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Short communication

Improving access to medicines for rare disease treatment: addressing the challenges

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Introduction

Orphan medicinal products (OMPs) are intended for diagnosis, prevention or treatment of life-threatening or very serious conditions that affect no more than 5 in 10,000 people in the European Union (EC, Orphan medicinal products, 2026). According to the Program for rare diseases in North Macedonia, an orphan drug is a drug intended to treat rare diseases defined as a heterogeneous group of generally chronic disorders that reduce the quality and/or length of life of affected individuals with prevalence that does not exceed 1 in 100,000 inhabitants (Official Gazette, No. 33/2026).

Ensuring patient access to OMPs remains challenging in both the EU and North Macedonia, as marketing authorization alone does not guarantee availability, which depends on national reimbursement decisionsNorth Macedonia's national rare disease program, established in 2009, currently provides medicines to about 420 of the 1,093 registered patients (December 2025). Medicines are centrally procured by the Ministry of Health and distributed through hospital pharmacies. For 2026, the program is funded with approximately EUR 17.5 million, including EUR 5.4 million from the state budget and EUR 12.1 million from the Ministry of Health (Official Gazette No. 33/2026).

Public healthcare institutions submit semi-annual reports through the national electronic health system on patient numbers, medicine stocks, and required quantities (Official Gazette No. 33/2026).

This research aimed to identify and critically assess the main challenges affecting access to medicines for rare diseases in North Macedonia.

Materials and methods

Literature research was performed using relevant scientific databases PubMed, ScienceDirect, Google Scholar, as well as official websites of the European Medicines Agency (EMA) and Macedonian Agency for Medicines and Medical Devices (MALMED), Health Strategy of the Republic of North Macedonia 2021–2030, including North Macedonia Drug registry and Official Gazette of the Republic of North Macedonia and other publicly available documents.

Results and discussion

The research and analysis of the available documents resulted in identification of the following challenges to the acess to rare disease medicines in North Macedonia:

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- *Limitations in the structural Funding of the National Rare Disease Program* - As a small country with restricted financial capacity, North Macedonia relies predominantly on central budget allocations to fund rare disease treatment, supplemented by resources from the Ministry of Health, which also finances broader public health programs involving prevention and early detection (Health Strategy of the Republic of North Macedonia 2021–2030). Budget forecasts for 2026 indicated a reduction of the National Rare Disease Program budget, from EUR 24 million to a proposed EUR 17.5 million. Persistent financial constraints within the national rare disease program limit the patient access to essential therapies (Official Gazette, No. 33/2026).

- *Regulatory Shortcomings Limiting Access to Innovative and Orphan Medicines* - North Macedonia's legislation does not formally recognize orphan medicinal products, and no dedicated framework regulates their authorization, designation, and import. This regulatory gap limits patient access. Only part of the orphan medicines in the national rare disease program have a standard marketing authorization, while the remaining products are unregistered and supplied through special import permissions (Drug registry of MALMED).

- *Administrative delays in medicine supply* - Regulatory gaps for orphan medicines, including their lack of formal recognition in national legislation, lead to delayed procurement of rare-disease therapies. Delays are even greater for unregistered medicines because of additional administrative and import requirements.

- *Limited pharmaceutical market attractiveness and implementation of pharmacoeconomic guidelines* - The presence of innovative companies is chalenged by limited funding, low GDP, a small market, small patient base, lack of pharmacoeconomic guidelines as well, which restricts access to modern therapies, especially for rare and highly specialized diseases.

To bridge this gap, the country relies on alternative pathways, mainly through local representatives or authorized distributors on behalf of the innovative companies (Kamusheva et al., 2018).

- *Difficulties in diagnosing patients with rare diseases, and/or incomplete patient registries* - North Macedonia faces a lack of disease-specific information and limited access to qualified specialists, alongside inadequate healthcare services that may exclude patients even after a correct diagnosis. Patients also encounter administrative barriers when seeking treatment or accessing social protection rights (Tasic et al., 2018).

Conclusion

Overall, the results indicate that access to orphan medicines in North Macedonia is limited by regulatory gaps, financial constraints, administrative delays, market-related, and diagnosis-related barriers. System performance can be improved through well defined legislation procedures, stable long-term funding, and optimized procurement procedures. Targeted policy and legislative reforms are therefore crucial to enhance medicine availability, ensure continuity of care, and better align national practices with international standards.

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