

## Written Opinion

from

**Prof Ilko Nikolaev Getov, PhD**

Organization and Economics of Pharmacy Department,  
Faculty of Pharmacy, Medical University - Sofia

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. Tzvetomir Mario Deliyki, MSc Pharm**

With topic:

**HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH VASCULITIS ASSOCIATED WITH ANTINEUTROPHILIC CYTOPLASMIC ANTIBODIES BY BIOLOGICAL TREATMENT**

Scientific supervisors: Assoc. Prof Emil Hristov, MD, PhD  
Assoc. Prof Lubomir Marinchev, MD, PhD

The dissertation presented for evaluation comprehensively and in depth examines the quality of life of patients with vasculitis who undergo biological treatment. With a volume of 154 pages, excellently illustrated with 42 tables, 33 figures, 2 photos, appendices and an exhaustive list of literature sources, the scientific work reviews, comments and analyzes the results of biological treatment in patients with vasculitis associated with antineutrophil cytoplasmic antibodies.

The pre-defined goals and tasks of the dissertation fall within the scope of the scientific specialty of the doctoral program and correspond to the content and conducted research. The research methods and materials are correctly selected and described, which shows knowledge of the subject, in-depth approach and good balance in terms of contributions of scientific-theoretical and scientific-applied nature formulated by the dissertation.

The paper provides a thorough literature review on the topic, based on PRISMA. Multilateral and multifaceted sources are used as references - Bulgarian and mostly foreign, all with results of diagnostic, therapeutic, prophylactic, prognostic and economic nature. The dissertation is the first comprehensive scientific study on medical and social aspects the importance and cost-benefit ratio of biological therapy in patients with vasculitis, with a special focus put on pharmacoeconomics.

In my opinion, the choice of topic is determined by the personal scientific, regulatory and practical experience and interests of the applicant, as he demonstrates in-depth training and free handling of

pathogenesis, modern guidelines and recommendations for vasculitis treatment, methodological tools for assessing quality of life and multifaceted pharmacoeconomic studies.

The goals and objectives section clearly and precisely formulates the scope and content of the research work, positively showing the expert guidance of the scientific supervisors.

The methodological part presents a protocol and design of a two-center, prospective, observational, non-interventional, controlled study in two periods, with auto-controls, specifically developed for the purposes of the dissertation.

The study results section is comprehensive and properly structured. The review and results sections are well balanced. In the dissertation, the results are presented in six chapters covering 53 pages - representativeness and demographic characteristics of the analyzed cohort of patients; clinical characteristics of the study group; assessment of health status using the EuroQol 5D-5L instrument before and after rituximab biological therapy; assessment of health status using the SF-36v2 Health Survey before and after biological treatment.

The economic analyzes commented in the dissertation are focused on innovative biological therapy and show that rituximab treatment is reimbursed only in patients with Wegener's granulomatosis and is highly cost-effective. It is correctly stated that the full and thorough assessment of the effect of application in the other two not reimbursed by the NHIF diseases – microscopic polyangiitis and eosinophilic granulomatosis with polyangiitis (Cherg-Strauss syndrome) - , is difficult and can be performed only after necessary scientific, regulatory and legislative changes are made in order to ensure that these patients too have access to treatment.

In relation to the dissertation, all 5 full-text publications and participation in scientific forums are presented. There is one publication in Bulgarian, ONE article is referenced in SCOPUS. The quantitative requirements of the University Regulations are met, and the doctoral student is the first author in one of the publications.

I acknowledge the results obtained and the conclusions made in the dissertation, which logically follow the goals and objectives and prove the research hypothesis - the health-related quality of life in patients without treatment and standard treatment of vasculitis is much worse than the general population. The application of biological drugs and timely initiation of treatment leads to rapid control of clinical symptoms and entry into prolonged remission.

The statistical analysis used in the processing of the results are modern, comprehensive and accurate. The presented abstract meets the requirements. Some general remarks can be made on the technical level and use, e.g. of "retrograde" instead "retrospectively", but in no way does this change the value of the work.

The formulated conclusions and contributions correspond to the results achieved, for me the leading ones being contribution 3 of scientific-theoretical and contribution 1 of methodical ones. The latter could be extrapolated to studies in other diseases using the same methodical apparatus.

**Conclusion:**

The dissertation presented for discussion and evaluation is of high quality and will have added value for the study of both vasculitis and results of biological treatment from a medico-social, pharmacoeconomic and clinical point of view.

The dissertation for the acquisition of PhD of Mr. Tzvetomir Mario Deliyiski, PhD student in self-study, meets the requirements, is focused in a specific multidiscipline scientific area, represents a novelty for Bulgaria and has significant contributions to the evaluation of new therapies and decision-making.

After I got acquainted in detail with the presented set of materials on the procedure of defense of the dissertation, I believe that the topic, volume, obtained results, conclusions made and formulated contributions fully meet the requirements of the Regulations of Sofia University "St. Kliment Ohridski ", the training in the doctoral program at Faculty of Chemistry and Pharmacy and 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. Tzvetomir Mario Deliyiski for the conducted study presented as dissertation thesis, author's abstract of doctoral dissertation, results achieved, publications and contributions.

Signature:

Sofia,