Medicinal products for human use: pharmacovigilance of products

2008/0260(COD) - 22/09/2010 - Text adopted by Parliament, 1st reading/single reading

The European Parliament adopted by 569 votes to 8, with 15 abstentions, a legislative resolution on the proposal for a directive of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.

The Parliament adopted its position at first reading under the ordinary legislative procedure (formerly known as the codecision procedure). The amendments adopted in plenary are the result of a compromise reached between the European Parliament and the Council. They amend the Commission's position as follows:

Market autorisation: the national competent authorities shall make publicly available without delay the marketing authorisation together with the package leaflet, the summary of the product characteristics, together with any deadlines for the fulfilment of the conditions where necessary for each medicinal product which they have authorised. The public assessment report shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

Market authorisation: **post authorisation efficacy and safety studies**: the amended text stipulates that it is necessary from a public health perspective to complement the data available at the time of authorisation with **additional data about the safety** and, in certain cases, also about the efficacy of medicinal products authorised.

The Commission should therefore be empowered to require the marketing authorisation holder to **conduct post-authorisation studies on safety and on efficacy**. It should be possible to impose this requirement at the time of granting the marketing authorisation or later, and it should be part of the marketing authorisation. These additional studies may be aimed at collecting data to enable the assessment of safety or efficacy of medicinal products in everyday medical practice.

Products subject to additional monitoring: some medicinal products are authorised subject to additional monitoring. This includes all medicinal products with a new active substance and biological medicinal products including biosimilars for which pharmacovigilance activities are prioritised. This may also apply, at the request of the competent authorities, to specific products, subject to the requirement to conduct a post-authorisation safety study or subject to conditions or restrictions with regard to the safe and effective use of the medicinal product that will be specified in the risk management plan.

Products subject to additional monitoring should be identified as such by a **black symbol** and a corresponding **explanatory sentence** on the summary of product characteristics and on the patient information leaflet, and a publicly available list of such medicinal products should be maintained up to date by the European Medicines Agency.

For all medicinal products, a standard text shall be included expressly asking healthcare professionals to report any suspected adverse reaction in accordance with the national spontaneous reporting system. Different ways of reporting, including electronic reporting, shall be available.

Suspicion of an adverse drug reaction: the suspicion of an adverse drug reaction, meaning that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, should be sufficient reason for reporting. Without prejudice to the existing Union and national provisions and practices on medical confidentiality, Member States should ensure that reporting and processing of personal data related to suspected adverse reactions including those associated with medication errors is on a confidential basis.

The text stipulates that Member States should operate a pharmacovigilance system to collect information useful in the surveillance of medicinal products including information on suspected adverse drug reactions, arising from use of a product within the terms of the marketing authorisation as well as from any other use, including overdose, misuse, abuse and medication errors, and those occurring after occupational exposure and ensure its quality through the follow up of suspected adverse drug reaction cases.

The **Eudravigilance** database should be equipped to immediately forward reports on suspected adverse reactions received from marketing authorisation holders to the Member States on whose territory the reaction occurred.

Assessment report: in the two years following the publication of the Directive, the Commission shall, in collaboration with EMA and national competent authorities and following consultations with organisations representing patients, consumers, doctors and pharmacists, social health insurers, and other interested parties, present to the European Parliament and the Council an assessment report regarding the readability of the summaries of product characteristics and the packaging leaflets and their value to the healthcare professionals and the general public. The Commission shall, if appropriate, bring forward proposals to improve the layout and the content of the summaries of product characteristics and of the packaging leaflet to ensure they are a valuable source of information for healthcare professionals and the general public as appropriate.

Strengthened Risk Assessment Committee: in order to fulfil its new tasks, the coordination group should be further strengthened through the adoption of clear rules as regards the expertise required, the procedures for reaching agreements or postions, transparency, independence and professional secrecy of its members, and the need for cooperation between Union and national bodies. With a view to ensuring that the same level of scientific expertise in the area of pharmacovigilance decision-making at both Union and national levels, when fulfilling pharmacovigilance tasks the coordination group should rely on the recommendations of the Pharmacovigilance Risk Assessment Committee.

Regardless of whether the urgency procedure or the normal procedure is applied, and whether the medicinal product was authorised through the centralised or non-centralised procedure, the Pharmacovigilance Risk Assessment Committee should always give its recommendation when the reason for taking action is based on pharmacovigilance data. It is appropriate that the coordination group and the Committee for Medicinal Products for Human Use should rely on this recommendation when performing their assessment of the issue.

Inspections: the competent authority of the Member State concerned shall, in cooperation with the Agency, ensure that the legal requirements governing medicinal products are complied with, by means of inspections, if necessary unannounced, and, where appropriate, by asking an Official Medicines Control Laboratory or a laboratory designated for that purpose to carry out tests on samples. This cooperation shall consist in sharing information on planned and conducted inspections with the Agency. Member States and the Agency shall cooperate in the coordination of inspections in third countries.

Uniform conditions: a recital states that uniform conditions be established as concerns the contents and maintenance of the pharmacovigilance system master file, as well the minimum requirements of the

quality system for the performance of pharmacovigilance activities by the national competent authorities and marketing authorisation holders, the use of internationally agreed terminology, formats and standards for the conduct of pharmacovigilance, and the minimum requirements for the monitoring of data in the Eudravigilance database to determine whether there are new or changed risks.

The format and content of electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders, the format and content of electronic periodic safety update reports and risk management plans and the format of protocols, abstracts and final study reports for the post-authorisation safety studies should also be established. In this respect, pending the adoption of a new Regulation based on Article 291 of the TFEU, Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission continues to apply, with the exception of the regulatory procedure with scrutiny, which is not applicable.

Transitional provisions: with regard to the requirements for the marketing authorisation holder to submit information on suspected adverse reactions electronically to the Eudravigilance database, the Member States shall ensure that these requirements apply 6 months after the functionalities of the database are established and have been announced by the Agency.

Until the Agency can ensure the functionalities of the Eudravigilance database:

- marketing authorisation holders shall be required to report, within 15 days of the day on which the holder concerned gained knowledge of the event, all serious suspected adverse reactions that occur in the Union, to the competent authority of the Member State on whose territory the incident occurred and shall report all serious suspected adverse reactions that occur on the territory of a third country to the Agency and, if requested, to the competent authorities of the Member States in which the medicinal product is authorised;
- the competent authority of a Member State may require marketing authorisation holders to report to it all non-serious suspected adverse reactions that occur on the territory of that Member State, within 90 days of the day on which the marketing authorisation holder concerned gained knowledge of the event.

During this period, Member States shall ensure that reports that occurred in their territory are made available promptly to the Eudravigilance database, and in any case within 15 days of the notification of suspected serious adverse reactions.

With regard to the requirements for the marketing authorisation holder to submit periodic safety update reports to the Agency, the national competent authorities shall ensure that these requirements apply 12 months after the functionalities of the repository have been established and have been announced by the Agency.

Until the Agency can ensure the functionalities agreed for the repository of the periodic safety update reports, the marketing authorisation holders shall be required to submit the periodic safety reports to all Member States in which the product has been authorised.