MEMO/

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Strengthening pharmacovigilance to reduce adverse effects of medicines

Medicinal products contribute considerably to the health of EU citizens. They can, however, also have adverse effects. It is estimated that 5% of all hospital admissions are due to an adverse drug reaction (ADR), and that ADR is the fifth most common cause of hospital death. In light of experience and following an assessment made of the EU pharmacovigilance system (supervision and monitoring of ADR) made by the Commission it has become clear that new measures are necessary to improve how the EU rules operate on the pharmacovigilance of medicinal products. Today's proposals seek to change the existing EU legislation on pharmacovigilance (provisions in Regulation (EC) No 726/2004 and Directive 2001/83/EC). They aim at strengthening and rationalizing the EU pharmacovigilance system, with the overall objectives of better protecting public health, ensuring proper functioning of the internal market and simplifying the current procedures.

Some adverse reactions can only be detected after a medicine has been authorised. The full safety profile of medicines can only be known once they have entered the market. The supervision and monitoring of adverse reactions of authorised medicines are carried out through the EU's pharmacovigilance system. This system ensures that any product, which presents an unacceptable level of risk, can be rapidly withdrawn from the market. Thus pharmacovigilance comprises collecting and managing data on the safety of medicines, evaluating this data and deciding to act to protect public health. It is estimated that 197,000 deaths per year in the EU are caused by ADRs and that the total cost to society of ADRs in the EU is €79 billion. Today's proposals are aimed at further improving the current system. They will save many lives per year across the EU. In addition, they will help to cut red tape by decreasing the administrative burden by ca. € 145 billion p.a.

What are the key measures proposed?

The improvement in the protection of public health will be achieved through:

1. Providing **clear roles and responsibilities for the key responsible parties** and clear obligations (see point 1 below for more details);

2. Strengthening **transparency and communication on medicine's safety issues** to increase the understanding and trust of patients and health professionals and improve the penetration of key warnings (see point 2 below for more details);

3. Strengthening **companies' pharmacovigilance systems**, allowing companies to improve their systems regularly whilst reducing administrative burden (see point 3 below for more details);

4. Introducing a **risk management planning** for each new medicinal product (see point 4 for more details).

5. Strengthening the **reporting system for adverse reactions** by rationalising current system and involving all stakeholders in pharmacovigilance (see point 5 below for more details);

6. Ensuring the **proactive and proportionate collection of high quality data** relevant to the safety of medicines through risk management and structured data collection (see point 6. for more details).

In addition to achieving better protection of public health the proposals will also **simplify** the current EU procedures with consequent efficiency gains for both the pharmaceutical industry and medicines' regulators.

Some of the proposed new rules in more detail:

1. Clear roles and responsibilities

- **Member States** should remain central to the operation of pharmacovigilance, with increased cooperation and work-sharing mechanisms (Member States not the Commission).

- **Companies' responsibilities** are clarified, in particular as regards the scope of their obligation to continuously monitor the safety of products thereby ensuring that all information available is brought to the attention of the authorities.

- A new scientific committee, the **Pharmacovigilance Risk Assessment Advisory Committee**, is created within the EMEA and it will play a key role in the pharmacovigilance assessments in the EU.

- The **mandate of the coordination group** composed of Member States representatives is enhanced for the sake of closer cooperation between the Member States and in order to increase work-sharing.

- The EU procedure for the **assessment of serious safety issues for nationally authorised products** is stream-lined through clear and binding initiation criteria for the Member States.

2. Transparency and communication

Clear, EU coordinated messages about specific safety risk issues:

- The **Eudravigilance database** should become the single point of receipt of pharmacovigilance information for medicinal products authorised in the EU.

- EU coordination of **communication about safety issues** and establishment of a European medicines **safety web-portal**.

- Introduction of a **new 'key information' section** in the summary of the product characteristics and the package leaflet.

3. Pharmacovigilance obligations by industry

Currently legislation requires a 'detailed description of the pharmacovigilance system' to be submitted in marketing authorisation applications. Today's proposals simplify the existing requirement by introducing the "**Pharmacovigilance system master file**". In the applications **only key elements** of the pharmacovigilance system should be submitted, but this is balanced with a requirement for companies to maintain a detailed file on site.

4. Risk management planning and non-interventional safety studies

In the existing provisions, companies may provide a **risk management system for specific medicinal** products if considered appropriate, and there is no explicit legal basis for competent authorities to request it. Today's proposals require:

- A **risk management system for each new medicinal product** (or for existing products on the basis of safety concerns), which should be proportionate to the identified risks, potential risks, and the need for additional information on the medicinal product.

- **Harmonised guiding principles** and a procedure for the supervision of non-interventional post-authorisation safety studies (i.e. safety studies of authorised products that are not clinical trials), in particular to ensure that they are non promotional, and the follow-up of any safety date generated in such studies.

5. Adverse drug reaction case reports

Current reports are submitted to several authorities if a product is authorised in more than one Member State, and **lead to duplicative assessments** as there is no provision to group assessments by products or substances. The proposals are intended:

- To make **reporting proportionate to risks**;

- To empower **patients to report their side effects**;

- To ensure that **overdoses and medication errors** are reported;

- To **simplify adverse reaction reporting.** It is proposed to report all adverse reaction data directly to the Eudravigilance database.

- For the Agency to take on a new task for the **monitoring of selected scientific literature** and for entering case reports of adverse effects onto the Eudravigilance database.

- For **medication errors** that result in an ADR to be reported to the competent authorities for medicines. Member State authorities should ensure that data is shared (including between the authorities for medicines and any authorities for patient safety) and make clear the **legal basis for patients to report** suspected adverse drug reactions.

6. Periodic safety update reports and other safety related assessments

As there is currently no provision for group submissions and assessments on products or substances, this leads to **duplicative submissions and assessments**. The **update of product information** as a result of these assessments is not governed in detail by the actual legislation. The proposals:

- Simplify **periodic safety update report submission** by industry and make it proportional to the knowledge about the safety/risk of the product;

- Would introduce **work-sharing mechanisms for the assessments**, with a prominent role in all cases by the Pharmacovigilance Risk Assessment Advisory Committee (see 1. above), and faster updating of product information;

- Amend the **scope of periodic safety update reports** to become an analysis of the risk-benefit balance of a medicinal product rather than a detailed presentation of individual case reports as a result of the submission of all ADR data directly to the Eudravigilance database,;

- Make the requirements for **periodic safety update reports proportional to the risks** posed by medicinal products, and routine reporting is no longer necessary for products considered low risk or where reporting would be duplicative (with the possibility for ad-hoc requests for such products).

- Make explicit provision for the **regulatory follow-up of assessments of periodic safety update reports**, to ensure a clear link between pharmacovigilance evaluations and the review and updating of marketing authorisations authorised in the EU.

- Create the **framework for the shared use of resources** between competent authorities for the assessment and follow-up of periodic safety update reports, with a strong involvement of the Agency's Pharmacovigilance Risk Assessment Advisory Committee.

- Foresee a **single assessment of periodic safety update reports** for medicinal products authorised in more than one Member State,(including all products containing the same active substance),. This will also be the case for products authorised by the Member States and/or by the Commission.

Finally, the proposals also contain two provisions to improve the availability of medicine in Member States, in particular the smaller ones.

When will this become law?

The proposals will now be transmitted to the European Parliament and the Council where it will be discussed and voted in the “co-decision procedure”.

More information on pharmacovigilance

More information on the complete pharmaceutical package

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