

News from the EMA

SECTION EDITORS



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New guidance and process improvement for periodic safety update reports

April, 6, 2017 – Following two years of experience with safety monitoring of nationally authorised medicines via the single assessment of periodic safety update reports (PSURs), the EMA has issued additional guidance and recommendations as part of its commitment to continuous process improvement. Two new documents aim at improving the safety information and benefit-risk assessment of medicines in the context of the periodic safety update single assessment (PSUSA): *Explanatory note to GVP Module VII* and *Assessors' questions and answers (Q&A) guidance on PSUR single assessment (PSUSA)*.

PSURs are reports that evaluate the benefit-risk balance of a medicine as evidence is gathered in clinical use. They are submitted by marketing authorisation holders at defined time points following a medicine's authorisation. The agency uses the information in PSURs to determine if there are new risks linked to a

medicine or if the balance of benefits and risks of a medicine has changed. Based on this information, EMA decides whether further investigations are needed or whether measures have to be taken to protect public health. If medicinal products contain the same active substance or the same combination of active substances, the related PSURs will be jointly assessed in a single assessment procedure.

The agency has carried out single assessments of PSURs for nationally authorised medicines containing the same active substances or combinations of active substances since 2015. Before that, PSURs for medicines containing the same active substance or the same combinations were submitted for assessment by their respective marketing authorisation holders to different national competent authorities at different times. The introduction of single assessments helped to streamline the process and to ensure that all the evidence generated about medicines containing

the same active substance is reviewed at the same time by one authority, resulting in consistent safety information.

The PSURs submitted by marketing authorisation holders are assessed by EMA's Pharmacovigilance Risk Assessment Committee together with a leading assessor from one nominated national authority for medicines regulation, the so-called lead Member State. The recommendations made during the assessment are legally binding, applicable to all Member States and implemented across the EU. The joint assessment helps to optimise use of resources between national competent authorities.

Single assessments of PSURs are a key post marketing regulatory tool to ensure patients receive up-to-date information on the safety of medicines. PSURs provide regular opportunities for monitoring medicines in a public health space that covers nearly 500 million people.

Reporting irregularities that may affect medicines

April 10, 2017 – The European Medicines Agency's (EMA) Management Board has adopted a new policy on how EMA handles allegations of improprieties received from external parties. These improprieties may include allegations of departures from standards of good practices that could have an

impact on the evaluation and supervision of medicines. The goal is to create an environment where individuals from outside the agency feel confident to raise their concerns on improprieties in their area of work. The policy helps EMA assess these reports and coordinate any further investigation in a structured way, while protecting the confidentiality of the reporter.

A dedicated email inbox, reporting@ema.europa.eu, has been created. Individuals external to EMA can raise their concerns by sending a message or providing information to this address. They can also send a letter to the agency. Their identity will be kept confidential.

If the allegations concern a centrally authorised medicine, EMA will coordinate the investigation. If there are any concerns that the improprieties may affect the balance of benefits and risks of the medicine, EMA's scientific committees may consider regulatory action. If the allegations concern a nationally authorised

medicine, EMA may, on a case-by-case basis, refer the matter to the national medicines agency in the European Union (EU) Member State where the concerned medicine is authorised. If there is a suspicion that fraud is involved, EMA will transmit the report to the European Anti-Fraud Office (OLAF) in accordance with the existing arrangements between the two institutions.

Since 2013, EMA has received a total of 43 reports that relate, for example, to the manufacturing of medicines or the conduct of clinical trials. Although no formal policy has existed until now, all reports were dealt with in line with the principles included in the new policy.

The policy was adopted by the Management Board at its March meeting and came into effect on 17 March 2017. It was prepared in consultation with the European Commission and OLAF.



New guide on biosimilar medicines for healthcare professionals

May 5, 2017 – The EMA and the European Commission have published an information guide for healthcare professionals on biosimilar medicines. Biosimilars are biological medicines that are highly similar in all essential aspects to a biological medicine that has already been authorised. The objective of the guide is to provide healthcare professionals with reference information on both the science and regulation underpinning the use of biosimilars.

The guide is a joint initiative of EMA and the European Commission. It was developed in collaboration with EU scientific experts, in response to requests from healthcare professionals. Organisations from across the EU representing doctors, nurses, pharmacists and patients have also shared useful views, to ensure that the guide adequately addresses questions relevant to healthcare professionals.

The guide was launched on 5 May 2017 at the European Commission's third stakeholder event on biosimilar medicines, a discussion

forum that provides a platform for stakeholders interested in biosimilars, including healthcare professionals, patients, payers, regulators, and industry.

The EU has pioneered the regulation of biosimilar medicines by establishing a solid framework for their approval and by shaping biosimilar development globally. Since the EU

approved the first biosimilar in 2006, the evidence gained from clinical experience shows that biosimilars approved in the EU are as safe and effective in all their approved indications as other biological medicines. To date, the agency's Committee for Medicinal Products for Human Use (CHMP) has recommended 28 biosimilars for use in the EU.



Green light given for the new EudraVigilance system for collection and monitoring of suspected adverse reactions

May 25, 2017 – The EMA will launch a new and improved version of EudraVigilance, the European information system of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the European Economic Area (EEA). The new version of EudraVigilance will go live on 22 November 2017 with enhanced functionalities for reporting and analysing suspected adverse reactions.

Users of the system, i.e. national competent authorities, marketing authorisation holders and sponsors of clinical trials, have to make final preparations to ensure that their processes and local IT infrastructure are compatible with the new system and the internationally agreed format. The EMA will support national competent authorities, marketing authorisation holders and sponsors of clinical trials in the EEA through targeted e-learning and face-to-face trainings, webinars and information days.

The enhancements for reporting and analysing suspected adverse reactions of the new EudraVigilance system will support better safety monitoring of medicines and a more efficient reporting process for stakeholders.

Expected benefits include:

- Simplified reporting of individual case safety reports (ICSRs) and the re-routing of ICSR reports to Member States as marketing authorisation holders will no longer have to provide these reports to national competent authorities, but directly to EudraVigilance, which will ultimately reduce duplication of efforts. An ICSR provides information on an individual case of a suspected adverse reaction to a medicine;
- Better detection of new or changing safety issues, enabling rapid action to protect public health;
- Increased transparency based on broader access to reports of suspected adverse reactions by healthcare professionals and general public via the adrreports.eu portal, the public interface of the EudraVigilance database;
- Enhanced search and more efficient data analysis capabilities;
- Increased system capacity and performance to support large volumes of users and reports (including non-serious adverse reactions originating from the EEA);

More efficient collaboration with the World Health Organisation (WHO) as EMA will make the reports of individual cases of suspected adverse reactions within the EEA available to the WHO Uppsala Monitoring Centre directly from EudraVigilance; Member States will no longer need to carry out this task.

The reporting of adverse reactions by patients and healthcare professionals to national competent authorities based on local spontaneous reporting systems will remain unchanged. There will also be no changes to the reporting of suspected unexpected serious adverse reactions during clinical trials until the application of the new Clinical Trial Regulation.



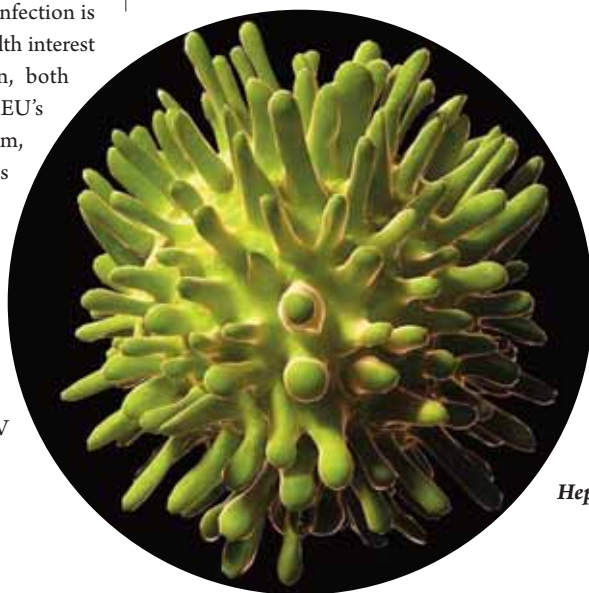
Two new medicines evaluated under accelerated assessment recommended for the treatment of chronic hepatitis C

June 23, 2017 – The EMA has recommended granting marketing authorisations in the EU for Maviret and Vosevi, two new medicines indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults.

Hepatitis C virus infection is a major public health challenge. It affects between 0.4% and 3.5% of the population in different EU Member States and is the most common single cause of liver transplantation in the EU. Approximately 15 million people are chronically infected with HCV throughout Europe. As HCV infection is considered to be of major public health interest in terms of therapeutic innovation, both medicines were evaluated under the EU's accelerated assessment mechanism, which aims to speed up patients' access to new medicines where there is an unmet medical need. Maviret and Vosevi are the first medicines for which accelerated assessment has been carried out within 120 days.

Maviret and Vosevi belong to the direct acting antivirals that block the action of proteins essential for HCV

replication. This type of medicine achieves high cure rates of the infection and does not require the concomitant use of interferons, medicines which are associated with poor tolerability and potentially serious side effects. Both Maviret and Vosevi are active against all genotypes of the virus and, with some differences between the two medicines, may be specifically useful in some patients who failed or cannot use previously available therapies.



Hepatitis C

The effects of Maviret were studied in a total of 2,376 patients who participated in eight pivotal and three supportive clinical trials, and the effects of Vosevi were studied in over 1700 patients in four main clinical trials. The HCV could no longer be detected in over 90% of patients 12 weeks after the end of treatment with either drug. If the blood of patients is clear of HCV for more than 12 weeks they are generally considered as being cured of the infection. Adverse events reported with Maviret were generally mild, including headache, fatigue, diarrhoea, nausea and abdominal pain. With Vosevi, mild nausea, headache and diarrhoea were the most common side effects; other potentially related adverse effects were decreased appetite, vomiting, muscle spasms, and rash.

The opinions adopted by the CHMP at its June 2017 meeting are an intermediary step on Maviret's and Vosevi's path to patient access. The CHMP opinions will now be sent to the European Commission for the adoption of decisions on EU-wide marketing authorisations through an accelerated procedure.

Probiotic Symbioflor 2 recommended for continued use in the treatment of irritable bowel syndrome but not of other gastrointestinal disorders

June 23, 2017 – A review by the EMA has concluded that the probiotic Symbioflor 2 and associated names can continue to be used for treatment of irritable bowel syndrome (IBS) in adults. However, the medicine should no longer be used more widely to treat so-called functional gastrointestinal disorders, a group of



disorders with a variety of causes that may require different treatment approaches.

Symbioflor 2, which contains *Escherichia coli* bacteria, has been described as a probiotic, which means that it encourages the growth of beneficial organisms (flora) in the gut. It was first made available in Germany in the 1950s and subsequently in Austria and Hungary.

In reaching its conclusions, EMA's Committee for Medicinal Products for Human Use (CHMP) reviewed all available evidence on the effectiveness and safety of Symbioflor 2. The data included clinical studies, scientific publications, post marketing experience, as well as information provided by the company and the views of an expert group formed for evaluating Symbioflor 2. The review did not find any new evidence on the effectiveness of Symbioflor 2 since the product was last approved. Available evidence

suggests that the risk of harm from Symbioflor 2 is low. Benefit has not yet been established in children with IBS.

Since the available data are not sufficiently robust for the CHMP to draw conclusions on how well Symbioflor 2 works and whether it is effective for any particular type of IBS, the CHMP has asked the company to carry out a well-designed study on effectiveness and safety among patients with different features of IBS (e.g. those with diarrhoea or with constipation as an important feature). Submission of the study report to national authorities will be a condition for maintaining Symbioflor 2's marketing authorisation. The CHMP recommendation will now be sent to the European Commission for a legally binding decision that will be valid throughout the EU.