Safety Alerts: An Observational Study in Portugal

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ABSTRACT

Purpose: The information that is available when marketing authorizations are approved is limited. Pharmacovigilance has an important role during the postauthorization period, and alerts published by national authorities allow health care professionals to be informed about new data on safety profiles. This study therefore sought to analyze all safety alerts published by the Portuguese National Authority of Medicines and Health Products I.P. (INFARMED).

Methods: We conducted an observational study of all alerts published on the INFARMED website from January 2002 through December 2014. From the data included in the alerts, the following information was abstracted: active substance name (and trade name), event that led to the alert, and the resulting safety measures. Active substances were classified according to the Anatomical Therapeutic Chemical (ATC) code.

Findings: A total of 562 alerts were published, and 304 were eligible for inclusion. The musculoskeletal system was the ATC code with more alerts (n = 53), followed by the nervous system (n = 42). Communication of the information and recommendations to the health care professionals and the public in general was the most frequent safety measure (n = 128), followed by changes in the Summary of the Product Characteristics and package information leaflet (n = 66). During the study period, 26 marketing authorizations were temporarily suspended and 10 were revoked.

Implications: The knowledge of the alerts published during the postmarketing period is very useful to the health care professionals for improving prescription and use of medicines and to the scientific community for the development of new researches. (*Clin Ther*. 2015;37:2122–2128)

Key words: pharmacovigilance, Portugal, safety alerts, National Regulatory Agency, adverse drug reactions, safety measures.

INTRODUCTION

The development process for new medicines includes preclinical and clinical studies whose objective is to evaluate their tolerability and efficacy.[1] However, the information that is available when marketing authorizations (MAs) are approved is limited. Among other limitations illustrated by the clinical trials is the fact that the population exposed to the pharmaceutical drug being studied is subject to strict inclusion and exclusion criteria, is homogenous, and does not always have similar (clinical, demographic, social, or other) characteristics to the real population.[2–7] This fact is at the root of the importance of continuously monitoring the safety profiles of medicine. Thus, triggered essentially by the thalidomide phenomenon in the 1960s,[8] pharmacovigilance systems were developed in various countries.[4,6,9] In

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Portugal, the National Pharmacovigilance System was created in 1992.[9]

Safety profile information gathered after the medicine is placed on the market is obtained through spontaneous reporting of adverse drug reactions by health care professionals, by the MA holders, and since July 2012,[10] to comply with the European directive, by patients. After spontaneous reporting, information is evaluated and coded by the pharmacovigilance systems, later being incorporate into the regulating agencies' databases.[11–16]

As a result of this entire process and once the hypothesis being studied is confirmed (frequently complemented by epidemiologic evidence), a safety alert is issued by the competent regulating authorities. This contributes toward improving knowledge about the medicine's safety profile.

Thus, to evaluate the clinical information included in the published alerts, the objective of the present study is to characterize the frequency, through a code of the Anatomical Therapeutic Chemical (ATC) classification system, and the adopted measures of all the safety alerts published in Portugal by the competent regulatory authority, the National Authority of Medicines and Health Products I.P. (INFARMED), on its website.

MATERIALS AND METHODS

Research Strategy

From the INFARMED website,[17] which contains the safety and quality alerts published in Portugal, alerts were selected taking into account the following inclusion criteria: (1) safety alerts; (2) alerts relative to medicines for human use; (3) alerts published from January 2002 (date when this information began to be available on the INFARMED website) through December 2014; and (4) alerts with recommendations and information released to health care professionals and the public in general (Direct Healthcare Professional Communication, changes to the Summary of Product Characteristics and the package information leaflet, suspension of MAs by a competent authority, such as INFARMED and/or the European Medicines Agency), and revocation of MAs. Exclusion criteria were as follows: (1) quality alerts; (2) alerts relative to medical devices, biosimilars, cosmetic and body hygiene products, homeopathic pharmaceutical products, and in vivo diagnostic devices; and (3) alerts relative to vaccines, batches, or manufacturing and supply process and/or replenishment of supply and alerts related to MA or clinical trial processes.

Data Collection and Statistical Analysis

The following information was taken for each alert included in the analysis: publishing date of the alert on the INFARMED website, active substance name (and trade name), event that led to the alert, and the safety measures that resulting. Active substances were classified according to the ATC code.

Correlation between time and alerts publication and ATC group was assessed using nonparametric Spearman correlation coefficient r values (2-tailed). All statistical analyses were performed using SPSS statistical software for Windows, version 21.0 (SPSS Inc, Chicago, Illinois).

RESULTS

Research Results

Figure 1 illustrates the results of the research performed and of the selected safety alerts.

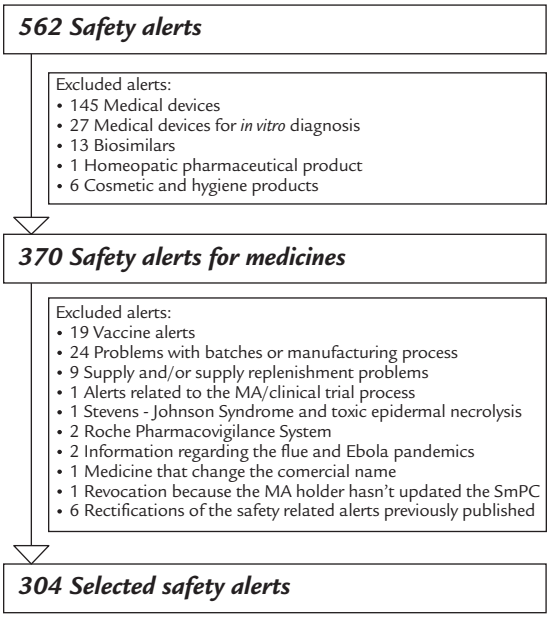

Figure 1. Flowchart of the research process and selection of safety alerts. MA = marketing authorization; SmPC = Summary of the Product Characteristics.