a serious public health challenge. It often affects people from the most vulnerable communities, including migrant workers, refugees, displaced persons, prisoners or drug users.

Today's existing TB treatments cannot effectively combat the disease because they are lengthy, complex, and generally show reduced efficacy against MDR-TB, imposing a heavy burden on patients, families and healthcare

systems. New TB medicines and regimens (a combination of medicines) that are simpler to administer, are of shorter duration, and can overcome drug resistance are urgently needed.

In recent years, there has been a shift towards developing entirely new regimens to treat TB, rather than focusing on single medicines. The revised guidance takes into account this development.

The guidance also clarifies the European Union's regulatory requirements with regard to data that should be generated to support the approval of new medicines or combinations of medicines, and provides direction on the following topics:

- Evaluation of the efficacy of individual new medicines and regimens in light of recently approved medicines
- Evaluation of new regimens including at least one new medicine
- Role of biomarkers to predict the effectiveness of the medicine(s) during clinical development
- Comments on the draft guideline should be sent to idwpssecretariat@ema.europa.eu using the form provided.

SECTION EDITORS



Section Editor:

Anuradha Alahari

Anuradha.Alahari@parexel.com



EMA contact:

Monika Benstetter

press@ema.europa.eu

Adaptive pathways: key learnings and next steps EMA publishes report on pilot project

August 03, 2016 – The EMA has published a final report on the experience gained during its pilot project on adaptive pathways, a product development concept for medicines that address patients' unmet medical needs.

The pilot project, which has now ended, showed that adaptive pathways can bring multiple stakeholders together – regulators, health technology assessment (HTA) bodies, healthcare professionals and patients – to agree on a prospective plan to generate data on a medicine across its lifespan in areas of unmet medical need. Adaptive pathways can support medicine development in therapeutic areas where evidence generation is challenging, such as infectious diseases, Alzheimer's disease, degenerative diseases, and rare cancers.

Adaptive pathways can be defined as a planned, progressive approach to bringing a medicine to patients. It is not a new route of marketing authorisation; it makes use of existing regulatory tools. Under this approach, the medicine will first be authorised in a small patient population that is likely to benefit most from the medicine. Then, additional evidence is gathered over time resulting in progressive licensing adaptations to extend or restrict the previously authorised indications of the medicine.

In March 2014, EMA launched a pilot project to explore the practical implications of the adaptive pathways concept with medicines already under development. EMA invited companies to submit ongoing medicine development programmes which fulfil the characteristics of adaptive pathways: a staggered approval from very small, restricted patient

populations to increasingly wider populations; a binding plan of post-licensing evidence gathering; and involvement of key stakeholders in the process.

The pilot helped to identify a number of aspects for further reflection. These include the need for increased involvement of patients to assist in the selection of candidates for adaptive pathways, the definition of methodologically-sound strategies of real-world evidence collection to support the assessment of both efficacy and effectiveness and the potential involvement of payers – Member States' organisations responsible for decision on pricing and reimbursement – to provide input on pricing strategies.

Adaptive pathways: a lifespan approach to learning

Adaptive pathways makes use of existing approval tools, in particular conditional marketing authorisation which has been in operation in the European Union (EU) since 2006. It also builds on the experience gained with strengthened post-marketing monitoring tools introduced by the 2012 pharmacovigilance legislation.

This concept of medicine development and data gathering is not meant to apply to all medicines, but only to medicines that are likely to address an unmet medical need. The medicine development also needs to meet the characteristics of adaptive pathways.

A key aspect of adaptive pathways is the involvement of all relevant decision makers across the lifespan of a medicine, including those who decide about patient access in the Member States. It is particularly important that all involved stakeholders agree upfront on a plan of post-licensing knowledge generation for a medicine, before it is authorised, and that the marketing authorisation holder commits to carrying out this plan. Once a marketing authorisation has been granted, the post-authorisation plan becomes a legally binding regulatory obligation.

Adaptive pathways is still a developing concept which will be refined as more medicines are considered for this approach. Cooperation between stakeholders and a strong pharmacovigilance system are the basis for a systematic monitoring of the safety and the overall performance of a medicine in clinical practice.



Better monitoring of biological medicines

New chapter in guidelines on good pharmacovigilance practices

August 15, 2016 – The EMA has adopted a new chapter to its guidelines on good pharmacovigilance practices (EU-GVP), entitled “Product-or population-specific considerations II: Biological medicinal products”. Good pharmacovigilance practices are a set of measures designed to ensure the robustness of the system of safety monitoring. The new chapter provides guidance on how to better monitor and manage the safety of biological medicines to optimise the safe and effective use of these products in Europe.

Biological medicines contain one or more active substances made by or derived from a biological source, such as blood or plasma. Some of them may be already present in the human body and examples include proteins like insulin and growth hormone. The active substances of biological medicines are larger and more complex than those of non-biological medicines. Only living organisms are able to reproduce such complexity. Their complexity as well as the way they are produced may result in a degree of variability in molecules of the same active substance, particularly in different batches of the medicine.

Therefore the guidance seeks to support those responsible for monitoring these medicines by:

- Highlighting specific issues and challenges for the pharmacovigilance of biological medicines, e.g. in relation to variability of the active substance or traceability of products
- Providing recommendations on how to address these specificities and challenges
- Outlining the roles and responsibilities of the various actors

The new chapter applies to biological medicines, biosimilars (medicines that are developed to be similar to an existing “reference medicine”) and medicines which contain the same or a closely related active substance but are not authorised as biosimilars. It does not apply to vaccines or advanced therapy medicinal products as separate guidance already exists for these.

EU-US collaboration to boost medicine development for rare diseases

New working group will share information and best practices

September 26, 2016 – The EMA and the United States Food and Drug Administration (FDA) have set up a new ‘cluster’ on rare diseases to share experiences and best practices on each

other's regulatory approach to the development of medicines for these diseases.

While rare diseases are estimated to affect 30 million people in the EU and approximately the same number in the United States, each disease individually concerns a limited number of patients. Therefore, global collaboration in this area is particularly important to ensure that the limited number of studies that can be conducted, due to the small populations, can benefit all patients regardless of where they live.

The agencies will exchange information on various aspects of the development and scientific evaluation of medicines for rare diseases. These include topics such as:

- Design of clinical trials in small populations and the use of statistical analysis methods
- Selection and validation of trial endpoints, i.e. target outcomes of a trial
- Preclinical evidence to support development programmes



- Design of post-marketing studies, in particular in the context of early access mechanisms such as EMA's conditional marketing authorisation and FDA's accelerated approval

- Risk management strategies for long-term safety issues with medicines for rare diseases

The creation of this cluster is the latest step in EMA's and FDA's wider objective to expand and reinforce international collaboration. The cluster will provide a forum for confidential exchange of draft documents, policies under development, and more detailed information supporting the scientific basis for decision making on medicine development. The currently existing EMA/FDA clusters discuss issues related to patient engagement, biosimilars, orphan medicines, medicines to treat cancer, medicines for children, and pharmacovigilance, among other topics.

New medicine to protect honey bees against Varroa mites VarroMed recommended for marketing authorisation

October 07, 2016 – At its October meeting, the Committee for Medicinal Products for Veterinary Use (CVMP) of the EMA recommended the granting of a marketing authorisation in the EU for VarroMed (oxalic acid dihydrate/formic acid). This antiparasitic medicine treats the Varroa mite infestation in honey-bee colonies, which is considered to be the most significant parasitic health concern affecting honey bees worldwide. The CVMP opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation.

Honey bees are essential for pollination of crops and wild plants in Europe. The European Commission estimates that pollinators, including honey bees, bumble bees and wild bees, contribute at least 22 billion euros each year to European agriculture and pollinate over 80% of crops and wild plants on the continent. However, beekeepers around the world have reported losses of honey-bee colonies, which are considered to be caused by a combination of different factors such as habitat loss, climate change, pesticide use, and also diseases

affecting bee health. A continued decline of these pollinators could lead to serious biological, agricultural, environmental and economic difficulties.

The main parasite affecting honey bees is the Varroa mite, an invasive species from Asia that has affected bee colonies worldwide. The Varroa mite feeds on the circulatory fluid of bees and brood (bee larvae) and can also contribute to the spread of viruses and bacteria.

VarroMed is a liquid which is trickled onto bees in the hive. It contains a fixed combination of two organic acids, oxalic acid dihydrate and formic acid. The medicine is not expected to pose a risk to human or animal health or the environment. Treatment should only be given at times when honey is not produced by bees.

VarroMed is intended to be used as part of an integrated Varroa control programme, which includes not only treatment with medicines but also non-chemical techniques like queen trapping or drone brood removal. It can be used either as a single-dose treatment during the broodless period (winter treatment) or in the presence of brood (spring or autumn), which will

usually require repeated treatments.

The effectiveness and safety of the product in the protection of honey bees against Varroa mites was tested in laboratory and field studies in different European climate conditions. VarroMed was effective in killing more than 80% of mites, which is below the effectiveness level of 90% recommended by the CVMP Varroa guideline. However, CVMP agreed that a lower level of 80% could be accepted when integrated Varroa control techniques are put in place. Repeated treatment of VarroMed might also result in increased bee mortality, and careful dosing is recommended to avoid overdosing.

The medicine has been classified as MUMS (minor use minor species/limited market), and, therefore, reduced data requirements apply, and these have been considered in the assessment. EMA's MUMS policy aims to stimulate the development of new veterinary medicines for minor species and for diseases in major species for which the market is limited and that would otherwise not be developed under current market conditions.