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Pharmacovigilance in the post-marketing period

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One of the important forms of the pharmacovigilance activities in the post-marketing period is sending of Individual Case Safety Reports (ICSRs) for suspected adverse drug reactions (ADRs) from healthcare professionals and collecting them into a single national database. Speaking about Bulgaria, this is the suspected adverse drug reaction's database within the Bulgarian Drug Agency (BDA). Collecting of data on ADRs was officially started in 1971 and was carried out by the institutions preceding BDA. By now, the national suspected adverse reaction's database includes about 7,700 cases. In the last years, the annual input of ADR's numbers about 160 reports.

Reports on ADRs from healthcare professionals are validated, assessed for seriousness, expectedness and causal relationship. The drug database is ground for signal generation; the signal is further investigated, evaluated and, as a result of this evaluation, a regulatory change with important clinical impact could be put in to effect.

Since 1974, all ICSRs received in the Bulgarian drug agency have been forwarded to the WHO ADRs Monitoring center in Uppsala, Sweden. After the accession of Bulgaria to the European Union on 1st January 2007, ICSRs are sent also to the European Drug Data Base – EUDRA VIGILANCE, located in the European medicines Agency (EMEA). Eudra Vigilance has started as a pilot project on 01.01.2002 and since November 2007 became mandatory as a single point of collection of ICSRs for all medicinal products, authorized in the countries of the European Union. This database currently numbers more than 1 300 000 cases and it grows monthly by about 10–15 000 reports. Quantitative methods of analyses within Eudra Vigilance are based on the statistical methodology of detection of Signals of Disproportionate reporting (SDRs) and the specific disproportional measure implemented in Eudra Vigilance Data analyses system is the proportional reporting ratio (PRR). As a consequence of our input for the fulfilment of the Eudra Vigilance, any ICSR sent by healthcare professional from Bulgaria has a much fold-increased chance for contributing in the signal detection process.

Referring to data from EMEA, the most common reasons for withdrawals of Marketing authorizations on the ground of safety concerns are: hepatobilliary disorders (26%); blood disorders (10%), cardio-vascular disorders (9%); skin disorders (6%), malignancies (6%). Most commonly withdrawn medicinal products for safety reasons belong to the following groups: medicinal products affecting the nervous system (31%); medicinal products acting on the musculoskeletal system (16%); cardio-vascular drugs (15%); analgesics (8%); antidepressants (7%); vasodilatators (6%); antipsychotics (4%); others (13%).

Important changes in safety data that recently have affected therapeutic behaviour are: the discovery of nephrogenic systemic fibrosis and its relationship to the gadolinium containing MRI contrast mediums; genetic predispositions for severe adverse reactions to Carbamazepin, abacavir, allopurinol; emerging of suicide ideations under treatment with antidepressants and antiepileptic; myocardial ischemia under treatment with long acting beta agonists; influence of NSAIDs on the cardio-vascular system and skin disorders etc.

Conclusion Several examples could demonstrate the importance of the pharmacovigilance for the clinical practice. The role of health care professionals in this respect is essential. Regardless of the possibilities given to us by the access to Eudra Vigilance, the number of ICSRs originating from Bulgaria is too low. Means for increasing the adverse reaction reporting activities of healthcare professionals is needed at all levels: medical universities; specialized medical associations; professional unions; health insurance funds; drug regulatory authority.