

STATEMENT

Subject: Doctor of Philosophy in Health and Sport Professional field - 7.3 Pharmacy, Scientific specialty „Social Medicine and Organization of Social Medicine and Pharmacy“

by Prof. Irina Nikolova Nikolova, PhD

Member of the scientific jury, in fulfillment of the Order of the Rector of Sofia University "St. Kliment Ohridski" No. RD-38-593/24.10.2023.

Author of the dissertation: M. pharm. Stefka Stoyanova Stoyanova, PhD student at the Department of Physicochemistry, Faculty of Pharmacy, Sofia University "Sv. Prof. Dr. Emil Ivanov Hristov, Ph.

"Analysis of diagnostic and therapeutic strategies in patients with arterial hypertension by the methods of measuring drug utilization and rational drug use at macro level in Bulgaria".

The dissertation work is devoted to the analysis of drug utilization and rational drug use in the treatment of uncomplicated essential hypertension in Bulgaria, using quantitative and qualitative measures at national level, as well as comparing diagnostic and therapeutic strategies in patients with uncomplicated essential hypertension with treatment standards and valid national and international pharmacotherapeutic guidelines. Within the period of the dissertation development, a research program was implemented with the following main tasks: analysis of national programs for the prevention of arterial hypertension; determination of the total number of patients diagnosed with primary hypertension who are part of the drug therapy reimbursement system; determination of the percentage of patients with different types of complication of primary essential hypertension (by ICD); identification of the most prescribed medicinal products by INN, according to the amounts paid by the NHIF budget; identification of the most prescribed medicinal products by INN, defined as the absolute number of DDD; presentation of the costs of medicinal products calculated as the number of packages; identification of the top 10 mono products by INN, quantity of active substance and number of tablets per package, calculated according to the indicator DDD/per patient/per year; identification the most prescribed combination medicinal products as DDD/year containing fixed dosage forms by trade name and INN; calculation of DDD per capita for 1 year and DDD per 1000 capita for 1 year.

The topic of the PhD thesis is very innovative and has potential for future, more detailed research. The dissertation is formatted according to the standard requirements for

this type of scientific work - it is written in 124 typewritten pages and includes 46 figures and 19 tables. The bibliography includes 198 references.

From the detailed and thorough analysis of the problem presented in the literature review, it is evident that M. Pharm. Stefka Stoyanova Stoyanova shows a thorough knowledge in the field of treatment and pharmacotherapy of hypertension, as well as the importance of early detection and diagnosis of essential hypertension as a socially significant disease. The aim of the dissertation is clearly stated, and to achieve it, tasks related to the analysis of rational drug use are formulated.

The methodological set is adequately chosen to meet the set tasks, and all methods are described in detail, allowing them to be generally reproducible. It is evident from the presented methodological part that the PhD student has mastered a number of modern methods both in the field of data analysis and in terms of their evaluation and statistical processing. The original data section is exemplary as the data obtained are well described and aptly illustrated with a large number of figures and tables.

In the framework of the dissertation realization, publicly available data from NHS registries related to arterial hypertension were analyzed and drug utilization was analyzed according to the WHO ATC/DDD methodology. The results were processed using descriptive statistical methods and presented in absolute and relative values, mean, median, mode.

It has been established that Bulgaria does not have a national pharmacotherapeutic guideline for the treatment of arterial hypertension and there is no adequate mechanism for the follow-up of patients with essential hypertension undergoing treatment in the so-called "free market". The practice of direct referencing of medical professionals to European and international standards has been adopted. In clinical practice in Bulgaria, the real choice for the treatment of patients with essential hypertension (ICD I10) are mono-products - they occupy 2/3 of the total share of antihypertensive drugs. The data obtained show that the costs of treating ICD I10 patients decreased with each passing year within the 5-year study, in contrast to the total costs of the NHIF, which showed an increasing trend. In clinical practice, beta-blockers, respectively the INN Nebivolol, have a significant share among the most prescribed medicines, defined through the NHIS treatment costs as well as by number of packages. The group of centrally acting anti-adrenergic drugs (Moxonidine, Rilmenidine), which, however, according to the current recommendations of the ESC and ESH, can be used only in resistant hypertension when all alternatives are ineffective, occupies a serious share.

From the research conducted, 12 main conclusions are summarized, with separate perspectives and contributions, to the formulation of which I have no objections. As a result of the studies conducted, the doctoral student concluded that diagnosis of essential hypertension is usually delayed and consequently the initiation of drug treatment is delayed. In clinical practice, there are no adequate prevention programmes in place that are non-patient-oriented and produce positive results.

The Author Executive Summary correctly reflects the dissertation by focusing on the results of the analyses, their discussion and the contributions of a scientific-theoretical, methodological and applied nature.

One full-text scientific publication with impact factor has been realized on the topic of the dissertation, in journal with Clarivate Analytics impact factor. The dissertation results have also been presented at one international forum and in 5 articles published in non-refereed journals.

Conclusion: The dissertation is written clearly and concisely. The amount of work done is sufficient, using an adequate range of research approaches and methods, and the data analysed is well processed and illustrated. The work presented and the scientific metrics clearly demonstrate the personal contribution of the PhD student to the realisation of the research programme. Undoubtedly, in the process of developing the PhD thesis, M.Sc. Pharm. Stefka Stoyanova Stoyanova has acquired sufficient theoretical knowledge and practical skills adequate for obtaining the PhD degree. The presented data and considerations give me grounds to confidently conclude that the submitted thesis meets the national and institutional regulatory requirements and the relevant quantitative criteria relevant to the present procedure. This gives me grounds to recommend to the Honourable Members of the Scientific Jury to vote in the affirmative for the award of the degree of education and research "Doctor" to M. Pharm. Stefka Stoyanova Stoyanova.

Sofia, 22.11.2023.

Prepared by:

/Prof. Irina Nikolova, MD, PhD/