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It is our great pleasure to present this Supplement Issue on "*Macedonian Pharmaceutical Bulletin*" to the scientific and professional community. This supplement includes the short communications from the *Sixth Congress of Pharmacy in Macedonia with International participation*, as the largest gathering for the pharmacy profession held in the Republic of Macedonia. The main theme of the Congress was "Modern pharmacist - bridging science with practice".

A broad spectrum of topics within the pharmaceutical sciences and practice carefully selected for this special occasion in order to build up a highly interesting and comprehensive program were covered. The contributions submitted to the Congress included 6 plenary lectures, 84 section lectures, and more that 240 posters. This Congress, followed the excellent international tradition, was attended by close to 1000 domestic and foreign participants. We received 326 short paper submissions from more than 25 countries. These numbers show that our Congress is aiming for the highest scientific standards, and that it can be considered a well-established venue for researchers in the broad fields of Pharmaceutical sciences and practice.

We would like to thank all internationally prominent researchers for their contribution to reinforcing the overall quality of the Congress. They give the state of the art of the recent advances in the field of pharmacy research.

Sincere thanks to the hosts of the Sixth Congress of Pharmacy in Macedonia with International participation, Macedonian Pharmaceutical Association and Faculty of Pharmacy, Ss Cyril and Methodius University in Skopje for their vision and commitments.

We acknowledge the sponsoring companies: the platinium sponsor AD ALKALOID, Skopje, the golden sponsor PLIVA, the silver sponsor EUROFARM and the bronze sponsor SEPTIMA, for the permanent support to our efforts during the organization.

We would also like to thank our members of the Scientific Committee for their volunteer time and dedication to the critical peer review process and in the organization of the program. We also wish to thank all the members of the Organizing Committee, whose work and commitment was invaluable.

On behalf of the Advisory and Scientific Committees, we would like to especially thank the authors, whose work was the essential part of the congress and contributed to a very successful event. Besides the many academic staff and professionals who contributed to the success of the Congress, we are grateful to the students who participated with oral presentations and posters.

The pharmaceutical sciences continue to grow as dynamic scientific interdisciplinary fields. We believe that published short communications will be an excellent source of scientific material in the fast evolving fields in Pharmaceutical sciences and practice.

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The present issue *of Macedonian Pharmaceutical Bulletin* is a special issue of the 6th Congress of Pharmacy in Macedonia with international participation.

This issue of *Macedonian Pharmaceutical Bulletin* contains short papers accepted by the scientific committee for the presentation at the Congress.

The authors are fully responsible for the contents of their short papers.

All reviewers that were involved in the short papers revision process are sincerely acknowledged.

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Short communication

Model framework for off label use of medicines

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Background

The drug licensing regulatory system ensures that marketed drugs to be used, meet the high standards and requirements for quality, efficacy and safety. Unfortunately, in practice, prescribers are often obliged to deviate from granted medicine marketing authorisation, due to the lack of availability of appropriate medicines for patient's therapeutic needs and progress. This concept of medicines use not mentioned in the approved labelling (FDA Modernization Act) or outside of the terms of Summary of Product Characteristics regarding indication, age, dosage, pharmaceutical form and route of administration (British NHS Guideline) is defined as off-label use of licensed medicines.

On the global level, many supportive evidence and health care needs confirm that off-label medicines use occurs in every country and each level or specialty area of healthcare (Conroy, 2003). Moreover, it is an integral part of Good Medical Practice and may provide the best available option or even the standard of care in a particular health condition (Dresser and Frader, 2009). In general, this concept is legal and may be appropriate, but it can be associated with safety, clinical and ethical concerns, emphasizing the increased incidence of adverse events associated with off-label medicines uses in particularly vulnerable patient groups (Gazarian and Kelly, 2006).

A concerning issue is that the majority of all off-label uses have limited to no scientific support (Radley et al., 2006) and a considerable number of prescribers have no or limited knowledge about off-label medicine use or do not meet regulations regarding off-label use, if they exist. (Piñeiro Pérez et al., 2014).

Experience shows that to ensure the quality of off-label use of medicines, there should be a formal mechanism to assess the feasibility, monitoring the safety and efficiency of medication used based on this concept.Thus, in continuum, the off-label use of medicines has been an essential part of the ethical and legal considerations as well as, many regulatory initiatives.

The overall objective is to present a model regulatory framework setting out guidelines and recommendations for quality use of off-label medicines within the national profile of health care policy.

A literature search was undertaken to identify the issues and challenges related to off-label medicines use including clinical, safety and ethical concerns.

Recommendations for model framework

Principles of good practice for off-label use of medicines should include the following elements: identifying the medical needs; compilation of a consensus list of accepted, scientific based off-label uses; creating an official expert group for the evaluation and approval of specific off-label uses; and, providing a safe and effective supply. The main guiding principles and developed activities to support a responsible decision-making with regard to off-label medicines include: 1) the medical need- the best avail-

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able treatment in cases of specific characteristics when authorized medicines cannot meet the patients' need; 2) sufficient scientific basis and/or clinical practice experience to justify their action. Distinguish the routine off-label use, which is the use of these medicines based on "high quality" evidence and the use in specific exceptional circumstances; 3) information duty and a high degree of respect for patient rights, involving the patient/carer in decision-making process; 4) monitoring and reporting the outcomes, efficiency and adverse reactions; 5) considering self-monitoring of prescribing practices, liability and accountability. An additional special responsibility which among others falls on pharmacists should be to ensure that the prescriber is conscious for off-label prescribing and the reasons for that 6) production of compendia of certain medicines, enlisting those off-label uses judged to be legitimate.7) financial sustainability of an off-label use in medical practice. Before deciding to compound a patient-specific preparation, a step by step evaluation of alternatives should be made. These alternatives include a therapeutic alternative, dose rounding or manipulation of licensed dosage forms (splitting tablets, crushing tablets/opening capsules, dispersing their content in water or food, splitting suppositories, the use of a preparation designed for another route of administration).

Conclusion

Prescription, compounding, dispensing and administration of off label use of medicines should be regulated within the national profile of health care policy.

The regulation regarding the practice of off-label medicine use differs between countries. Some countries have this practice regulated by law, while in others it is covered by good practice regulations or general professional recommendations and ethical standards. Assuming that there is no any general rule to regulate the "accurate" off-label use of medicines it is of paramount importance for the countries to find a national solution to fulfil the ethical and legal demand, especially in the areas of pharmaceutical law and health insurance law. The common elements of these regulatory frameworks are the physicians' freedom to prescribe off-label medicines if the scientific evidence exists and the need to inform patients when making this decision. Making policy efforts, by adopting appropriate guidelines for off-label medicines use, based on scientific evidence, with specifications of healthcare professionals' responsibilities and a registry of off-label drug use in every day practice, would make possible a valuable approach towards ensuring a quality use of these medicines. Recommended solutions, as practiced in some countries, would support prescribes in more direct and active approach to handle the ethical and legal phenomenon associated with the off-label use of medicines

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CONTENTS

Opening lecture

Closing lecture

Plenary lectures

Pharmacoeconomy / Social pharmacy / Drug information

Pharmaceutical analysis / Quality assurance / Regulatory affairs

Clinical biochemistry / Toxicology / Food and nutrition

Pharmaceutical technology and biotechnology/ Cosmetology / Biopharmacy

Medicinal and aromatic plants

Clinical pharmacy / Pharmaceutical chemistry / Biomolecular sciences

Continual professional development

Student session