Statement

from

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Regarding the dissertation on the topic: "Retrospective study of the medicinal use, availability and accessibility of biosimilar medicinal products containing monoclonal antibodies in Bulgaria", presented for public defense before a scientific jury for awarding the educational and scientific degree "doctor" in the professional field 7.3 Pharmacy, scientific specialty "Social medicine and organization of healthcare and pharmacy.

Author of the dissertation: Emanuil Plamenov Yordanov , PhD student at the Department of Physical Chemistry, Faculty of Chemistry and Pharmacy, Saint Kliment Ohridski University, Sofia

Scientific supervisors: Prof. Dr. Emil Hristov,

The topic of the dissertation is interesting, relevant and significant. The dissertation contains 113 pages and is illustrated with 15 tables and 48 figures. The used literature includes 126 sources. The work is constructed consistently and logically. Includes introduction, literature review, aim and objectives, materials and methods, results of own research and analysis, discussion of results, conclusion, conclusions, bibliography.

Originality and significance of the dissertation: for the first time in Bulgaria, a study of medicinal use at the national level is conducted and the availability and accessibility of biosimilar medicinal products containing monoclonal antibodies in Bulgaria are analyzed; for the first time, a systematic review of scientific publications was carried out according to the PRISMA standard for evaluating the medicinal usability of biosimilar medicinal products containing monoclonal antibodies; for the first time in Bulgaria, the level of knowledge of biosimilars and biological products containing monoclonal antibodies among medical specialists from real practice is measured; the study reveals new theoretical aspects of the processes of pricing and reimbursement of medicinal products in the solidarity insurance systems for health care.

The in-depth literature review on the subject based on PRISMA includes 468 sources. In the work, a comprehensive literature review on the subject was made. It introduces us to the modern knowledge of the problem and indicates the reasons for the present work. A systematic review of scientific publications was performed in accordance with the recommendations of the Cochrane Collaboration

and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A study protocol was drawn up in accordance with the PRISMA 2009 Checklist, with predefined: subject, design, search strategy, inclusion and exclusion criteria, data collection methods, data analysis and statistical evaluation, conclusions. Over a period of 12 years, 100 scientific publications were found in which biosimilar medicinal products were considered.

Competence, thoroughness of the problem and the skills of the PhD student to work with literary sources are demonstrated.

The purpose of the development is defined clearly and precisely and corresponds to the title.

From the overview and the objectives, the corresponding **six tasks** arise.

The formulated goals and objectives of the dissertation work and their implementation have allowed the Pharm. Emanuil Yordanov to develop the chosen topic excellently.

The methods used in the dissertation can generally be defined as general research methods, specific methods, statistical and others - (Desk research, survey method in the form of a written questioning (survey card). We used two main approaches when conducting the survey - in-person questioning, through a direct group survey and in-person absentee questioning through a direct e-mail survey An original survey protocol and design was developed to assess scientific knowledge regarding the knowledge of new medicinal products among doctors of various specialties.

The obtained results are presented and well illustrated, fully covering all the tasks set by the dissertation.

From the analysis of the results, it is clear that medical professionals must have a clear idea about the specific features and characteristics of biosimilar medicinal products in order to be able to make motivated and correct decisions about their rational prescription. Biosimilar medicinal products have physical, chemical and biological properties that are very similar to those of the reference biological medicinal product, although due to the natural variability of the biological source and the manufacturing process that is unique to each manufacturer, there may be slight differences between them . This means that they can provide the required therapeutic benefits in a manner very similar to the reference biologic drug with a proven similar efficacy, safety and immunogenicity profile. The regulatory process for authorizing biosimilar medicinal products differs from that for generic medicinal products. For biosimilar medicinal products, complete pharmaceutical quality data are required, as well as additional quality studies comparing the structure and biological activity of the biosimilar and the reference biological medicinal product. Development is based on demonstrating biosimilarity to the reference using comparability studies to demonstrate similarity in chemical structure, biological function, efficacy, safety and immunogenicity. This process ensures that biosimilar medicinal products are of high quality and can be used interchangeably with reference biological medicinal products in appropriate clinical cases. Therefore, it is essential that medical professionals have an excellent knowledge of biosimilar medicinal products in order to make informed decisions and achieve rational prescribing. Biosimilar medicinal products often appear to be more affordable than the reference biological medicinal product. Their wider use could help increase competition in the segment and lead to lower prices. This, in turn, should help make these important medicinal products more accessible to patients who need them.

A medicinal product can only be defined as available if it is authorized for use and has a registered price. The same medicinal product is defined as affordable if it is available and included in a system of reimbursement from public funds. Under the terms of Bulgaria's membership in the EU, as of January

1, 2007, Bulgarian citizens have a guaranteed availability of high-quality, safe and effective biosimilar medicinal products, equal to other EU citizens. The authorization for the use of biosimilar medicinal products is centralized at the EU level and is ensured through the rules introduced by Directive 2001/83/EC and Regulation (EC) No 726/2004. The relative share of biological products is 17%, which shows excellent availability, accessibility and macro-level usability assessed through budget indicators. The rule that the price of BPLP cannot exceed 80% of the registered price of the reference biological product leads to a reduction of the total costs of treatment within the budget of the NHIF and provides access to treatment for a larger number of patients. The obtained results show that the prescription and dispensing of biosimilar medicinal products is at a negligible low level - only 4.75% of the total prescription estimated through the budgetary costs of the NHIF.

In the discussion section, the author successfully analyzes the results of his own study. In the dissertation, 12 conclusions are systematized in response to the tasks set. Formulated conclusions and contributions correspond to the achieved results.

The submitted abstract meets the requirements.

An important contribution of the dissertation is that the study enriches healthcare professionals' knowledge of the practical application and medicinal use of biosimilar medicinal products containing monoclonal antibodies worldwide and reveals their impact on pricing and reimbursement systems.

There are presented publications and reports published in scientific issues, referenced and indexed in world-famous databases with scientific information - 3; publications and reports published in non-refereed journals with scientific review or published in edited collective volumes - 8. The PhD student participated in the Seventh Congress of Pharmacy with international participation, November 21 - 24, 2019, Hotel "Rila", Borovets, Bulgaria, as awarded with the "Best Oral Presentation of a PhD Student or Young Scientist". He also received the "Alma Mater" award for the academic year 2019/2020 by order of the Rector No. RD27-1596 of 20.11.2020. He also participated in project 3717/2022., Comparative analysis of pricing and reimbursement systems between Italy and Bulgaria , Head, Targeted funding from the state budget. FNI SU "St. Kliment Ohridski"

The dissertation contain applied results, which represent an original contribution to science and meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria the Regulations for the Implementation of this law and the relevant Regulations of SU "Sveti Kliment Ohridski", Sofia. The presented materials fully comply with the specific requirements of the "Sveti Kliment Ohridski" University of Sofia, Sofia.

The dissertation shows that the PhD student possesses theoretical knowledge and professional skills in the scientific specialty, demonstrating qualities and skills for independent conduct of scientific research. Due to the above, I confidently give my **positive assessment** of the conducted research, dissertation, achieved results and contributions, and offer to the esteemed members of the jury to evaluate positively the dissertation work for the acquisition of the educational and scientific degree "Doctor" of the {hD student Emanuil Plamenov Yordanov in professional direction 7.3 Pharmacy, scientific specialty "Social medicine and organization of health care and pharmacy.

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