Macedonian pharmaceutical bulletin, 68 (Suppl 1) 535 - 536 (2022)
Online ISSN 1857 - 8969
DOI:10.33320/maced.pharm.bull.2022.68.03.257
Short communication

Requirements and possibilities for reporting ADRs: a comparative analysis between Bulgaria and the Republic of North Macedonia

Violeta Getova[1], Radiana Staynova[2], Hristina Lebanova[3], Svetoslav Stoev[3], Ilko Getov[1]

[1]*Faculty of Pharmacy, Medical University-Sofia, 1000 Sofia, Bulgaria*
[2]*Department of Pharmaceutical Sciences, Faculty of Pharmacy, Medical University of Plovdiv, 4002 Plovdiv, Bulgaria*
[3] *Faculty of pharmacy, Medical University-Pleven, 5800 Pleven, Bulgaria*

Introduction

The continued surveillance and monitoring of safety is a crucial, mandatory part of the life cycle of medicinal products. The monitoring and assessment of drug-related problems, adverse drug reactions and adverse events begin from the earliest phases of drug development and expand into later phases. By the time of the marketing authorization application, the available data must be sufficient to prove a positive benefit/risk balance. However, the safety surveillance continues in the post-marketing phase with detection, collection, assessment and understanding of information on adverse drug reactions and other drug-related problems, known as the science of pharmacovigilance. (Rolfes et al., 2017) The sources of information on the safety of medicines are numerous and include scientific literature, clinical trials and post-marketing studies. Furthermore, the systems for spontaneous reporting of adverse drug reactions (ADR) are believed by many to be the most valuable source of safety information on medicines. (Health on the net foundation; World Alliance for Patient Safety, WHO Draft guidelines, 2005) Since 2012 the legislation of the European Union allows patients and consumers to report directly to the national competent authorities cases of adverse drug reactions. (Directive 2010/84/EU) This concept is now fully acknowledged by many countries within and outside the EU, as reports coming from patients do not differ significantly in quality of information while at the same time providing a more personal view on the burden of the adverse reactions to the everyday life. (Heringa et al., 2018; Macedonian agency for medicines and medical devices) Having in mind the importance of spontaneous reporting in the assessment of medicines' safety, the creation and maintenance of a system for collection of patients' ADR reports is considered a significant part of the activities of national regulators. The current study aims at exploring the existing possibilities for direct patient reporting of adverse reactions in Bulgaria and the Republic of North Macedonia as well as a parallel between the legislative framework in both countries.

Materials and methods

For the purpose of the study, a comparison between the legal documents on medicines in the two countries has been made. The main focus was requirements on activities and stakeholders in the field of post-marketing drug safety surveillance. The responsibilities of the national regulators have been analyzed as well as the functionalities for online ADR reporting on the corresponding sites. Ad-hoc search of the pharmacovigilance information on the websites was conducted in terms of essence and frequency of publication of the available information.

Results and discussion

Legal framework - In Bulgaria, the main legal document on medicines is the Law on medical products for human use where Chapter 8 is entirely dedicated to drug safety activities and the national pharmacovigilance system. A separate Ordinance № 8/2008 on requirements for collecting information on adverse drug reactions within the country used to exist but it is no longer applicable to local reporting from 2012. All individual case reports for adverse reactions must be submitted by the Bulgarian drug agency (BDA) to the European medicines agency (EMA)

*v.getova@pharmfac.mu-sofia.bg

via the Eudravigilance system. In addition to the national law, the European guidelines on Good pharmacovigilance practice are also applicable to pharmacovigilance activities. Bulgarian representatives take part in the monthly EMA's Pharmacovigilance risk assessment committee meetings. In Bulgaria requirements and activities related to medical devices are detailed in a separate Law on medical devices. (Law on medical devices, 2020; Law on medicinal products for human use, 2020). In the Republic of North Macedonia, the main law on medicines is called Law on medicines and medical devices where section III.6 is dedicated to pharmacovigilance. (Law on medicines and medical devices, 2007). In both countries, there are separate national institutions responsible for drug regulation. In the context of pharmacovigilance, the abovementioned national competent authorities are responsible for the collection and analysis of drug safety information.

National competent authorities - In both countries, institutions responsible for the regulatory affairs related to medical products are established. In Bulgaria, this is the Bulgarian drug agency (BDA) and in the Republic of North Macedonia – the Macedonian agency for medicines and medical devices (Malmed). Both agencies are responsible for medicinal products for human use and medical devices. In Malmed there is a division on pharmacovigilance and materiovigilance. According to the Malmed website, all pharmacovigilance activities are exercised by the National pharmacovigilance center. In BDA all activities regarding medical devices are performed by division "Medical devices". Pharmacovigilance is a separate sub-structure in the department "Pharmacovigilance and Clinical trials". (Bulgarian drug agency, Macedonian agency for medicines and medical devices)

Functionalities of websites - On the websites of Malmed and BDA organigrams and contact details of the head of departments are available. In a separate section are published the latest versions of legal documents applicable to the pharmaceutical sector. On the Malmed website, there are two sections dedicated to safety surveillance: pharmacovigilance and materiovigilance. On BDA's website, there is no separate section dedicated to materiovigilance. On both websites patients and consumers have the opportunity to report ADR via an online reporting form. Healthcare professionals (HCP) can also report drug-related problems using a different online form. On Malmed there are also patient and HCP's forms for reporting incidents (adverse events) related to medical devices. This functionality could not be found on BDA's website. However, there is a direct link to the EMA's list of medicines under additional monitoring. On the websites of the national competent agencies, educational materials and direct healthcare professionals' communications related to new information on drug safety are frequently uploaded. (Bulgarian drug agency, Macedonian agency for medicines and medical devices).

Conclusion

The conducted study showed a lot of similarities in the organization of national pharmacovigilance systems in Bulgaria and the Republic of North Macedonia. In both countries patients and consumers have the opportunity to report adverse reactions which is of utmost importance in drug safety surveillance. Differences are seen mostly in medical devices regulation and materiovigilance. Future collaboration between BDA and Malmed could be useful for the improvement of national pharmacovigilance systems and strengthening the role of drug safety specialists in the Balkan region.

References

Bulgarian drug agency, http://www.bda.bg/index.php

Directive 2010/84/EU. Directive 2010/84 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use. 2012 http://ec.europa.eu/health/files/eudralex/vol-1/dir_2010_84/dir_2010_84_en.pdf

Health on the net foundation, http://www.hon.ch/Global/pdf/TrustworthyOct2006.pdf

Heringa, M., Floor-Schreudering, A., Wouters, S., De Smet, P., Bouvy, M., 2018. Preferences of patients and pharmacists with regard to the management of drug-drug interactions: a choice-based conjoint analysis, Drug Safety (41), 179-189.

Law on medical devices, 2020, https://www.bda.bg/images/stories/documents/regulations/zakoni/ZMI.pdf

Law on medicinal products for human use, 2020, https://www.bda.bg/images/stories/documents/regulations/zakoni/%D0%97%D0%9B%D0%9F%D0%A5%D0%9C.pdf

Law on medicines and medical devices, 2007, https://malmed.gov.mk/wp-content/uploads/2-Zakon-za-lekovite-i-medicinskite-pomagala-osnoven-tekst-Sl.Vesnik-br.106-od-2007.pdf

Macedonian agency for medicines and medical devices, https://malmed.gov.mk/

Rolfes, L, van Hunsel, F., van der Linden, L, Taxis, K., van Puijenbroek, E., 2017. The Quality of Clinical Information in Adverse Drug Reaction Reports by Patients and Healthcare Professionals: A Retrospective Comparative Analysis. Drug Saf. 40(7), 607-614. 10.1007/s40264-017-0530-5

World Alliance for Patient Safety. WHO Draft Guidelines for Adverse Event Reporting and Learning Systems. World Health Organization (WHO/EIP/SPO/QPS/05.3). 2005.