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Plan for implementation of the pharmacovigilance legislation by the European Medicines Agency

Activities to protect and promote public health 2012 in partnership with European Member States

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Introduction

New pharmacovigilance legislation (Directive 2010/84/EU and Regulation (EU) No 1235/2010) amending existing legislation was adopted in the European Union (EU) in December 2010. The European Medicines Agency and the European Member States[1] are responsible for implementing much of the new legislation.

The legislation aims to promote and protect public health by strengthening the Europe-wide system for monitoring the safety and benefit-risk balance of medicines. It builds on the existing processes and structures for pharmacovigilance such as the EudraVigilance system for monitoring suspected side effects. Most of the legislation applies from July 2012.

This document provides a summary of the activities the Agency will implement in 2012 and those that it will focus on beyond 2012. Activities are grouped into four main topic areas reflecting the overall process for safety monitoring in the European Union.

- Collection of key information on medicines
- Better analysis and understanding of data and information
- Regulatory action to safeguard public health
- Communication with stakeholders

The need for prioritisation results from budget and resource restrictions. Activities contributing to public health have been given the highest priority, followed by activities increasing transparency and improving communication and then by activities that simplify processes.

An additional document *European Medicines Agency and Member States Joint Implementation Check-list* which is currently online will be updated by the end of March 2012. This will provide a more detailed implementation schedule listing core tasks and will be aimed at pharmaceutical industry and national medicines regulatory authorities.

[1] The term European Member States refers to the European Economic Area (EEA): The EEA was established on 1 January 1994 following an agreement between the member states of the European Free Trade Association (EFTA) and the European Community, later the European Union (EU). Specifically, it allows Iceland, Liechtenstein and Norway to participate in the EU's Internal Market without a conventional EU membership. In exchange, they are obliged to adopt all EU legislation related to the single market, except laws on agriculture and fisheries. One EFTA member, Switzerland, has not joined the EEA.

Collection of key information on medicines

Being able to collect key information on the safety of a medicine is critical to ensuring the safe and effective use of that medicine. In line with the requirements of the new legislation, the Agency will implement a number of new activities in 2012 to ensure that data-and-information collection procedures provide a solid foundation for regulatory action to protect public health.

Risk management plans

The new legislation strengthens procedures for the submission of risk management plans to the Agency. In the European Union, companies submit a risk management plan at the time of application for a marketing authorisation. The plan includes information on how the medicine will be monitored for safety during its lifetime and describes risk minimisation activities. In 2012, the Agency will work on establishing the new procedure for requesting and assessing risk management plans from the pharmaceutical industry while in February the Agency will publish a draft good pharmacovigilance practice (GVP) module on risk management plans for consultation. After 2012, the Agency will begin work on establishing a risk-management effectiveness monitoring system.

Periodic safety update reports (PSURs)

Periodic safety update reports (PSURs) are documents that provide an evaluation of the benefit-risk balance of a medicine. They are submitted by marketing authorisation holders at defined periods during the post-authorisation phase. In February 2012, the Agency will publish a draft good pharmacovigilance practice (GVP) module on PSURs for consultation. The Agency will also implement new procedures related to PSURs during 2012 for medicines authorised through the central authorisation procedure. In 2012, the Agency will also publish a list of Union reference dates for the preparation and submission of PSURs. Beyond 2012, work will focus on PSURs for nationally authorised medicines.

Post-authorisation safety and efficacy studies (PASS/PAES)

A new approach to the use of post-authorisation safety and efficacy studies (PASS/PAES) is foreseen in the legislation and implementation will begin in 2012. A PASS is a study of an authorised medicine which identifies, characterises or quantifies a safety hazard, confirms the safety profile of the medicine, or gauges the effectiveness of risk management measures during its lifetime. A PAES aims to clarify the efficacy for a medicine on the market including efficacy in everyday medical practice. The purpose of the information in a PASS/PAES is to support regulators in decision-making on the safety and benefit-risk profile of a medicine.

The Agency will publish a draft Good Pharmacovigilance Practice (GVP) module on post-authorisation safety studies (PASS) for public consultation in February 2012. A scientific guideline for public consultation on post-authorisation efficacy studies (PAES) will also be published by the Agency during the year. This scientific guideline aims to support the delegated act the European Commission may adopt that will determine the situations in which post-authorisation efficacy studies may be required. A key task of the new Pharmacovigilance Risk Assessment Committee (PRAC) will be to approve new PASS protocols when it starts to meet from July 2012. The ability to require and enforce PASS/PAES studies will become part of the Agency's toolkit for improving the benefit-risk monitoring of medicines.

Full operation of the procedure for protocol approval and results management for centrally authorised medicines will begin in 2012. The Agency will focus on nationally authorised medicines after 2012.

Electronic submission of core medicine information by pharmaceutical industry

The pharmaceutical industry is required to provide the Agency with key information on all authorised and registered medicines in line with Article 57 of the new regulation. The deadline for submission of information by industry is July 2012. Once received, this information will be used by the Agency to support the safety-monitoring of medicines and to protect public health. Following discussions with European industry associations, the Agency intends to publish a revised legal notice and guidance in February 2012 specifying the information that must be submitted by July 2012.

Reporting by patients

The legislation introduces the right of individual European citizens to report suspected side effects from medicines directly to national medicine regulatory authorities. During 2012, the Agency will cooperate with European Member States to provide information to patients on direct reporting.

Better analysis and understanding of data and information

The ability to query, analyse and understand data is particularly important when applied to the safety and benefit-risk profile of a medicine. During 2012, the Agency will continue to invest in signal-detection tools and will prepare for the development of new IT systems beyond 2012.

EudraVigilance and signal detection

The legislation foresees strengthening and increased functionality of EudraVigilance, a system designed for collecting reports of suspected side effects. These reports are used for evaluating medicines during their development and monitoring their safety following their authorisation in the European Economic Area (EEA). As of July 2012, the Agency will begin to operate a revised signal detection process for centrally authorised medicines. For nationally-authorised medicines the Agency will further improve access to EudraVigilance data for national medicine regulatory. Throughout 2012, the Agency will continue to work on improving the quality of EudraVigilance data.

Additional monitoring

During 2012, the Agency will work with the European Member States to establish the first list of medicines subject to additional monitoring. This list, and the subsequent changes to package leaflets for medicines on the list, will encourage reporting of suspected side effects and increase transparency for patients on medicines that are being closely monitored.

IT systems to support processing and analysis of data

New IT systems are required to support certain provisions in the legislation, such as a repository for periodic safety update reports (PSURs). The development of IT systems requirements in coordination with key stakeholders such as national medicines regulatory agencies and pharmaceutical industry will continue at the Agency during 2012 however due to budget and resource restrictions, the full development of new IT systems will not begin until after 2012.

Regulatory action to safeguard public health

Ensuring that the Agency and the European Member States can respond to emerging or urgent health issues in a timely and efficient way is a key deliverable of the legislation. As such, the legislation increases the opportunities for quick regulatory action through a new committee and a strengthened Coordination Group and through new procedures that fast-track the decision-making process when public health is at risk. Priority will be given to these activities in 2012.

Scientific committees and decision-making

A new Pharmacovigilance Risk Assessment Committee (PRAC) will begin meeting from July 2012 with monthly meetings from September 2012. The PRAC will focus on the planning, assessment and monitoring of safety issues with human medicines. The Committee for Medicinal Products for Human Use (CHMP) will start to adopt opinions based on recommendations from the PRAC.

The legislation has also revised the mandate of the existing Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) so that it will lead on decision-making based on recommendations from the PRAC for nationally-authorised medicines. The legislation introduces an opinion-making power either by consensus or majority vote, which in the latter case is transformed into a binding European Commission decision. These changes will ensure harmonised implementation of safety recommendations across the EU. The CMDh will begin meeting based on its new responsibilities from September 2012.

Strengthening referral procedures

During 2012, the Agency will implement a major new referral procedure (known as the urgent Union procedure) specifically designed to rapidly assess significant emerging safety issues linked with a medicine available in the EU regardless of its initial authorisation route (being centralised or national authorisation). A referral is a procedure used to resolve disagreements and address concerns. In a referral, the European Medicines Agency is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. This assessment procedure is conducted through the PRAC and/or CHMP in conjunction with the CMDh in the case of nationally authorised products. Final decisions can result in changing the product information (summary of product characteristics/patient information leaflet), restricting the use of the medicine or withdrawing the medicine from the market.

A key aspect of the new procedure will be the systematic involvement of the PRAC in providing safety expertise to drive the primary assessment and to identify appropriate regulatory actions to be taken for subsequent adoption by the CHMP or CMDh. This new procedure will enhance transparency of the process through the publication of related information online and the opportunity for the public to engage with the Agency through public hearings.

Communication with stakeholders

A commitment to openness and transparency is explicit in the legislation. With new provisions on public access to agendas and minutes of regulatory meetings on safety issues, the legislation aims to increase public confidence in the safety monitoring system. A good pharmacovigilance practice (GVP) module on public participation will be released for consultation later this year. New activities to highlight medicines with safety concerns more proactively are also part of the Agency's implementation plan for 2012.

Online publishing of information

During 2012, the Agency will begin publishing the agendas and minutes of the PRAC, CMDh and CHMP and the assessments, approvals, recommendations, opinions and decisions from the PRAC, CMDh and CHMP through its corporate website at www.ema.europa.eu. Beyond 2012, the Agency will launch a complete European medicines web portal which will link to national medicines web portals.

Coordination of safety messages

Building on its existing role in communicating safety issues for centrally authorised medicines and referral procedures for nationally authorised medicines the Agency will take an active role in supporting the coordination of safety announcements for nationally authorised products with European Member States. The goal is to ensure that the European public receives consistent and coherent safety advice on medicines that are authorised through national procedures but available in more than one Member State.

Public hearings

2012 will see the introduction of public hearings for referrals which fall within the urgent Union procedure when this is considered necessary by the PRAC.