NATIONAL CENTER OF PUBLIC HEALTH AND ANALYSES

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ORGANIZATION AND MANAGEMENT OF THE SUPPLY CHAIN OF MEDICINAL PRODUCTS FOR THE SPECIFIC TREATMENT OF COVID-19 IN HOSPITALS IN BULGARIA

ABSTRACT

OF A DISSERTATION THESIS

for the award of the educational and scientific degree “Doctor” in the doctoral program “Social Medicine and Health Management”,

professional field 7.1. “Medicine”,

within the field of higher education 7. “Health Care and Sports”

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The dissertation thesis comprises 154 standard typed pages and is illustrated with 22 figures and 12 tables. The bibliography includes 188 references, of which 54 are in Cyrillic. In relation to the dissertation, 4 scientific articles have been published.

The dissertation has been reviewed and approved by an extended scientific collegium of the Department "Classification Systems, Standards and Innovations" at the National Center of Public Health and Analyses and has been proposed for defense before a scientific jury.

Note: The numbering of the tables and figures in the abstract does not correspond to the numbering in the dissertation thesis

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Introduction

The organization and management of the supply chain of medicinal products in healthcare facilities are acquiring increasing importance and significance for modern healthcare systems, and in particular for hospitals. The combination of the significant number of hospital healthcare establishments in the country, their heterogeneous therapeutic activity profiles, together with numerous suppliers and an extensive nomenclature of medicinal products used in the therapeutic process, makes these activities difficult to manage, cumbersome, and complex to regulate.

In the context of a global pandemic, this entire process becomes further complicated and puts at risk the provision of adequate and comprehensive medical care. Under such conditions, when supplies are hindered by diverse production and logistical reasons, and at the same time a timely response and securing of the healthcare system with the necessary resources are required in order for it to adequately respond to the global health threat, an entirely new approach is needed to address these emerging problems. In this new reality, under a global health threat, the role of the state and the Ministry of Health of the Republic of Bulgaria, as the responsible national health institution, is to act as an initiator and driving force in the processes of contracting, provision, logistics, and delivery of medicinal products to healthcare facilities. The establishment of a regulatory framework and the search for conditions that regulate the timely and equitable distribution of medicinal products, regardless of the type of ownership, constitute its primary task.

The issue of the existence of clear regulatory conditions governing the timely and equitable distribution of medicinal products in the event of extraordinary circumstances such as pandemics, natural disasters, or other crises is extremely important and relevant in the contemporary world. In recent years, particularly during the COVID-19 pandemic, it has clearly been demonstrated how vulnerable healthcare systems can be and how critical the role of the legal framework is in resource management.

In the absence of an adequate regulatory framework, there is inevitably a risk of chaos, inequality, and even unfair and unregulated practices in the supply of medicinal products. This may lead to serious consequences, both for the health of individual patients and for society as a whole. Pharmaceutical regulation should ensure equal access to life-saving medicinal products, regardless of the social status, geographical location, or economic capacity of patients.

Furthermore, under clearly established and regulated rules for distribution and prioritization, the work of healthcare institutions, pharmaceutical companies, and logistical units is facilitated. Through predeveloped plans and coordination, panic and stockpiling can be avoided, and it can be ensured that the most vulnerable groups receive timely and adequate assistance.

Last but not least, such a regulatory framework plays a key role in public trust in state institutions. When people are aware that fair mechanisms for crisis management exist and that efforts are being made to protect their health, they are more likely to cooperate and follow the guidance of the authorities.

The need for regulatory rules and conditions for the supply and distribution of medicinal products under extraordinary circumstances is not merely an administrative formality, but a matter of public responsibility, equity, and health security.

Scientific Hypothesis, Aim and Objectives Scientific

Hypothesis

The introduction of a specific procedure and model for the supply of certain medicinal products to hospital healthcare facilities (outside traditional distribution channels) allows for more efficient management of the supply chain. This leads to optimization of the treatment process and improvement of the operational efficiency of the system. As a result, faster access of Bulgarian patients to innovative medicinal products is ensured in emergency situations related to threats to public health.

Aim

The aim of the present study is to analyze the organization and management of the supply chain of medicinal products for the specific treatment of COVID-19 in hospital healthcare facilities in Bulgaria, with a focus on the applied mechanisms for planning, provision, distribution, and control. As a secondary aim within the conducted analyses, the role of institutional coordination is assessed, in particular that of the Ministry of Health, as well as the effectiveness of the applied logistical models

under pandemic conditions. On this basis, key factors are identified and guidelines are formulated for the optimization and sustainable management of the supply chain under extraordinary circumstances.

Objectives

To conduct a comprehensive review of the therapeutic approaches adopted during the COVID-19 pandemic.

To perform an analysis of the use of RDV in hospital healthcare facilities in Bulgaria.

To analyze the supply chain logistics of RDV in the country.

To examine the institutional role, functions, and management mechanisms of the Ministry of Health in the organization, coordination, and control of the supply chain of medicinal products during the COVID-19 pandemic.

To investigate the impact of the efficiency of supply chain management of Remdesivir on age-specific mortality by regions and gender in the country.

To assess the relationship between logistical accessibility and health outcomes, by examining the dependence between the distance from the central warehouse, regional differences in mortality, and formulating recommendations for more efficient resource allocation under conditions of shortage. To determine whether there are significant differences in mortality depending on the distance of the regions from the central distribution warehouse of the medicinal product RDV.

Materials and Methods

In order to achieve the set research objectives, a comprehensive methodological framework was applied, combining retrospective, documentary, and sociological analysis. The dissertation is based on the empirical foundation of the author’s direct professional experience in managing the provision of resources for healthcare facilities during the pandemic crisis. This approach ensures not only access to relevant regulatory and operational information but also the authenticity of the conclusions. The data extraction process encompasses a wide range of verified sources, subjected to systematic interpretation.

A review of multinational experience and specialized scientific literature in the field of pharmaceutical logistics, access to medicinal products, and the management of health crises was conducted. The search for scientific information was carried out in internationally established databases, including PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, using combinations of keywords and logical operators (Boolean operators), such as: COVID-19, Remdesivir, drug supply chain, medicine shortages, centralized procurement, pharmaceutical

logistics, pricing and reimbursement. The selection of publications was performed based on their scientific relevance, the availability of a DOI, as well as their correspondence to the subject of the study, with priority given to sources from the period 2020–2024.

A detailed review of the legislation and departmental acts regulating the distribution channels in Bulgaria was conducted, including the Medicinal Products in Human Medicine Act, the Public Procurement Act, secondary legislation, as well as official documents and guidelines of the Ministry of Health and other competent institutions.

In the analytical part, datasets from the National Health Information System (NHIS) and its COVID19 module were used, as well as various registries and information datasets of the Ministry of Health, together with international statistical platforms for monitoring the epidemiological situation and the burden on healthcare systems.

The validity and objectivity of the data related to hospital hospitalization, the applied therapy, and the distribution of medicinal products were ensured through officially provided data from information datasets under the Access to Public Information Act. The data were obtained from the Ministry of Health through "Information Services" JSC, in its capacity as operator of the NHIS. The provided information was extracted from the National Information System for Combating COVID-19 and was supplied in anonymized form, without containing personal data or identifying information, in compliance with the requirements of the applicable legislation on personal data protection. This approach ensures a high degree of reliability and eliminates the risk of subjective influence on the analysis.

The processing of the collected dataset was carried out using the tools of economic and statistical analysis. Alternative and variation methods were applied for the study of frequency distributions and structural deviations in the data. A comparative approach was used, based on predefined indicators for the evaluation of logistical models. Of key importance for the formulation of strategic guidelines is the method of expert evaluation, through which the factors defining the effectiveness of national and pan-European supply chains were synthesized. It should be noted that the study was conducted in strict compliance with ethical standards, without processing confidential corporate information or personal data.

Own Research – Results and Discussion

The present section aims to present and interpret the results of the conducted study, focused on evaluating the organization and management of the supply chain of medicinal products for the specific treatment of COVID-19 in hospital healthcare facilities in Bulgaria. The selection of the applied indicators is aligned with the need for a comprehensive approach that encompasses both the clinical and the logistical aspects of the problem under consideration.

The main groups of analyzed indicators—mortality, use of Remdesivir, use of monoclonal antibodies, and the characteristics of the supply chain—are determined by the objective of tracing the relationship between the availability and access to specific therapy, the effectiveness of its application, and the final health outcomes.

The analysis of mortality is used as the primary integral indicator of the effectiveness of the healthcare system under pandemic conditions. It allows for the assessment of the extent to which the provision of therapeutic resources and their timely application influence the outcome of the disease. At the same time, the indicators related to the use of Remdesivir and monoclonal antibodies provide an opportunity for a detailed review of the applied therapeutic approaches and the degree of access of patients to innovative medicinal products.

The inclusion of the analysis of the supply chain is essential for achieving the objective of the dissertation, as it is precisely through it that the mechanisms for the provision, distribution, and control of medicinal products are examined. This analysis allows for the identification of organizational and managerial factors that determine the effectiveness of the system, as well as the potential limitations and risks in its functioning under extraordinary epidemic conditions.

The combined consideration of these indicators provides an opportunity to establish the relationship between logistical processes and clinical outcomes, which is in direct accordance with the formulated aim of the dissertation. In this way, a substantiated basis is provided for drawing conclusions and formulating recommendations aimed at optimizing the management of the supply chain of medicinal products in future health crises.

Mortality Analysis

The analysis of mortality is aimed at examining mortality as the final and most generalized indicator of the effectiveness of the treatment process. Through it, the foundation is laid for the subsequent consideration of the role of therapeutic approaches and logistical mechanisms in the formation of health outcomes. In order to verify the distribution of Remdesivir and the effectiveness of the management of its supply chain to hospital healthcare facilities in the country, an analysis of

agespecific mortality by gender and by region was conducted in relation to their distance from the central warehouse from which the distribution of medicinal products is carried out. The aim of the study is to identify differences in mortality across regions and to group the regions accordingly. Knowledge of regional differences in mortality allows, under conditions of resource shortage, for timely decisionmaking regarding the redistribution of vital medicinal products and equipment at regional level.

Data on age-specific mortality by gender for the period 08.03.2020–30.05.2024 were used, obtained from Information Services. Mortality was calculated based on the population as of 31.12.2019, as the closest date to the beginning of the observation period, and is expressed per 1000 population (‰).

The data show that mortality rates increase progressively after the age of 40–45, reaching their peak among individuals over 75 years of age. Statistical processing establishes that the difference in mortality between genders becomes significant only after the age of 60 ($p=0.040$), which highlights the need for specific resource planning for these high-risk groups.

In order to define regional specificities in supply needs, a cluster analysis of mortality levels by region was applied. The results outline three clearly distinguishable clusters: the first with relatively low levels (Kardzhali region), the second with persistently high values (Gabrovo, Pazardzhik, Plovdiv, Ruse), and the third—intermediate. This territorial differentiation is key in determining the allocation limits of medicinal products across regions.

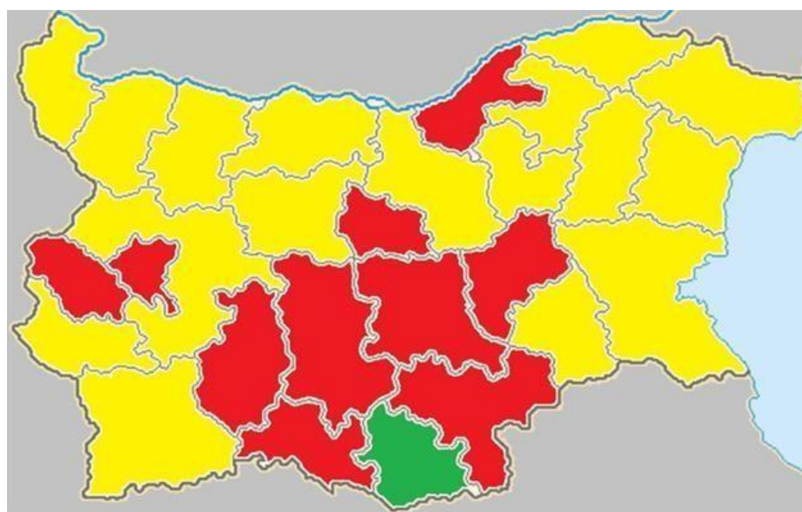

Figure 1. Map/Diagram of the territorial distribution of mortality across the three clusters

The probable reason why the regions of Sofia (capital) and Plovdiv are among those with the highest mortality rates, despite the concentration of hospitals, physicians, and equipment, is precisely their better level of provision. It is likely that the most severe cases are referred specifically to hospitals in

these regions. It is also possible that the differences are due to underreported or overreported mortality. This is particularly valid for smaller settlements in more remote regions.

Analysis of RDV Use

Proceeding to the analysis of therapeutic access, the study focuses on the dynamics of the use of Remdesivir (RDV), with the aim of verifying the effectiveness of the management of the supply chain of one of the main medicinal products for the treatment of coronavirus infection to hospital healthcare facilities in the country. An analysis of the lethality caused by the disease across different regions of the country was performed, compared with the proportion of patients treated with the medicinal product, including those requiring intensive care and those with milder forms of the disease. Below are presented the summarized results reported by hospital healthcare facilities within the respective territorial scope of the Regional Health Inspectorates (RHI) by regions, for hospitalized and deceased patients, compared with the specific consumption of RDV.

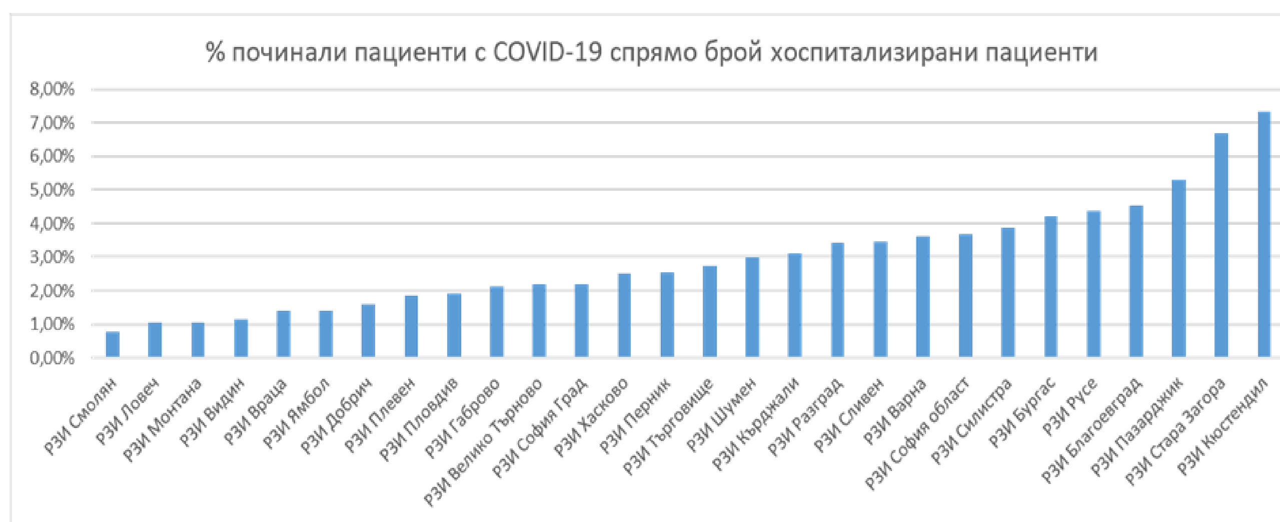

Figure 2. Percentage of deceased COVID-19 patients relative to the number of hospitalized patients in the respective region

A clear overall effectiveness of the therapy in healthcare facilities across the respective regions for patients with COVID-19 in the country can be observed. The following conclusions can be drawn: The lowest percentage of deceased patients, relative to the total number of hospitalized COVID-19 patients, is observed in the healthcare facilities in the regions of Smolyan, Lovech, and Montana, respectively 0.77%, 1.05%, and 1.06%.

The highest percentage of deceased patients, relative to the total number of hospitalized COVID-19 patients, is observed in the healthcare facilities in the regions of Pazardzhik, Stara Zagora, and Kyustendil, respectively 5.3%, 6.70%, and 7.32%.

The figure below presents the proportion of patients in different regions of the country who were placed on intensive care, compared to the total number of hospitalized patients.

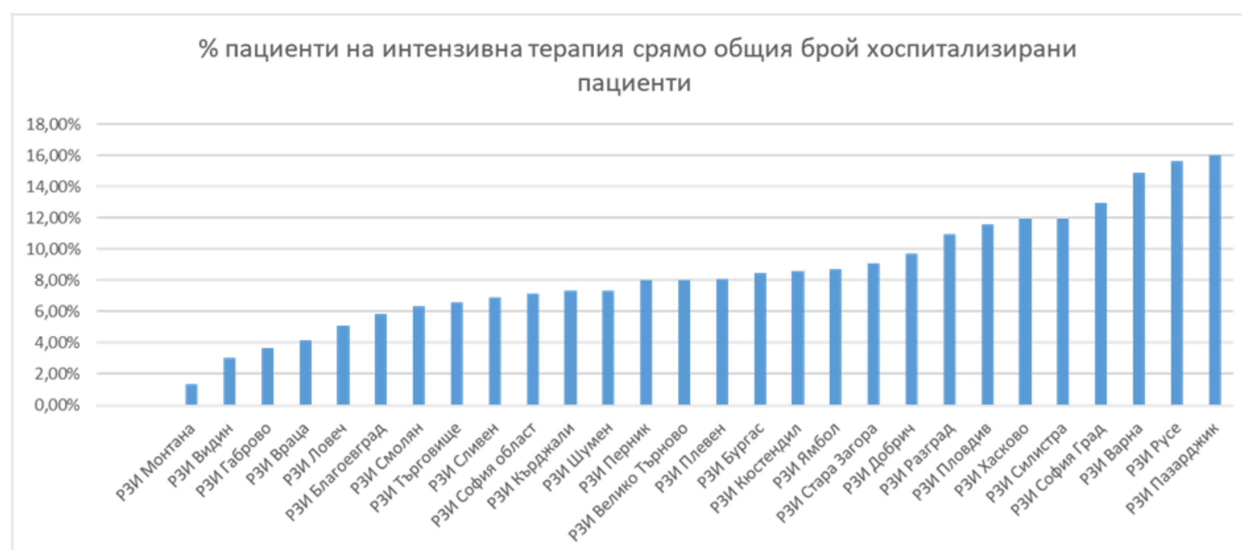

Figure 3. Percentage of COVID-19 patients in intensive care relative to the total number of hospitalized patients by regions

It can be observed what percentage of hospitalized COVID-19 patients were on intensive care, regardless of whether Veklury was included in the therapeutic regimen. The lowest percentage of patients on intensive care is observed in the regions of Montana, Vidin, and Gabrovo, respectively 1.32%, 3.05%, and 3.66%. The highest percentage of patients on intensive care, relative to the total number of hospitalized COVID-19 patients, is observed in the healthcare facilities in the regions of Varna, Ruse, and Pazardzhik, respectively 14.90%, 15.67%, and 16.03%.

The next figure shows the percentage of patients treated with RDV relative to the total number of hospitalized COVID-19 patients in healthcare facilities across different regions.

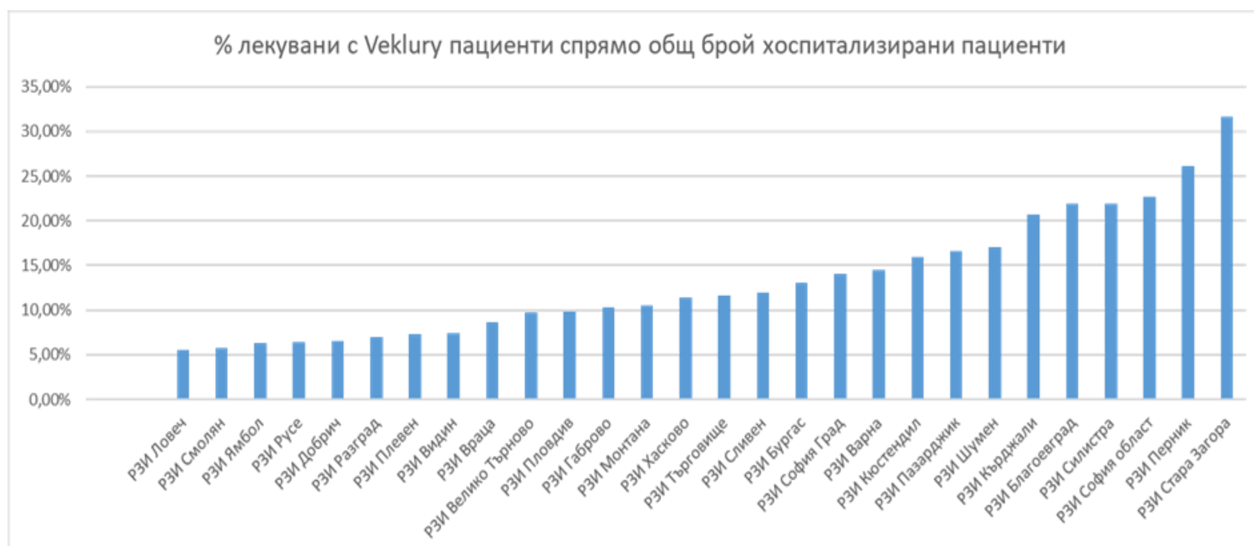

Figure 4. Percentage of COVID-19 patients treated with Veklury relative to the total number of hospitalized patients by regions

The figure indicates what proportion of hospitalized COVID-19 patients in healthcare facilities were treated with RDV as part of the therapeutic regimen. The lowest proportion of patients, relative to the total number of hospitalized COVID-19 patients, treated with Veklury is observed in the healthcare facilities in the regions of Lovech, Smolyan, and Yambol, respectively 5.56%, 5.80%, and 6.25%. On the other hand, the highest proportion of patients treated with RDV is observed in the healthcare facilities in the regions of Sofia Region, Pernik, and Stara Zagora, respectively 22.66%, 26.16%, and 31.70%.

Figure 5. Percentage of patients initiated on Veklury therapy compared to the total number of patients admitted to intensive care by regions

**In some regions, the percentage exceeds 100% because RDV was also administered to patients who did not require intensive care.*

The percentage of patients included in RDV therapy relative to the total number of patients placed on intensive care in healthcare facilities in the respective region has been defined.

In the analysis of the data, it is observed that in absolute terms the total number of patients receiving RDV is lower than the total number of hospitalized COVID-19 patients requiring intensive care. The following figure presents the percentage of deceased patients treated with RDV relative to the total number of patients treated with RDV.

Figure 6. Percentage of deceased COVID-19 patients treated with Veklury relative to the number of patients treated with Veklury by region

From the presented graph, a conclusion can be drawn regarding the effectiveness of RDV therapy in accordance with the applied therapeutic regimen and the timing of its inclusion in patient treatment. The lower the percentage of deceased patients in whom the medicinal product was included as part of the therapeutic regimen, the more effectively it was used. The available data, supported by the results of conducted clinical studies, indicate that Veklury is most effective in the early days of the disease, when it is included in the therapeutic regimen between the 2nd and the 10th day of the infection. It can be concluded that the healthcare facilities in the regions of Pernik, Montana, and Smolyan demonstrate the best indicators of effectiveness in the use of the medicinal product, where the percentages of deceased patients relative to the total number of patients treated with Veklury are as follows: 9.70%, 10.17%, and 13.25%. The regions with the poorest indicators in terms of effectiveness of the application of the medicinal product are Kyustendil, Razgrad, and Ruse, where the percentages are as follows: 45.99%, 49.28%, and 68.56%.

Figure 7. Overall distribution in the country of quantities of the medicinal product Veklury by weeks

The results show that the centralized planning mechanism has demonstrated high adaptability. The monitoring of the quantities delivered to hospital pharmacies reveals a strong correlation with epidemic waves, which indicates the absence of systemic logistical deficits at the national level. Variations in consumption across regions are interpreted as a result of clinical decisions rather than a failure in the supply chain.

Analysis of the Use of Monoclonal Antibodies

Information was collected and analyzed from 97 hospital healthcare facilities, representing 100% of the facilities that included medicinal products representing monoclonal antibodies in their therapeutic protocols for the treatment of COVID-19.

From the collected and summarized information, it can be observed that:

The total number of patients treated with monoclonal antibodies for the period from 01.11.2021 to 21.01.2022 in hospital healthcare facilities in the country is 2077. Of these:

49% are female and 51% are male.

The majority of patients are under 65 years of age (60%), while the remaining 40% are aged 65 and above.

Monoclonal antibodies were administered in over 95% of cases (or 1980 patients out of a total of 2077 patients) in accordance with the provided summaries of product characteristics (within 7 days from the onset of symptoms).

Out of a total of 2077 patients undergoing therapy with monoclonal antibodies, 1443 patients had the presence of risk factors as an indication for the initiation of monoclonal antibody therapy. The highest

number of patients with risk factors undergoing monoclonal antibody therapy was observed in the regions of Pazardzhik, Plovdiv, Sofia City, and Sofia Region.

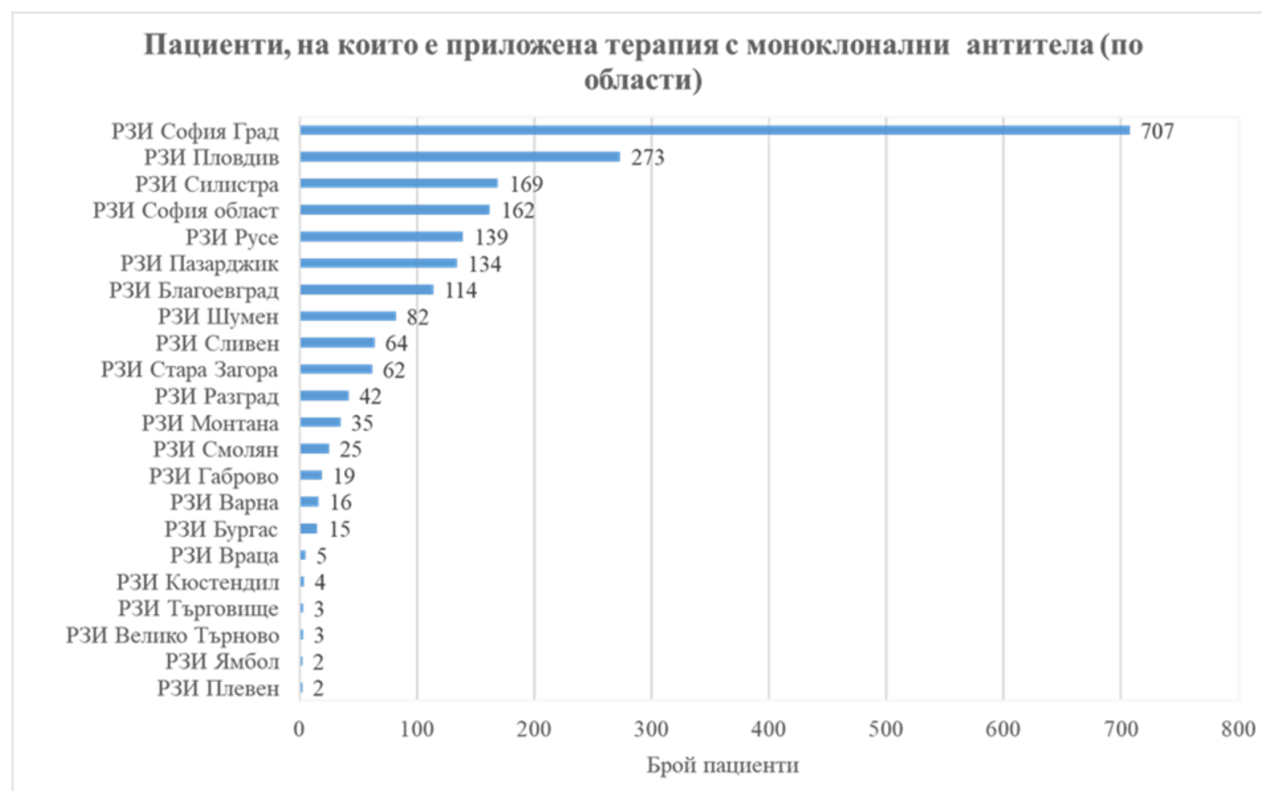

Figure 8. Patients treated with monoclonal antibodies (by region)

Our data for 2077 patients showed that hospitalization occurred in only 6% of the cases following the administration of the therapy. This result is direct evidence of the importance of timely logistical response—the effectiveness of these products critically depends on the speed of the supply chain from the central warehouse to the patient in an outpatient setting or in an early phase of hospitalization.

Provision of Medicinal Products for the Treatment of COVID-19 at National Level

Under the conditions of the COVID-19 pandemic, the provision of medicinal products to hospital healthcare facilities in Bulgaria is not carried out through a single universal mechanism, but through a combination of several parallel models, activated depending on the nature of the medicinal product, the degree of shortage, its regulatory status, the need for urgency, and the available financing options. Practical experience has shown that under conditions of an extraordinary epidemic situation, the system has functioned through a combination of centralized, decentralized, and compensatory mechanisms.

Among the main mechanisms for the provision and delivery of medicinal products for COVID-19 to hospital healthcare facilities are: centralized supply by the Ministry of Health under international agreements, centralized procurement by the Ministry of Health from the domestic market, decentralized supply by healthcare facilities through public procurement procedures and tenders, donations, as well as redistribution among already secured quantities and available reserves. The comparison between the individual mechanisms shows that centralized supply by the Ministry of Health has the highest values in terms of degree of central control, equality of access, traceability, accountability, and economic efficiency. Procurement by hospitals provides higher logistical flexibility but is associated with weaker coordination and lower resilience in conditions of shortage. Donations retain their importance as a rapid compensatory mechanism but have limited predictability and low sustainability as a systemic solution.

The most significant role during the pandemic is played by the centralized approach to supply, implemented by the Ministry of Health, especially with regard to medicinal products with limited availability, high cost, or strategic importance, such as Remdesivir. Within this model, the Ministry acts as a central coordinator and contracting entity, ensuring the necessary quantities through participation in international framework agreements, joint European procurement mechanisms, or through direct contracts with manufacturers.
As a complement to this model, procurement by the Ministry of Health from the domestic market should also be considered. This approach was applied in the provision of monoclonal antibodies for the treatment of COVID-19, as quantities of the respective medicinal product were available within the country. Compared to international deliveries, the response time here is usually shorter, but the effectiveness of the mechanism is directly dependent on the availability on the domestic market and the possibilities for timely contracting.

Alongside the centralized mechanisms, throughout the entire period of the pandemic, the decentralized model of supply also functioned, whereby healthcare facilities independently ensured the necessary medicinal products through public procurement procedures, electronic tenders, framework agreements, or direct deliveries from licensed wholesalers. This is the traditional model of supply in the Bulgarian hospital system. Its advantage is that it provides greater operational freedom to healthcare facilities and allows for a faster response when resources are available on the market. However, under conditions of global shortage, its limitations become evident, related to competition between individual hospitals, uneven access, and differences in pricing conditions.

Hospital pharmacies also occupy an essential place in the process, as they ensure the final stage of medicinal supply. Regardless of the way in which a given medicinal product is delivered, it is the hospital pharmacy that receives, stores, records, and provides it for administration. Donations also have a complementary role, which under conditions of shortage act as a temporary compensatory mechanism but do not represent a sustainable source of supply.

Centralized Provision of RDV

At the national level, decisions regarding the provision of medicinal products for the treatment of COVID-19 for the needs of the healthcare system in the country were adopted in connection with the initiated conclusion of a Framework Agreement for joint procurement of medical countermeasures by the European Commission, ratified by the National Assembly of the Republic of Bulgaria by law (promulgated in State Gazette, issue 26 of 2020). This mechanism created a legal and organizational opportunity for joint procurement of medicinal products, medical devices, and other means to combat serious cross-border threats to health.

Following the adoption of a Decision of the Council of Ministers, formalized in Protocol No. 59 of 21.10.2020, the necessary financial resources were allocated, and the procurement of the medicinal product Veklury (INN Remdesivir) from the pharmaceutical company Gilead Sciences Ireland UC, which is the marketing authorization holder, was authorized. The procurement was made possible through the pan-European joint procurement agreement. Bulgaria participated in two consecutive framework contracts of the European Commission. Under the first framework contract No. SANTE/2020/C3/048, signed on 07.10.2020, the Ministry of Health concluded four bilateral contracts to secure the necessary quantities. In total, under this mechanism, the country purchased 207,360 vials against a contractual minimum of 98,593 vials, which is twice the initially agreed minimum quantities. The second framework contract of the European Commission—No. HERA/2022/NP/Q001—was concluded on 18.07.2022. Under it, Bulgaria concluded a bilateral contract for the purchase of 43,000 vials, but due to the subsiding of the pandemic by the end of 2022, an annex was signed and only 8,000 vials, planned for delivery in September 2022, were utilized. As an addition to this central mechanism, at the end of 2020 a significant donation of financial resources was made by a commercial company to the Bulgarian Red Cross, with the condition that the funds be used for the procurement of medicinal products for the specific therapy of COVID-19. The example of Bulgaria and the timely provision of Veklury in 2020 demonstrates the advantages of the Joint Procurement Agreement

compared to the standard procedures through which medical products pass in the European Union. This approach allows faster access to innovative therapy under emergency conditions and creates a stronger position in negotiating quantities and delivery terms.

Regulatory and Organizational Framework

Alongside the provision of medicinal products, specific regulatory and organizational measures were adopted in Bulgaria to ensure their delivery, accountability, and control over their use. Amendments to Ordinance No. 3 of 05.04.2019 created the possibility for the Ministry of Health to subsidize healthcare facilities for maintaining the readiness of infectious disease clinics and wards, as well as for maintaining reserves of medicinal products included in the list under Article 262, paragraph 1 of the Medicinal Products in Human Medicine Act, necessary for the treatment of the infectious disease that caused the epidemic spread.

The provisions of Article 263 of the Medicinal Products in Human Medicine Act made it possible, with funds from the state budget outside the scope of compulsory health insurance, to pay for medicinal products that are not included in the Positive Drug List but are necessary for prophylaxis or treatment in epidemics, pandemics, and other serious threats to public health. On this regulatory basis, the medicinal products Veklury (INN Remdesivir), Casirivimab and Imdevimab 120 mg/ml concentrate for solution for infusion, and Regkirona (INN Regdanvimab) were provided in the country, included in the list under Article 266a, paragraph 2 of the Medicinal Products in Human Medicine Act by respective orders of the Minister of Health.

The delivery of Veklury on the territory of the Republic of Bulgaria is carried out in accordance with the conditions of the framework contracts, with the receiving entity designated by the Ministry of Health being the state-owned company BUL BIO – NCIPD Ltd., holding a valid wholesale distribution authorization for medicinal products. The specific distribution and supply of healthcare facilities are carried out on the basis of orders of the Minister of Health, which approve guidelines for the provision, accountability, and control of the use of medicinal products intended for the treatment of coronavirus infection.

In summary, practice during the pandemic shows that the provision of medicinal products for the treatment of COVID-19 in Bulgaria was implemented through a mixed model, in which the leading role is played by the centralized coordination of the Ministry of Health, complemented by decentralized hospital supply practices, donations, and extraordinary regulatory mechanisms. This combination ensures a relatively high degree of control, traceability, and adaptability under conditions

of an extraordinary epidemic situation and confirms the importance of institutional coordination for the sustainable functioning of the supply chain.

The logistics processes were implemented at national level through a specifically structured supply chain. During the pandemic, Bulgaria applied a specific model in which the state assumed the role of central coordinator through the Ministry of Health and the Regional Health Inspectorates. The supply process was organized through weekly requests from hospital pharmacies, which are verified based on actual hospitalizations and are fulfilled through centralized delivery from “Bul Bio–NCIPD” to regional hubs.

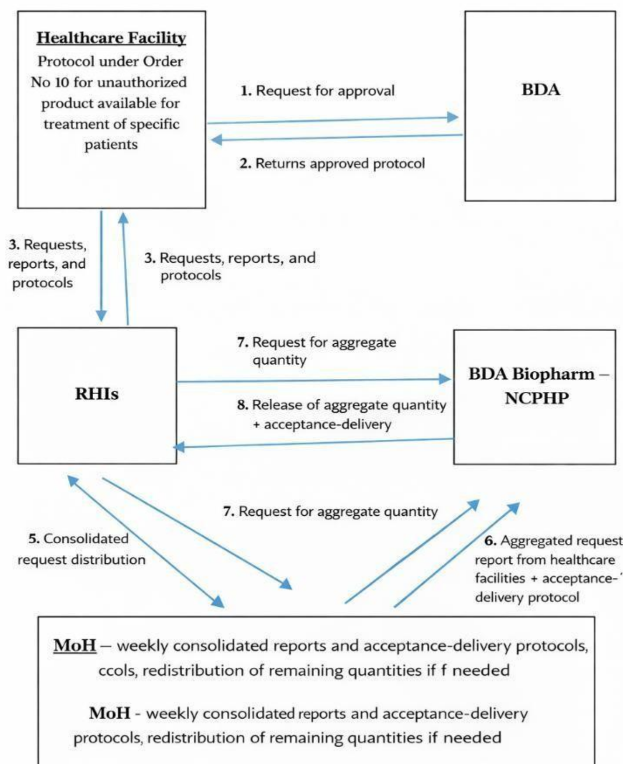

Figure 9. Algorithm for the provision, accountability, and control of medicinal products

Comparative Analysis of Distribution Models

A central place in the study is occupied by the comparison between the two main models of supply organization applied under crisis conditions (centralized and decentralized model):

Decentralized (Market-Oriented Model)

The distribution of medicinal products to hospital healthcare facilities in Bulgaria is carried out through a decentralized model, in which multiple participants interact within a clearly regulated chain: manufacturer or importer → wholesaler → hospital pharmacy → patient. At the beginning of this chain stands the manufacturer or the marketing authorization holder (MAH), who determines which licensed wholesalers may distribute the respective medicinal product on the Bulgarian market. This selection falls within the competence of pharmaceutical companies, and national institutions do not directly participate in it.

Wholesalers play a key role in the decentralized model, ensuring the physical movement of medicinal products to healthcare facilities. They function as independent intermediaries and must hold a license from the Executive Agency for Medicines (EAM), as well as comply with the requirements of Good Distribution Practice (GDP). The EAM exercises control over their activities through licensing, inspections, and monitoring of compliance with regulatory requirements. In addition, all participants in the chain, including hospital pharmacies, are obliged to apply systems for the verification of medicinal products in accordance with European requirements, with the aim of preventing the entry of falified medicines.

Hospital pharmacies represent the final point of distribution before the medicinal product reaches the patient. They are supplied exclusively by licensed wholesalers and are responsible for the storage, traceability, and dispensing of medicines within the healthcare facility. Pharmacists in hospital pharmacies perform an important function both in terms of quality and safety, as well as in internal cost control and accountability to financing institutions.

The National Health Insurance Fund (NHIF) participates indirectly in the system by financing a significant portion of medicinal products used in hospital care. Payment is carried out based on reported quantities and under conditions of established ceiling prices approved by the National Council on Prices and Reimbursement (NCPR). This mechanism aims to control public expenditures and limit price disparities.

The role of the Executive Agency for Medicines is not limited only to the control of distributors. It is also responsible for pharmacovigilance, authorization of emergency import of medicinal products, as well as the management of shortages through mechanisms for restricting re-export. By maintaining

registers and applying regulatory instruments, the agency aims to prevent disruptions in the supply chain.

The decentralized model operates within a broad regulatory framework, mainly governed by the Medicinal Products in Human Medicine Act, which defines the requirements for all participants in the chain—from production to use. The Act introduces mechanisms for traceability, quality control, and prevention of falsification, including through mandatory verification of medicinal products. In addition, the Public Procurement Act regulates the rules for purchasing medicines with public funds, with recent amendments aimed at harmonizing conditions for all healthcare facilities.

The system is further complemented by secondary legislation, including Ordinance No. 10/2009 regulating reimbursement mechanisms by the NHIF, as well as Ordinance No. 10/2011, which regulates access to unauthorized medicinal products through a special regime. These mechanisms allow the provision of treatment in the absence of alternatives while ensuring strict control and traceability.

The decentralized distribution model in Bulgaria is characterized by the participation of multiple independent actors, a high degree of regulation, and clearly defined responsibilities. It ensures flexibility and competition in supply, while the regulatory framework aims to balance accessibility, cost control, and the guarantee of quality and safety of medicinal products. In the context of contemporary challenges, including medicine shortages and supply crises, a trend towards strengthening mechanisms for centralization, resilience, and control is observed, including at the European level.

Centralized Model

An alternative to the decentralized distribution approach is a centralized logistics system, in which all or most deliveries to hospital facilities are carried out through a single distribution center or central warehouse. This means that instead of each hospital ordering and receiving medicines from different wholesalers, a central warehouse—most often state-managed or operated by a selected operator—assumes the functions of storage and distribution of medicinal products to hospitals across the country.

The centralized model has several significant advantages compared to the decentralized one. It allows for better control over inventories and more effective management of shortages. In such a system, stocks of key medicinal products can be monitored and managed at the national level, creating opportunities for more precise planning, increasing deliveries in anticipation of rising demand, and

redistribution between regions in cases of local shortages. This is difficult to achieve in a fragmented system where each healthcare facility maintains its own limited stock. The central warehouse can also serve as a state reserve for critical medicines, which can be activated in emergency situations. Centralization creates conditions for higher efficiency and professional management. A large warehouse base, equipped with modern inventory management software and automated storage systems, can operate more efficiently than multiple separate storage structures within healthcare facilities. The introduction of technologies such as automatic tracking of batches, expiry dates, and minimum stock levels reduces the risk of human error and facilitates timely distribution. This also limits the likelihood of costly medicines being discarded due to expiration.

The centralized model creates economies of scale and opportunities for lower prices. By consolidating demand, it can conduct public procurement procedures for significantly larger volumes, increasing purchasing power and enabling the negotiation of more favorable pricing conditions. This also reduces disparities between large and small hospitals and leads to a more equitable use of public funds.

The centralized system introduces standardization and transparency. A unified electronic mechanism for submitting and executing requests facilitates the tracking of the entire process and limits opportunities for irregular practices. At the same time, the stronger centralized position provides the state with greater capacity to act in crises, when direct negotiations with manufacturers, participation in international mechanisms, and the imposition of requirements for minimum stock levels are necessary.

Alongside these advantages, the centralized model is also associated with a number of risks and limitations. First, it creates a risk of a single point of failure (SPOF). Concentrating supply through one center means that a technical failure, accident, fire, or other incident in the central warehouse may affect the supply of all hospitals. In contrast, the decentralized system has multiple parallel channels, which to some extent provide redundancy. A similar risk arises in the event of transport disruptions—road blockages or interruptions of logistical links may temporarily leave parts of the country without access to supplies.

Lack of flexibility and delays in deliveries represent another weakness of the centralized approach. In the decentralized model, hospitals often maintain local stocks and can be supplied relatively quickly by regional distributors. In a centralized system, requests must pass through the central system and be transported to the respective healthcare facility, which may take more time, especially in remote areas. This necessitates extremely precise logistical planning and, where necessary, the establishment of regional hubs.

Limited competition and the risk of corrupt practices should also be taken into account. Centralized public procurement concentrates significant financial resources in a limited number of contracts, creating conditions for pressure, lobbying, and dependence on a small number of suppliers. If control is not sufficiently effective, instead of multiple local risks, a single large systemic risk may emerge. A comparison is presented, constructed directly on defined indicators related to supply and logistics, using a four-level scale of impact:

Indicator	Centralized Supply by the Ministry of Health	Decentralized Supply	Donations
Speed of provision	3	2–3	2
Degree of central control	4	1	2
Equity of access	4	2	1
Resilience under shortage	3	2	1
Logistical flexibility	2	3	2
Traceability and accountability	4	3	1
Economic efficiency	4	2	2

Scale: 1 – Low impact | 2 – Moderate | 3 – High | 4 – Critical

Table 1. Comparative assessment of mechanisms for the supply of medicinal products during COVID19

Large centralized structures are often more bureaucratic and more difficult to adapt. Therefore, such a model should provide for flexible exceptions and the possibility of urgent individual deliveries.

In summary, the centralized distribution model offers significant advantages in terms of control, economic efficiency, transparency, and crisis resilience, but at the same time creates risks related to concentration, reduced flexibility, bureaucratization, and institutional vulnerability. For this reason, its implementation should be accompanied by compensatory mechanisms that limit its weaknesses and preserve the necessary operational adaptability of the system.

The analysis of these two models shows that neither of them is universally effective under pandemic conditions. The centralized model ensures strategic stability, while the decentralized model ensures tactical speed.

Proposal for an Optimized Hybrid Logistics Distribution Model

Based on the identified advantages and disadvantages, the dissertation proposes the implementation of a Hybrid logistics model. It combines the economic strength of centralized contracting with the operational resilience of decentralized infrastructure. The model relies on information connectivity between distributors' warehouses and the national system, allowing dynamic inventory management and rapid redirection of resources to critical points.

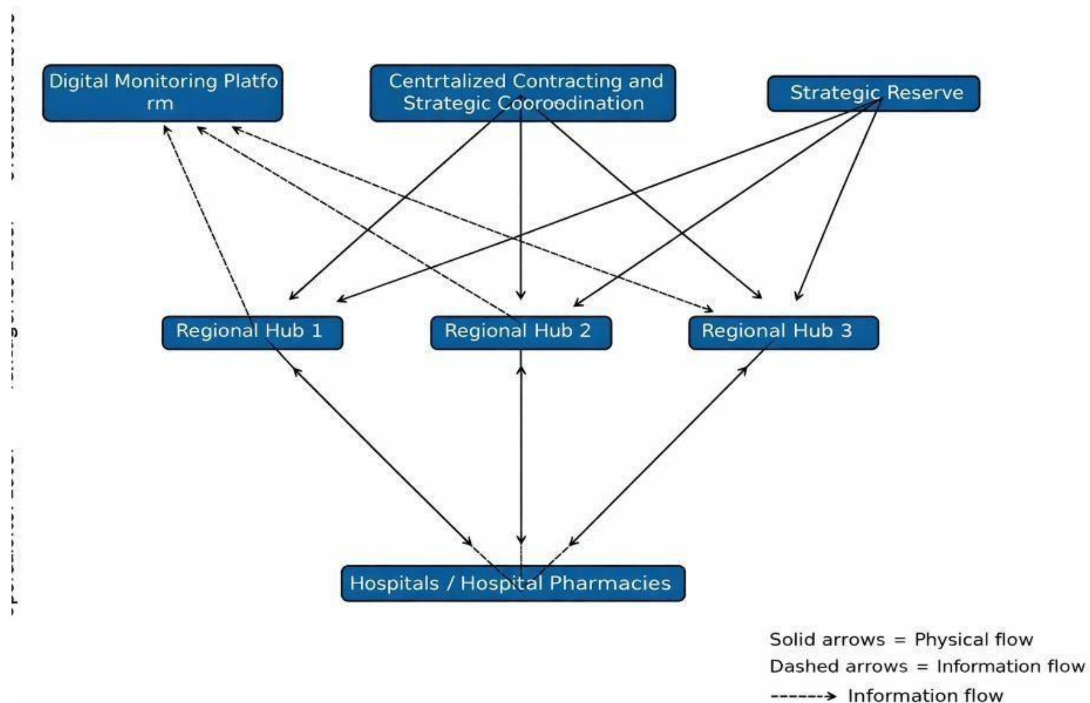

Figure 10. Conceptual hybrid model for the supply of medicinal products to healthcare facilities

The proposed model integrates centralized strategic management with decentralized operational distribution through three interconnected levels:

Strategic level: A central coordinating body manages the system at national level through centralized contracting (public procurement), maintenance of a national strategic reserve, and a digital monitoring platform. The platform collects real-time data on availability and consumption, enabling early identification of shortages.

Tactical level: Implemented through a network of regional logistics hubs. They function as intermediate centers for storage and distribution, diversifying the infrastructure and eliminating the risk of a "single point of failure" characteristic of strictly centralized systems.

Operational level: Covers hospital pharmacies as the final point of the chain. They manage hospital inventories and provide feedback to higher levels regarding actual therapeutic needs.

The functioning of the model is based on the synchronization between the physical flow (movement of products from the central reserve through regional hubs to the patient) and the information flow (exchange of real-time data on availability and forecasts).

Of particular importance is the embedded crisis management mechanism, which in emergency situations allows prioritization of deliveries and mobilization of strategic reserves. In summary, the hybrid model combines the economic efficiency of centralized contracting with the operational resilience of decentralized infrastructure. However, its successful implementation requires a modern digital and storage base, a clear legal framework, and political will for reforms in the sector.

Conclusions

Within the presented dissertation research, a critical review of the deficiencies in pharmaceutical supply chains under crisis scenarios has been carried out. Based on a multidisciplinary approach, including a detailed literature review and empirical analysis of operational-logistical indicators, a conceptual framework for increasing system resilience has been formulated. The scientific contribution of the work is synthesized in the following key directions:

The thesis of the operational superiority of the hybrid configuration in supply is substantiated. The study demonstrates that the integration between centralized strategic planning (ensuring economies of scale) and decentralized local execution is the only mechanism capable of eliminating critical points in the distribution network.

The imperative need for reorganization of the state reserve in Bulgaria is identified. The analysis of the pandemic experience confirms that market mechanisms are insufficient under force majeure conditions. A model of a “strategic buffer stock” is proposed, functioning as a subsidiary system guaranteeing the availability of critical medicinal products without distorting standard commercial channels.

The role of information provision as a foundation of security is defined. The expansion of the functionalities of the NHIS to the level of intelligent real-time monitoring is considered not merely as

a technological upgrade, but as a tool for preventing market failures and optimizing resource provision at national level.

It is established that centralized state intervention under conditions of a health crisis does not disrupt, but complements market mechanisms, creating a balanced environment between public interest and the logic of the free market. This is manifested through increased coordination between institutions, improved cost control, and minimization of the risk of parallel shortages and price imbalances.

It is demonstrated that the introduction of a specifically centrally coordinated mechanism for the supply of certain medicinal products (outside traditional distribution channels) leads to a significant increase in the efficiency of supply chain management. Empirical results show a reduction in procurement time, limitation of variations in access between healthcare facilities, and improvement in supply predictability.

It is confirmed that the formulated scientific hypothesis—that the introduction of a specific order and model for the supply of certain medicinal products to hospital healthcare facilities, outside traditional distribution channels, allows for more effective supply chain management—is valid. This is expressed in the optimization of the treatment process, increased operational efficiency of the healthcare system, and provision of faster and equitable access of patients to innovative medicinal products in emergency situations related to public health threats.

In conclusion, based on the conducted comparative analysis, the dissertation proposes a transition to a sustainable hybrid model that institutionalizes the state reserve as a guarantor of security without disrupting the competitive environment of private distributors.

The dissertation demonstrates that the organization of the supply of medicinal products to hospitals under crisis conditions is not merely a logistical issue, but a matter of national and regional security. The application of the principles embedded in the model for management and analysis of the supply chain of medicinal products can significantly improve the preparedness of the healthcare system and minimize the social and economic impacts of future epidemic and other emergency crises.

Future research could focus on the quantitative modeling of the financial benefits of implementing the supply chain management model, as well as on the development of metrics for assessing supply chain resilience in the pharmaceutical sector.

VI. Recommendations

Based on the conducted analyses and the derived conclusions, the following recommendations are formulated, addressed to the competent institutions and stakeholders in the supply chain of medicinal products:

1. Institutional and Structural Recommendations

To the Ministry of Health (MoH) and the Council of Ministers (CoM):

- It is recommended to establish a National Strategic Logistics Reserve through the creation of a centrally state-managed logistics center for critical medicinal products and medical supplies. This center should function as a strategic buffer (“second echelon”), activated in emergency situations, shortages, or disruptions in the supply chain.
- To the Ministry of Health (MoH), jointly with the National Assembly: It is necessary to introduce regulatory provisions for a hybrid model of medicinal supply through amendments to the Medicinal Products in Human Medicine Act and the related secondary legislation. The aim is to create a legal framework allowing the combination of centralized public procurement (at national or European level) with decentralized operational distribution at regional level.

2. Technological and Innovation Recommendations

- To the Ministry of Health (MoH) and “Information Services” JSC (operator of the NHIS): An upgrade of the National Health Information System (NHIS) should be implemented through the introduction of intelligent early warning algorithms that automatically signal critical reductions in the availability of medicinal products across regions and healthcare facilities.
- To the Ministry of Health (MoH), the Executive Agency for Medicines (EAM), and healthcare facilities: It is recommended to establish a regulated mechanism for horizontal resource exchange, enabling the redistribution of available stocks between healthcare facilities in the event of shortages. This requires both regulatory amendments and the development of a technical platform for traceability and coordination.

3. Operational Recommendations (Risk Management)

- To hospital healthcare facilities: Internal protocols for logistical flexibility should be developed and implemented, including pre-identified alternative suppliers, transport routes, and action scenarios in the event of supply disruptions, in order to limit the risk of "single points of failure" (Single Point of Failure – SPOF).

- To the Ministry of Health (MoH), jointly with the EAM and the Regional Health Inspectorates (RHI): It is recommended to introduce the practice of periodically conducting national "stress tests" of the medicinal supply system through simulations of crisis scenarios (pandemics, supply disruptions, shortages), in order to assess system preparedness and identify weaknesses.

4.Communication and Coordination Recommendations

- To the Ministry of Health (MoH) and the Executive Agency for Medicines (EAM): It is necessary to establish and maintain a sustainable mechanism for information exchange between regulatory authorities, wholesalers, and healthcare facilities, including through regular operational channels and digital platforms for sharing data on availability, deliveries, and expected shortages.
- To wholesalers of medicinal products (distributors): An obligation should be introduced for proactive notification of regulatory authorities in cases of expected disruptions in the supply chain, including delays, shortages, or risk of re-export, in order to enable timely implementation of compensatory measures.

The proposed recommendations are aimed at building a more resilient, coordinated, and adaptive medicinal supply system, capable of ensuring timely and equitable access to therapy in future emergency situations, while simultaneously improving the efficiency of management and control of resources within the healthcare system.

Contributions

The present dissertation contributes to the development of scientific knowledge and practice in the field of organization and management of the supply chain of medicinal products under emergency conditions, by providing a systematized and empirically grounded analysis of the functioning of the Bulgarian model during the COVID-19 pandemic.

The scientific contribution of the study is expressed in the development and application of an integrated analytical approach that links clinical indicators (mortality, therapeutic outcomes) with logistical and organizational characteristics of the medicinal supply system. For the first time in the national context, a comprehensive analysis of the relationship between access to specific therapy (Remdesivir and monoclonal antibodies), their distribution mechanisms, and final health outcomes, including age-specific and regional mortality, has been conducted. Through the use of statistical methods, including cluster analysis, regional differences have been identified and patterns of distribution of health risk have been outlined, contributing to a deeper understanding of the factors influencing the effectiveness of the healthcare system under crisis conditions.

A substantial contribution of the work is also the analysis of the institutional role of the Ministry of Health, examined in the context of the actually applied mechanisms for centralized planning, contracting, and distribution of medicinal products. The study demonstrates the transformation of the traditionally decentralized system into a hybrid management model, combining market mechanisms with centralized coordination under conditions of an extraordinary epidemic situation.

The applied contribution of the dissertation is expressed in the formulation of specific conclusions and recommendations for optimizing the supply chain of medicinal products, including the need to establish mechanisms for dynamic redistribution of resources, improvement of logistical traceability, and introduction of tools for early identification of shortages. The proposed guidelines have the potential for practical application in future health crises and may serve as a basis for the development of a more resilient and adaptive model of medicinal supply in Bulgaria. The dissertation demonstrates that the implementation of a coordinated, institutionally supported, and logistically secured supply model is a key factor in ensuring timely access to innovative therapy and improving health outcomes under pandemic conditions.

List of Scientific Activity Related to the Dissertation

Scientific Publications

1. Nedev O., Grigorov E. – *"REMDESIVIR – THE MEDICINAL PRODUCT THAT PROVED TO BE A SUCCESSFUL NEW HEALTH TECHNOLOGY IN THE FIGHT AGAINST COVID-19"*, *Yearbook of Hospital Pharmacy*, 2022, Vol. 3, pp. 38–55. (ISSN 2367-8763)
2. Nedev O., Galeva S., Grigorov E. – *"THE ELECTRONIC PLATFORM FOR PROCUREMENT OF MEDICINAL PRODUCTS FOR HOSPITALS – A NEW CHALLENGE FOR PHARMACISTS"*, *Yearbook of Hospital Pharmacy*, 2017, Vol. 8, pp. 13–18. (ISSN 2367-8763)
3. Toshev A., Nedev O., Georgiev S. – *"FROM THE RESPONSE TO COVID-19 AND MPOX TO SUSTAINABLE VACCINATION POLICIES: THE STRATEGIC ROLE OF DG HERA"*, *Vaccine-Preventable Diseases. Proceedings of the IV National Conference on VaccinePreventable Diseases*, 2025, Vol. 4, Issue 4, pp. @–@. (ISSN 3033-2176) **accepted for publication**
4. Nedev O., Toshev A., Salchev P., Grigorov E. – *"CENTRALIZED VERSUS DECENTRALIZED LOGISTICS OF MEDICINAL PRODUCTS IN HOSPITAL SUPPLY DURING CRISES"*, *Bulgarian Journal of Public Health*, 2026, Vol. 18, Issue 1, pp. 18–38. (ISSN 1313-860X)

Participation in Scientific Events with Posters

1. Nedev O., E. Grigorov. *MANAGEMENT OF THE SUPPLY CHAIN OF SPECIFIC MEDICINAL PRODUCTS FOR THE TREATMENT OF COVID-19 IN HOSPITAL CARE*

INSTITUTIONS IN BULGARIA. VIII Congress of Pharmacy with international participation, 27–30 April 2023, Hotel “Rila”, Borovets Resort. Electronic abstract book (ISBN 9789548137-16-4), poster 125.

2. Nedev O., A. Toshev, E. Grigorov, P. Salchev, S. Georgiev. *ORGANIZATION OF THE SUPPLY OF SPECIFIC MEDICINAL PRODUCTS FOR THE TREATMENT OF COVID-19 IN HOSPITAL CARE INSTITUTIONS IN THE COUNTRY.* XI Festival “Sea and Health”, 16–17 May 2025, Varna, Varna Medical Forum. 2025:14(Suppl.1):108–109.
3. Nedev O., A. Toshev, S. Georgiev, E. Grigorov. *MANAGEMENT OF THE SUPPLY CHAIN OF MEDICINES TO HOSPITAL CARE INSTITUTIONS – ANALYSIS OF MODELS*, IX Congress of Pharmacy with international participation “PharmaceuticAI Science Revolution”, 30.10 – 02.11.2025, Abstract Book (ISBN 978-619-7063-81-3), p. 337.
4. Nedev O. *ESTABLISHMENT AND FUNCTIONING OF THE CENTRAL PURCHASING BODY IN THE HEALTHCARE SECTOR THROUGH THE IMPLEMENTATION OF AN ELECTRONIC PLATFORM FOR PROCUREMENT OF MEDICINAL PRODUCTS FOR THE NEEDS OF HEALTHCARE INSTITUTIONS IN THE REPUBLIC OF BULGARIA*, XVI National Conference on Hospital Pharmacy, 14–16 October 2020, Borovets, Hotel “Samokov”

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