

## REVIEW

**Subject:** Dissertation for the degree of Doctor of Science - Scientific field: 7. Health Care and Sports, Professional field – 7.3 Pharmacy, Scientific specialty "Pharmacoeconomics and pharmaceutical regulation"

by Prof. Irina Nikolova Nikolova, MD, member of the scientific jury, in compliance with Order No. P-109-94 of 12 February 2026 of the Rector of MU-Varna.

**Author of the dissertation:** MPharm. **Lada Aleksandrova Andreeva**, PhD student at the Department of organization and economics of Pharmacy, Faculty of Pharmacy, Medical University of Varna, with scientific supervisors Assoc. Prof. Anna Todorova, PhD, and scientific consultant Prof. Valentina Petkova, PhD, DSci.

**Dissertation title:** "Investigating the Potential of Pharmaceutical Care to Improve Therapeutic Outcomes and Prevent Complications in Patients with Ankylosing Spondylitis"

The dissertation presents an in-depth study of ankylosing spondylitis (AS), a chronic, progressive inflammatory disease with pronounced social significance. The focus is on the potential for optimizing pharmaceutical care across its entire spectrum – from early screening and prevention to monitoring drug therapy and improving patients' quality of life – which determines the interdisciplinary nature of the dissertation.

MPharm. Lada Andreeva graduated Faculty of Pharmacy, MU-Sofia in 2007 with the "Golden Galen" award. Since 2023, she has been an Assistant at the Department of Healthcare, Faculty of Public Health and Healthcare at Angel Kanchev University of Ruse. Since July 2024, MPharm. Lada Andreeva has been a self-funded PhD student at the Department of Organization and Economics of Pharmacy, Faculty of Pharmacy at the MU-Varna.

The dissertation is 145 pages long, of which the literature review covers nearly 40 pages, the results and discussion section approximately 50 pages, and includes 254 cited references. It contains 38 tables and 4 figures, with nearly 70% of the cited literature being from the last 10 years.

### 1. Literature review

The literature review represents an extensive and in-depth overview of current knowledge regarding AS, therapeutic approaches, and the role of pharmaceutical care. It covers three main thematic sections – the nature and characteristics of the disease, therapeutic

strategies, and the regulatory-practical framework of Good Pharmaceutical Practice with an emphasis on pharmaceutical care in AS. Overall, the review demonstrates the author's excellent familiarity with the complex subject matter and a good ability to synthesize information from diverse sources. By systematizing current knowledge, the literature review builds a solid foundation for demonstrating the need to introduce a multidisciplinary approach in which the pharmacist has a clearly defined and active role.

The review stands out for its exceptional timeliness. The author not only presents the classical views on pathogenesis (the role of TNF- $\alpha$ , HLA-B27) but also discusses the latest data on the IL-23/IL-17 axis, including the paradox of the ineffectiveness of IL-23 inhibitors in axial manifestations. This attests to a deep knowledge of modern immunology. In the therapeutic section, not only are established NSAIDs and TNF inhibitors examined, but also the newer IL-17 inhibitors (secukinumab, ixekizumab) and JAK inhibitors, which gives the review high practical value. Particularly valuable is the detailed analysis of prognostic factors for response to biologic drugs (male sex, smoking, elevated CRP, short disease duration).

The strongest part of the review is the section on Good Pharmaceutical Practice and pharmaceutical care. The evolution of the concept is traced – from the classic definition by Hepler & Strand, through the later definitions by PCNE. Specific elements are also included – identifying drug-related problems, periodic therapy review, adherence monitoring, database creation. The pharmacist's role is examined from a practical perspective – the pharmacist not only as a consultant but also as an active participant in early screening by recognizing inflammatory pain and referring patients to a rheumatologist.

Overall, the literature review provides a solid foundation for a dissertation. It introduces the complex subject matter of AS, justifies the need for pharmaceutical care, and outlines specific interventions (early screening, chronopharmacological optimization of NSAIDs, adherence monitoring).

## **2. Goal and objectives**

The aim of the dissertation is clearly formulated and includes: (1) investigating the attitudes and competencies of pharmacists for providing pharmaceutical care to patients with AS, and (2) analyzing the potential for integrating the pharmacist into the multidisciplinary approach. The aim is realistic, achievable, and has a clear practical orientation. It allows for covering two mutually complementary perspectives – that of the pharmacists (the care providers) and that of systemic integration.

The six tasks are logically arranged and follow the sequence: survey among pharmacists → development of algorithms → survey among patients → assessment of disease activity →

assessment of quality of life → assessment of adherence. The tasks are specific and measurable, using validated instruments (BASDAI, BAS-G, EQ-5D-5L, MMAS-8).

### **3. Materials and methods**

The study covers two target groups: (1) Master of Pharmacy graduates from Northeastern Bulgaria (the regions of Ruse, Varna, and Dobrich) and (2) patients diagnosed with AS from the Ruse region. Two independent surveys were conducted – an online anonymous questionnaire among pharmacists (20 closed-ended questions, 4 modules, January–June 2025) and a face-to-face interview questionnaire among patients (November 2024 – November 2025). For the patients, three validated instruments were used: BASDAI for disease activity, EQ-5D-5L for health-related quality of life, and the Morisky 8 (MMAS-8) for medication adherence. The documentary method (analysis of guidelines and summaries of product characteristics), sociological method (questionnaire surveys), and statistical data processing were applied.

### **4. Results**

The study includes 260 pharmacists – 77% women, 23% men. Pharmacists who graduated more than 10 years ago were approximately 50%, and those without postgraduate specialization were 87%. The presented results outline a clear picture of a discrepancy between high motivation and low preparedness for providing pharmaceutical care to patients with AS. The three main findings support each other: (1) 84% of pharmacists consider their involvement necessary, but (2) 55% do not feel prepared, and (3) 70% cannot distinguish inflammatory pain from mechanical pain. This triad (motivation, lack of preparedness, specific knowledge deficit) constitutes a strong argument for the necessity of educational interventions. The PhD candidate skillfully uses these data to justify the developed algorithm and screening questionnaire.

The statistical processing is correct and transparent. Particularly valuable is the correlation analysis, which shows that the ability to differentiate pain, rather than general theoretical knowledge, is a key predictor of readiness for pharmaceutical care. This is a practically oriented conclusion. The developed algorithm and screening questionnaire (five questions reflecting the ASAS criteria) are directly applicable in pharmacy practice.

The educational materials for patients with AS represent the practical application of the data achieved. They were developed using a multidisciplinary and collaborative approach (Medical University of Varna, University of Ruse, Astra Pharmacies, the Bulgarian Association of Patients with Ankylosing Spondylitis), which guarantees their relevance. The materials cover the entire spectrum of pharmaceutical care – from early recognition to

adverse reaction monitoring – and are practically oriented, with clearly delineated boundaries of pharmaceutical competence.

## **5. Discussion**

In the discussion section, the author provides a correct and well-argued interpretation of the empirical results obtained, comparing them with current international data and placing them within the context of contemporary understanding of pharmaceutical care for chronic inflammatory rheumatic diseases. Particularly valuable is the finding that disease activity in the studied cohort is higher than European reference levels, which points to the need for optimizing therapeutic control. The PhD candidate convincingly demonstrates the strongest negative associations – smoking and insufficient sleep – which are potentially modifiable through pharmaceutical consultations. The paradoxical finding of the lowest medication adherence precisely among patients with higher education is correctly interpreted as an indicator of the need for targeted pharmaceutical support, rather than as a discouraging result. The positive correlation between adherence and disease activity in women is explained through the hypothesis of reverse causality, which is scientifically sound.

The author demonstrates the necessary critical self-assessment by explicitly stating the main limitations of the study – the regional nature of the samples, the risks of subjectivity inherent in self-assessment instruments, and the lack of a longitudinal design in the patient survey. This transparency increases confidence in the conclusions. The discussion is logically structured, the interpretations are balanced and data-driven, and the conclusions drawn convincingly support the main thesis of the dissertation – that the pharmacist has a significant and as-yet-untapped role in the comprehensive care of AS, which can be realized through targeted training, screening tools, and therapy monitoring.

## **7. Conclusions**

The conclusions of the dissertation are clearly formulated, follow logically from the presented results, address the stated aim and objectives, and correctly summarize the most important findings – the relationship between professional experience and pharmacist competence, the barriers to pharmaceutical care, the factors for high disease activity, the paradoxically low adherence among highly educated patients, and the lack of correlation between disease activity and quality of life in the overall sample. They demonstrate the author's ability to synthesize empirical material and draw generalizations with practical relevance.

## **8. Recommendations**

The recommendations represent the logical culmination of the scientific research. They are addressed to specific institutions – the National Assembly, the Ministry of Health, the National Health Insurance Fund, the pharmaceutical faculties, the Bulgarian Pharmaceutical Union, pharmacy owners, and patient organizations. This is extremely important because a recommendation without a designated addressee remains merely a declaration. The author clearly distinguishes between different levels of responsibility – legislative, regulatory, financial, educational, and organizational. The recommendations are hierarchically structured – from the most general (regulatory framework) through the educational and financial levels to specific partnerships. This pyramidal structure allows the various addressees to find their share of responsibility. The author demonstrates an ability to think not only as a researcher but also as a health policy expert, which is a high mark of the applied value of the dissertation. The PhD candidate correctly understands that without a legislative or regulatory framework, pharmaceutical care remains a voluntary activity dependent on the goodwill of individual pharmacists.

**In summary**, the topic of the doctoral thesis is highly relevant, both at the institutional and national level as well as globally, and holds potential for future research.

From the obtained results, eight conclusions have been adequately derived, along with three contributions of a scientific-theoretical nature and four of a practical-applied nature. These are based on solid empirical data, addressed to specific institutions, and cover different levels of intervention – regulatory, financial, educational, organizational, and collaborative. I highly appreciate the fact that the doctoral candidate does not limit herself to scientific conclusions alone, but makes an attempt to influence real-world practice and policy. The recommendations constitute a significant contribution and demonstrate the author's commitment to the real problems of patients and the healthcare system.

On the topic of the dissertation, five full-text scientific publications have been published. The results of the dissertation have also been presented at two international and one national scientific forum.

## **Conclusion**

The dissertation is written clearly, concisely, and with a thorough understanding of the subject matter. The volume of work completed is sufficient, employing an adequate set of research approaches and methods with the application of validated instruments. The analyzed data have been correctly processed and illustrated through tables and figures, which facilitates tracking the findings. The presented results, although regional in scope (Northeastern Bulgaria), have national significance, as this is the first time in the country


that the attitudes and competencies of pharmacists for providing pharmaceutical care in ankylosing spondylitis, as well as the clinical and behavioral characteristics of patients with this disease, have been systematically investigated. The developed algorithm, screening questionnaire, and educational materials represent a direct applied contribution and can be used in pharmacy practice. I highly appreciate the doctoral candidate's aspiration to influence real-world practice and policy, demonstrating commitment to the problems of patients and the healthcare system.

The presented work demonstrates the personal contribution of the doctoral candidate to the implementation of the research program. In the process of developing the doctoral thesis, MPharm. Lada Andreeva has acquired in-depth theoretical knowledge and practical skills, adequate for obtaining the educational and scientific degree of "Doctor".

**Based on the above, I confidently give a positive conclusion that the presented work meets the national and institutional regulatory requirements and the relevant quantitative criteria applicable to this procedure. I recommend to the esteemed members of the scientific jury to vote positively for the award of the educational and scientific degree of "Doctor" to Master of Pharmacy Lada Aleksandrova Andreeva.**

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Reviewed by

  
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