Written Opinion

from
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On the dissertation paper for obtaining Doctor's Academic and Science Degree under a PhD Program "Social Medicine and Organization of Healthcare and Pharmacy",
Higher Education Area 7. Healthcare and Sports; Professional Direction 7.3 Pharmacy

By ***Mr. EMANUIL PLAMENOV YORDANOV, MSc Pharm***

With topic:
RETROSPECTIVE STUDY ON DRUG UTILIZATION, AVAILABILITY AND AFFORDABILITY OF BIOSIMILAR MEDICINAL PRODUCTS CONTAINING MONOCLONAL ANTIBODIES IN BULGARIA

Scientific supervisor: Prof Emil Hristov, MD, PhD

The dissertation submitted for evaluation examines in a focused and comprehensive manner the medicinal use, availability and accessibility of biosimilar medicinal products containing monoclonal antibodies in Bulgaria.

In a volume of 129 pages and illustrated with 15 tables, 48 figures and 1 appendix, the scientific work presents a comprehensive list of 126 literary sources, mostly in English. The dissertation examines comments and analyzes the results of a study conducted on the use of biosimilar medicinal products, the possibilities for saving public costs and the attitude of prescribing medical specialists on the issue of biological and/or biosimilar medicines.

The defined goals and tasks of the dissertation work are within the scope of the scientific specialty of the doctoral program and correspond to the content and the conducted studies. The methods and materials for each element of the studies are correctly selected and described. The PhD student shows excellent knowledge of the subject and a thorough approach. From the point of view of the formulated contributions, they are grouped as scientific-theoretical, methodical and scientific-applied. Some specific and sensitive methods were used, such as desk research and moving average.

In the work, a comprehensive literature review on the subject was made, based on PRISMA and the PRISMA 2009 Survey Checklist. One hundred twenty six sources were used as references, which comprehensively and multifaceted, mostly in English, cover the topic and provide a solid theoretical basis for the study. In its entirety, the dissertation is the first comprehensive scientific study on the regulatory, medico-social and financial aspects of the use of biosimilar medicinal products.

The choice of the topic, in my opinion, has its continuation and solid foundation in the primary unit of the dissertation and is determined by his personal and practical experience and interests. The PhD

student demonstrates in-depth preparation and free handling of the terminology, research tools and makes serious, thorough and rational conclusions about the practice in Bulgaria.

Already in the introduction, the grounds and findings of the problem are presented, and the scope and content of the research work are clearly and precisely formulated in the aim and tasks section. It should be emphasized that the scientific leader is a leading specialist, expert and researcher of the regulatory and practical aspects of biological medicinal products in Bulgaria, which also has an impact on the quality of the development.

In the methodological part, a valuable and in-depth approach of presenting the materials and methods separately for each of the implemented tasks is used. The use of heterogeneous data sources and a wide range of classical methods of medico-social studies is impressive.

The study's results section include analysis of results for each task. Assumptions have been adopted that comprehensively and correctly describe the use of biological and biosimilar medicines. The periods after authorization for use of the reference biological medicinal products and their biosimilar medicinal products when they become available for Bulgarian patients are defined, i.e. after the fulfillment of the two cumulative conditions – authorization for use and registered price. The authors conclude that the period in Bulgaria is below the EU average. The prices of medicinal products, as well as the price of one therapeutic course, significantly exceed the average income of Bulgarian citizens, which is why these types of products are considered affordable only after their inclusion in the reimbursement system. According to one of the tasks, it has been proven that the share of the studied products is close to 1/5 of the total costs for drug therapy in Bulgaria in general, and the use of biosimilar medicinal products is negligible.

A survey of the knowledge of specialists prescribing biological and biosimilar medicinal products containing monoclonal antibodies in Bulgaria was also conducted. The survey was conducted among doctors with a specialty that is among the leaders in prescribing biological drugs. The presented sample covers 1/3 of all doctors specializing in rheumatology in Bulgaria, which allows the national representativeness of the findings. Descriptive statistical methods were applied to analyze the results. The author comments on the results of the studies in a separate section. The annotated economic data show that the relative share of biological products is 17% of the public expenditure on medicines. The data is indicative of excellent availability, accessibility and usability at a macro level, assessed through budget indicators.

The obtained results also show that the prescription and dispensing of biosimilar medicinal products is at a negligible low level – only 4.8% of the total prescription, estimated through the budget expenditures of the NHIF. An attempt was made to identify the main reasons for this negative result - the lack of adequate national standards for the substitutability/interchangeability of biological and biosimilar medicinal products with biological and/or biosimilars, prescribing by trade names, conservatism and mistrust of prescribers to the so-called substitute therapies, aggressive drug promotion to medical specialists, etc. The survey found that most respondents were willing to prescribe biosimilars to patients who had already been treated with them, but were less likely to

prescribe them to patients who had not previously been treated with biosimilars or with other biological medicinal products. This suggests that there may be concern and uncertainty among professionals about the use of biosimilar medicinal products, particularly among patients requiring de novo biologic therapy.

In connection with the dissertation work, the publication activity is presented in a modern and adequate way. The articles in referenced and indexed world-famous databases with scientific information are 3, in English, in only one scientific journal - Journal of Generic Medicines, which is logical and shows that the wide scientific community has gained access to the research. The applicant is FIRST author in one of the publications. There are 8 publications and reports (from scientific forums) in non-refereed editions, the PhD student is the FIRST author in one as well. There are data on participation in a scientific project with targeted funding, as well as awards from scientific forums and the Rector of SU St. Kliment Ohridski".

I accept the results obtained and the conclusions drawn in the dissertation, which follow logically from the set goals and objectives and prove the research hypothesis. Modern, comprehensive and accurate scientific language, methodological tools and statistical analysis were used in processing the results.

The submitted abstract meets the requirements.

I have general notes on a technical level and about spelling mistakes. My only conceptual question has to do with the preference for using the term "utilization" instead of "use" in Bulgarian language translation and the grounds for doing so.

The formulated contributions correspond to the achieved results, and I consider that leading contributions are contribution 3 from the scientific-theoretical and contribution 2 from the scientific-applied.

Conclusion:
The dissertation submitted for discussion and evaluation is of high quality and will contribute to the study of drug use, the practice of biologic substitution, and the clinical and regulatory rationale for monoclonal antibody biologic therapy of patients in rheumatology and gastroenterology. The dissertation work for the acquisition of the PhD of mag.-pharm. Emanuil Plamenov Yordanov, a full-time PhD student, meets the requirements, is a novelty for Bulgaria and has significant contributions. After having familiarized myself in detail with the presented set of materials for the protection procedure, I consider that the requirements of the Regulations of SU "St. Kliment Ohridski", studies on the PhD program of the Faculty of Chemistry and Pharmacy and they are the result of the author's own research and development.

In view of the above outlined arguments and the dissertation thesis, **I confidently give my positive evaluation** and would like to suggest to the Honorable Members of the Scientific Jury to confer ***Doctor's Academic and Science Degree (PhD) on*** Mr. Emanuil Plamenov Yordanov.

Signature:

Digitally signed by Ilko Nikolaev Getov
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The present written opinion was prepared in accordance with Art. 69, par. 4 of the Rules on the Terms and Conditions for Obtaining Science Degrees and Academic Positions with the Sofia University St. Kliment Ohridsky and in conjunction with Order No. RD-38-116/08.02.2023 of the Rector.