ACCESS TO ESSENTIAL MEDICINES IN THE REPUBLIC OF MOLDOVA

Final report

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Summary

Ensuring continuous access to essential and affordable medicines of good quality is one of the key components of a functional health system. The commitment of the Government of the Republic of Moldova to the implementation of the concept of essential medicines is stipulated by a series of strategic documents: National Health Policy, State Medicines Policy as well as by regulatory documents that translate this concept into practice.

The first national list of essential medicines was approved in 1996, and was revised four times later. The first and only Regulation on the National List of Essential Medicines (NEML) was approved in 2007. In total, four editions of NEML were approved, the last one in 2011. The WHO essential medicines list (WHO EML) is, however, revised every 2 years, the last edition being approved in 2017.

Access to essential medicines in the Republic of Moldova remains a challenge for the health system and for every medicine user. The WHO Study[1] on the availability and affordability of medicines in the Republic of Moldova, found that the NEML was accounted for 40.89% of all medicines procured on centralized basis from public funds and the share of expenditures for essential medicines reached 43.14% out of the total expenditures as a result of centralized procurements in 2011.

This study aims to analyze and evaluate the implementation of the concept of essential medicines in the national health system and to identify determinants to improve the application of the concept in practice. In order to achieve the proposed goals the general and special legislative and normative framework regarding the essential medicines in the health system were analyzed. Another focus of examination was how the NEML could be aligned with the WHO EML and the use of NEML in public procurement of medicines and in the process of development and approval of the list of reimbursed medicines within mandatory health insurance.

Following the examination of the regulatory framework on the concept of essential medicines, a number of weaknesses have been identified. The NEML regulatory documents do not set the context for comprehensive implementation of the essential medicines concept in practice. The Regulation of Essential Medicines, approved in 2007, which name the actors responsible for the management, development and implementation of NEML, does not establish an algorithm that would explicitly clarify the steps to be taken for medicines inclusion and/or exclusion in/from the NEML and the documentation and information flow relevant to this process. In addition, as the result of the analysis of the regulatory framework there has been found deficiencies in the procedures related to:

- Order of submission and examination of applications.
- File structure.
- List of documents required to support the information presented in the application file.

[1] Availability and affordability of medicines and assessment of quality systems for prescription of medicines in the Republic of Moldova, OMS 2012

- Referencing sources officially accepted for the evidence on cost-effectiveness of medicines.
- Ensure the security of the files submitted to the Permanent Commission for the development, evaluation and updating of the Essential Medicines List.
- Structure and organization of the Permanent Commission for the development, evaluation and updating of the Essential Medicines List.

Despite the fact that the Regulation of Essential Medicines establishes the institution responsible for coordinating the implementation and monitoring of the application of NEML, neither this document, nor any other specifically developed document on holistic and systematic follow-up of NEML implementation can provide a set of indicators for monitoring and evaluating the concept of essential medicines as well as its related procedures. Current activities and indicators for monitoring the implementation of essential medicines address sporadically this group of medicines and do not supervise systematically the access to essential medicines by monitoring the impact of implementing the regulatory framework on the marketing authorization of the medicines, pricing policies, public procurement of medicines, etc., as well as their alignment with the new provisions of the WHO and other recognized international institutions.

The comparative analysis of the 2011 edition of the NEML (635 molecules) with 2017 edition of WHO EML (532 molecules) reveals that 337 molecules [2] are common to both lists. At the same time, it was found that there are 152 molecules in the last edition from 2017 of the WHO essential medicines list, which were not included in the 2011 NEML. At the same time, 263 molecules of WHO EML are not present in the 2017 edition, but they are included in the NEML of the RM from 2011. By this comparison we can point out that the deficiencies in the functioning of the review and completion mechanism result in differences between the NEML and the WHO EML. Therefore, the delay in reviewing the NEML according to the WHO recommendations could affect the selection of medicines for supply and subsequently the quality of medical services and the rational use of public budgets. The consequences in the healthcare in the context of the changes that have occurred in the latest WHO EML editions versus the NEML of the RM can be studied through a further analysis which main goal would be the rational use of medicines and would involve evaluations based not only on the lists of essential medicines, but also on the Pharmacotherapeutic Formulary and national clinical protocols.

Another difference that has been noted is the lack in national practice of the separate lists of essential medicines for adults and children unlike the WHO EML structure model.

The analysis of access to essential medicines based on public procurement shows an increase in the share of essential medicines in the list of medicines procured through centralized tendering system - from 47.01% in 2015 to 51.61% in 2017. In 2015, a total of 585 INNs were procured, of which 275 INNs (47.01%) were EM, in 2016 the share of EM slightly increased by 23 INNs (49.58% - 298 INNs) out of a total of 601 INNs procured, and in 2017 the EM share reached 51.61% and accounted for 289 INNs out of a total of

[2] In this study, the term "molecule" refers to the generic name of INN of a medicine.

560 INNs. The number of essential medicines in the list of requested medicine for public procurements for 2016-2017 was of 293 molecules/INN, which represented about 46% of the total of 635 molecules/INN included in NEML in 2011.

Among the factors that would influence the access to essential medicines are the marketing authorization, import authorization, pricing and reimbursement policies including price registration in the National Catalogue of ex-factory manufacturer prices for medicines etc. According to the data collected for 2015-2017, it was noted that the share of essential medicines was on average of 40% out of the total number of authorized medicines to be placed on the market. The evolution of the share of essential medicines authorized for placing on the market depends on a number of factors: the characteristics of the pharmaceutical market, measures undertaken to implement the concept of essential medicines, the legislative and procedural facilitations of essential medicine placement on the market. The share of essential medicines that have the price registered in the National Catalogue of ex-factory manufacturer prices for medicines is of 43.75%. It is worth mentioning that a large number of essential medicines are imported into the country under external financial assistance (anti-tuberculosis, antiretroviral, vaccines etc.), being procured from international procurement agencies or through international procurement mechanisms. In many cases, these medicines are imported as unauthorized medicines and their price is not registered in the National Catalogue of ex-factory manufacturer prices for medicines. Thus, the import of essential medicines under external financial assistance increases the share of essential medicines on the national market even though they do not have a marketing authorization and do not have their price registered in the National Catalogue of ex-factory manufacturer prices for medicines. The impact of the registration procedure in the National Catalogue of ex-factory manufacturer prices for medicines on the access to essential medicines on the local market could be examined in a later study.

One of the factors that would contribute to increased access to essential medicines is the application of zero or differentiated VAT rate, practically used in European countries. At present, the essential medicines are subject to 8% VAT, which is similar to other medicines, and which adds to their final cost. Revision of medicine pricing regulations by differentiating approaches for essential medicines versus other medicines would help increase access to them.

Conclusions

The government has committed to implement the concept of essential medicines in the country. In this respect, separate provisions were included in the State Medicines Policy. New regulations, approaching the NEML from different perspectives were adopted, which also establishes the institutions responsible for the NEML development and its adjustment to the WHO EML and the implementation and monitoring of the NEML.

The new draft law on medicines, developed by the MoHLSP and presented for public debates in the first half of 2018, legally defines the definition of essential medicines and establishes the authority responsible for approving the list of essential medicines[3].

In the last three years, the EM share in the list of medicines procured on centralized basis increased from 6.11% in 2015 and to 10.72% in 2017 compared to 2011. In 2011, the EM constituted 40.89% of the list of medicines procured on centralize basis through public tenders, and the share of expenditures was of 43.14% from the total amount contracted for the centralized procurement of medicines. In 2011, the EM constituted 51.61% of the list of medicines procured on the centralized basis through public tenders for that specific year, and the share of expenditures was of 65.94% from the total amount contracted for the centralized procurement of medicines.

The national list of essential medicines is not systematically reviewed. The latest version of the national list of essential medicines was approved in 2011, while the existing regulatory framework stipulates the revision of the NEML every two years.

The National List of Essential Medicines is not developed individually for adults and children, as is the case with WHO EML. Unlike the WHO EML model, the NEML is not structured in chapters based on levels of healthcare services, such as palliative care.

The regulatory framework that establishes the process of developing, reviewing and approving the national list of essential medicines is incomplete. The regulations on the evaluation and approval of medicines for inclusion in the list of essential medicines are outdated (approved in 2007). The Regulation does not provide for an algorithm or procedures in the national practice for adapting NEML to the WHO EML. These rules, therefore, do not provide clarity, predictability and accessibility for the development, revision and approval mechanism of the essential medicines list, aligned to the last WHO recommendations and international practices.

There are no precise rules on the entities who should submit the request, and the procedures for submitting the request for NEML review by subsequent inclusion or deletions of medicines in the NEML. The current normative acts state that the NEML review request may be submitted by a specialist who signs the application and

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[3] The government bill for the approval of the draft Law on Medicines http://www.particip.gov.md/proiectview.php?l=ro&idd=5261

applies the stamp of the organization. At the same time, the requirements for supporting evidence for inclusion of the medicine in the NEML and the reference documents require more special experience and training in the preparation of the request application file. In this context, the provisions of the Regulation on Essential Medicines are not fully applicable.

The transparency of the NEML development and review processes for the professional and for public is not ensured. The regulation on development the NEML, approved in 2007, does not establish deadlines for review requests submission, rules for publishing invitation for participations in review process, the list with requirements for the publication of the results of application evaluation and the decisions taken, terms of reference for selecting and approving the composition of the Permanent Commission for the development, evaluation and updating of the EML.

Ensuring participation in the NEML elaboration and review process is mentioned in the specific regulatory framework, but it does not expressly stipulate how participation is ensured. The normative acts do not provide an express algorithm for the participation of the healthcare and pharmaceutical community, professional and patient associations, as well as the consumers in the process of NEML development and review.

The evaluation criteria of the medicines to be included in the NEML represent a list of principles, but their application is not supported by an effective methodology. The lack of clarity in the regulations on essential medicines creates confusion in interpreting and application of the evaluation criteria.

NEML implementation monitoring is not based on a comprehensive list of indicators and a functional monitoring system. Public authorities responsible for ensuring the access to medicines, monitoring the pharmaceutical market, quality assessment of medical and pharmaceutical services use a set of indicators which address only some aspects of essential medicines, and data collection and analysis is not systematically done. In addition, the used indicators are incomplete and do not reflect the key requirements for monitoring the availability and affordability of essential medicines at each level of healthcare, implementation of the NEML within public and private healthcare institutions, the level of coverage of the pharmacotherapeutical groups, the continuity of supply essential medicines to healthcare institutions and pharmaceutical units etc.

Comparative Analysis of NEML 2011 edition (635 molecules) with WHO EML 2017 edition (532 molecules) reveals that 337 molecules are commonly shared. At the same time, it was found that there are 152 molecules in the WHO list of essential medicines, the last edition of 2017, which were not included in the 2011 NEML. At the same time, it was found that there are 263 molecules which were not included in the last edition from 2017 of WHO list of essential medicines, but are present in the 2011 NEML. The relevance of including 152 molecules in the NEML or the exclusion of 263 from the 2011 edition, taking into account the latest WHO EML adjustments, requires a methodological evaluation with taking into account the criteria and tools of analysis of

the NEML, established by the MoH order, with involvement clinical experts, pharmacists and public health economists.

The results of the comparison the NEML and WHO EML reveal deficiencies in the functioning of the NEML review and completion mechanism, which could consequently affect negatively the quality of healthcare services.

From the total number of medicines contracted through public procurements for healthcare institutions and for national and special programs, the essential medicines accounted for 47.01% - in 2015, 49.58% - in 2016 and 51.61% - in 2017. However, the share of essential medicines in the list of medicines procured on the centralized basis has not reached a majority level.

The share of essential medicines in the list of medicines requested for public procurements in the period 2016-2017 is about 48% of the total number of molecules/INNs included in the NEML 2011.

The share of essential medicines that have the price recorded in the National Catalogue of ex-factory manufacturer prices for medicines is of 43.75%. It is worth mentioning that a large number of essential medicines are imported into the country under external financial assistance being procured from international agencies or through international procurement mechanisms. In many cases, these medicines are imported as unauthorized medicines and their price is not recorded in the National Catalogue of ex-factory manufacturer prices for medicines. The lack of registration in the National Catalogue of ex-factory manufacturer prices for medicines is one of the limitations for the entry of medical products on the market and for their availability in healthcare and pharmaceutical institutions. Currently, national legislation does not provide for mechanisms that would facilitate the entry of essential medicines on the market in the absence of producer price registration. In the view of the purpose of the essential medicines list, they must be affordable and accessible on the market. The option offered by the current legal framework is the import of these medicines as non-registered medicinal products, if requested by an economic entity and if the conditions stipulated in the Article 11, Paragraph 7 of the Law on Pharmaceutical Activity are respected [4]. However, this provision for unauthorized import does not form a sustainable framework, because the economic entity is more often motivated by the market driven factors and less by a public health interest. Moreover, the import authorization for non-registered medications may have a negative impact on the motivation to apply for marketing authorization for medicines which represents a stage of the quality assurance system for the pharmaceutical market.

[4] The MoHLSP order no. 559 of 29/06/2017 Regarding Regulation on the Authorization of Imports of Medicines, Other Pharmaceutical Products, Parapharmaceuticals and Non-Authorized Medicines in Moldova
http://amed.md/sites/default/files/Medicamente/Ordin%20MS%20nr.%20559%20din%2029.06.2017.pdf

In case of diseases with the highest rates of mortality in Moldova, the medicines included in the list of public procurement medicines represent 44-55% of the NEML: cardiovascular diseases, cancer, digestive diseases, respiratory diseases.

The share of cardiovascular, gastrointestinal, antineoplastic , immunosuppressive medicines and respiratory system medicines procured through public tenders, represents 44-55% of the total number of INNs included in the NEML. Taking into account the number of accepted essential medicines under these therapeutic groups in the NEML, **their share in public procurement lists should be between 80-100%**, if considered by the number of INNs present in each therapeutic group and available budgets.

The share of the contracted budget for the procurement of essential medicines in the total contracted amount for public procurements of medicines accounted for 64.75% in 2015, 62.29% in 2016 and 65.94% in 2017. In 2011 the share of the contracted budget for the procurement of essential medicines in the total contracted amount for public procurements of medicine constituted 43.14%.[5] Based on collected data, the procurement budget for the period 2015-2017 was about 430.3 million MDL including VAT in 2015, reached 681.9 million MDL including VAT in 2016 and about 451.2 million MDL including VAT - in 2017.

The comparative analysis of the 2011 NEML with the current List of Reimbursed Medicines (LRM) (June 2018) reveals that EM represents 72.95% (116 INNs) of the total 159 INNS included in the LRM. When comparing the obtained data with the data included in WHOevaluation of access to medicines and their quality[6], it can be noticed that in the last years the share of essential medicines in the LRM has increased by 26.09% compared to 2011.

Based on the results of this research, we conclude that **a comprehensive and thorough monitoring by the public authorities in charge for supervision of the pharmaceutical market is clearly necessary to make decisions supported by persuasive and systematically collected evidence that would improve access to essential medicines.**

[5] Availability and affordability of medicines and assessment of quality systems for prescription of medicines in the Republic of Moldova, OMS 2012
[6] Ibidem

Recommendations for interventions:

Revision of the mechanism for the development, adjustment and approval of the NEML

- Regulating the methods of the NEML examination, evaluation and alignment to the WHO EML.
- Develop the methodology for applying the eligibility assessment criteria for medicines to be included in the list of essential medicines.
- Develop the NEML structured by different age groups: adults and children.
- Develop a customized NEML focused on different levels of healthcare: primary care, hospital care, palliative care.
- Exhaustive regulation of the process of evaluation and decision-making regarding the applications for inclusion of medicines in the list of essential medicines and systematic review of the NEML.
- Establishing the requirements for recording the evaluation and decision-making procedure and management of the applications for drug inclusion in the list of essential medicines.
- Clarifying the responsibilities of each actor involved in the process of developing and reviewing the NEML.
- Define the duties, responsibilities, activity and reporting procedures of the Permanent Commission for the elaboration, evaluation and updating of the NEML.
- Developing of guidelines for applicants requesting the inclusion of medicines in the national list of essential medicines regarding the compiling of the application file, the requirements for the sources and documents providing the scientific evidence on the medicinal product.
- Improve the transparency of developing, reviewing and approving of the list of essential medicines and the consultation processes at all levels.
- Active promotion amongst doctors and pharmacists of the concept of essential medicines.

Developing a mechanism to monitor the implementation of the concept of essential medicines at the level of all stakeholders

- Developing a system for monitoring the implementation of the concept of essential medicines by strengthening the indicators pursued by MMDA, NPHA, NHIC.
- Develop a list of relevant monitoring and evaluation indicators for the concept of essential medicines that would reflect the following:
  - the presence on the pharmaceutical market and the impact of the regulatory framework on the pharmaceutical market authorization, the import of medicinal products, the registration in the National Catalogue of ex-factory manufacturer prices for medicines;
  - ensuring continuity in supplying the essential medicines to the health care system;

- implementation of the concept of essential medicines in hospital and outpatient institutions and in community-based pharmacies;
- ensuring the affordability of the essential medicines by supervising the evolution of prices and the cost of treatment in comparison with the days' wage, etc.

Improve the practice of compiling lists of medicines for centralized procurement: selecting medicines and estimating quantities

- Active use of the ABC/VEN methodology as an effective tool for prioritizing and optimizing costs on medicines. The implementation of VEN and ABC analysis will help the healthcare institutions to optimize the practices of selecting and formulating the list of medicines, rational use of public money and improving the quality of healthcare services. Develop the ABC/VEN tool implementation guide[7].

Enhancing accessibility to essential medicines

- Reviewing the VAT enforcement policy for this group of medicines by exempting or setting a lower VAT for essential medicines that would help increase the end-user access to essential medicines.
- Revision of essential medicines prices monitoring system and determining the needs of medicine pricing policies review.

Rational use of medicines

- The level of potential impairment in the quality of healthcare services, in the context of changes in the latest editions of WHO essential medicine lists versus the NEML of the Republic of Moldova, and the differences between the included molecules can be evaluated by a separate study that would focus on the rational use of medicines and would be based not only on the list of essential medicines, but also on the pharmacotherapeutical formulary and the national clinical protocols.
- Implement a system of monitoring drug prescription and compliance with the treatment standards.
- Developing a strategy for informing and educating the population on essential medicines.

[7] Group V (Vital Medicines)/Group E (Essential)/Group N (Non-Essential) // The ABC System examines the annual consumption of medicines which are classified into 3 groups and their procurement costs in relation to medicine expenditures.

Abbreviations

ATC	Anatomical, Therapeutic and Chemical Classification
CCPPH	Center for Centralized Public Procurement in Health
Center PAS	Center for Health Policies and Studies
EMA	European Medicines Agency
EMs	Essential Medicines
EU	European Union
FDA	Food and Drug Administration
GF	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	Good Manufacturing Practices
GD	Government Decision
MDL	Moldovan Leu
MHI	Mandatory Health Insurance
MMDA	Medicine and Medical Devices Agency
NHIC	National Health Insurance Company
INN	International Non-Proprietary Name
HTA	Health Technology Assessment
HCI	Healthcare institutions
MHIF	Mandatory Health Insurance Funds
MPSU	Medical and Pharmaceutical State University
PHCI	Public Healthcare Institution
NEML	National Essential Medicines List
LRM	List of Reimbursed Medicines
RM	Reimbursed Medicines
MoH	Ministry of Health
MoHLSP	Ministry of Health, Labor and Social Protection
WHO	World Health Organization
OTC	Over- the- Counter
SMP	State Medicine Policy
VAT	Value Added Tax
TB	Tuberculosis
VEN	Vital, Essential, Non-essential
USD	American Dollar
UNDP	United Nations Development Programme

Contents

Introduction

Ensuring the availability and affordability of medicines is a challenge for any health system, whether it is part of a developed country (with high income) or a developing country. This responsibility of the health system becomes more evident for countries with small and medium budgets. The response of health systems to this challenge lies in approving and maintaining a national medicine policy updated to the needs of the healthcare system and in the regulatory framework for marketing authorization, selection, procurement and use of medicines. Access to necessary medicines and vaccines is part of Agenda for the implementation of Sustainable Development Goals (SDG) 2030. Objective 3 of the SDG is focused on ensuring a healthy lifestyle and promoting the well-being of all citizens, regardless of age, and the underlying provisions include the measures to increase access to essential, high-quality, safe and effective essential medicines. Also, Objective 3 of the SDG envisages support for the research and development of vaccines for communicable and non-communicable diseases that primarily affect the developing countries and better access to essential medicines and vaccines under the Doha Declaration on the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which supports and confirms the right of developing countries to apply the flexibility provided in the Agreement to improve access to medicines[8].

The concept of essential medicines is recognized throughout the world as a tool to improve equity in healthcare and promote rational use of resources. Essential medicines are one of the basic benchmarks in the process of ensuring access to medicines for healthcare consumers. The judicious choice of a limited number of essential medicines also results in improved quality of care, and improved drug management.

In 1977, the World Health Organization (WHO) developed the Essential Medicines List (EML), which is updated every two years. The WHO EML serves to inform and guide the countries in developing the National List of Essential Medicines (NEML). The WHO also recommends a regular review of the NEML to ensure the credibility, timeliness and relevance of the drug selection process to meet the needs of the health sector and the rational use of the country's budget.

The Analysis Report on Access to Essential Medicines highlights the progresses and weaknesses of the national regulatory framework and the practical application of the concept of essential medicines in the Republic of Moldova.

[8] Transforming our world: the 2030 Agenda for Sustainable Development
https://sustainabledevelopment.un.org/post2015/transformingourworld

Study Methodology

The purpose of this study was to analyze the implementation of the concept of essential medicines in the national health system and to identify the factors that would improve the concept implementation.

The study on the implementation of the concept of essential medicines was conducted using the following methods:

- Analysis of the general and specific legislative and regulatory framework on essential medicines in the national health system.
- Researching the alignment of the National List of Essential Medicines with the WHO Essential Medicines List and the role of the National List of Essential Medicines in the preparation of the list of medicines for public procurements and the list of reimbursed medicines.

In order to carry out the research, necessary data were collected to evaluate the regulations, procedures for the approval and implementation of the national list of essential medicines. The main source of information was the official websites of the Ministry of Health, Labor and Social Protection (MoHLSP), the National Health Insurance Company (NHIC), the Medicines and Medical Devices Agency (MMDA), as well as those of the pharmaceutical and health service providers.

The success in implementing the concept of essential medicines is driven by commitments and the involvement of several sectors and stakeholders at different levels, such as: the institutions responsible for policy development and approval; the agency responsible for policy implementation in the field of medicine and pharmaceutical activity; institutions responsible for health education and professional training, institutions responsible for the implementation of NEML, authorities responsible for the management of resources for healthcare and pharmaceutical services and those responsible for providing access to information on medicine and medical device. However, taking into account the research objectives, this study does not foresee the evaluation of NEML implementation by all reference sectors and the involvement of the institutions responsible for the implementation of this concept. Thus, the study does not reflect the results of the implementation of the concept of essential medicines by the health education and training institutions, the health care entities and the pharmaceutical sector.

Structure of the study. The first chapter of the study provides a general description of the main policy documents and normative acts regarding the development and implementation of NEML in the health system, as well as the potential factors contributing to the presence of essential medicines on the pharmaceutical market, such as: medicines and import authorization, pricing policies and reimbursement regulations. In addition, the first chapter analyzes the mechanism of development, approval and implementation of NEML. Chapter Two presents the results of the NEML examination in relation to the WHO EML, and NEML representation in the list of medicines procured through public mechanisms and in the list of reimbursed medicines.

Methodological limitations in summarizing key study results

Public information on medicines procured with public funds differs from one year to another and is presented in various ways. At the same time, not all information on medicines procured with public funds was available, in particular we refer to the final list of medicines which failed to be contracted due to lack of bids for the 2015 public tenders. Generally, it has been noticed that the procurement of the medicines required by healthcare facilities is made by repeated procedure of public tenders. This is caused by a number of factors such as: lack of bids at the initial tender, nominal or quantitative adjustment requests for some INNs, etc. Moreover, for some acquisitions, the published information on bidding results was confusing in terms of data on contract award. For example, it has been noted that for some bids, the published information reveals duplications in terms of quantity, costs and item names proposed for contracting; information on bidding results for 2016 includes the unit of measure and the unit price, while the bidding results table for 2017 shows the total amount instead of the price per unit in the "unit price" section. The absence of a standardized format used annually to publish bidding results and contract awards limits the possibilities for a complex and comparative analysis between years. Also, there is no a practice to publish an Information note at the end of all tenders that would containing a summary of the number of repeated procedures for the medicines included in the tender documents. Availability of an Information note on tenders might reduce confusion in the process of tracking the results of the bids. Moreover, the public information note for organized tenders would strengthen the evidences on the number of bids submitted for a group of products and would stimulate the analysis of the reasons, in particular for products not covered by bids in the first procurement procedure, with subsequent decisions made by public authorities to facilitate the procurement process.

The smaller number of International Non-proprietary Name (INN) included in the analysis of the 2017 bids is also determined by the fact that not all bids and, respectively, lists of winning offers were available in full form for public access. For the year 2017, public procurements were made through two different structures: Center for Centralized Public Procurement in Health (CCPPH) and UNDP. The data published by UNDP on the official website provides a brief summary of the tenders organized for the public procurement of medicines and medical devices for national and special programs. The published information does not provide details of the list of medicines such as name and concentration, pharmaceutical form, quantity, unit price according to INCOTERMS, manufacturer and holder of the marketing authorization of the medicinal product included in the tender and procurement contract. The UNDP official website provides the information regarding the signed contracts specifying the supplier's name, the total contracted amounts, the pharmacotherapeutic group or the national or special procurement program, such as antiretroviral medicines or the National Program for Prevention and Control of Diabetes Mellitus and so on. The information about the detailed list of pharmaceutical products or medical devices in most cases is not provided by UNDP. In spite of limited information regarding the list of medicines or medical devices procured through UNDP, the study authors admitted that the contracted list of names is factually

in line with the list of medicines/INNs requested by the country central public authorities and the number of product names procured through UNDP was considered in the analysis of the total assortment of medicines procured with public money for 2017.

CHAPTER I. THE ANALYSIS OF PUBLIC POLICIES AND REGULATORY FRAMEWORK REGARDING THE IMPLEMENTATION OF THE CONCEPT OF ESSENTIAL MEDICINES

Policies on the implementation of the concept of essential medicines

The law on pharmaceutical activity establishes, by article **18[1]**, the right of citizens to receive medical care based on the following provisions:

- provide good quality, effective and safety medicines in accordance with the minimum guaranteed medical insurance,
- emergency provision of medicines by any pharmaceutical or health facility, irrespective of the type of property and subordination;
- ensuring access to information on the quality and safety of medicines, obtainable from pharmaceutical companies and institutions, health care facilities and public health institutions, information attesting the quality and safety of medicines;
- the right to address expert bodies, institutions and organizations and to access conclusions on the quality, efficacy, and safety of medicines and the level of health care services.

The Government's commitment to implement the concept of essential medicines is stipulated in the National Health Policy[9], the State Medicine Policy[10] and in the regulatory documents which transposes this concept into practice.

Thus, the National Health Policy establishes the provision of access to essential and quality medicines as one of the basic factors for achieving new performances in the health care system. For a comprehensive approach to ensuring the access to essential, quality, effective and safety essential medicines, in 2002 the Government of the Republic of Moldova approved the State Pharmaceutical Policy, a document focused on pharmaceutical and medicine sectors. This strategic document is a fundamental component of the National Health Policy.

The state medicine policy focuses its general objectives on providing efficient, safety, good quality and affordable medicines covering the real needs of society, taking into account the frequency of illnesses and the public health development programs, ensuring the rational use of medicines and the non-discriminatory access of all citizens to essential medicines.

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[9] Government Decision no. 886 of 06.08.2007 regarding the approval of the National Health Policy http://lex.justice.md/md/324940/

[10] Parliament Decision no. 1352 of 03.10.2002 regarding the approval of the State Medicine Policy http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=307874

The state medicine policy addresses the concept of essential medicines through a number of provisions: it includes essential medicines as part of the overall objective of this document and sets out the requirements of selecting key medicines.

Regulations and procedures on development of the list of essential medicines

General Provisions

The implementation of the State Medicine Policy (SMP) was supported by the elaboration and approval of a set of legislative and normative acts that establish the public authorities in charge and their responsibilities in the implementation of the SMP, regulate the placing on the market of high-quality, efficient, safety medicines, as well as their import, distribution, dispense and rational use. In 1997, the Law on Medicine was enacted to ensure that people have access to good quality, efficient and safety medicines, as well as the maintenance of affordable prices and non-admission of abusive medication.

The implementation of the concept of essential medicines is regulated by several documents. The State Medicine Policy specifies a set of criteria and requirements for the development and revision of the national list of essential medicines, which must:

- meet the real needs of the population,
- be reviewed periodically,
- take into account the structure of morbidity, mortality and demographic indicators,
- take into consideration the proposals of specialists from different levels of the health system,
- take into account the results/novelties of the world science in the field of pharmacy, pharmacology and pharmacotherapy,
- be updated in accordance with the latest version of the WHO EML.

Under the national regulatory framework, essential medicines are defined as medicines that meet the needs of the majority of the population in the treatment of the most widespread diseases and which must be available at all times and in the required quantities. Essential medicines must be available in appropriate and high-quality forms and offered at affordable price for each patient and for the whole population, with assured access to drug information.

The WHO initial definition of essential medicines as of 1977 provided that essential medicines are "the most important and indispensable for the health needs of the population."

The WHO definition, revised in 2002, states that "Essential medicines are those that satisfy the priority health care needs of the population." Essential medicines are selected with due regard to disease prevalence and public health relevance, evidence of clinical efficacy and safety, and comparative costs and cost-effectiveness.

Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford.

Implementation of the concept of essential medicines must be flexible and adjustable to many situations considered essential[11]. At the same time, which medicines are regarded as essential remains a national responsibility.

By comparing the WHO definition of essential medicine and the national one, it can be noted that the key requirements of the WHO definition are found in the national framework, such as: cover the needs of the health system for the most widespread diseases, be available at all times and in the required amount, at high quality and affordable prices, with accessible information about the medicine.

In May 2018, the MoHLSP proposed a new draft law on medicine for public discussions, to adjust the EU Directives on medicinal products for human use which included certain stipulations on essential medicines. The draft law on medicines establishes by virtue of Article 11 "Essential Medicines" the criteria for qualifying the medicine as essential: they are defined based on the health priorities of the country, they meet the health protection needs of the majority of the population and are available at any time in the required amount and in appropriate forms and dosages and affordable prices. The same article specifies the requirements for the presentation of essential medicines, such as International Non-Proprietary Name, pharmaceutical form, concentration and method of prescribing. The draft law provides that the List of Essential Medicines for Human Use will be determined by the order of the Ministry of Health, Labor and Social Protection. Moreover, another article of the draft law sets out provisions for a rapid procedure for obtaining the marketing authorization for medicines, which will also include essential medicines.

The first list of essential medicines was approved by the Ministry of Health in 1996. In 2007, the Ministry of Health approved a new list of essential medicines and the first edition of the NEML[12]. The subsequent reviews of the essential medicines were approved in 2009 and 2011, with due adjustment and completions of the list of essential medicines. However, the 2009 and 2011 orders did not foresee changes to the NEML regulation which was approved in 2007. It means that the NEML in the Republic of Moldova has been revised 4 times since the first edition in 1996, followed by the editions of 2007, 2009 and 2011. However, taking into account the provisions of the Regulation approved in 2007 by the MoH, 6 revisions should have been carried out since 2007. If compared to the WHO EML, the NEMLs approved by the MoH starting with the first national list of essential medicines from 1996, about 13 editions were to be approved by now (Table 4).

The 2007 NEML Regulation sets out the basic terms and the way to implement the concept of essential medicines in the national health system, namely: defines the essential

[11] World Health Organization's Essential Medicines List: From Idea to Implementation, https://www.cugh.org/sites/default/files/106_WHO_Essential_Medicines_List_from_Idea_to_Implementation_FINAL.pdf

[12] MoH Order no. 162 of 23.04.2017 regarding the approval of the Regulation and the List of Essential Medicines

medicines, the areas of use of NEML, set out the criteria and requirements for inclusion/deletions of medicines in/from the NEML and for the procedure of essential medicines selection; designates the institution responsible for updating and implementing NEML. The same regulation provides for other aspects necessary to ensure the NEML's functionality, such as update frequency and the development of lists of essential medicines based on levels of healthcare services.

Since 2007 there has been no other regulation that would make any modifications to the document. Moreover, other regulatory documents on the rational use of medicines do not provide details on the NEML development, review and implementation procedures. All changes that have been made and approved since 2007 to the present day refer to the NEML's immediate review and completion, but not to the regulation of the procedures for developing, reviewing, adjusting and approving of the list.

Including medicines in the List of Essential Medicines

The 2007 NEML Regulation names the stakeholders responsible for the management, development, and implementation of the NEML, but does not set up an algorithm that would explicitly describe the procedure of medicines inclusion and/or deletion in/from the NEML and the relevant information flow related to this procedure.

The sequence of application submission actions

The 2007 LNME Regulation specifies the content of an application for inclusion/deletion of medicines in/from the EML which in addition to the general characteristics of the medicinal product, should be accompanied by a set of documents providing data on the drug efficacy, bioequivalence study results, safety, therapeutic equivalence, pharmaco-economic studies with due sources of reference.

The data requested for the application include: International Non-proprietary Name (INN) , pharmaceutical form, pharmacotherapeutic group, therapeutic indications.

The annex to the NEML regulation stipulates that the request for inclusion or deletion of the medicine from the list is signed by the specialist submitting the NEML review request. Assessing by the items included in the structure of the application, it is understood that any specialist belonging to the healthcare system is entitled to make such an application. At the same time, the requirements for formulating a request include the confirmation of the signature by the organization's stamp, which underlines that the applicant is part of a medical organization.

At the same time, the Regulation does not set the time limit and the deadline for submission of applications, the period for the examination of applications, the institution receiving the application files.

Following the analysis of NEML legal framework we conclude the following: the lack of a mechanism that would clarify the order of file submission procedure and the frequency of their examination, the content of the application file, the legal address for filing the applications and the ensuring storage and archiving of the files submitted to the Permanent Commission.

The order no.165 of 23.04.2007 of the MoH does not provide a separate regulation that would govern the procedure of submitted request and files evaluation and the decision-making process regarding the changes of the NEML. Other MoH orders by which the updated NEMLs were approved also fail to provide above mentioned regulations.

Examining the request for inclusion and deletion of medicines in/from NEML

The NEML regulation contains the following criteria for the selection and use of essential medicines:

- Efficacy and safety proven in various circumstances.
- Cost-effectiveness and risks. Assessing the cost of the drug involves determining the full cost of the treatment and its effectiveness.
- Medicines production and storage conditions.
- Selecting the most optimal pharmaceutical form that ensures good quality and bioavailability.
- Most essential medicines should be formulated as single compounds.
- Fixed-doses combination medicines are selected based on evidence of the benefits of therapeutic effect and safety, especially for reducing the risk of developing resistance during TB/HIV, TB treatment .

The requirements for the essential medicines selection process envisage transparency by setting up the inclusion and deletion criteria, consulting clinical treatment standards, providing sources of evidence, commissions' decisions, consulting the opinions of all participants in the implementation of the list of essential medicines, especially those provided by practitioners.

Basically, the regulation sets out a number of criteria to ensure transparency in the process of drafting, approving and revising the NEML. At the same time, the regulation does not clearly express the procedure to ensure the widest participation of all potential stakeholders involved in the development, approval and implementation of the NEML and last, but not least of the EMs beneficiaries.

The Ministry of Health assigns[13] the Medicines Agency the responsibility for the management of NEML and the establishment of a Permanent Commission for the elaboration, evaluation and updating of NEML (hereinafter referred to as the Permanent Commission). At the same time, the NEML regulation does not contain separate provisions on the Permanent Commission activity, decision-making, NEML evaluation and updating tools, the duration of the examination of the applications and submitted files, the management of incomplete files and other possible situations, the model of data evaluation report for inclusion or deletion of medicines in/from the NEML, ensuring the transparency of procedures for submitting applications to the Permanent Commission and its decisions. In addition, there is no framework to define the establishment of the Permanent Commission, the way of selecting and approving the list of members and the periodicity of reviewing the list of members of the Permanent Commission. Although, NEML is largely based on the WHO EML 2011, the adjustment of the national list to the WHO EML and the inclusion of additional medicines should be guided by a regulation that

[13] MoH Order no.165 of 23.04.2007 Regarding the approval of the Regulation and the List of Essential Medicines

exhaustively describes all the requirements, tools, the duration of each stage, and the procedures for each participant involved in the NEML drafting/reviewing process, as well as the work of the Permanent Commission.

In accordance with WHO recommendations and international practices, the development of the List of Essential Medicines is a multi-stage structured process based on a well-defined methodology, ensuring active involvement of public sector institutions, professional associations, practitioners, patient associations, civil society, etc. in the process of reviewing and adjusting the EML. Adjustment of the national list of essential medicines based on the level of medical services is a practice used by both countries with limited budgets and high income countries. For example, Sweden has developed a Wise List that includes 200 essential medicines to primary health care[14]. A similar practice is also implemented in the UK. The table below summarizes the result of the adjustment of the preliminary list of essential medicines for primary care in Canada[15](box).

[14]The 'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential medicines in ambulatory care in Stockholm.
https://www.ncbi.nlm.nih.gov/pubmed/21414143
[15]''Development of a preliminary essential medicines list for Canada''
http://cmajopen.ca/content/5/1/E137.full

Box: Development of a Preliminary Essential Medicines List for Canada

The summary below is taken from the article ''Development of a preliminary essential medicines list for Canada''

Premises. The large number of medicines available in Canada poses a challenge for clinicians. There is list at provincial level such as the Ontario Drug Benefit formulary, the Alberta Drug Benefit List and the Quebec Public Prescription Drug Insurance Plan which include more than 3800, 4000 and 7000 medicines, respectively. A short list of essential medications might make it easier for clinicians to prescribe the most effective, safety and appropriate medications for their patients in Canada.

The results of the WHO essential medicines list adaptation

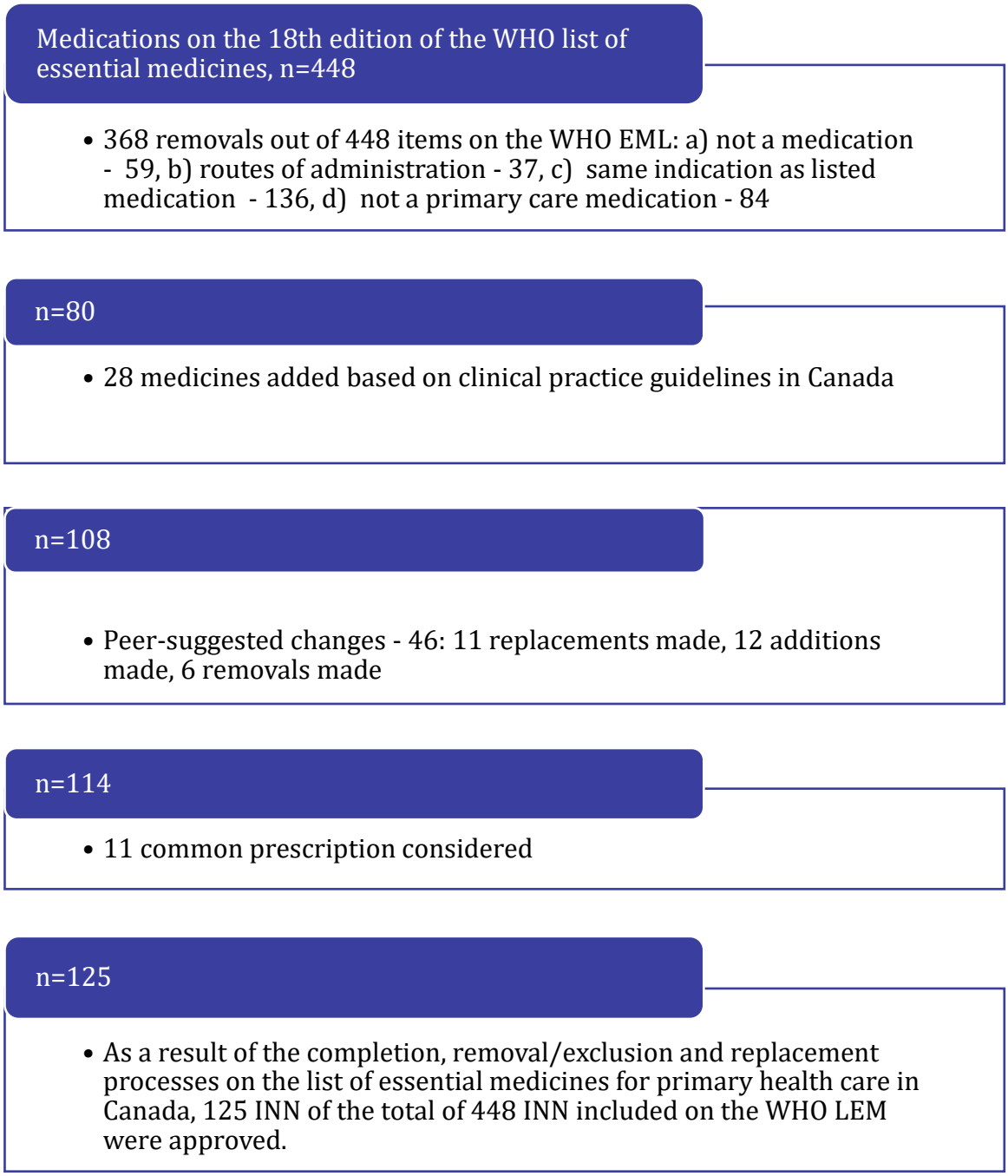
The WHO's List of Essential Medicines was adapted using a 4-step process involving a small group of Canadian clinicians and clinician-scientists.

The preliminary essential medicines list for Canada contains only 125 medications, about half of the number of medications on the Swedish Wise List and about a quarter of the medications on the WHO list. The small size of the list might allow clinicians to learn more information about fewer medicines and improve the practice of medicine prescription.

The limited list of essential medicines for primary care included more than 90% of prescribed medicines, which was subsequently confirmed by the clinic's audit; in more than 90% of patients it was observed that all or at least one prescribed drug was on the List. These preliminary results suggest that, although smaller than the essential medicines list of other countries, this list still covers most medicines and patients. Through a more comprehensive assessment of national coverage by the preliminary medicines List, it could be used as a national list of essential medicines officially approved by the Federal Minister for Health.

The WHO list contained 448 items. At design of the initial list, 368 items were removed. Deletions included 59 items that were not medicines (e.g., condoms), 37 had other medicines on the list with better-tolerated routes of administration, 136 medicines had the same indication as other listed medicines (e.g., metoclopramide is listed, but ondansetron is not), 52 medicines were used for uncommon indications in Canadian primary care (e.g., the antiparasitic ivermectin), and 84 were medicines used by specialists (e.g., the chemotherapeutic agent vincristine). Twenty-eight medicines were added to the list based on Canadian clinical practice guidelines, systematic reviews, health technology assessment reports and international primary care formularies (e.g., the bisphosphonate alendronate).

Additions, removals and replacements to the list of essential medicines for Canada throughout development.



Ensure transparency and participation in the NEML development and review process

The transparency of the NEML development and review is regulated by the general framework for decision-making transparency. Although the NEML regulation establishes the process of selecting essential medicines by providing a set of specific requirements, including transparency and consultation, this document does not contain a framework to regulate these requirements. According to the current regulation, all participants in the process have the right to express their opinion and practitioners and MoH specialists can be involved. However, the document does not stipulate the minimum period for placing the NEML draft for public discussions and the deadline for submission of proposals following the debates, the routes to facilitate the involvement of

practitioners, patient organizations, the community in the examination of the lists by sending personalized invitation to participate in the debate, including the draft list; the terms of submission of applications and the requirements for the publication of the NEML review announcement notice (period, place of publication, etc.); terms of examination of the applications by the Permanent Commission and publication of decisions, etc.

Analyzing the WHO EML adjustment practice, we note that the standard EML review procedure sets a deadline for submitting the applications; requires to publish the names of the official authorities responsible for the results of the examination of all applications and comments on the official website; appoints the person responsible for verifying the fullness of the data published on the official web site; specifies the role of patient organizations and their involvement, as well as the degree of consideration of the comments /recommendations of these participants in the final decision-making process. As an example of review terms and conditions set out above, we bring some of the WHO procedures applied to the EML review:

"The application should be received at least four months before the meeting of the Expert Committee. The summary of the considerations and other relevant information are posted on the WHO web site and the secretary of the Expert Committee checks the application for completeness. The final results of the evaluation by the Expert Committee are published in the WHO Technical Report Series. Patient advocacy groups and representatives of the health care industry are invited to comment on the applications and draft recommendations."

Approval and frequency of NEML review

The 2007 Ministry of Health order, which approves the NEML regulation, assigns MMDA a number of tasks related to the implementation of NEML which include:

- ensure the access to NEML information by publishing it,
- train and ensure a Permanent Committee to carry out activities on the NEML development, evaluation and update,
- manage changes and additions to NEML.

Once NEML is reviewed, the draft document is examined and approved by the MoHLSP. The regulations in force provide for the revision of the NEML once every two years.

Thus, the normative acts expressly establish the institutions empowered to review and approve the NEML, the frequency of NEML update, the routes of informing the healthcare practitioners and the population about it. Moreover, the MoHLSP order requires the creation of a Commission that will directly manage the process of development and adjustment of NEML.

The study examined the information published by the public authorities responsible for the coordination and implementation of NEML[16] and found that the last NEML review was conducted in March 2011. Compared to the WHO EML editions published on the WHO official website, 3 new WHO EML editions were approved for adults and children from 2011 to 2018. The WHO EMLs are developed separately for different age groups: adults and children.

We find, therefore, that NEML has not been revised since 2011, although the regulation provides for its adjustment and completion every two years, and the WHO has adjusted EML three times during this period. We also noted that the reports on evaluation and inclusion of essential medicines in NEML are not published, nor the results of the Permanent Committee's work on the development, evaluation and updating of NEML.

Dissemination and monitoring of the NEML the implementation

The dissemination of information on NEML should be done through several routes if we rely on the rules contained in the Essential Medicines regulation. In this regard, the regulation specifies the following: publishing in specialized journals, placing on the MoHLSP, MMDA, and "Nicolae Testimitanu" MPSU website. Examining the official webpages of these public authorities, only the official MMDA website contains the NEML from 2011. The official websites do not include previous NEML editions, as is the case with the WHO NEML.

Monitoring the application of NEML in medical and pharmaceutical practices is part of the regulations and procedures of several public institutions responsible for medicine and pharmaceutical sectors coordination, assessment, control, accreditation, and funding from the health care system.

MMDA, as a key institution for the implementation of medicine and pharmaceutical policies, annually presents and publishes on its official website reports on its activity and on the resources and on the pharmaceutical system operation in Moldova (Statistical Yearbook). In the annual MMDA reports for 2008-2017, available on the official webpage, there is not any particular information about the Agency's initiatives and systematic activities aimed at implementing the concept of essential medicines, with some exceptions for the reports from 2009 and 2013. The 2009 MMDA Activity Report mentions the involvement of MMDA in the review of the list of essential medicines, later proposed for MoH approval, as well as in the review of the list of medicines which prices are monitored, the latter being supplemented with medicines belonging to the OTC (over the counter) subgroups and essential ones.

The 2013 MMDA Annual Activity Report contains a list with a series of MMDA objectives part of the Action Plan for 2014, including the specific objective of developing a system for monitoring and evaluating the availability and affordability of vital and essential medicines . Achieving the objective based on the list of essential and life-saving medicines set for 2014 was not reflected in the 2014 MMDA Annual Activity Report, which does not allow us to conclude whether or not a system has been set up to monitor

[16] http://amed.md/ro/list-of-medicine Chapter MEDICINES, subchapter LIST OF ESSENTIAL MEDICINES

and evaluate the affordability and availability of essential and life-saving medicines. At the time of the analysis, no publicly available tools were found on public authorities' websites that would reflect the price analysis of essential medicines and their evolution. Even the MMDA annual activity reports do not contain information on essential medicines price developments and their affordability for consumers. MMDA annual reports do not provide data on the work of the Permanent Commission for the development, evaluation, and updating of the NEML, although according to the provisions of the 2007 MoH Order, MMDA is responsible for the creation of the Permanent Commission.

At the same time, the statistical yearbook on the pharmaceutical system operation for the years 2012-2015, published on the MMDA website, presents more information related to the implementation of NEML, with data with following indicators being reflected:

- The total number of essential medicines registered in the report and the total number of authorized medicines, and the evolution of essential medicines authorized in Moldova compared to the year before the reporting period.
- Analysis of drug registration by groups of countries, including essential medicines manufactured in the Republic of Moldova.
- Determining the rating of the top 10 medicine manufacturers with the highest number of registered products, including the share of essential medicines.
- Analysis of the share of essential medicines registered by the local manufacturers in the total number of essential medicines authorized for marketing in the reporting year.

From the analyzed documents regulating the attribution of responsibilities for coordination and monitoring of NEML implementation, it is noticed that a safe practice of systematic follow up and evaluation is not formed and there is the need for a set of indicators to measure the implementation of the concept of essential medicines. Reporting on Essential Medicines in the Statistical Yearbooks on the pharmaceutical system operation published until 2015, contain a number of indicators mainly related to the authorization of medicines on the national market. At the same time, in order to facilitate the monitoring of the implementation of the list of essential medicines, it is necessary to establish a list of certain indicators for a comprehensive follow-up of this group of medicinal products. Developing a potential list of indicators to follow up the implementation of the list of essential medicines should take into account such aspects as: the existing constraint for essential medicines in accessing the market caused by the lack of marketing authorization or by the lack of price registration in the National Catalogue of ex-factory manufacturer prices for medicines; the share of essential medicines in the list of medicines procured with public funds for the needs of healthcare facilities; the affordability of essential medicines in pharmaceutical facilities of different levels; interruptions in the supply of essential medicines to healthcare facilities, pharmacies and pharmaceutical warehouses; affordability of essential medicines released through community pharmacies for end-consumers, etc.

When examining the legislative framework regarding the health system, among the authorities that monitor the quality of the medical services rendered to the

population there is the National Council for Health Evaluation and Accreditation[17], which recently underwent reorganization and was included in the structure of the National Public Health Agency (NPHA)[18] and the National Medical Insurance Company[19]. The regulations, standards and procedures used by these public authorities have an essential contribution to facilitating and monitoring the use of essential medicines, complementary to the activities directly attributed to MMDA on this component. According to the basic standards in the assessment and accreditation of health care institutions and pharmaceutical companies, a number of quality indicators are used that tangentially cover the subject of essential medicines, such as: the list of hospital indicators for the evaluation of the hospital pharmacy activity includes evaluation of the presence of the list of essential medicines in the range of medicines and medical devices. The results of this evaluation is rated by three criteria: "appropriate", "partially appropriate" and "not appropriate". The list of indicators used within the standard of community-pharmacies accreditation contains an indicator that would monitor the medicine support of the population. According to the title and description of this indicator, it generally refers to the maintenance of a complex assortment of medicines and pharmaceuticals, highlighting the necessity of availability of medicines and medical devices of social importance, according to the legislation in force. In fact, the indicator does not focus on essential medicines.

The list of indicators used at the evaluation and accreditation of Health care facilities and pharmaceutical entities, makes clear that the list of key medicines is taken into account by specialists, especially at the evaluation of hospitals providing in-patient services. However, when evaluating and accrediting the activity of community-pharmacies providing services to ambulatory patients, the indicator measures the list of medicines of social importance. According to the MoH order, issued in the autumn of 2012 and revised in 2016, community pharmacies have the duty to ensure the availability of the medicines that are included in the List of Medicines and Medical Devices of social importance[20]. The term "medicines of social importance" is defined as high-priority

[17] Government Decision no. 526 of 29.04.2002 regarding the National Council for Health Assessment and Accreditation, http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=302751
[18] Government Decision no. 1090 of 18.12.2017 regarding the organization and functioning of the National Public Health Agency, http://lex.justice.md/md/373337/.
[19] Health system review Republic of Moldova, https://www.ecoi.net/en/file/local/1248465/1930_1421316901_hit-moldova.pdf
[20] MS Order no. 959 of 01.10.2012 regarding the access of the population to medicines and medical devices of social importance, http://usmf.md/wp-content/uploads/2013/legi/acces%20la%20medicamente.pdf

medicines that meet the needs of consumers [21]. The total number of medications and medical devices included in the List of medicines and medical devices of social importance 2016, is of 65 and 19 respectively, counted by INN. The review of the list of medicines of social importance, approved by the MoH Order from 2016, includes 43 INNs found in the NEML. 22 INNs from the list of medicines of social importance are not part of the NEML.

The list of social medicines and the list of essential medicines are not replaceable if their current content is taken into account and it is necessary to review the list of indicators for monitoring the availability of essential medicines supply in community pharmacies within the accreditation process.

Indicators for the accreditation of primary care institutions do not reflect the concept of essential medicines. In case of these institutions, the indicators used for the evaluation and accreditation of medicine-based assistance measure the drug-administration errors and reporting of adverse reactions.

The National Health Insurance Company (NHIC) is the public institution responsible for the management of mandatory health insurance funds in accordance with the legislation. One of the goals of NHIC is to control the quality of health care provided and to implement the statutory framework for mandatory health insurance[22]. From the Annual Reports on NHIC activity, there are a number of indicators related to compensated medicines, such as the dynamics of EML adjustment, the share of population claims regarding the access to medicines, the amount of financing of compensated medicines, the number of beneficiaries and prescriptions, etc. In the list of indicators monitored by NHIC, the published data show that access to essential medicines is not monitored within the quality assessment of hospital services. Taking into account the role of essential medicines in ensuring the equity in the access to medicines and in cost optimization, NHIC evaluation of the quality of healthcare services should also include the prescription of essential medicines according to the clinical treatment protocols as well as recording changes in treatment regimen determined by stock-out of essential medicines, as part of list of indicators for evaluation of the implementation of the concept of EMs.

In conclusion to the analysis of Health Evaluation and Accreditation Department of the NPHA and NHIC participation in the monitoring of the implementation of the list of essential medicines, as part of service quality evaluation carried out by the PHCI and the pharmaceutical units, we mention:

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[21] Ministry of Health Order no.765 of 06.10.2016 regarding the amendment of the annex to the Ministry of Health Order no. 959 of October 1, 2012 http://amed.md/sites/default/files/Legislatie/Ordine%20ale%20MS/nr.765%20din%2006.10.2016.PDF

[22] GD no. 156 of 11.02.2002 regarding the approval of the Statute of the National Health Insurance Company http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=295866

- the currently used indicators provide insufficient information for a complex assessment of the provision of essential medicines in hospitals,
- the monitoring of the use of medicines from the NEML is not reflected by the indicators used to measure the evaluation of institutions in the primary health care system and the pharmaceutical units.
- Moreover, the indicators gathered by NPHI and NHIC are not part of a consolidated monitoring system for essential healthcare products that would ultimately facilitate the decision-making.

Key Stakeholders and Responsibilities

According to international practices, the implementation of the concept of essential medicines involves the participation of different actors in the health system. The table below presents a model list of stakeholders from different structures and levels and their responsibilities in implementing the concept of essential medicines in the health system.

Table 1. List of potential actors and stakeholders responsible for the implementation of the concept of essential medicines

Stakeholders	Potential responsibilities
Government	Develop and implement the national medicine policy as part of health policy. Raising the awareness of healthcare professionals and general population on the importance of the list of essential medicines. Facilitate the registration of safety, high – quality and effective medicines by forming or strengthening the capacities of the regulatory authority in the field of medicine.
Pharmaceutical industry	Provide complete and impartial information about medicines to all stakeholders - government institutions, medical and pharmaceutical staff, consumers. Act in accordance with medicine promotion criteria and implementation of ethical code for medicine promotion. Respond to the needs of developing countries through low-cost drug offers. Develop new medicines for rare/neglected diseases with uncovered needs.
Healthcare staff	Rational prescription of medicines in line with patient's health condition and the social and economic criteria of the healthcare services beneficiaries. Provide transparent and safe information on patient's health condition and prescribed medication.

Academic and training institutions	Improve the medical staff training on health management and rational use of medicines. Implement the concept of essential medicines. Ensure continuous education of healthcare providers. Provide health education to population.
Service consumers, patients	Improve the quality and relevance of information to the public. Collaboration with public authorities and NGOs in the education of medicines consumers. Support the program of essential medicines. Request compliance with established advertising criteria for medicinal products and raise awareness of health authorities on suspected violations.
Mass media	Provide relevant and balanced information on health, use of medicines. Educate the population about the rational use of medicines. Facilitate advertising for those who respect ethical criteria.

According to national policy documents, the responsibility for ensuring access to effective, safety and high quality essential medicines for all categories of population is attributed to the Government [23] through the Ministry of Health, Labor and Social Protection and other specialized and/or subordinate public authorities. The specialized public authority responsible for the implementation of medicine and pharmaceutical policies and for the supervision of the medicines and pharmaceuticals quality is the Medicine and Medical Devices Agency, an institution under the authority of the Government[24].

The Law on Medicines establishes that the MoHLSP strategically coordinates the activities in the field of medicine, conducts financial and administrative activities to ensure the monitoring and development of the medicine and pharmaceutical sector in line with the national medicine policy; elaborates and approves normative acts on

[23] Parliament Decision no. 1352 of 03.10.2002 regarding the approval of the State Medicine Policy http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=307874
[24] The Law on Medicines no. 1409 of 17.12.1997 (// -http://lex.justice.md/index php?action=view&view=doc&lang=1&id=311586) (Published OM: 11.06.1998 in the Official Monitor No. 52-53 Art. 368)

medicinal products (class of medicines, standardization, approval, manufacture and registration of medicinal products, including those of vegetable origin)[25].

According to pharmaceutical and medicine legislation, MMDA is the institution that ensures the efficiency and safety of medicines and their compliance with the quality standards. It is clear from the analysis of MMDA competences established by the Law on Medicines that it contributes to the development of the concept of essential medicines in the health system[26]

MMDA regulation, approved by the Government Decision in 2013, as amended, establishes the functions and duties, the rights, the structure and the administration of the institution. The MMDA Regulation provides for a number of Agency's functions associated with the implementation of NEML, such as: to promote and monitor the rational use of medicines; to monitor the market of medicinal products and medical devices and their quality; to coordinate the process of providing the health care system on a continuous and timely basis with efficient, safety, affordable and good quality medicines; monitor and periodically review prices for the medicines on the pharmaceutical market, thereby ensuring its transparency and affordability; provide healthcare specialists with information on the medicines.

In the light of the functions assigned to MMDA, we note that this institution is the key actor in ensuring NEML updating, creating the proper conditions for essential medicines supply by tracking imports, monitoring stocks and prices, analyzing affordability, monitoring the prescriptions and drug consumption and processing of reported indicators. According to the MMDA organizational chart, prior to the last MMDA reform in 2017, the institution had a department that dealt with the issue of rational use of medicines.

The national health, pharmaceutical and medicine legislation regulates the concept of essential medicines through provisions on rational prescription, ethical promotion of medicines, ongoing education and training of specialists in the field and of the general population. In this respect, we can mention the MoH orders with reference to the prescription and release of medications [27], the regulation on the approval of promotional materials, the order on the introduction of the VEN/ABC methodology and the responsibilities of health and education institutions in using this method.

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[25] The Law on Medicines no. 1409 from 17.12.1997 (// -http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=311586) (Published OM: 11.06.1998 in the Official Monitor No. 52-53 Art. 368).

[26] Government Decision no. 71 of 23.01.2013 regarding the approval of the Regulation, structure and stuff of the Medicines and Medical Devices Agency http://lex. justice.md/md/346518

[27] Order no. 960 of 01.10.2012 regarding the prescription and release of medicines http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=345095,

At the same time, the regulatory framework formally addresses the media, consumers, and the pharmaceutical industry's involvement in issues related to the development of NEML.

We conclude that MMDA is the institution designated to ensure the development of NEML and the systematic adjustment of the list using the collected evidence, its implementation and monitoring, identification and analysis of deficiencies and challenges in access to essential medicines.

The scope of NEML and the target groups

The list of essential medicines is not only an instrument that help public healthcare institutions to ensure non-discriminatory access to medicines and their rational use, but also a requirement imposed on private institutions active in health sector. This requirement, valid for institutions in both sectors, public and private, is defined by task no. 5 of the 11 main tasks of the medicine policy.

The analysis of the latest national documents, which approves the NEML, reveals that there are no separate lists of essential medicines per healthcare level, such as: primary care, hospital care, palliative care. Lists of essential medicines are not approved according to the beneficiaries 'age criteria – individually for adults and children. If we look at WHO EML evolution, we find that starting with 2007, WHO introduced separate EMLs for children's needs. Moreover, the WHO EML is composed of two basic and complementary lists. Currently, there is a single list in the national health system and there is not a separate list for children; there are no separate lists for different levels of assistance: primary, hospital, palliative care (the MoH order 144 of 28.02.2011)[28].

According to the same 2007 regulation approved by the MoH as "The List of Essential Medicines", the areas of NEML use are:

- training doctors and pharmacists,
- medicine procurements,
- developing the list of compensated medicines,
- medication donations,
- monitoring the range and prices of medicines,
- public information.

Based on the methodology of this evaluation, the second chapter of the report presents the results of the NEML analysis in some of the above mentioned areas, such as the medicine procurement, the representation in the list of reimbursement medicines.

Determinants on placing and supply of essential medicines on the pharmaceutical market

The availability of medicines in the health system and the insurance of affordability and availability for end-users are conditions determined by a number of

[28] On the amendment of Annex no. 2 to the Ministry of Health Order no. 162 of April 23, 2007 "On the Approval of the Regulation and the List of Essential Medicines" http://amed.md /sites/default/files/Medicamente/Med-te%20esentiale%202011.pdf

factors such as: authorization of medicines, import regulation, pricing policy, medication reimbursement, healthcare and pharmaceutical services, public procurements of medicines, intellectual property in the field of medicines, licensing of activities.

In the next subchapter of the report we will analyze the impact of the factors mentioned above in order to understand the potential positive effects or limitations of different regulations.

Marketing Authorization of medicines and approval the import of pharmaceuticals products

The introduction of essential medicines on the market is generally facilitated by the provisions of the State Medicine Policy (SMP), which sets priorities in the order of authorization of medicines. SMP establishes that the medicines included in the list of essential medicines, as well as the National Pharmacotherapeutical Formulary, approved by the Ministry of Health, are of highest priority in the authorization of medicines. At the same time, the orders and regulations governing the procedure for the authorization of medicinal products in the Republic of Moldova do not provide specific facilities for this group of medicines, such as for the duration of the examination of the application for authorization of the essential medicines, or a priority provision on the order of applications examination.[29] The medicine authorization procedure provides for a shorter evaluation period of the application for the registration of medicinal products, up to 60 days compared to the standard period of up to 210 days, if the medicine are registered by the EMA or by a country of the European Economic Area or Switzerland, USA, Canada, Japan, Australia. Under these circumstances, a simplified registration procedure is applied.

The new draft law on medicine (Article 47. Recognition and rapid procedure), in addition to the recognition procedure, opts for the introduction of a rapid authorization procedure for medicinal products that are non-authorized and which are included in the List of Essential Medicines approved by MoHLSP. The draft law on medicines stipulates a 150 day term for the rapid procedure[30]. According to data collected for the last years, it has been noted that on average, the number of authorized medicines per year is about 830, of which about 40% are essential medicines. The evolution of the share of essential medicines authorized for placing on the market depends both on the characteristics of the pharmaceutical market and on the need to extend the validity of the marketing authorization, taking into account the expiry date of the certificate.

[29] MoH Order no. 739 from 23.07.2012 regarding the Regulation of the authorization of medicinal products for human use and the introduction of post-authorization modifications, published in OM no. 254-262 of 14.12.2012 http://lex.justice.md/md/345886/

[30] http://particip.gov.md/proiecte.php?l=ro&tag=6

Table 2. Analysis of the number of essential medicines authorized for marketing in the period 2015-2017

Year	Number of authorized medicines	Number of essential medicines	The share of essential medicines in the list of authorized medicines for placing on the market
2015	804	344	42%
2016	869	324	37%
2017	951	361	37,96%

In the absence of authorization for some medicines included in the list of essential medicines, it is very important to monitor more actively the availability and affordability of NEML medicines on different criteria in order to reduce the risks of discontinuing the treatment and/or limiting the therapeutic options. Also, it is necessary to introduce legislative provisions that would facilitate the registration, the presence on the pharmaceutical market of products from the list of essential medicines.

Medicines can only be imported if they are authorized in the country. At the same time, the law on pharmaceutical activity, by the provisions of paragraph 7 of art. 11, establishes the conditions for the import, distribution and the use of unauthorized medicinal products in the healthcare practice in the Republic of Moldova. Such situations include cataclysms, catastrophes, epidemics, epizootics, mass poisoning, other cases threatening people's health; the absence of analogues or substitutes on the pharmaceutical market, the need to reduce the costs of public procurement of medicines, parapharmaceuticals and medicinal raw materials unauthorized in the Republic of Moldova, but authorized in the country of origin.

The responsibility for authorizing the import of unregistered medicines belongs to MMDA. Systematic monitoring of NEML through a set of key indicators that would include tracking the share of essential medicines imported as unauthorized based on pharmaco-therapeutical groups would serve as evidence to support proposals and initiatives to ensure access to essential medicines.

Regulation of medicine prices

The Government is responsible to ensure the affordability of medicines and other healthcare products in the country. Pricing policies for medicines have undergone several revisions between 1997 and 2018. At present, medicine price regulations include the registration of producer price, the inclusion of mark-ups. The distributor's margin, as one of the aspects of pricing regulations of medicines, along with the criteria and the method of wholesale and retail price-formation was introduced in 1997[31]. In 2015, the regulation

[31] Government Decision no. 603 of 02.07.1997 on the approval of the Regulation on the pricing of medicines and pharmaceutical and parapharmaceutical products. http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=296542

on distributors' margins is revised by introducing a differential regressive margin of 5-tier mark-ups[32]. The end-price of medicines may be marked up at most as much as 40% to the manufacturers' delivery price or the procurement price and if the price according to the National Catalogue of ex-factory manufacturer prices for medicines is up to 30 lei (of which the cumulative wholesale mark-up for both local and imported products is 15%, and up to 25% for retail mark-ups), the minimum distributors' margin should be of up to 16% (of which 5% - wholesale mark-ups and 11% - retail mark-ups). This trade-related regulation does not provide for special requirements for medicinal products included in the NEML.

At the same time, the normative framework sets out special regulations for medicines included in the list of reimbursed ones, stipulating by law the obligation of the National Health Insurance Company to negotiate the value of the mark-ups with the pharmacies at signing the agreements for delivery of the compensated medicines but which will not exceed the limits established by the 5-tier distribution margin. According to the regulations, the negotiation of the mark-ups by the National Health Insurance Company and the community pharmacies can be done based on a mechanism established by the Government. Following the plan, the access to reimbursed medicines will be analyzed in detail in the context of the second objective of this project, detailing the functioning of the mechanism for negotiating the mark-ups between NHIC and community pharmacies.

The aforementioned documents regulate prices for all types of medicines , with no exceptions for essential medicines.

Another regulation of the prices of medicines is the registration of the producer price of medicines, approved in 2010 by the Government of the Republic of Moldova, which does not provide facilities for the essential medicines[33].

The content of this regulation is based on the analysis and use of the external reference price in a number of countries selected as a benchmark for country assessment of the producer price to be recorded in the National Catalogue of ex-factory manufacturer prices for medicines.

If the medicines are not registered in the National Catalogue of ex-factory manufacturer prices for medicines, they cannot be imported into the country. Exceptions to this provision are medicinal products imported under the special conditions regulated by Article 11 (7) of the Law on Pharmaceutical Activity.

According to the law, if the price of essential medicines is not registered in the National Catalogue of ex-factory manufacturer prices for medicines, the medicines cannot be imported into the country. Accordingly, these medicines cannot be included in the

[32] Law no. 1456 of 25.05.1993 on pharmaceutical activity no. 1456 of 1993 http://lex.justice.md/index.php?action=view&view=doc&id=313276

[33] Government Decision no. 525 of 22.06.2010 on the approval of the Regulation on the method of approval and registration of producer prices for medicines, http://lex.justice.md/md/334986/.

public procurement list and distributed to hospitals and cannot be found in community pharmacies even if they are authorized for placing on the pharmaceutical market. Thus, the regulation imposing price registration in the National Catalogue of ex-factory manufacturer prices for medicines might be one of the impediments to placing a certain item on the list of centralized public procurements, if the marketing authorization is mandatory.

When comparing NEML with the list of medicines registered in the National Catalogue of ex-factory manufacturer prices for medicines, it was found that out of 875 medicines (INN + dose + pharmaceutical form) only 375 (42,857%) are registered in the Catalogue. The distribution of these medicines according to the pharmacotherapeutic groups is as follows:

Table 3. The registration of the essential medicines prices in the National Catalogue of ex-factory manufacturer prices for medicines

Section	Therapeutic group	Medicine from the NEML (total positions), 2011	Authorized prices, # medicine (positions) Year 2018 (first semester)
1	**Anesthetics**	29	13
2	**Analgesics, antipyretics, anti-inflammatory, non-steroidal, anti-gout, anti-rheumatic**	53	35
3	**Antiallergics medicines used in anaphylaxis**	22	11
4	**Antidotes and other preparations used in poisoning**	17	4
5	**Anticonvulsants/Antiepileptics**	25	7
6.	**Anti-infectives**		
6.1	Anthelmintics		
6.2	Antibacterials		
6.2.4	TB medicines	235	84
6.3	Antifungal medicines		
6.4	Antivirals		
6.5	Antiprotozoal medicines		
7	**Antimigraine medication. Cerebral hemodynamic and metabolic medicines**	20	15
8	**Antineoplastic, immunosuppressive medicines**	65	31
9	**Antiparkinsonism medicines**	5	2
10	**Medicines affecting blood**	32	19
11	**Blood products and plasma substitutes**	3	0
12	**Cardiovascular medicines**	59	36
13	**Dermatological medicines**	25	6
14	**Diagnostic agents**	7	4
15	**Disinfectants and antiseptics**	5	1

16	**Diuretics and medication for prostate disorders**	14	7
17	**Gastrointestinal medicines**	42	24
18	**Hormonal, endocrine medication and contraceptives**	40	21
19	**Immunological medicines/Vaccines**	32	3
20	**Muscle relaxants**	7	3
21	**Ophthalmology**	18	6
22	**Ocytocic**	9	3
23	**Dialysis medications**	1	0
24	**Psychotropic**	26	11
25	**Respiratory system medications**	22	15
26	**Medicines used in hydroelectrolytic equilibrium disruptions**	9	1
27	**Vitamins and minerals**	27	11
28	**Ear nose throat for children**	4	2
29	**Newborns**	4	0
30	**Varia**	0	0
	Total	**857**	**375**

Another factor that influences the final cost of medicine is the value-added tax (VAT). In Moldova, the VAT on medicines is of 8% and was introduced in 2006. The analysis of international practices on the application of VAT on medicines reveals different approaches. For example, in European countries the VAT varies from 0 to 25%. According to the WHO publication, countries like Malta and Cyprus have zero VAT on medicines; countries with up to 8% VAT on medicines are Turkey (8%), Poland (7%), Belgium, Netherlands and Portugal (6%), Lithuania and Hungary (5%), Spain (4%), Luxembourg (3%), Switzerland (2.4%), France (2.1%). Some countries in Europe also apply differentiated VAT to medicines. For example, in France the VAT on reimbursed medicines is of 2.1% and of 5.5% for non-reimbursed medicines; Lithuania has set 5% VAT for reimbursed and 21% for OTC; Cyprus - zero VAT on medicines and 15% on diagnostic products, Sweden set 25% VAT for medicines, except for prescription medicines for which the VAT is zero; Romania applies 9% VAT on prescribed medicines and 12% VAT - on OTC medicines[34].

According to WHO recommendations, in order to increase end-user access to essential medicines, it is necessary to grant VAT exemption or facilitation for this group of medicines[35].

Another government initiative to increase access to medicines, announced in the autumn of 2016, was to establish a list of 160 brand names (65 INNs) qualified as socially

[34]WHO Guideline on Country Pharmaceutical Pricing Policies
http://apps.who.int/medicinedocs/documents/s21016en/s21016en.pdf
[35] WHO guideline on country pharmaceutical pricing policies.
http://apps.who.int/medicinedocs/documents/s21016en/s21016en.pdf

important medicines for which it was proposed to reduce the price by 40 %. The price reduction initiative is based on the outcome of negotiations between the Government and pharmacy networks. The selection of medicines in the list of socially important medicines is based on the criteria of the most needed and most commonly used pharmaceuticals by citizens. Such an initiative was approved by the Ministry of Health in 2012 by introducing a list of medicines and devices of social importance that should be available in community pharmacies[36]. However, after the introduction of the list of socially important medicines, there haven't been any evaluation reports in terms of affordability and availability of medicines in rural and urban pharmacies, and the continuity of this model.

Some drug prices indicators included in the MMDA annual report and the Statistical Yearbook are the following: the price index showing the evolution of retail prices per year and per month for a pre-established list of medicines, the share of producer prices registered in the National Catalogue of ex-factory manufacturer prices for medicines by geographical area[37].

An initiative introduced in MMDA activity plan for 2018 and mentioned in the MMDA reports is to modify the regulatory framework by establishing the maximum wholesale and retail prices and informing the population on the price ceiling of pharmaceuticals on the market[38].

However, the annual reports and analyzes published by MMDA do not provide comprehensive information on price monitoring indicators and do not provide separate data on price developments for the essential medicines group. The "Price Index" indicator is calculated according to the data collected on the basis of a predetermined list of medicines, but this list is not publicly available in the MMDA reports or on their official website to track the share of NEML items included in the list of monitored medicines by price index and the evolution of this index for essential medicines. Moreover, the analysis of the impact of medicine price regulation should be more comprehensive by examining not only the evolution of prices according to the price index or the consolidated analysis for the whole price catalog, but also the changes in the contribution by out of pocket payments, as well as the availability of medicines on the pharmaceutical market, and their affordability for consumers, etc.

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[36] MoH Order regarding the access of the population to medicines and medical devices of social importance no. 959 of 01.10.2012, http://usmf.md/wpcontent/uploads/2013/legi/ acces%20la 20medicamente.pdf

[37]Activity Report 2016 http://amed.md/sites/default/files/Despre%20Agentie/Raport%20%20AMDM%202016%20general.pdf

[38] Activity Report 2017 http://amed.md/sites/default/files/Despre%20Agentie/Raport%20pe%20activitate%20AMDM%202017.pdf

Public Procurement of Medicines

Medicines account for an essential share of spending incurred by Healthcare facilities. Currently, the pharmaceutical market operates with an impressive number of medicine names, and the selection and formation of a list of essential medicines is one of the most cost-efficient actions to ensure the ongoing supply and rational use of medicines. Under a limited budget, focusing on a list of key medicines makes it easier to use funds wisely and meet the real needs of the population. Also, reducing the list of medicines will simplify other processes of the supply system such as storing, inventorying and record keeping.

In the Republic of Moldova, the public procurement of medicines and medical devices is carried out at the central level. The centralized public procurement of medicines and medical devices for the health system was driven by the need to improve the procurement practice of these products, to streamline the use of public money, and to ensure that medicines are procured at standards that meet the needs of public health care institutions[39].

In 2016, the last adjustments and additions to centralized procurement of medicines and medical devices were approved and introduced. Between 2005 and 2016, procurement procedures for medicines and supplies for the health care system were carried out on centralized basis by MMDA, and since 2017 this function has been taken over by the Center for Centralized Public Procurement in Health (CCPPH).

The Center for Centralized Public Procurement in Health (CCPPH) - the central authority for the procurement of health products - was established by the Government Decision no.1128 of 10.10.2016. The Government Decision approved the CCPPH operating regulation, the instruction for the procurement of medicines, other medical products and medical devices for the health system and the fees for public healthcare procurement.

The approved regulations stipulate the following competencies for CCPPH: planning and carrying out procedures for procurement of medicines, other medical products and medical devices; awarding of public procurement contracts, evaluation and supervision of healthcare goods procurement from the national and local budgets, public institution and mandatory health insurance funds and from external loans in proportion to direct or guaranteed state debts. Healthcare institutions are responsible for determining the needs for medicines and medical devices to be procured from public money. In case of national and special programs, the needs are determined by specialized committees in collaboration with MoHLSP specialists.

[39] Government Decision no. 1128 of 10.10.2016 regarding the Center for centralized public procurement in health, Official Monitor no.353-354 / 1210 of 11.10.2016

Under the procedures in force, the Healthcare facilities with the help of Pharmacotherapeutical Committees and the Procurement Group within HCI, develops the list of needs to ensure the functionality of the sanitary institution. The variables that influence the formulation of the list of medicines for procurement are[40]:

- Institutional Pharmacotherapeutical Formulary.
- National Clinical Protocols approved by MoHLSP.
- Morbidity.
- Required quantity per patient.
- Available stocks of medicines.
- The planned budget for this group of products.
- Marketing authorization status of the medicine in Moldova.

In order to understand the practical application of the provisions by which essential medicines gain priority, this review examined the list of medicines for centralized procurement for the years 2015-2017, officially published on the website of the institution responsible for centralized procurement of medicines and medical devices. The results of NEML and public procurements list compliance evaluation reveal that essential medicines account for 49% of the total list of public procurements of medicines. This fact was also noted in the study on medicines availability and affordability conducted with WHO support in 2011, showing that the share of essential medicines in the list of centralized medicine procurement is of 40% [41]. The nearly 10% increase in the share of essential medicines in the general list of medicines procured from public money over the last 6 years since WHO assessment is praiseworthy, but this share has not reached majority and is only 49%. The trend of growth indicates that the list of essential medicines is used to select medicines to meet the needs of the HCI and ensure the quality of medical services, but they still do not form the majority.

The analysis of the current practices of public procurements of medicines based on NEML, reveals deficiencies in developing and prioritizing the list of medicines for public procurements in relation to available budget. As a consequence, conditions that impair the quality of medicine provision to HCI are created. One way to improve the practices of need assessment and amount estimation would be to apply the VEN/ABC methodology as an effective tool for prioritizing and optimizing spending on medicines. This tool was approved by the WHO in January 2012[42]. However, the results of the evaluation of the lists of essential medicines procured over the last three years show that

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[40] Regulation on the procurement of medicines, other medical products, medical devices, specialized medical transport, maintenance services for medical devices and information systems included in the Medical Register, medical waste treatment and disposal services for the needs of the health system, Annex no. 3 to the Government Decision no.1128 of 10 October 2016http://lex.justice.md/md/367038/

[41] Availability and Affordability of Medicines and Assessment of Quality Systems for Prescription of Medicines in the Republic of Moldova (2012;), WHO, http://apps.who.int/medicinedocs /documents/s20000en/s20000en.pdf

[42] MoH Order no. 68 of 30/01/2012 regarding the implementation of the VEN/ABC analysis

the VEN /ABC tool for medicines needs and quantity assessment, approved in 2012 by MoH, is not used in practice.

The VEN system determines the priorities for selection, procurement and use according to the potential health impact of each medicine.

VEN relates each medicine included in the pharmacotherapeutical formulary or the list of essential medicines to one of the 3 groups:

Group V (vital) - includes life-saving medications, the unavailability of which can cause serious health consequences and/or impair illness prevention, or are crucial for the provision of basic health services. The absence of these medicines on the pharmaceutical market is inadmissible.

Group E (essential) - Essential medicines are those used in the treatment of less severe diseases, but which are prescribed for the most prevalent illnesses in the general population. This group is not absolutely vital for providing basic health care.

Group N (non-essential) - medicines defined as non-essential are not included in the previous two groups: V or E, are prescribed for treatment of insignificant diseases (self-medicating) or medications of minor importance but very expensive and with limited effect.
Being qualified as non-essential does not imply that these medicines may no longer be included in pharmacotherapeutical formulary or essential medicines list. In many cases, these medicines for minor illnesses and symptoms that do not require the doctor's consultation are part of the list of essential medicines, but they are given less attention in the procurement process. Grouping of medicines by VEN is a dynamic process that requires regular revisions and adjustments.

The ABC system is a tool for selection, procurement, distribution management and promotion of the rational use of medicines.
This system is based on the examination of information on annual consumption of medicines and the costs involved in procuring them and classify the medicines into 3 groups based on the medicine expenses incurred by HCI:

Group A includes 10 to 20% of the medicines nomenclature, for which approximately 70-80% of the financial resources are spent;

Group B includes 10-20% of the medicines nomenclature and expenditures amounting to 15-20% of the total financial resources;

Group C includes 60-80% of the medicines nomenclature with a total cumulative cost of about 5-10%.

Source: http://apps.who.int/medicinedocs/documents/s19617en/s19617en.pdf

A detailed presentation of the NEML reflection in the list of medicines procured on a centralized basis is presented in Part II of this study.

Reimbursement of medicines

In 2015, the MoH reviewed and approved changes to the mechanism of inclusion of medicines for reimbursement from Mandatory Health Insurance Funds [43]. The MoH reviewed and approved changes to the mechanism of inclusion of medicines in the list of reimbursed medicines; assigned the entity responsible for inclusion/deletion of medicines in/from the list of reimbursed ones - the Council for inclusion/deletion of compensated medicines from the mandatory health insurance funds; the Council Secretariat (hereinafter referred to as the Council) is responsible for data processing and submission of proposals for the list of compensated medicines; the methodology for calculating the fixed reimbursement amount for the medicines included in the List of Reimbursed Medicines procured from the Mandatory Health Insurance Funds and other aspects of the organization and functioning of the Council and the Secretariat. In 2017, by common order of MoHLSP and NHIC the nominal composition of the Council of Reimbursed Medicines and of the Council Secretariat (order No. 1063/639-A of 27.12.2017) was approved[44]. Thus, the 2017 order makes amendments only to 2 annexes of order no. 600/320 of 24.07.2015 and these refer to the change of the name of the Council and the Council Secretariat and to their composition.

By virtue of the specific objectives set forth by this study, the team of experts focused on the use of the concept of essential medicines in the practice of medicine compensation. Comprehensive evaluation of the mechanism for inclusion/deletion of medicines in/from the list of compensated medicines is the objective of the second stage of the operational research. In the context of Objective 1 of the review of the regulation on the inclusion/deletion of compensated medicines in/from the list of medicines covered by Mandatory Health Insurance Funds, it was noted that the List of Essential Medicines is a key indicator in determining the priorities for reimbursement of medicines from Mandatory Health Insurance Funds along with other indicators, such as National Clinical Protocols and Standard Medical Guidelines. The regulation also specifies other requirements that influence the decision on inclusion of medicines in the list of compensated ones, as:

- Medicines should be authorized in Moldova.
- Medicines should be registered in the National Catalogue of ex-factory manufacturer prices for medicines.

Moreover, the principles of inclusion of new products in the List of Reimbursed Medicines are largely common with the principles for selection of medicines for the list of essential medicines approved by the MoH, and are as follows:

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[43] Ministry of Health Order no. 600/320 of 24.07.2015 regarding the mechanism of inclusion of medicines in the system of compensation from mandatory health insurance funds, Official Monitor no. 247-252 art no: 1629 of 04.09.2015, http://lex.justice.md/viewdoc.php?action =view&view=doc&id=366925&lang=1

[44] Order of the MoHLSP and NHIC no. 1063/639-A of 27/12/2017 „ On approval of the nominal composition of the Council for Compensated Medicines and of the Council Secretariat. http://www.cnam.md/httpdocs/editorDir/file/Legislatie/ordine/2018/639-A%20-%201069%20din%2027_12_17%20cons_med_comp_.pdf

- Efficiency evaluation based on scientific evidence.
- Systematic review of results published in scientific literature for the collection of evidence.
- The number of patients requiring treatment for one efficiency unit.
- Medicine safety.
- Pharmacoeconomic assessment.

Another order of the MoH with regard to the compensated medicines covered mandatory health insurance funds, which approves the List of Reimbursed Medicines, the prescription form and the prescription instruction for the reimbursed medicines from the Mandatory Health Insurance Funds, stipulates the responsibilities of MoH and NHIC in informing about the way of reimbursement, the periodicity of the revision of the List of Reimbursed Medicines; MMDA responsibilities for informing NHIC about authorized medicinal products to be placed on the market, the registration in the National Catalogue of ex-factory manufacturer prices for medicines, the list of trade names for INNs included in the List of Reimbursed Medicines.[45].

Thus, the common criteria for selecting essential and reimbursed medicines are: efficiency, safety, cost-effectiveness, morbidity. As a result, these two procedures can support each other through exchange of experience and practice.

Intellectual property

A key factor in ensuring access to medicines is intellectual property law. In February 2017, amendments were approved to the law on pharmaceutical activity, which introduced the legal norm on data protection and the protection of pharmaceuticals marketing. This rule states that holders of an original medicinal product, authorized for marketing,will be granted a period of 5 years from the date of authorization and an additional period of 2 years of protection for the placing on the market of the medicinal product concerned. If during the period of tests and studies data protection, the holder of the marketing authorization obtains an authorization for one or more new therapeutic indication of this very product, which was scientifically proved, prior to the authorization of the medicinal product, to provide significant clinical benefits compared to existing therapies, the 2-year protection period for placing on the market may be extended to a maximum of 3 years. As shown by previous studies of the Center for Health Policies and Studies[46] and by international sources, the impact of preclinical tests and clinical studies data protection on access to generic medicines/generics is considerable. As a result, there is an increase in medication costs determined by the fact that only the original medicine is on the pharmaceutical market. The recent change introduced in the

[45] Order no. 492/139 of 22.04.2013 regarding the Medicines compensated from Mandatory Health Insurance Funds
[46] Negative impact of data exclusivity to medicines access http://pas.md/ro/PAS/Studies/Details/11

Pharmaceutical Law on preclinical testing and clinical studies data protection may be a potential barrier to essential medicines if this list will include patented molecules[47].

CHAPTER II. ANALYSIS OF THE NATIONAL LIST OF ESSENTIAL MEDICINES: ALIGNMENT TO THE WHO ESSENTIAL MEDICINES LIST, REPRESENTATION IN THE LIST OF CENTRALIZED PUBLIC PROCUREMENTS AND IN THE LIST OF REIMBURSED MEDICINES

The structure of the NEML is based the WHO EML model and is subdivided into chapters that are classified according to the farmacoterapeutic groups. Medicines are written by their generic name or international common name (INN). The NEML evaluation provides a comparative analysis with the WHO Essential Medicine List, in order to identify gaps and align this list and the mechanisms of development and review to the most recent WHO documents.

Method of Analysis:

For the quantitative analysis of NEML approved in Moldova, an observational, descriptive study was carried out. The paper copy of NEML 2011 was transferred into a Microsoft Excel document to facilitate the process of evaluation according to the following parameters: presence by INN and pharmaceutical form; the authorized/unauthorized status of the molecule; use in pediatrics; inclusion in the List of Compensated Medicines, etc.

NEML has been evaluated for quantitative changes taking into consideration the number and ratio of molecules, pharmaceutical forms, drug additions and deletions in the process of NEML development, review and adjustment of.

EMLs from 1996, 2007, 2009, 2011 were used in the study comparing the latest approved NEML and the WHO EML of 2017. Medicines (molecules or compounds) that were not found in the NEML, but were present in the last edition of the WHO EML were considered absent and recorded in a separate table. The term "molecule" refers to the generic name or INN of a drug. Analysis of changes in NEML was made by comparing updated versions of the NEML of 1996, 2007, 2009, 2011. The NEML approved in 2009 was not found on the official pages of the country public authorities, thus the source used was the list published on the WHO webpage under the Republic of Moldova profile. A new occurrence of a molecule in the updated version was considered an ''addition'' to the list, while the omission of a molecule from a later version was considered a ''deletion''. Duplicates are molecules listed multiple times in the same list within different sections for different therapeutic groups. The list of molecules for each NEML was analyzed by marking and identifies a molecule that appears multiple times in the same list. As a result, the number of duplicate molecules that reoccur in the list was counted. This number of duplicates was deduced from the total number of molecules in NEML to get the number

[47] Intellectual Property Rights and Access to Medicines: A South-East Asia perspective on global issues http://www.searo.who.int/entity/intellectual_property/trh.pdf
http://law.haifa.ac.il/images/documents/BenolielChirwa.pdf

of unique molecules. The WHO EML model is structured according to the pharmaco-therapeutic classification. NEML has been developed by classifying the medications based on their therapeutic group starting with the 2007 edition.

The results of the NEML analysis

The first NEML (1996) contained 108 molecules, including duplicates (or 106 molecules, excluding duplicates). The latest 2011 NEML contains 635 molecules (or 576 molecules, excluding duplicates). In this regard, an increase in the total number of molecules has been noted when comparing the NEML of 1996 and NEML of 2011, with 527 molecules including duplicates or 470 molecules, excluding duplicates. The quantitative changes in the compositional of the NEML are presented in Table 4.[48]

Table 4. Evolution of the number of molecules in the NEML, 1996-2011

Year	WHO EML	NEML (molecule)
1977	204	-
1979	235	-
1983	243	-
1985	263	-
1988	280	-
1990	293	-
1992	300	-
1995	301	-
1996	-	108
1997	310	-
1998	317	-
2000	322	-
2002	341	-
2003	331	
2005	319	-
2007	337 (main list)	504
2009	352 (main list)	578[49]
2011	358 (main list)	635
2013	374	-
2015	414	
2017	532	

The data included in Table 5 indicates that after three updates of the NEML there has been a considerable increase in the number of molecules, including the increase in the share of pharmaceutical forms per molecule, the numerical completion of the

[48] The source for analyzing the evolution of the number of molecules in the WHO EML is the study "Report of the Core-Committee for revision of National List of Essential Medicines", http://cdsco.nic.in/WriteReadData/NLEM-2015/Recommendations.pdf

[49] NLEM 2009/WHO website, http://www.who.int/selection_medicines/country_lists/mda_2009.pdf?ua=1

pharmaceutical forms and the doses per molecule. This confirms the development of the therapeutically qualified options as essential and their inclusion in the NEML to ensure the quality of medical services. Also starting with the list approved in 2007, there is a change in the NEML structure that is now grouped by therapeutic classes.

Table 5. Quantitative evolution of the NEML by molecules and molecules + pharmaceutical forms

Year of NEML approval	Total number of molecules (excluding duplicates)	Total number of molecules (including duplicates)	Total number of pharmaceutical forms	Rate of pharmaceutical form per molecule	Total number of therapeutic categories
1996	106	108	147	1,36	0
2007	475	504	718	1,42	29
2009	519	578	819	1,41	27
2011	576	635	856	1,34	29

The analysis of the NEML of 2007 and 2011, which have the same medicine grouping system, reveals that the number of medicines in some sections has expanded considerably during this time. The most obvious addition was noted for the following groups: antiprotozoal products (ratio of 3.66); antimigraine medication, medicines to regulate cerebral hemodynamics and cerebral metabolism (ratio 2), antiparkinsonian (ratio 1.66); antiviral (ratio 1.65); antiallergic medicines used in anaphylaxis (ratio 1.44); antidotes and other preparations used in poisoning (ratio 1.36). Simultaneously there have been noticed substantial reductions in the ratio for diagnostic agents (ratio 0.3), dialysis preparations (ratio 0.5). Following the NEML revisions in 2007, the following sections were completed:

- antiprotozoic - with 24 molecules,
- cardiovascular medicines - with 23 molecules,
- immunological / vaccines - with 14 molecules,
- hormonal, endocrine, other contraceptive medication - with 16 molecules,
- dermatological medicines - with 13 molecules,
- gastrointestinal disease medication - with 12 molecules,
- antivirals - with 11 molecules,
- anesthetics - with 8 molecules.

At the same time, molecules in the following sections were excluded from the NEML of 2007:

- diagnostic agents - 21,
- cardiovascular medicines - 16,
- hormonal medication, endocrine, other contraceptives - 12,
- anti-neoplastic, immunosuppressive, palliative medication - 11,
- products obtained from blood and plasma substitutes - 10.

- For the 2011 NEML the most remarkable change was incurred by 17 positions, exclusions from the diagnostic agents' section (21 positions), antineoplastic, immunosuppressive, palliative medication - 8 excluded positions. At the same time, the completions registered in 2011 concerned the following sections: ophthalmic - 13, immunological/vaccines - 12, antiviral - 11, antiprotozoic - 9, dermatological (topical) medicines - 8 molecules.
- The data in Table 6 reflects the evolution of the number of molecules in the NEML of 1996, 2007, 2009, 2011, considerable changes being revealed for certain pharmacotherapeutic groups, which registered a significant increase in the number of molecules. These changes cover sections that include antiprotozoal products (ratio 3.66); antimigraine medication, medicines to regulate cerebral hemodynamics and brain metabolism (ratio 2), antiparkinsonian (ratio 1.66); antivirals (ratio 1.65); antiallergics used in anaphylaxis (ratio 1.44); antidotes and other preparations used in poisoning (ratio 1.36).
- There was a substantial decrease in the ratio for diagnostic agents (ratio 0.3) and dialysis preparations (ratio 0.5)
- As mentioned above, the NEML is structured by therapeutic groups, but medicine classification does not coincide in all cases with WHO EML. For example: The WHO EML of 2017 contains the group of "Medicines for pain and palliative care", while in the NEML such a pharmacotherapetuic group is missing. In WHO EML of 2017, the group "Medicines for pain and palliative care" contains 22 INNs, which represent 46 pharmaceutical forms, 13 of which are liquid oral and suppository (pediatric) doses that can be administered to children. In the NEML of 2011, while such a group is missing, most INNs are found under other classification, such as:

  1. Anesthetics - 1.3. Preoperative medication and short-term sedation
  2.1. Non-opioid analgesics and non-steroidal anti-inflammatory medicines;
  5. Anticonvulsants/antiepileptics
  7. Antimigraine medication, medicines to regulate cerebral hemodynamics and brain metabolism - 7.1 Attack treatment,
  10.2 Medicines that affects clotting
  12.5 Antithrombotics,
  17.2 Antiemetics
  17.5.3 Antidiarrheal medication for adults
  24. Psychotropic preparations, 24.5 Medicines used in substance dependence programs
- However, the NEML of 2011 does not contain 17 pharmaceutical forms of the 46 pharmaceutical forms included in the WHO EML of 2017.

Table 6. NEML evolution 1996, 2007, 2011 by number of molecules, including additions and deletions in the period of 2007-2011.

Section	Therapeutic class	NEML 1996	D*	A**	NEML 2007	D	A	NEML 2009	NEML 2011	Report	Net modifications
1	Anesthetics	7	0	9	16	1	8	25	22	1.44	7
2	Analgesics, antipyretics non-steroidal, anti-inflammatory, anti-rheumatic	5	3	25	27	5	7	31	29	1,06	2
3	Antiallergic medicines used in anaphylaxis				9	0	4	9	13	1.44	4
4	Antidotes and other preparations used in poisoning				11	0	4	14	15	1.36	4
5	Anticonvulsants/Antiepileptics	6	0	4	10	0	1	10	11	1.1	1
6.	Anti-infectives	23						110			
6.1	Anthelmintics				6	0	6	6	12	2	6
6.2	Antibacterials	16	2	25	39	0	7	42	46	1.25	7
6.2.4	TB medicines	4	0	10	14	0	7	14	21	1.5	7
6.3	Antifungal medicines	3	0	5	8	0	3	7	11	1.4	3
6.4	Antivirals				17	0	11	22	27	1.65	11
6.5	Antiprotozoal medicines				9	0	24	11	33	3.66	9
7	Antimigraine medication, cerebral hemodynamic and metabolic medicines				7	3	10	8	14	2	7
8	Anti-neoplastic, immunosuppressive medication				57	11	3	62	49	0.85	-8
9	Antiparkinsonien				3	0	2	4	5	1,66	2
10	Blood disease medicines				17	4	3	16	16	0,94	-1
11	Blood products and plasma substitutes				13	10	3	15	6	0.46	-7
12	Cardiovascular medicines	19	6	29	42	16	23	51	49	1.16	7
13	(Topical) dermatological medicines	3	2	19	20	5	13	19	28	1.4	8
14	Diagnostic agents				25	21	4	24	8	0.3	-17
15	Disinfectants and antiseptics				0	0	6	-	6	0	6
16	Diuretics and medication for prostate disorders				8	1	4	7	11	1,37	3
17.1	Medication for gastrointestinal	12	5	15	19	4	12	26	27+ 4	1.4	8

	disorders										
17.2	Anti-diarrheal medicine	4	4	3	3	2	3	1	1	1.33	1
18	Hormonal, endocrine medication, other contraceptives	3	0	29	32	12	16	36	36	1,12	4
19	Immunological medicines/Vaccines				14	2	14	14	26	1,85	12
20	Muscle relaxants				5	0	2	7	7	1.4	5
21	Ophthalmology				14	1	6	15	19	1.35	13
22	Ocytocic				6	3	7	7	11	1.66	4
23	Dialysis medications				2	0	0	2	1	0,5	0
24	Psychotropic				14	0	8	19	22	1,57	8
25	Respiratory system medications				17	3	2	20	16	0,94	-1
26	Medicines used in hydroelectrolytic equilibrium disruptions				6	2	3	7	7	1,16	1
27	Vitamins and minerals				14	3	8	15	19	1,35	5
28	Ear nose throat for children							-	4		
29	Newborns							-	4		
30	Bisphosphonates	3						3			
Total		**108**			**504**	**109**	**234**	**569**	**635**		

Note: D -deleted; A- addition.

Comparative analyzes of NEML 2011 and WHO EML 2017

The comparative examination of WHO EML of 2017 and the most recent approved version of NEML published in 2011, aims to determine the differences between the molecules found in the WHO list of 2017 and missing in the NEML of 2011 or not included under a specific therapeutic group, the analysis being performed on each individual therapeutic group.

The study reveals a partial inconsistency in the classification by therapeutic groups, which made the comparative analysis more difficult, for example **Medicines for pain and palliative care** are not found in NEML of 2011, respectively all the medicines that are part of this group are not present in this section. At the same time, medications that refer to the non-existing group in the 2011 edition can be found under other therapeutic groups, for example: *dexamethasone* is included in the NEML, but under section **8. Antineoplastic, immunosuppressive, palliative medication;** *lactulose* **- 17. Medicines for gastrointestinal diseases, etc.**

At the same time, the NEML 2011 therapeutic category **2. Analgesics, antipyretics, nonsteroidal anti-inflammatory medicines, antigout and antirheumatic medicinal products** includes a number of other medicines not found in the WHO EML under this therapeutic group.

The comparative analysis has determined that the largest number of medicines that are missing in the NEML 2011 compared to WHO EML are those in the following categories: antidotes and other preparations used in intoxications (5), antiviral (15), antiprotozoic (5) hormonal, endocrine, other contraceptives (5) immunological/vaccines (3). In total, 94 medicines (67 basic and 27 complementary) were omitted or not included in the analogue pharmacotherapy groups.

Comparative analysis of the NEML 2011 (635 molecules) with the WHO EML 2017 (532 molecules) reveals that 337 molecules are common to both lists (Table 7). At the same time, we have noted that 152 new molecules were included in the latest edition of the WHO list. It was also found that 263 molecules from the 2011 edition of the NEML of RM are not found in the WHO EML of 2017. By this comparison study we pointed out that the deficiencies in the functioning of the review and completion mechanism according to the frequency regulated by the normative framework lead to NEML content differences in relation to WHO EML. The delay in reviewing and adjusting NEML in accordance with WHO recommendations could influence the selection of medication for supply and the quality of medical services. The level of influence on the quality of medical services in the context of the changes that have been made in the latest editions of the WHO's list of essential medicines versus the NEML of the Republic of Moldova can only be understood by an additional analysis on the rational use of the medicines in terms of the list of essential medicines, the Pharmacotherapeutical Formulary and the national clinical protocols. The study did not analyze the relevance of inclusion of 152 molecules into the NEML or the exclusion of 263 molecules from the WHO EML, but present in the 2011 edition of the NEML because such an analysis requires separate research with the application of NEML criteria and analysis tools established in the country through the MoH order and those recognized at the international level, with the involvement of clinicians, economists, pharmacists.

Table 7. Comparative analysis of NEML 2011 and the WHO EML 2017 by the number of included molecules

Section	Therapeutic classs	Total NEML 2011	Deletions from WHO EML 2017	Additions to the WHO EML 2017	Total, EML/ WHO 2017	Shared molecules
1	Anesthetics	22	10	2	14	12
2	Analgesics, antipyretics, non-steroidal, anti-inflammatory, anti-rheumatic	29	23	16	22	6
3	Antiallergic medicines used in anaphylaxis	13	8	0	5	5
4	Antidotes and other preparations used in poisoning	15	6	6	15	9
5	Anticonvulsants/Antiepileptics	11	3	3	11	8
6.	Anti-infectives					
6.1	Anthelmintics	12	1	2	13	11
6.2	Antibacterials	46	0	0	38	
6.2.4	TB medicines	21	5	8	24	16
6.3	Antifungal medicines	11	4	2	9	7
6.4	Antivirals	27	14	23	37	14
6.5	Antiprotozoal medicines	33	3	6	36	30
7	Antimigraine medication, cerebral hemodynamic and metabolic medicines	14	10	0	4	4
8	Anti-neoplastic, immunosuppressive medication	49	18	23	41	31
9	Antiparkinsonien	5	3	0	2	2
10	Blood disease medicines	16	13	4	17	13
11	Blood products and plasma substitutes	6	2	8	12	4
12	Cardiovascular medicines	49	28	10	30	20
13	(Topical) dermatological medicines	28	12	2	18	16
14	Diagnostic agents	8	3	2	7	5
15	Disinfectants and antiseptics	6	0	1	7	6
16	Diuretics and medication for prostate disorders	11	6	3	8	5
17	Medication for gastrointestinal disorders/anti-diarrheal medications	32	23	2	11	9
18	Hormonal, endocrine medication, other contraceptives	36	15	10	31	21
19	Immunological medicines/Vaccines	26	8	5	32	18

20	Muscle relaxants	7	2	1	6	5
21	Ophthalmology	19	8	5	16	11
22	Ocytocic	11	7	2	5	3
23	Dialysis medications	1	0	0	1	1
24	Psychotropic	22	8	4	17	13
25	Respiratory system medications	16	11	1	6	5
26	Medicines used in hydroelectrolytic equilibrium disruptions	7	1	0	8	8
27	Vitamins and minerals	19	8	1	12	11
28	Ear nose throat for children	4	0	0	4	4
29	Newborns	0	0	0	6	4
30	Varia	0	0	0	7	0
Total		**635**	**263**	**152**	**532**	**337**

The study has also revealed certain medicines that are included in the 2017 WHO EML, but which are missing in the 2011 NEML (Table 8). At the same time, Table 8 a number of medicine names marked with asterisks which indicate that this items are not included in the NEML in the same therapeutic group as in the WHO EML, but are found under other NEML therapeutic groups. In total, there are 67 medicines in the main list and 27 in the WHO complementary EML list which are not found in the NEML.

Table 8. Medicines not present in the NEML/2011 versus EML/WHO 2017

No.	Therapeutic class	Basic list	Additional list
1	Anesthetics	nitrogen oxide,	
2	Analgesics, antipyretics, non-steroidal anti-inflammatory, anti-gout, anti-rheumatic medicines NEML 2011 WHO of 2017 - Medicines, Antialgia and medicines used for palliative treatment	*methadone *, amitriptyline *, cyclizine[c] dexamethasone *, sodium docusate, fluoxetine, haloperidol *, hyoscinebutylbromide, lactulose * [c], loperamide *, metoclopramide *, midazolam *, ondansetron *, senna**	
3	Antiallergics used in anaphylaxis		
4	Antidotes and other preparations used in poisoning	methylthionine chloride, potassium iron hexacyanoferrate(II)	*Deferoxamine, fomepizole, sodium calcium edetate, succimer*
5	Anticonvulsants/Antiepileptics	midazolam	
6.	Anti-infectives		
6.1	Anthelmintics		
6.2	Antibacterials		

6.2.4	TB medicines	rifapentine*	Delamanide, clofazimine, bedaquiline, linezolid, *streptomycin*
6.3	Antifungal medicines	itraconazole *, voriconazole *	
6.4	Antivirals	Darunavir, raltegravir, abacavir + lamivudine, efavirenz + lamivudine + tenofovir, isoniazid + pyridoxine + sulfamethoxazole + trimethoprim, valganciclovir, entecavir, tenofovir disoproxil fumarate, sofosbuvir, simeprevir, daclatasvir, dasabuvir, ledipasvir + sofosbuvir, ombitasvir + paritaprevir + ritonavir, sofosbovir + velpatasvir	*Peginterferon alfa (2a or 2b) **
6.5	Antiprotozoal medicines	Miltefosin, artesunate + amodiaquin *, artesunate + mefloquine, artesunate + pironarid tetraphosphate, dihydroartemisinin + piperaquin phosphate	
7	Antimigraine medication, cerebral hemodynamic and metabolic medicines		
8	Anti-neoplastic, immunosuppressive, palliative medication		8.2: bendamustine, trans-retinoid acid (ATRA), dasatinib, imatinib, nilotinib, tioguanin, zolendronic acid 8.3 - anastrozole *, bicalutamide *, leuprorelin, methylprednisolone *
9	Antiparkinsonien		
10	Blood disease medicines		*erythropoiesis stimulating agents, deferoxamine *, hydroxycarbamide*
11	Blood products and plasma substitutes	Fresh-frozen plasma, erythrocyte mass, leukocyte mass,	

		Antirabic immunoglobulin, Antitetanos immunoglobulin	
12	Cardiovascular medicines	Clopidogrel *	
13	(Topical) dermatological medicines	Mupirocin, calamine,	
14	Diagnostic agents		*barium sulfate *, meglumine iotroxate*
15	Disinfectants and antiseptics	Alcohol-based disinfectants	
16	Diuretics and medication for prostate disorders		
17	Medication for gastrointestinal disorders/anti-diarrheal medications		
18	Hormonal, endocrine medication, other contraceptives	Ulipristal, etonogestrel release implant, progesterone vaginal ring *, gliclazide *, glucagon,	
19	Immunological medicines/Vaccines	Tifoidvacc, the tick-borne encephalitis vaccine, HPV Vaccine	
20	Muscle relaxants		
21	Ophthalmology	Azithromycin *, erythromycin *, natamycin, latanoprost	*Bevacizumab*
22	Ocytocic		
23	Dialysis medications		
24	Psychotropic	Clozapine,	
25	Respiratory system medications	budesonide + formoterol	
26	Medicines used in hydroelectrolytic equilibrium disruptions		
27	Vitamins and minerals		
28	Ear nose throat for children		
29	Newborns	dexamethasone*	
30	Varia		
TOTAL		**67**	**27**

*Note: ** - the medicines that are not found within this therapeutic group but are included in NEML under a different section.

This study did not aim to analyze NEML as compared to National Clinical Protocols (NCPs), but to understand the NEML coverage in the NCP, two NCPs were selected for examination, i.e. the treatment of adult gastric and duodenal ulcers (National Clinical

Protocol 207) and epilepsy treatment in adult (National Clinical Protocol 290). It was found that:

- The group of medicines for adult gastric and duodenal ulcers contains 15 drug names. All the medicines are registered in Moldova. Of the 15 medicine names 7 are not found neither in the NEML nor in the WHO EML (Table 9).
- The section of adult epilepsy medication contains 24 medicine names, of which 13 are authorized to be placed on the market in Moldova. Out of the 24 names 13 are not found neither in the NEML nor in the WHO EML. 14 medicine names out of 24 are not found in the NEML (Table 10).

It should be noted that the Regulation of the List of Essential Medicines (MoH order no.162 of 2007) specifies along with other measures regarding the implementation of the essential medicine concept the necessity to select the essential medicines according to the standard clinical recommendations.

Table 9. Gastric and duodenal ulcers in adults - National Clinical Protocol 207

INN, concentration, pharmaceutical form	NEML	Authorized INN	WHO EML 2017
Amoxicillin, 500 mg capsules	present	present	
Tetracycline, 500 mg capsules	missing	present	missing
Clarithromycin, 500 mg tablets	present	present	
Bismuth salts, 120 mg film-coated tablets	missing	present	missing
Metronidazole, 250 mg tablets	present	present	
Tinidazole, 250 mg tablets	present	present	
Levofloxacin, 500 mg capsules	present	present	
Omeprazole, 20 mg capsules	present	present	
Rabeprazole, 20 mg capsules	missing	present	missing
Pantoprazole, 20 mg capsules	missing	present	missing
Esomeprazole, 20 mg capsules	missing	present	missing
Lansoprazole, 20 mg capsules	missing	present	missing
Misoprostol, 200 µg tablets	present	present	
Sucralfate tablets 1 g	missing	present	missing
Famotidine, 20 mg tablets	present	present	

Table 10. Epilepsy in adults - National Clinical Protocol 290

INN, concentration, pharmaceutical form*	NEML	Authorized INN	WHO EML 2017
Acetazolamide 250mg tablets	present for another therapeuti c group	present	present
Valproic acid, 100, 200,500 mg tablet/film-coated tablets; 500mg capsules; oral solution	present	present	present
Carbamazepine, 100, 200mg tablets	present	present	present
Clobazam	missing	missing	missing
Clonazepam 500 µg, 2 mg tablets;	present	present	
Eslicarbazepine	missing	missing	missing
Ethosuximide*	missing	missing	present
Felbamate*	missing	missing	missing
Phenytoin, 25 or 50 mg / 5ml oral solution; 50mg/5 ml injectable solution; 50 mg tablets, 25, 50 or 100 mg oral solid forms	present	present (injectable solution)	
Fenobarbital 100mg tablets; 200 mg/ml injectable solution	present	present	
Gabapentin, 300mg, 100mg, 400mg capsules	present	present (300mg)	
Lacosamide*	missing	missing	missing
Lamotrigin 100mg, 50mg tablets/film-coated tablets	present	present	present
Levetiracetam,	missing	present	missing
Oxcarbazepine*	missing	missing	missing
PREGABALIN	missing	present	missing
Rufinamide*	missing	missing	missing
Stiripentol*	missing	missing	missing
Tiagabine*	missing	missing	missing
Topiramatum	missing	present	missing
Vigabatrin	missing	missing	missing
Zonisamide*	missing	missing	missing
Thiopental Natrium 0.5; 1g powder for injectable solutions; 0.5; 1g lyophilisate for injectable solutions	present	present	present
Propofol 10 mg/ml emulsion for injection / emulsion for infusion	present	present	present

ANALYSIS OF THE NATIONAL LIST OF ESSENTIAL MEDICINES AND MEDICINES PROCURED WITH PUBLIC FUNDS

The existing statistical data on the imported and domestic medicines turnover show that the pharmaceutical market in the Republic of Moldova can be estimated at 2.7 bln. MDL annually.[50] A significant volume of the annual turnover of pharmaceuticals is attributed to products procured from public funds for the needs of national, special programs and public health care institutions. The section below shows the results of the study regarding the reference to the NEML in development of the list of medicines procured through centralized tendering system with public funds, including those required by public healthcare institutions and by national and special healthcare programs.

Methodology

For the analysis, the data on the results of centralized medicine procurement for the national programs and healthcare institutions carried out by MMDA and CCPPH for 3 consecutive years: 2015, 2016 and 2017, UNICEF - procurement of vaccines for 2016 and 2017, as well as UNDP data on medicine procurements for 2017.[51] A peculiarity of the centralized medicine procurement covered by the state budget to meet the needs of the national and special programs of 2017 is that it was carried out by UNDP, a UN international agency, on behalf of MoHLSP. The collaboration agreement was signed for 3 years[52]. Based on the collaboration agreement signed by UNDP and MoHLSP within the project "Procurement Support Services for the Ministry of Health, Labor and Social Protection", the international agency pledged to assist public health authorities in strengthening national capacities for the following activities:

- Procurement of medicines and medical devices included in the list of national and special health programs, such as diagnostics and treatment of HIV/AIDS and STI, oncological, hematological, tuberculosis, rare diseases, diabetes etc.
- Strengthen the capacity of the Ministry of Health, Labor and Social Protection to ensure a transparent, efficient and sustainable procurement process and to promote a coherent pharmaceutical policy.
- Modernizing the public storage areas for medicines in line with international standards of good distribution practices (GDP).

The lists of national tender results contain the following data related to medicines: International Nonproprietary Name (INN) and trade name, doses and pharmaceutical

[50] The average import turnover in the period 2011-2015, calculated by the authors on the basis of the data from "Resources and Activity of the Pharmaceutical System of the Republic of Moldova", Statistical Yearbook 2015, Medicines and Medical Devices Agency

[51] It does not include procurements through FG Grants

[52] Procurement support services for the Ministry of Health, Labor and Social Protection http://www.md.undp.org/content/dam/moldova/docs/Project%20Documents/Project%20document%20health.pdf

form, procured quantity (measured by tablets, ampoule/ml), unit price with and without VAT, the VAT value, the total amount including VAT. In some cases, only the total amount with and without VAT was specified in the information note on the signed contracts, without specification unit price. When estimating the contracted budget of centralized procurements, values (prices & sums) with VAT (VAT rate is 8%) were taken into account. The lists related to the medicines and devices procured via UNDP provides only general information such as: pharmacotherapeutic group, tender winners or directly contracted companies, and total amount per contract. Thus, the result list published by UNDP does not provide data on each medicine included in the procurement contract, unit price, or information about all direct and indirect costs that are included under the term "unit price". From the possible set of factors that would clarify the value of the unit price, it should be noted: the potential costs that are complementary to the product unit price to ensure the DDP (Incoterms) delivery, one of the conditions specified in the CCPPH procurement requests; medicine quality control costs, if delivery is not required to fulfill the DDP Incoterms to the Health Facility, procurement logistic costs etc. The limitations in evaluating the final cost of medicines and consumables procurement with MoHLSP funds through UNDP affected the estimations of the final contracted sum for essential medicines in 2017. Moreover, in the case of the vaccines procured through UNICEF, only the total contracted budget was considered.

The data obtained from the public sources (the official web pages of MMDA, CCPPH and UNDP) were evaluated using the observational and descriptive study method. The lists of medicines called for tender, specified by INNs, pharmaceutical form, and doses, were analyzed in nominal and quantitative terms by comparing the NEML and data of the procurement lists. As procurement list were considered the list with medicines procured based on submitted offers, winning bids and awarded contracts, as well as medicines for which no offers have been submitted and which have not been procured. The analysis was carried out with the help of a working tool in Microsoft Excel format. For the evaluation, the lists of medicines subject to procurement from public money during the period 2015-2017 were examined: in 2015 - 5 bids; in 2016 - 20 bids and in 2017 - 38 bids. The different number of bids per year is explained by the fact that for the lists of medicines for which no offers were submitted at the first bidding, the procedure was repeated. Therefore, the number of lists examined differs from year to year. When assessing the total number of molecules/INNs, the lists of vaccines procured under the agreement with UNICEF have also been taken into account.

The study was conducted by comparing the presence of medicines in both lists (NEML and offers) per molecule/INN. In the analysis of the list of purchased medicines, the term molecule/INN is defined similarly as in the NEML analysis and implies the *INNs, doses and pharmaceutical forms*. Analyzing the list of medicines procured with public money, it was observed that some molecules are included in several lists published on the official website of the authorities responsible for procurements. The reason that explains the reoccurrence of medicine names in several announced procurement lists for the same budget year would be the lack of offers at the first bidding and reposted call for proposals or identification of additional needs, etc. If some medicines reappeared in multiple biddings, INNs that have been identified in difference formulation in the bidding

lists were considered for the total estimated budget, but were not taken into account when estimating the number of molecules/INNs of essential medicines transposed in the procurement lists, to exclude the duplication of the number of INNs.

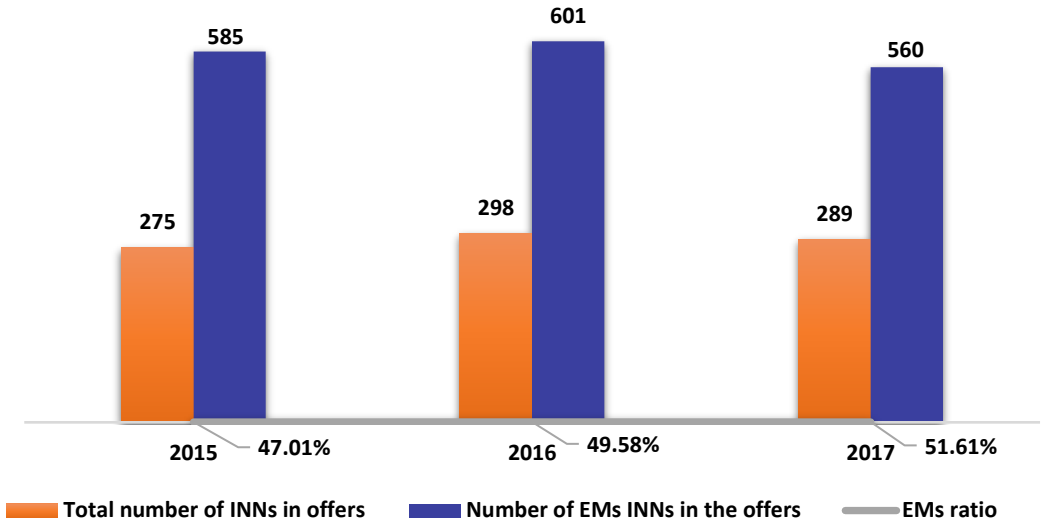
Analysis of the NEML representation index in the list of medicines procured with public funds

The evaluation of the lists of medicines procured with public funds over the past three years shows that Essential Medicines (EMs) account for about 49% (or about 287 molecules/INNs as an annual average) of the total of molecules/INNs procured on centralized basis annually. Thus, a total of 585 INNs were acquired in 2015, of which EMs accounted for 275 INNs (47.01%), in 2016 the number of EMs was slightly higher - up to 298 INNs (49.58%) of the total of 601 INNs, and in 2017 the share of EMs has reached about 51.61%, which represents 289 INNs/EMs of the total of 560 INNs. The decrease in the total number of molecules/INNs procured with public funds in 2017 did not essentially influence the share of EMs in the total amount of procured medicines, but as a share of total procured INNs there is an increase of about 2.02% compared to 2016 (Figure 1).

Comparing analyzed data with the latest WHO evaluation of access to medicines and their quality carried out in partnership with the national authorities in 2011[53], it can be noticed that in recent years the share of essential medicines in the list of medicines procured on centralized basis has increased by about 8 % compared to 2011. According to the WHO analysis, essential medicines constituted 40.89% of the list of medicines included in the 2011 call for tenders, and in terms of costs, these accounted for 43.14% of the total amount of medicines contracted for hospital treatment.

[53] Availability and affordability of medicines and assessment of quality systems for prescription of medicines in the Republic of Moldova, OMS 2012, http://apps.who.int/medicinedocs/documents/s20000en/s20000en.pdf

Figure 1. The share of Essential Medicines (EM) covered by bids in centralized procurements



Data from the table 11 shows an increase in the EMs/INNs share in the total number of molecules/INNs/medicines present in the bidding lists. The fluctuation of the absolute number of essential medicines also depends on the total number of medicines selected for procurement in each budget year. According to selection rules for medicine procurement, among the factors that determine the list of medicines are: treatment protocols and their amendments, estimated needs per year and current stocks, prescribing practices, the presence of the marketing authorization for medicinal products, the registration in the National Catalogue of ex-factory manufacturer prices for medicines etc. The term "number of medicines in the offer" includes the medicines for which bids have been submitted and procurement contracts have been signed. One of the reasons for a lower number of INNs in 2017, reflected in the report, is the absence of detailed data on biddings, including the list of medicines of the winning bids on official web sites of the responsible authorities.

As mentioned above, procurement for fiscal year 2017 was made through two different structures: CCPPH and UNDP. The data published by the UNDP on the official website provides a brief summary of the tenders organized for the procurement of medicines and medical devices from public money for national and special programs. Data provided on the UNDP page does not provide details on procured medicines, except for ARV and anti-TB medicines, such as name and doses, pharmaceutical form, quantity, manufacturer/ holder of marketing authorization for medicinal products included in the procurement contract. Another critical element in monitoring the procurement with public funds is the announcing of the unit price and the total amount specifying the INCOTERMS terms for each medicinal product or medical device as well as costs for logistics issues, customs clearance, quality control, and other costs if the pharmaceutical products were not procured under DDP(Incoterms) conditions. The UNDP official website provides only the list of signed procurement contracts, with the total amounts

per pharmacotherapeutic group or the name of the national or special program, such as antiretroviral medicines , the diabetes program etc.[54]

The announcement of a note covering the details for each medicine and/or medical device helps public authorities, end-beneficiaries, the community, key actors in organizing procurements to understand the budget involved for each medicine, what are the factors that drive high prices for high-cost rate medicines within the provided budget, etc. Moreover, providing comprehensive information helps increase the trust of the end consumers.

The reporting only of general information on the list of contracted pharmaceuticals determined the authors of the study to conclude that the factual contracted list of items corresponds to the list of medicines/INNs requested by MoHLSP or health institutions. On that basis, the number of items procured through UNDP was considered in the analysis of the range of medicines procured with the public money in 2017. From the UNDP procurement data, only ARV (unit price and total value) and TB procurements (total value) were available.

Table 11. The share of Essential Medicines (EMs) procured on centralized basis to cover the needs of healthcare facilities and national and special programs in the period of 2015-2017.

Year	2015	2016	2017
The total number of bidded INNs (procured)	585	601	560
Number of bidded EMs/INNs (procured)	275	298	289
Rate of bidded EM/INNs, %	47.01%	49.58%	51.61%

Table 12 shows the data for 2015-2017, specifying the total number of medicines requested through tenders, including the number of procurements with offers and those without offers, with separate data on essential medicines.

The analysis of the procurement lists reveals that there are cases of lack of bids including for essential medicines every year. The data for 2015 are incomplete because the sources used to collect the data did not contain information on the medicines for which no offers were submitted. For the years 2016-2017, the INNs proportion in the list of EMs without offers was of 5,10%, 16 INNs - in 2016 and of 3,99% (12 INNs) in 2017.

The number of EMs in the list of medicines for public procurement for 2016-2017 is around 293 molecules/INNs, making up 48.34% out of the total of 635 molecules/INNs included in NEML 2011 (Table 12).

[54] http://www.md.undp.org/content/moldova/ro/home/projects/servicii-de-sus_inere-a-achiziiilor-pentru-ministerul-sntii-/transparency-of-procurement.html

Table 12. The share of Essential Medicines (EMs) in centralized public procurements for 2015-2017.

Year	2015*	2016	2017
a.Total number of INNs in the procurement list:	*n/date*	723 (100%)	603 (100%)
Total INNs with offers (procured)	*585*	83,13%(601)	92.87% (560)
Total INNs without offers	*n/date*	16.87% (122)	7.13% (43)
b.The total proportion of EMs/INNs in the procurement list:	*n/date*	43,43%(314)	49.92% (301)
Total INNs/ EMs with offers (procured)	*275*	94,90% (298)	96.01% (289)
Total procured INNs/ EMs without offers	*n/date*	5.10% (16)	3.99% (12)

* There is no data available on the list of medicines for which offers were not submitted at procurements for 2015.

The analysis of the lists of medicinal products not covered by tenders and respectively not procured within the centralized procurement for 2016 and 2017, indicates that approximately 14 INNs/EMs from the ones requested by Health facilities are not procured annually. Thus, 16 INNs/EMs were not procured in 2016, and 12 INNs/EMs - in 2017, of which 3 INNs/EMs are found in the list of products without offers for both years: *Methyldopa 250mg, tablets, Streptokinase 1500000 IU, powder/infusion solution and Theofillin prolong –released capsules 200 mg and prolong –released capsules 300 mg* (table 13).

Table 13. The list of essential medicines for which offers were not submitted in 2016-2017.

2016			2017		
No.	**INNs EM without offers**	**Pharmaceutical form or doses**	No.	**INNs EM without offers**	**Pharmaceutical form or doses**
1	Dextromethorphan	m0.15% 150 ml, Oral solution	1	Alprostadil	Powder/infusion solution, 20 mcg
2	Ferric sulphate	325 mg, extended-release tablets	2	Azathioprine	tablets, 50 mg
3	Hydrochlorothiazide + Triamterene	tablets, 25 mg + 12.5 mg	3	Caffeine	injectable solution, 20% 1 ml
4	Interferon alpha	1000 UI, Powder/nose drops; 3000000 UI/ml-Injectable solution	4	Diltiazem	180 mg & 90 mg, extended-release tablets
5	Isosorbide dinitrate	extended-release tablets 20 mg; infusion solution 0.1% 10 ml Perf.	5	Erythromycin	250 mg, enteric-coated tablets
6	Lamivudine + Zidovudine	tablets, 150 mg + 300 mg	6	Fludarabine	50 mg, infusion solution
7	Methyldopa	tablets, 250 mg	7	Methyldopa	tablets, 250 mg

8	Miconazole	cream, 2% 15g	8	MESALAZINE	suppositories 500 mg; enteric tablets 500 mg
9	Permethrin	cutaneous solution 0.5% 60 ml	9	Potassium aspartate + Magnesium aspartate	injectable solution, 452 mg + 400 mg / 5 ml Inj.
10	Piridostigmine Bromide	tablets, 60 mg			
11	Repaglinide	tablets, 2 mg			
12	Retinol	drink drops 50000 IU / ml 10 ml	10	Vinorelbine	injectable solution, 50 mg/5 ml Perf.
13	Ritonavir	100 mg. Tablets			
14	Streptokinase	Powder/infusion solution 1500000 IU	11	Streptokinase	Powder/infusion solution 1500000 IU
15	Sumatriptan	tablets, 50 mg + 100 mg			
16	Theophylline	extended - release tablets 200 mg & 300 mg	12	Theophylline	extended - release tablets 200 mg & 300 mg

The lack of offers and contracts for these 16 pharmaceuticals, cannot in all cases be described as an interruption in the medicine supply to healthcare institutions. Under the current legislation, the MoHLSP has established a mechanism for importing unauthorized medicinal products into the country under a number of conditions, including the absence of analogues or substitutes on the pharmaceutical market, or when there is a need to reduce the costs of public procurement of medicines, parapharmaceuticals and raw material for unauthorized medicinal products in the Republic of Moldova, but registered in the country of origin. Considering these provisions, we could assume that some medicines for which no offers were submitted had been imported through this mechanism if requests were made. Unfortunately, there were not find any information on the medicines authorized for import under the conditions of the lack of marketing authorization in Moldova on the website of the NDRA, but accepted according to the terms described.

One of the examined aspects was the presence and distribution of Essential Medicines (INNs/EMs) according to pharmacotherapeutic groups in the lists of medicines procured with public money in the period 2015-2017 and their ratio against NEML of 2011. As an analysis criterion was the evaluation of pharmacotherapeutic groups, ranked in descending order, starting with those with most INNs included in the NEML 2011. The data presented in Table 14 shows that the group with the highest number of medicines in the NEML is "6. Anti-infectives "- 150 INNs, but the total number of bidded INNs/EMs was approximatively 59 (39%), followed by the medications of the groups "8. Antineoplastic, immunosuppressive, palliative medication "and" 12. Cardiovascular medicines "- with 49 INNs in the NEML and covered by bids in the proportion of 55% or 27 INNs out of the total number; the third group consists of "2. Analgesics, antipyretics,

non-steroidal, anti-inflammatory, anti-rheumatic medicines "with 29 INNs included in the NEML, which accounts for 69% of the total number (20 INNs).

At the same time, the highest rate of representation of Ems in bids compare to the 2011 NEML is for the medicines in the group "26. Medicines used in hydroelectrolytic imbalance and acid-base disorders "- 90% or 6 INNs of the 7 in the NEML of 2011, followed by the group" 9. Antiparkinsonian "- 80% (with 4 INNs out of 5 in the NEML) and after by group" 3. Antiallergic medicines used in anaphylaxis "with 10 INNs of 13 in the NEML accounting for 77%.

The lowest rate of presence is registered for the medicines in the groups "11. Products obtained from blood and plasma substituents "- 17% and" 13. (Topical) dermatological medicines "- 18% in the procurement lists for which 1INN of 6 and 5 INN of 28 respectively have been listed in NEML 2011.

At the same time, it was noted that for the group "23. Dialysis Solutions "containing only 1 DCI - Intraperitoneal Dialysis Solution, there was no offers submitted (0%). The product was not identifiable in the procurement lists, due to the fact that it is not specified in the NEML under a specific international non-proprietary name or as a component of a medicinal product.

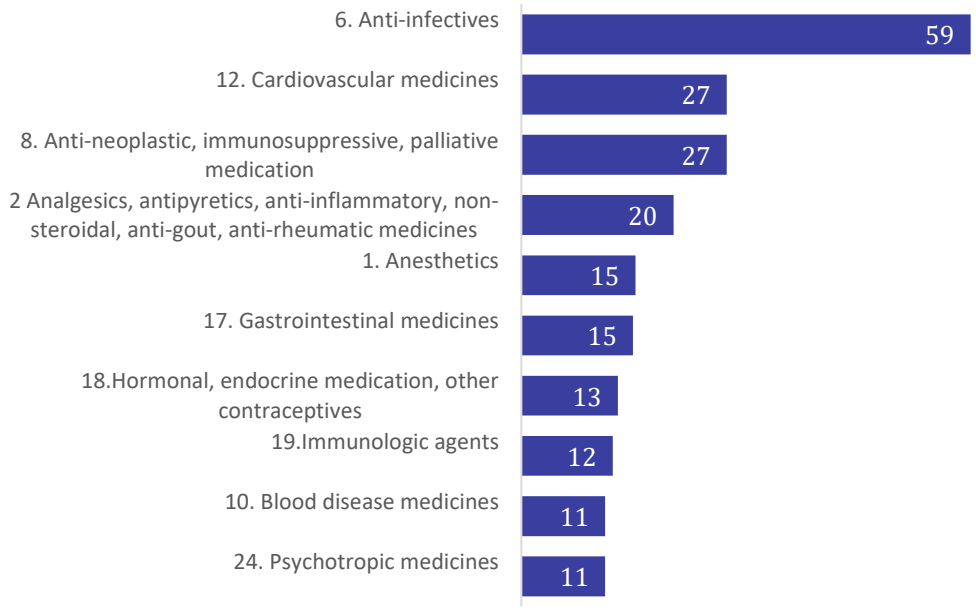
Table 14. The share of EMs in the lists of procured medicines

Therapeutic Group	Number of INNs in the NEML 2011	Number of INNs EMs in the offers	Rate of EMs (INN) in the offers
26. Medicines used in hydroelectrolytic imbalance and acid-base disorders	7	6	90%
9. Antiparkinsonien	5	4	80%
3. Antiallergic medicines used in anaphylaxis	13	10	77%
5. Anticonvulsants/antiepileptics	11	8	73%
2. Analgesics, antipyretics, non-steroidal, anti-inflammatory, anti-rheumatic medicines	29	20	69%
10. Blood disease medicines	16	11	69%
1. Anesthetics	22	15	68%
7. Antimigraine medication, cerebral hemodynamic and metabolic medicines	14	8	57%
8. Anti-neoplastic, immunosuppressive, palliative medication	49	27	55%
12. Cardiovascular medicines	49	27	55%
24. Psychotropic medicines	22	11	50%
15. Disinfectants and antiseptics	6	3	50%
17. Medication in gastrointestinal disorders	31	15	47%
19. Immunologic agents	26	12	46%
22. Oxytocin and tocolytics	11	5	45%
25. Respiratory system medicines	16	6	40%
6. Anti-infective	150	59	39%
14. Diagnostic agents	8	3	38%
18. Hormonal, endocrine medication, other contraceptives	36	13	35%
16. Diuretics and medication for prostate disorders	11	3	30%

21. Ophthalmic medications	19	6	30%
27. Vitamins and minerals	19	6	30%
20. Miorelaxants (peripheral-action) and cholinesterase inhibitors	7	2	29%
4. Antidotes and other preparations used in poisoning	15	4	27%
28. Ear, nose and throat for children	4	1	25%
29. Specific medicines for the care of newborns [c]	4	1	25%
13. (Topical) dermatological medicines	28	5	18%
11. Blood products and plasma substitutes	6	1	17%
23. Dialysis solutions	1	0	0%
TOTAL	**635**	**292**	**45.93%**

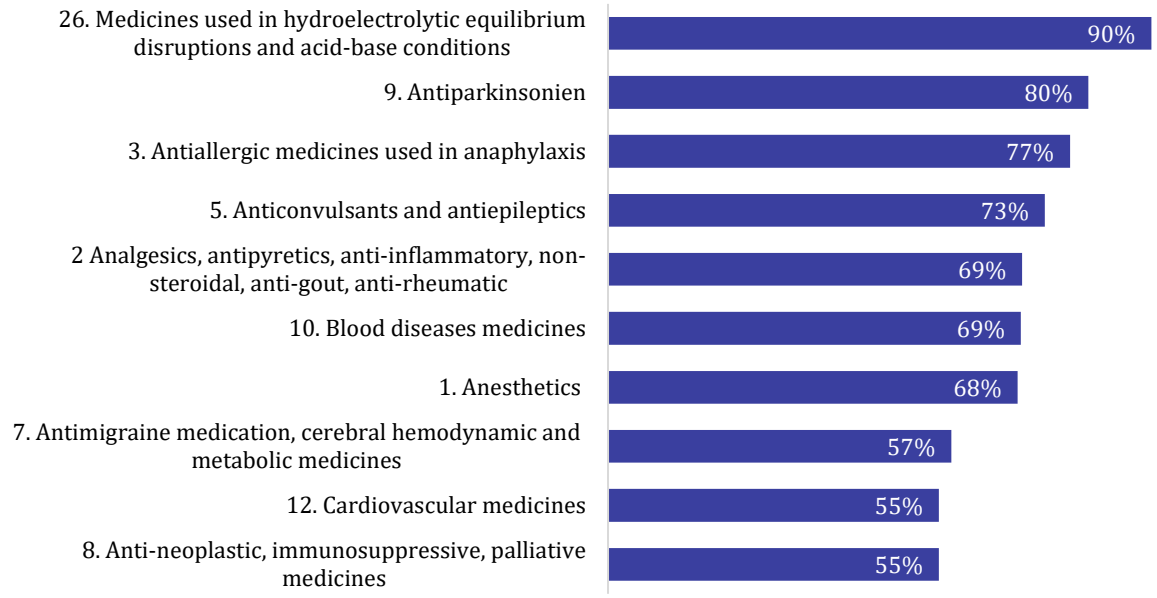
Figures 2 and 3 show the data for the top 10 therapeutic groups, selected by the highest number of molecules/INNs in the bids and their proportion in relation to the number of INN in the NEML. From these figures, it is clear that although the absolute number of medicines in the group of anti-infective, cardiovascular, gastrointestinal, antineoplastic and immunosuppressive medicines is higher, their share from the total number of medicines from the NEML is in the range of 36-55%. It should be mentioned that these medicines are used in the treatment of diseases with the highest death rates in Moldova: cardiovascular diseases, cancer, digestive system diseases, and respiratory diseases.

Figure 2. Top 10 therapeutic groups by the number of molecules/EMs INN present in the offers



From the evidence shown in Figures 2 and 3, it results that the top 10 consists of EMs from the same pharmacotherapeutic groups, both as a total number of INNs and their proportion of representation. The analysis of the top 10 therapeutic groups indicates that the first three positions are held by anti-inflammatory, cardiovascular, anesthetics, but as a share of representation the top also includes such groups as: medicines used in hydroelectrolytic equilibrium disruptions - 90%, antiparkinsonians - with a coverage of 80% and antimigraine medication – with a rate of 57% (Figure 3).

Figure 3. Top 10 therapeutic groups by the number of molecules/INN EMs present in the offers



The analysis of the NEML 2011, structured by therapeutic groups and its representation in the tenders for the last three years, is shown in Table 15. In this table, it can be seen that representation of 14 therapeutic groups EMs/INN in the lists of medicines procured from public funds is the same in the last 3 years.

Table 15. Structure of essential medicines procurements for the needs of health care facilities by therapeutic groups, 2015-2017

Therapeutic group	No. INN NEML, 2011	2015		2016		2017	
		EMs molecules/ INN in the offers per group		EMs molecules/INN in the offers per group		EMs molecules/IN N in the offers per group	
1. Anesthetics	22	15	68.18%	15	68.18%	15	68.18%
2. Analgesics, antipyretics, non-steroidal, anti-inflammatory, anti-rheumatic	29	19	65.52%	21	72.41%	20	68.97%
3. Antiallergic medicines used in anaphylaxis	13	10	76.92%	10	76.92%	10	76.92%
4. Antidotes and other preparations used in poisoning	15	4	26.67%	4	26.67%	4	26.67%
5. Anticonvulsants/antiepileptics	11	8	72.73%	8	72.73%	8	72.73%
6. Anti-infective medicines	150	53	35.33%	61	40.67%	63	42.00%
7. Antimigraine medication, cerebral hemodynamic and metabolic medicines	14	9	64.29%	8	57.14%	7	50.00%
8. Antineoplastics, immunosuppressive, palliative care medicines	49	28	57.14%	28	57.14%	25	51.02%
9. Antiparkinsonism medicines	5	4	80.00%	4	80.00%	4	80.00%
10. Medicines affecting blood	16	10	62.50%	11	68.75%	12	75.00%
11. Blood products of human origin and plasma substitutes	6	1	16.67%	1	16.67%	1	16.67%
12. Cardiovascular medicines	49	26	53.06%	27	55.10%	28	57.14%
13. Dermatological medicines	28	6	21.43%	5	17.86%	4	14.29%
14. Diagnostic agents	8	3	37.50%	3	37.50%	3	37.50%
15. Disinfectants and antiseptics	6	3	50.00%	3	50.00%	3	50.00%

16. Diuretics and medication for prostate disorders	11	4	36.36%	4	36.36%	2	18.18%
17. Gastrointestinal medicines	31	15	48.39%	15	48.39%	14	45.16%
18. Hormonal, endocrine medicines, other contraceptives	36	14	38.89%	12	33.33%	12	33.33%
19. Immunologic agents	26			12	46.15%	12	46.15%
20. Muscle relaxation and cholinesterase inhibitors	7	2	28.57%	2	28.57%	2	28.57%
21. Ophthalmological preparations	19	5	26.32%	6	31.58%	6	31.58%
22. Oxytocin and anti-oxytocisc tocolytic	11	5	45.45%	5	45.45%	5	45.45%
23. Dialysis solutions	1						
24. Psychotropic medicines	22	11	50.00%	11	50.00%	11	50.00%
25. Respiratory system medicines	16	7	43.75%	7	43.75%	5	31.25%
26. Medicines used in correcting electrolytes and acid-base disorders	7	6	85.71%	7	100.00%	6	85.71%
27. Vitamins and minerals	19	6	31.58%	6	31.58%	5	26.32%
28. Ear, nose and throat for children [c]	4	1	25.00%	1	25.00%	1	25.00%
29. Specific medicines for the neonatal care [c]	4			1	25.00%	1	25.00%
TOTAL	**635**	**275**	**44%**	**287**	**45%**	**264**	**42%**

The table below shows the information related to the 14 therapeutic groups with the same level of representation in the procurement lists of public tenders over the last three years examined in the study.

Table 16. List of therapeutic groups with a constant share of EMs molecules/INN present in public procurement lists during 2015-2017

Therapeutic group	No. INN NEML , 2011	The total number and the annual share of the INN	2015		2016		2017	
			EMs INNs in the offers per group/rate		EMs INNs in the offers per group/share		EMs INNs in the offers per group/rate	
1. Anesthetics	22	15/68,18 %	15	68.18%	15	68.18%	15	68.18%
3. Antiallergic medicines used in anaphylaxis	13	10/76.92 %	10	76.92%	10	76.92%	10	76.92%
4. Antidotes and other preparations used in poisoning	15	4/26.67%	4	26.67%	4	26.67%	4	26.67%
5. Anticonvulsants/antiepileptic	11	8/72.73%	8	72.73%	8	72.73%	8	72.73%
9. Antiparkinsonian medicines	5	4/80.00%	4	80.00%	4	80.00%	4	80.00%
11. Blood products of human origins and plasma substitutes	6	1/16.67%	1	16.67%	1	16.67%	1	16.67%
14. Diagnostic agents	8	3/37.50%	3	37.50%	3	37.50%	3	37.50%
15. Disinfectants and antiseptics	6	3/50.00%	3	50.00%	3	50.00%	3	50.00%
20. Muscle relaxations and cholinesterase inhibitors	7	2/28.57%	2	28.57%	2	28.57%	2	28.57%
22. Oxytocin and anti-oxytocic tocolytic	11	5/45.45%	5	45.45%	5	45.45%	5	45.45%
23. Dialysis solutions								
24. Psychotropic medicines	22	11/50.00 %	11	50.00%	11	50.00%	11	50.00%
28. Ear, nose and throat for children [c]	4	1/25.00%	1	25.00%	1	25.00%	1	25.00%
29. Specific medicines for the neonatal care [c]	4	1/25.00%	1	25.00%	1	25.00%	1	25.00%

Yearly differences between the list of EMs included in the bids and the NEML for the therapeutic groups which are not shown in Table 16 are insignificant, being within 1-2 molecules/INN.

The tendency to reduce the number of INNs was specific for the groups: 7. *Antimigraine medication, cerebral hemodynamic and metabolic medicines* and 13. *Dermatological medications*, with one INN, annually; For groups *8. Antineoplastic, immunosuppressive, palliative medication, 16. Diuretics and prostate disease medication, 17. Medication for gastrointestinal disorders, 18. Hormonal, endocrine medication, other contraceptives, 25. Respiratory system and 27. Vitamins and minerals*, but this reduction was only valid for 2017. The annual increase in the number of INNs was specific for groups *10. Blood disorders medication* (from 10 in 2015 to 12 in 2017) and *12. Cardiovascular medication* (from 26 INNs in 2015 to 28 INNs in 2017).

These deviations may be influenced by a number of factors such as: changes to the National Protocols as a consequence of their updating, marketing authorization medicines status and/or producer price registration in the National Catalogue of ex-factory manufacturer prices for medicines. This study did not look at national protocols versus NEML since it was not part of the proposed objectives. The impact of the status of "the medicine registered in the National Catalogue of ex-factory manufacturer prices for medicines " has not been analyzed, since there are not any records of all versions of the Catalogue with the changes made, annually publicly available.

The analysis of contracted budgets within public procurements of medicines 2015-2017

The value of centralized medicine procurements for Health facilities needs is estimated annually at around 500 million MDL including VAT (VAT rate 8%), estimated on the basis of data collected on MMDA and CCPPH pages.[55] According to the data analyzed, the contracted amount as a result of public procurements for the years 2015-2017 varied accounting for about 430.3 million MDL including VAT in 2015, 681.9 million MDL including VAT in 2016, and 451.2 million MDL including VAT - in 2017. The total amount for medicines procured through tenders on public money for 2017 includes both the amount of the CCPPH contracts, expressed in MDL, which include 8% VAT, as well as the amounts contracted for the public procurement of vaccines through UNICEF and the medicines included in the national and special programs procured through UNDP and recalculated in MDL without VAT (0% VAT rate) by the NBM average exchange rate for 2017: 1 USD = 18,4902MDL (source - official website of NBM https://www.bnm.md/ro/content/ratele-de-schimb).

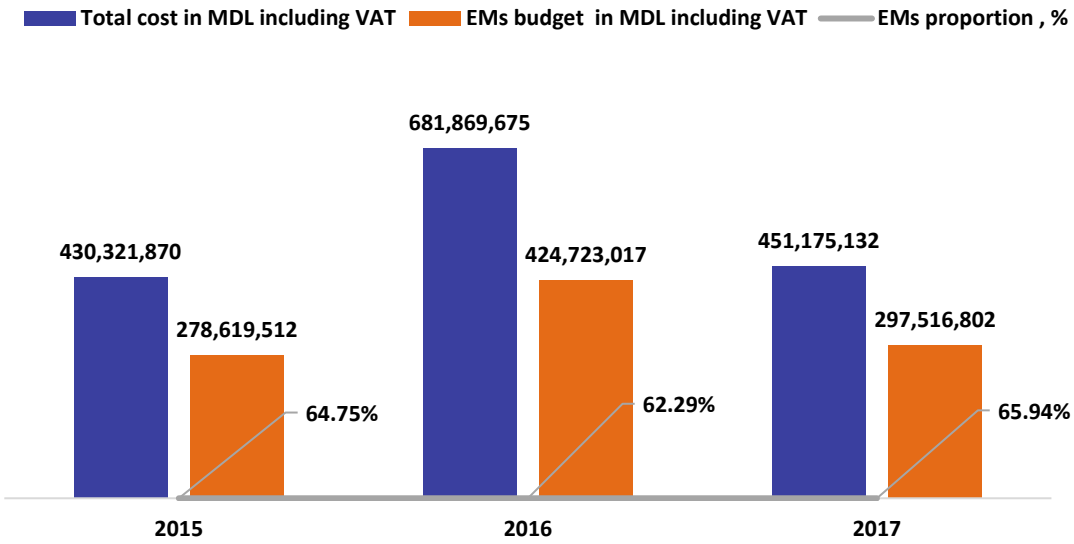
It should be noted that procurement through international agencies is exempted from VAT and other taxes, which influences total procurement costs. Exemption from VAT is not allowed for CCPPH procurement. Moreover, in the case of procurements through UNICEF and UNDP several variables have to be considered in interpreting the

[55] It does not include medicine procurements through the GF Grants.

total contracted budget: costs for logistics services that are not publicly displayed on the websites; additional costs for services related to delivery, depending of the selected INCOTERMS conditions. These characteristics can influence the total budget contracted, which is publicly displayed for medicines procured through UNICEF and UNDP.

The value of centralized procurements for all medicines over the period 2015-2017 is shown in Figure 4.

Figure 4. Value of public procurements of essential and non-essential medicines for 2015-2017



Note: The budget for 2017 also includes the procurement budgets of UNDP and UNICEF with "0" VAT. Limitations: Due to the lack of official data on the UNDP page on the structure of the total cost of the medicines included in the procurement contract, the value of the published procurement contracts was included in the report. However, this amount was not adjusted in relation to potential logistics costs linked to the procurement procedure The information on the cost of the medication does not reflect the unit price for a basic unit (tablet or ampoule), nor the potential costs of logistics, customs services and quality control, etc. to conclude the total cost covered from the public budget under the INCOTERMS - DDP delivery conditions, a term applied for public procurement of medicines by the CCPPH.

The annual proportion of the contracted budget for public procurements of EMs accounts for 64.3% of the total amount of medicine procurements and varies from 64.75% (278.6 million MDL including VAT) in 2015, 62.29% (424.7 million MDL including VAT) - in 2016 and up to 65.94% (297.5 million MDL including VAT) - in 2017.

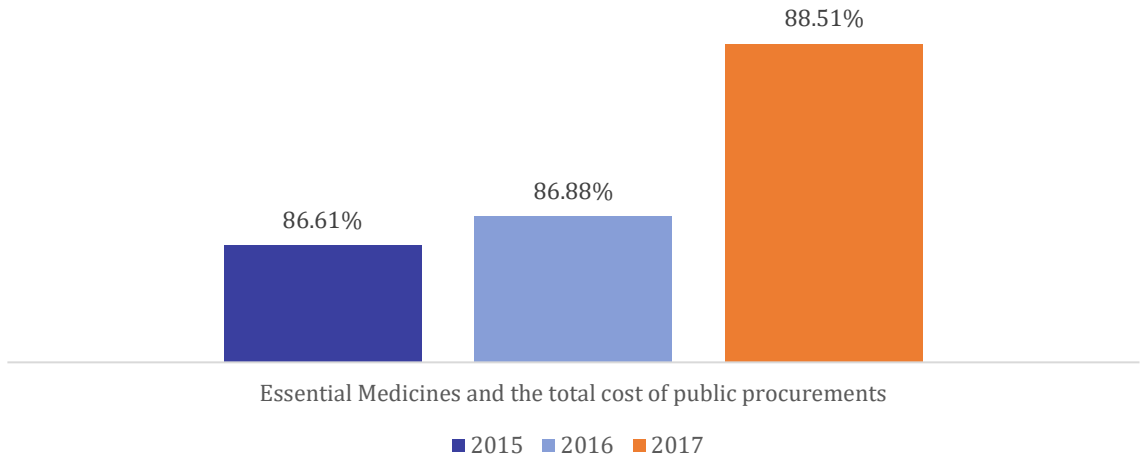
According to data on centralized drug procurements in 2015-2017, approximately 87% of the total amount per year are contracted for EMs in 10 therapeutic groups (out of a total of 29 groups in the NEML - Table 17 and Figure 6).

Table 17. Top 10 of EMs therapeutic groups that account for the highest share in the procurement budget for the years 2015-2017

Therapeutic group	EMs from the contracted budget of public procurements 2015	EMs from the contracted budget of public procurements 2016	EMs from the contracted budget of public procurements 2017
6. Anti-infective medicines	25.59%	27.61%	23.52%
8. Antineoplastics, immunosuppressive, palliative care medicines	11.48%	12.23%	12.34%
26. Medicines used in correcting water electrolytes and acid-base disturbances	11.30%	9.92%	12.44%
1. Anesthetics	8.39%	8.18%	8.22%
10. Medicines affecting blood	7.50%	8.75%	8.97%
17. Gastrointestinal medicines	7.16%	6.47%	6.19%
2. Analgesics, antipyretics, non-steroidal, anti-inflammatory, anti-rheumatic	5.69%	3.94%	6.07%
12. Cardiovascular medicines	3.71%	3.11%	3.92%
15. Disinfectants and antiseptics	3.64%	2.71%	4.37%
14. Diagnostic agents	2.15%	3.96%	2.46%
Total	**86.61%**	**86.88%**	**88.51%**

Thus, the rate of total procurement costs (2015-2017) for Essential Medicines in the top 10 therapeutic groups constituted 86.61% in 2015, 86.88% in 2016 and 88.51% in 2017 (i.e., an increase of 1.63% compared to 2016, Figure 5 and Figure 6).[56]

Figure 5. Share of the top 10 therapeutic groups costs in the contracted budget, 2015-2017

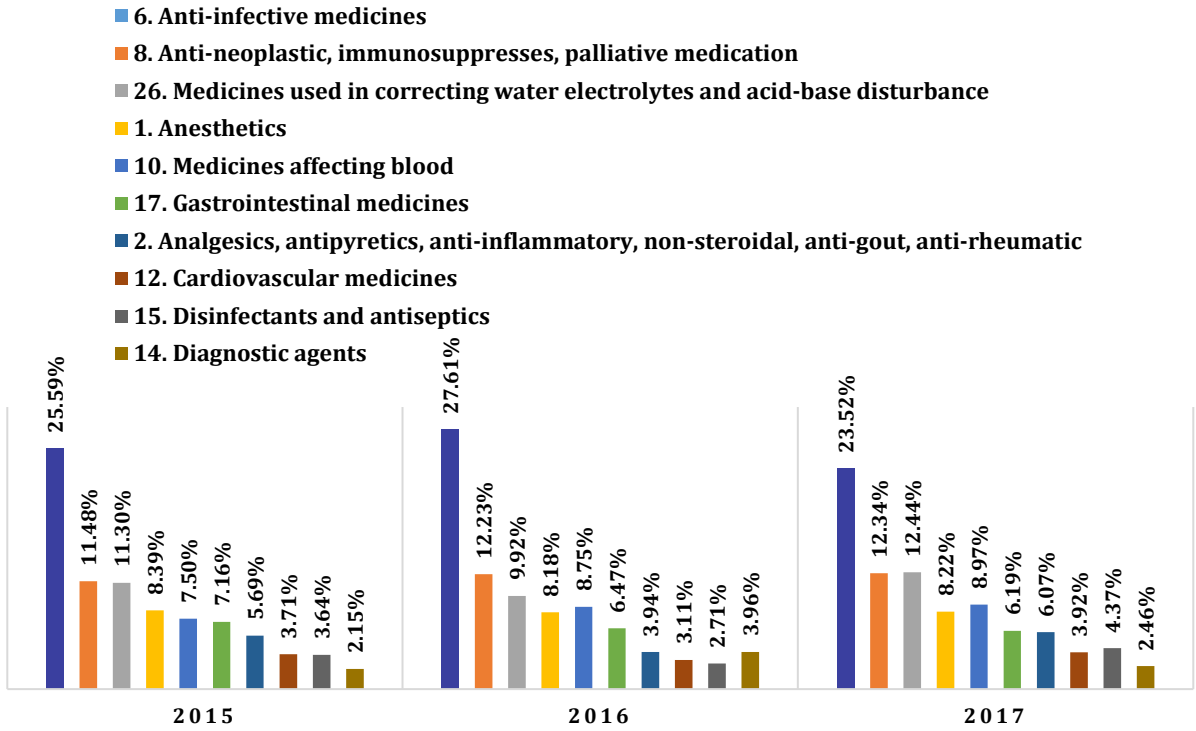


On the first 3 positions of the top 10 therapeutic groups with the largest contracted budget are the essential medicines in the therapeutic group *6. Anti-infectives* - on average 25.6% per year, followed by the group *8. Antineoplastic, immunosuppressive, palliative and anti-inflammatory medicines and group 26 Medicines used in hydroelectrolytic equilibrium disruptions and acid-base conditions* - with a share of about 11% per year.

[56] It does not include medicine procurements through the GF Grants

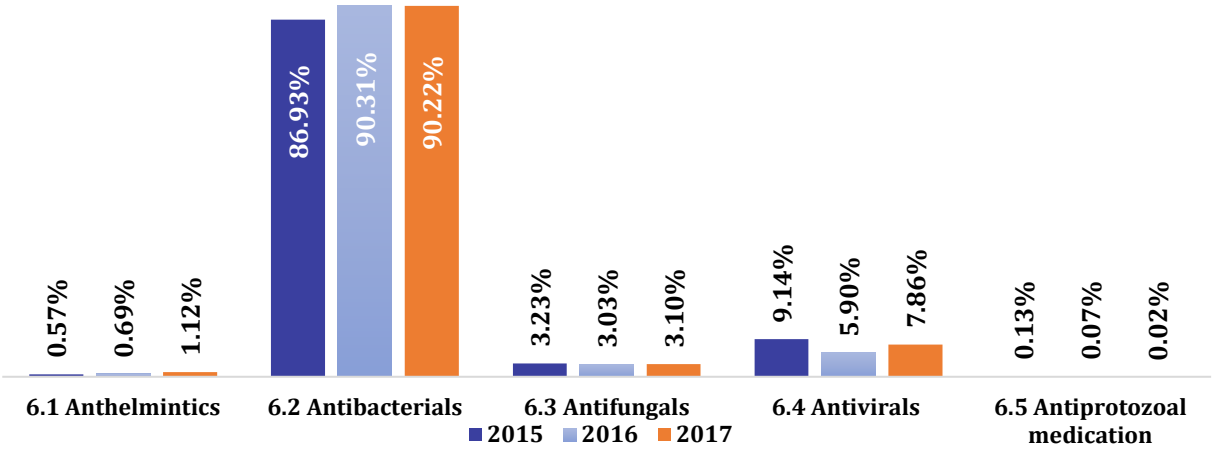
The analysis of the amounts contracted for bided EMs through centralized procurements for the years 2015-2017, based on the top 10 therapeutic groups with the largest contracted budget, reveals that in 2015 the value of procured essential medicines of the Group 6. Anti-infectives (top 1) amounted to 71.3 million.\ MDL including VAT, and in 2016 - to 111.3 million MDL including VAT (i.e. an increase of about 30 million MDL including VAT), while in 2017 there is a significant decrease in the value of these procurements - of about 60.96 million MDL including VAT (by 45.2% or about 50.34 million MDL including VAT compared 2016 and by 30.8% or about 22 million MDL including VAT - compared to 2015). The deviations pointed out for 2017 can be explained by the limitations of the study: the lack of unit price information for INNs procured from public funds through UNDP for 2017. Figure 6 shows the share distribution of contracted budgets for EMs in the top 10 therapeutic groups based on payed amounts.

Figure 6. Distribution of EMs contracted budgets in the top 10 therapeutic groups, 2015-2017.



For the detailed analysis of medicines by subgroups in the top 10 groups, only the therapeutic group with the highest budget involved was chosen - 6. Anti-infective medicines. Figure 7 shows that among the 5 therapeutic subgroups, the majority percentage is held by Antibacterial medicines (subgroup 6.2), namely about 89% throughout the period 2015-2017.

Figure 7. Distribution of contracted budgets for anti-infective medicines in the period 2015-2017.



Antibacterial preparations procured from public budget in the years 2015-2017 account for about 48% of the total number of molecules/INNs included in NEML 2011 in this therapeutic subgroup (6.2 Antibacterial) and about 60% of the group 6. Anti-infective medicines. This group of essential medicines also includes TB and ARV medicines .[57]

The estimated procurement expenditures for antibacterial EMs ranges from 61.97 million. MDL including VAT (86.93% of the total amount of Group 6. Anti-infective medicines) in 2015, up to 100.52 million MDL including VAT (with a rate of 90.31%) in 2016 and 54.99 million MDL including VAT (with a rate of 90.22%) in 2017 (about 55 million MDL including VAT, adjusted by the amounts contracted by UNDP, Table 18).

Table 18. Structure of the EMs amount and budget distribution in the group "6. Anti-infectives " within centralized procurements of 2015-2017

Group 6. ANTIINFECTIVES	EM INNs/NEML Group 2011	2015		2016		2017*	
		EM INNs in offers	Total cost, million MDL including VAT	EM INNs in offers	Total cost, million MDL including VAT	EM INNs in offers	Total cost, million MDL including VAT
6.1 Anthelmintics	12	5	408,760	5	764,767	5	553,311
6.2 Antibacterials	67	30	61,975,120	38	100,520,855	42	54,998,390
6.3 Antifungals	11	7	2,303,536	8	3,370,735	5	1,526,243
6.4 Antivirals	27	9	6,514,420	8	6,567,715	10	3,872,406
6.5 Antiprotozoal medication	33	2	93,909	2	78,279	1	10,908
Total	**150**	**53**	**71,295,746**	**61**	**111,302,350**	**63**	**60,961,259**

The value of procurement contracts signed by UNDP in 2017 for anti-tuberculosis medicines under the TB National Program constitutes 630,799 thousand US dollars (with

[57] TB and ARV medicine INNs are common for public procurement and GF grants

0% VAT) or about 11,663,598 million MDL (0% VAT), and for HIV ARV medicines under the HIV National Programm - 487,326 thousand US dollars (0% VAT) or 9,010,755 million MDL (0% VAT).

Data on procurements of anti-TB and ARV medicines through UNDP were included in the study, both by contract value and by the total number of Ems/ INNs, given that detailed information on UNDP contracts was available for these products (source - the official website of UNDP Moldova), while for other medicines in the national and special programs only the total budgets were considered while the total number of EMs/ INNs were not analyzed because of the lack of information. The study team concluded that all the medicines for other national and special programs, except for anti-tuberculosis medicines and ARVs, for which no detailed data were available, were contracted in 2017 based on calls to tender announced on the UNDP page.

It also should be taken into account that the Republic of Moldova annually receives antituberculous (anti-TB) and antiretroviral (ARV) medicines, procured under the Grants from the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF), to support the National Program for Tuberculosis Control and the National HIV/AIDS/STI Prevention and Control Program. TB grant covered the procurement of antituberculous medicines for the treatment of resistant TB (M/XDR-TB) forms in the Republic of Moldova.

The implementation of TB and HIV programs supported by the Global Fund Grant (GF) is carried out by the Public Institution "Coordination, Implementation and Monitoring Unit of the Health System Projects" (PCIMU), with anti-TB and ARV medicines being procured annually through international procurement agencies - Global Drug Facility (GDF), International Dispensary Association (IDA) and/or UNICEF. The table below provides data on procurements of anti-TB and ARV medicines under Global Fund grants (Table No. 19)

Table 19. Information on procurements of TB and ARV medicines carried out by PCIMU from GF Grants in the years 2015-2017

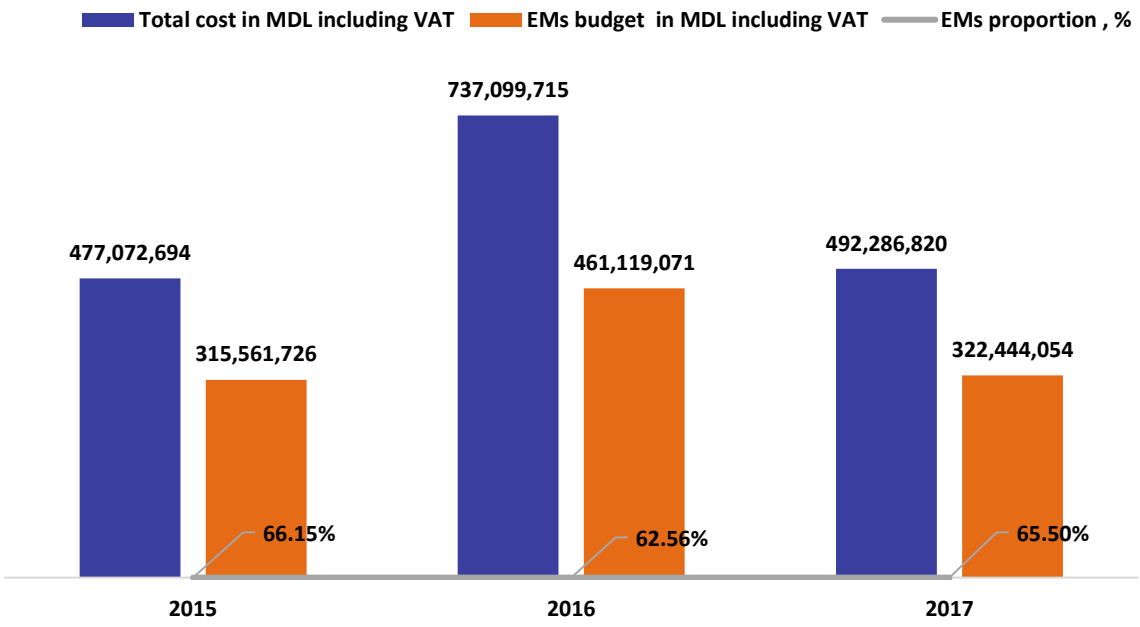
Therapeutic group	2015		2016		2017	
	Number of procured molecules/INNs	Total cost, million MDL (0 VAT)	Number of procured molecules/INNs	Cost total, million MDL (TVA 0)	Number of procured molecules/INNs	Total cost, million MDL (0 VAT)
TB medicines (6.2.4 Antituberculosis medicines)	11	29,980,236	14	46,880,466	13	24,892,675
ARV medicines (6.4.2 Antiretroviral medicines)	17	16,770,587	16	8,349,574	16	16,219,013
Total value, MDL (0 VAT):				**55,230,040**		**41,111,688**

Note: The total procurement costs covered by GF Grants are at the rate of ''0'' VAT and include delivery costs (freight insurance, transport costs) under CIP-Chisinau conditions, according to the INCOTERMS standards, and are recalculated in MDL exchanged at the National Bank of Moldova average currency rate for the year: 2015 - 1USD = 18,8161 MDL; 2016 - 1USD = 19.9238 MDL; 2017 - 1USD = 18.4902 MDL (source - official website of NBM https://www.bnm.md/en/content/ratele-de-schimb).

The value of anti-TB and ARV medicines procurements made by PCIMU, from GF sources represents 9.8% of the total cost of procured medicines with public money in 2015 with a total value of 46,750,824 million MDL (0% VAT), 7.49% or 55.230.040 million MDL (0% VAT) - in 2016 and 8.35% or 41,111,688 million MDL (0% VAT) - in 2017. The budgets for the procurement of anti-TB and ARV medicines from GF sources are determined by the unit price of the medication and the required quantities, which are adjusted based on the remaining stocks at the stage of determining the quantitative needs, the changes in the treatment schemes, etc.

TB and ARV molecules/INNs are found in the estimations of the total number of INNs under the therapeutic group 6. Anti-infective medicines. The total costs for anti-TB and ARV medicines covered by the GF Grants are not included in the total estimation of procurements with public money presented in the Figures 4 and 5, but are shown in Figure 8.

Figure 8. Total amount of procurements of essential and non-essential medicines from public money, including those covered by FG Grants, between 2015-2017



The EMs from 16 therapeutic groups (out of 29) contracted between 2015-2017, the cost of which accounted for more than 1% of the total value, retained the same share in the total public procurement budget in these three years (table 20).

Data evaluation reveals changes for the anti-infective therapeutic group, especially for 2017. For this group, the total amounts contracted for the anti-tuberculosis and antiretroviral subgroups were considered, the final amount does not include the 8% VAT, the logistics costs covered by UNDP and the possible differences in costs as a result

of INCOTERMS contracting conditions. These factors could be among those that caused the overall amount for 2017 to be lower versus 2016.[58] The final budget detailed in Table 19 does not include the amounts for antidiabetic medicines, medicines required for transplantation, for the treatment of mental illness, cancer treatment, rare diseases procured in 2017 through UNDP, because the UNDP official website does not display the factual lists included in the procurement contracts, but only the contracts with total amounts. For this reason, it was not possible to calculate the EMs budget quota to be included in the CCPPH medicines procurement analysis, which provides detailed information per INNs. Based on the presented information we conclude that the contracted amounts increased in 2016 versus 2015, but the number of EMs increased only slightly and only for certain groups. In 2017, the contracted budget is lower than in 2016, the explanation being that the procurements for national and special programs were made under different conditions previously described in this report. Procurements of EMs of Group 2. *Analgesics, Antipyretics, Anti-inflammatory* entailed constant amounts within the limit of 15 million MDL with annual VAT, as well as those of group 15. *Disinfectants and antiseptics* - which in the period of 2015-2017 remained at a relatively constant value of around 10 million MDL including VAT (10.13 million MDL including VAT in 2015, 10.91 million MDL including VAT in 2016 and 10.81 million MDL including VAT in 2017). The same situation was noted for group 25. *Respiratory system medication,* for which the annual costs are in the range of about 3.5 million MDL including annual VAT.

Table 20. List of 16 essential medicines groups with budgets over 1%, which were contracted through centralized procurement, 2015-2017

Therapeutic group	2015		2016		2017	
	EMs from the budget contracted through public procurements	Total cost, million MDL including VAT	EMs from the contracted budget through public procurements	Total cost , million MDL with VAT	EMs from the amount contracted through public procurements	Total cost, million MDL including VAT
6. Anti-infective medicines	25.59%	71,295,746	27.61%	111,302,350	23.52%	60,961,259
8. Antineoplastics, immunosuppressive, palliative care medicines	11.48%	31,989,470	12.23%	49,328,282	12.34%	30,533,475
26. Medicines correcting water, electrolyte and acid-based disturbance	11.30%	31,492,237	9.92%	39,979,195	12.44%	30,787,621
1. Anesthetics	8.39%	23,370,266	8.18%	32,992,681	8.22%	20,351,587
10. Blood disease medicines	7.50%	20,892,654	8.75%	35,297,291	8.97%	22,209,181
17. Gastrointestinal medicines	7.16%	19,961,532	6.47%	26,067,624	6.19%	15,329,381
2. Analgesics, antipyretics, non-steroidal, anti-	5.69%	15,840,314	3.94%	15,902,847	6.07%	15,013,089

[58] It does not include medicines procurement from GF Grants

inflammatory, anti-rheumatic						
12. Cardiovascular medicines	3.71%	10,340,579	3.11%	12,547,043	3.92%	9,702,272
15. Disinfectants and antiseptics	3.64%	10,129,631	2.71%	10,915,729	4.37%	10,810,202
3. Antiallergic medicines used in anaphylaxis	2.68%	7,464,880	2.57%	10,363,138	2.07%	5,118,554
14. Diagnostic agents	2.15%	5,992,901	3.96%	15,975,782	2.46%	6,088,156
7. Antimigraine medication, cerebral hemodynamic and metabolic medicines	1.93%	5,363,834	2.19%	8,825,567	2.30%	5,692,687
25. Respiratory system medicines	1.29%	3,594,881	0.88%	3,535,260	1.41%	3,485,389
27. Vitamins and minerals	1.25%	3,479,461	1.20%	4,833,957	1.11%	2,735,913
24. Psychotropic medication	1.15%	3,205,655	1.13%	4,537,055	1.01%	2,494,170
18. Hormonal, endocrine medicine and contraceptives	1.04%	2,902,258	0.90%	3,641,669	0.57%	1,408,416

In estimating the total expenditure for procurement of EMs from public money for the years 2016-2017, the value of the contracts for vaccines (Therapeutic Group 19. Immunological) procured through UNICEF (Figure 4 & 8) was also taken into account According to available data, UNICEF procured and delivered 11 vaccine /INNs in 2016, amounting to approximately 1,164,598 million USD or about 21,533 654 million MDL excluding VAT (0% VAT) and 10 vaccine INNs in 2017 amounting to 1,204,648 million USD or about 22,274,184 million MDL excluding VAT (Table 21).

Table 21. Data on the procurement of immunological products - Vaccines (Therapeutic Group 19. Immunological) with public money through UNICEF in the period of 2016-2017

Therapeutic group	2016		2017	
	Number of procured EM INNs	total cost, million MDL including VAT	Number DCI ME procured	Number of procured EM INNs
19. IMMUNOLOGICAL MEDICINES/Vaccines	11	21,533,654	10	22,274,184

ANALYSIS OF THE NATIONAL LIST OF ESSENTIAL MEDICINES AND REIMBURSED MEDICINES

The current list of medicine reimbursed from the mandatory health insurance funds (LRM) is established and approved by the joint order of MoH and NHIC no. 492/139A of 22.04.2013, as further amended and supplemented. The last adjustment of the LRM was approved by the Joint Order of MoHLSP/NHIC no. 729/230-A of 11.06.2018. The list of reimbursed medicines is structured in Sections (2) and Chapters (6) depending on healthcare levels, reimbursement rates and treatment groups:

Section I. List of Medicines reimbursed from Mandatory Health Insurance Funds for continuous treatment in outpatient conditions:

Chapter 1. Partially Reimbursed Medicines (on average 30%)
Chapter 2. Partially Reimbursed Medicines (50% on average)
Chapter 3. Partially Reimbursed Medicines (70% on average)
Chapter 4. Fully Reimbursed Medicines (100%)

Section II. The list of medicines reimbursed from mandatory health insurance funds for episodic treatment in the outpatient care department and at home treatments for some diseases commonly encountered in family doctor practice:

Chapter 1. Partially Reimbursed Medicines for Adults (over 70% on average) and fully reimbursed (100%) for children - 0-18 years of age.
Chapter 2. Fully Reimbursed Medicines (100%) for Children - 0-18 years of age.

Medicines are presented under international non-proprietary names with specification of strength and pharmaceutical form for which fixed costs in MDL are set off (including VAT and excluding VAT).

The comparative analysis of the 2011 NEML with the current list of compensated medicine (June 2018 edition) reveals that essential medicines represent 72.95% (116 INNs) of the total of 159 INNs included in the LRM. By comparison with WHO EML 2017 edition, it is noted that 8 of 43 INNs which are not found in the NEML 2011 are present in the WHO EML. 2 of 8 INNs correspond to the pharmaceutical form and dosages (amiodarone and pyridostigmine), 2 INNs are present in other doses (clozapine and gliclazide) and 4 INNs - in other pharmaceutical forms (pyridoxine hydrochloride tablets, thiamine hydrochloride tablets, methylprednisolone injectable solution, digoxin injectable solution).

When comparing data with the WHO Study on the availability and affordability of medicine in the R of Moldova carried out in 2011, it can be noticed that the share of essential medicines in the list of reimbursed medicines has increased by 26.09% compared to 2011. According to the analysis conducted by the WHO team jointly with the country team, the essential medicines on the list of reimbursed medicines in 2011 constituted only 92 INNs and of these mostly partially compensated: 11 INNs for chronic diseases are reimbursed at the rate of 50% and only 4 INNs - at the rate of 70% and 3 INNs - at the rate of 90%.

The analysis of the LRM (2018 edition) versus the NEML in force shows that the EMs/ INNs in the LRM increased compared to 2011 from 92 molecules/INNs to 116 molecules/INNs.

Also, in its current version, the LRM contains fully compensated medicines (100%), among which the share of EMs constitute 69,81% (or 37 INNs) of the total number of 53 reimbursed medicines as INNs provided for long-term care in outpatient conditions - Chapter 4 (Section I)[59]; also there is an increase in the number of EMs/ INNs with "the average compensation rate of 70%", from 4 INNs in 2011 to 17 in the LRM 2018, which represents 70.83% of the total number of 24 INNs included in LRM 2018 under the Chapter 3 (Section I - CM for long-term care treatment in ambulatory conditions)[60].

Thus, the EMs have a share of 73.49% of the total compensated medicines with 50%, 70% and 100% rate of reimbursement for ambulatory support treatment. In case of reimbursed medicines for the episodic treatment in the outpatient care and at home of some diseases commonly encountered in the practice of the family doctor (section II), the EMs account for 80.88 % or 55 INNs of the total of 68 INNs in the LRM in 2018 (Table 22).

Table 22. Representation of EMs in the list of reimbursed medicines and distribution by compensation rates

Section/Chapter	Reimbursement rate	INNs in the LRM	INNs in the NEML	present, %
Section I	LRM from MHIF for supportive (long-term) treatment under ambulatory conditions			
Chapter 1	Partially RM - on average by 30%	**4**	**0**	0.00%
Chapter 2	Partially RM - on average by 50%	**10**	**7**	70.00%
Chapter 3	Partially RM - on average by 70%	**24**	**17**	70.83%
Chapter 4	Fully RM - 100%	**53**	**37**	69,81%
Section II	LRM from MHIF for the episodic treatment in the outpatient care department and at home of some diseases commonly encountered in the practice of the family doctor			
Chapter 1	Partially RM on average by 70% (adults) and fully - 100% (children aged 0-18)	**53**	**40**	75,47%
Chapter 2	Fully RM - 100% (children aged 0-18).	**15**	**15**	100%
	TOTAL	**159**	**116**	**72,95%**

[59] Annex No. 1 to the Order of the MoH and NHIC no. 492 / 139A of 22.04.2013 on compensated medicines from MHIF
[60] Ibid.

Table 23. List of reimbursed medicines versus the National List of Essential Medicines 2011 and WHO EML 2017

No. d/o	INN Compensated Medicines	Essential Medicines, RM - 2011	WHO Essential Medicines -2017 (adults)	WHO Essential Medicines - 2017 (children)
SECTION I. List of Medicines Reimbursed from Mandatory Health Insurance Funds for supportive (long term) treatment in outpatient conditions (International Nonproprietary Names - INN)				
Chapter 1. Partially reimbursed medicines (on average by 30 %)				
1	ESCITALOPRAM	-	-	-
2	DONEPEZILI HYDROCHLORID	-	-	-
3	LERCANIDIPIN (for hypertensive patients with Amlodipine intolerance)	-	-	-
4	SALMETEROL+FLUTICASONE M	-	-	-
Chapter 2. Partially reimbursed medicines (on average by 50 %)				
5	ACETYLSALICYLIC ACID	+	+	+
6	AMIODARONE	+	+	-
7	DIGOXIN	+	+	+
8	ISOSORBIDE DINITRATE (40 mg capsules)	- only 5mg tablets	- only 5mg tablets	-
9	ISOSORBIDE MONONITRATE	-	-	-
10	WARFARIN	+	+	+
11	CLOPIDOGREL (for the treatment of patients after coronary angioplasty)	+	+	-
12	SIMVASTATIN (for patients with genetically determined lipidemia)	+	+	-
13	MESALAZINE	+	-	-
14	ACECLOFENAC	-	-	-
Chapter 3. Partially reimbursed medicines (on average by 70 %)				
15	BROMOCRIPTINE	-	-	-
16	LEVOTHYROXINE	+	+	+
17	THIAMAZOLE	-	-	+
18	BECLOMETASONE	+	+	-
19	FLUTICASONE	+	-	-
20	URSODEOXICHOLIC ACID	-	-	-
21	AMLODIPINE	+	+	-
22	BISOPROLOL	+	+	-
23	CARVEDILOL (treatment of patients with stable pectoral angina, heart failure)	+	+ as an alternative to bisoprolol	-
24	ENALAPRIL	+	+	+
25	INDAPAMIDE	+	-	-
26	LISINOPRIL	+	-	-
27	LOSARTAN	+	+	-

28	METOPROLOL	+	+ as an alternative to bisoprolol	-
29	NEBIVOLOL (for the treatment of hypertensive patients with heart failure over 65 years of age)	-	-	-
30	PERINDOPRIL (for the treatment of hypertensive patients with Ischemic Cardiopathy and Myocardial Infarction)	+	-	-
31	RAMIPRIL	+	-	-
32	SPIRONOLACTONE	+	+	+
33	TELMISARTAN (for the treatment of hypertensive patients with diabetes mellitus)	-	-	-
34	TORASEMIDE	-	-	-
35	VALSARTAN (for the treatment of hypertensive patients with diabetes mellitus and heart failure)	-	-	-
36	VERAPAMIL	+	+	-
37	DICLOFENAC	+	-	-
38	ALLOPURINOL	+	+	+
Chapter 4. Fully Reimbursed Medicines (100%) for treatment and prophylaxis in children aged 0-18 years				
39	ERGOCALCIFEROL	+	+ * Ca as an alternative to colecalciferol	+ * Ca as an alternative to colecalciferol
40	IRON (III) HYDROXIDE POLYMALTOSE	-	- IRON SALT	- IRON SALT
41	FLUTICASONE	+	-	-
42	FERROUS SULPHATE WITH ASCORBIC ACID	+	-	-
43	FOLIC ACID	+	+	+
44	VALPROIC ACID	+	+	+
45	CARBAMAZEPINE	+	+	+
46	LAMOTRIGINE	+	+	+
47	PHENOBARBITAL	+	+	+
48	TOPIRAMATE	-	-	-
49	VALPROAT NATRIUM M	+	+	+
50	LEVODOPA + CARBIDOPA	+	+	-
51	TRIHEXIFFENIDIL (Including for the treatment of mental illness)	+	-	-
52	AMITRIPTYLINE	+	+	+
53	CLONAZEPAM	+	-	-
54	CLOZAPINE	-	+	-
55	DIAZEPAM (Including epilepsy treatment)	+	+	+
56	PAROXETINE	-	-	-
57	RISPERIDONE	+	+	-
58	SERTRALINE	+	-	-
59	SULPIRIDE	+	-	-
60	TRIFLUOPERAZINE	+	-	-
61	HALOPERIDOL	+	+	+
62	LEVOMEPROMAZINE	-	-	-

63	GLIBENCLAMIDUM	+	+	-
64	GLICLAZIDUM (indicated in patients with cardiovascular pathology)	-	+	-
65	GLIMEPIRIDE	-	-	-
66	METFORMIN	+	+	+
67	REPAGLINIDE (indicated in patients with postprandial hyperglycaemia)	+	-	-
68	INSULIN HUMAN (ATC code: A10AB01)	+	+	+
69	INSULIN HUMAN (ATC code: A10AC0r)	+	+	+
70	INSULIN HUMAN (ATC code: A10AD01)	+	+	+
71	SALBUTAMOL	+	+	+
72	TEOPHYLLINE	+	-	-
73	METILPREDNISOLON (Cream & Ointment)	- only injectable forms & tablets	- only injectable forms	- only injectable forms
74	CLEMASTINE	+	-	-
75	DESLORATADINE	+	-	-
76	DEXPANTHENOL	-	-	-
77	MOMETASONE	-	-	-
78	CETIRIZINE	+	-	-
79	PREDNISOLONUM	+	+	+
80	METILPREDNISOLONE	+	+	+
81	METHOTREXATE	+	+	+
82	BRINZOLAMIDE	-	-	-
83	TIMOLOL	+	+	-
84	TRAVOPROST	-	-	-
85	TRAVOPROST M+TIMOLOL	-	-	-
86	BRIMONIDINE+TIMOLOL	-	-	-
87	PIRIDOSTIGMINE BROMIDE	+	+	+
88	PANCREATIN	+	+	+
89	TOBRAMYCIN	-	-	-
90	COLISTIN	-	+	+
91	INTERFERON -$_{\beta}$-1a	+ Interferon – beta	- pegylated interferon alfa (2a or 2b)	-
	SECTION II List of Reimbursed Medicines from the Mandatory Health Insurance Funds for the episodic treatment at in the outpatient care department and at home of some diseases commonly encountered in the practice of the family doctor			
	Chapter 1. Partially reimbursed medicines for adults (on average by 70%) and fully compensated - (100%) for children aged 0-18			
92	AMINOPHYLLINE	+	-	-
93	AMOXYCILLINE	+	+	+
94	AMOXICILIN + CLAVULANIC ACID	+	+	+
95	AMPICILLIN	+	+	+
96	AZITHROMYCIN	+	+	+
97	CAPTOPRIL	+	-	-
98	CEFTRIAXONE	+	+	+

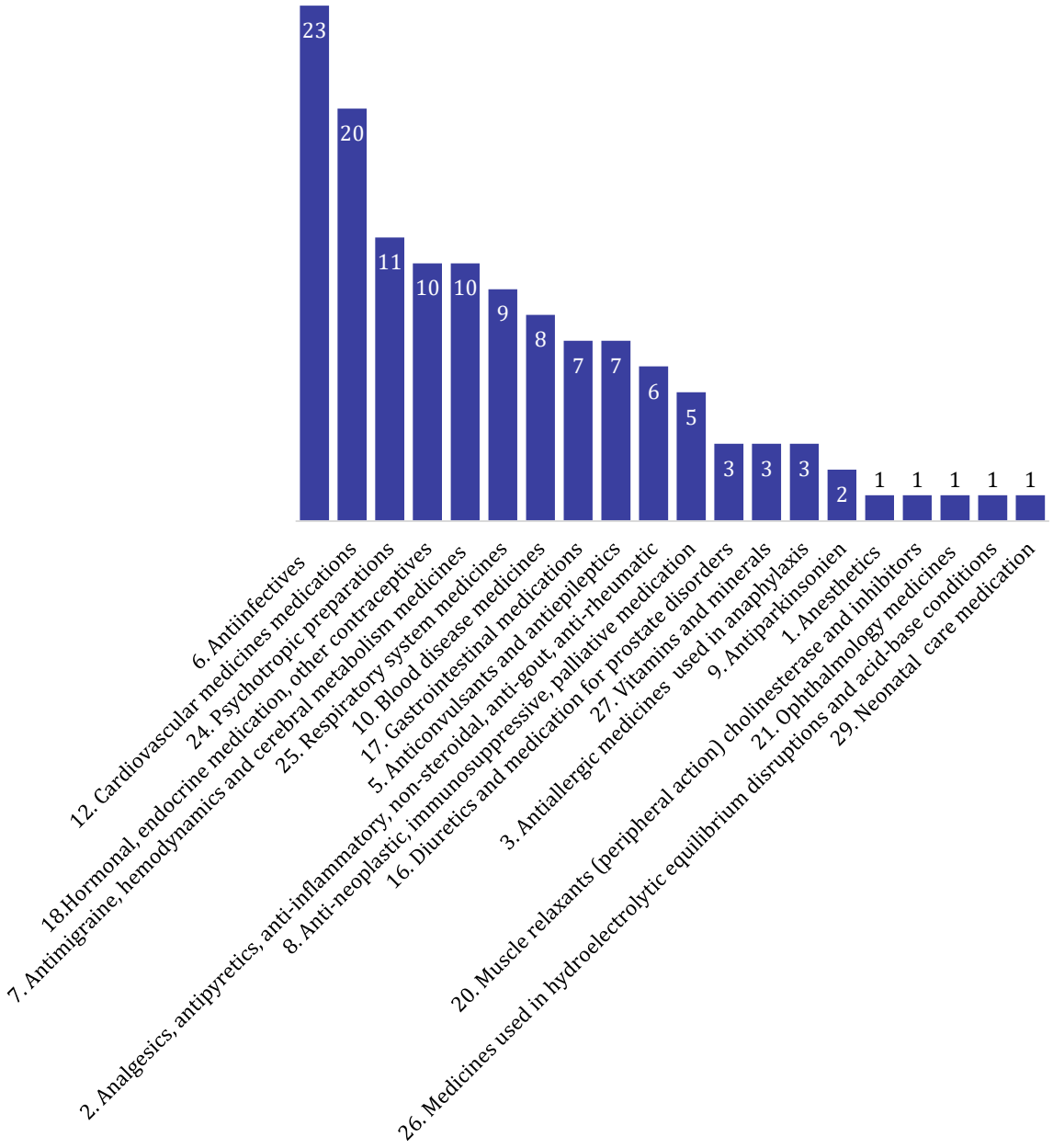
99	CEFOPERAZONE	+	-	-
100	CEPHALEXIN	+	+	+
101	CEFIXIME	+	+	+
102	CEFPODOXIME	-	-	-
103	CEFUROXIME	+	-	-
104	CIPROFLOXACIN	+	+	+
105	CLARITHROMYCIN	+	+	+
106	COLCHICINE	+	-	-
107	CYANOCOBALAMIN	+	-	-
108	DEXKETOPROFEN	+	-	-
109	DEXAMETHASONE	+	+	+
110	DICLOFENAC	+	-	-
111	DIPYRIDAMOLE	+	-	-
112	DOXYCYCLINE	+	+	+
113	FAMOTIDINE	+	-	-
114	IPRATROPY BROMIDE + FENOTEROL	*- only as 2 individual products)*	- only IPRATROPIUM	-
115	FLUCONAZOLE	+	+	+
116	FLUOXETINE	+	+	+
117	FUROSEMIDE	+	+	+
118	GABAPENTIN	+	-	-
119	KETOPROFEN	+	-	-
120	LEFLUNOMIDE	-	-	-
121	MELOXICAM	-	-	-
122	METRONIDAZOLE	+	+	+
123	NATRIUM CHLORIDE	+	-	-
124	NEOSTIGMIN METILSULFAT	+	+	+
125	NICERGOLINE	+	-	-
126	NIMESULIDE	-	-	-
127	OFLOXACIN	+	+	+
128	OMEPRAZOLE	+	+	+
129	PANTOPRAZOLE	-	-	-
130	PAPAVERINE	+	-	-
131	PENTOXIFYLLINE	+	-	-
132	PIRACETAM	+	-	-
133	PREGABALIN	-	-	-
134	PROPRANOLOL	+	+	+
135	PIRIDOXIN (injectable solution)	*- only tablets of 25mg*	*- only tablets of 25mg*	*- only tablets of 25mg*
136	RABEPRAZOLE	-	-	-
137	ROXITHROMYCIN	+	-	-
138	TRIMETHOPRIM-SULFAMETHOXAZOLE	+	+	+
139	SILYMARINE	-	-	-
140	SULODEXIDE	-	-	-
141	TETRACICLIN (tablets & capsules)	*- only ophthalmic ointment*	*- only ophthalmic ointment*	*- only ophthalmic ointment*
142	TIZANIDINE	-	-	-
143	TIAMIN HYDROCLORID (injectable solution)	*- only tablets of 50mg*	*- only tablets of 50mg*	*- only tablets of 50mg*
144	VINPOCETINE	+	-	-

Chapter 2. Fully reimbursed medicines (100%) for treatment and prophylaxis in children aged 0-18 years

145	IBUPROFEN	+	+	+
146	INTERFERON ALFA-2B	+ Interferon alpha	pegylated interferon alpha (2a or 2b) *	-
147	ACETYLCYSTEINE	+	+	+
148	CARBOCISTEINE	+	-	-
149	PANCREATIN	+	+	+
150	ALBENDAZOLE	+	+	+
151	AMBROXOL	+	-	-
152	AMOXYCILLINE	+	+	+
153	AMOXYCILLINE + CLAVULANIC ACID	+	+	+
154	AMINOPHYLLINE	+	-	-
155	AZITHROMYCINE	+	+	+
156	BENZATINBENZILPENYLICIN + BENZYLPENYLICIN	+ are found only separately, not in combination	+ are found only separately, not in combination	+ are found only separately, not in combination
157	CEFUROXIM (NOT INDICATED IN PNEUMONIA)	+	-	-
158	PARACETAMOL	+	+	+
159	TRIMETHOPRIM-SULFAMETHOXAZOLE	+	+	+

The therapeutic group distribution of essential medicines present in the LRM (2018) reveals that the LRM 2018 includes EMs of 20 therapeutic groups out of a total of 29 groups present in the NEML 2011, and the highest number of EMs INNs in the LRM is represented by medicines of the group (6) Antiinfectives - 23 INNs (of which 19 INNs are part of RM *for episodic treatment day healthcare/medical consulting rooms, treatment offices and at home of diseases commonly encountered in the practice of the family doctor)*,followed by 20 INNs from group (12) Cardiovascular medicines, 11 INNs - Psychotropic medications (group 24) and 10 INNs from group (7) antimigraine medicine and group (18) Hormonal medication (Figure 8).

Figure 9. Distribution of Essential Medicines presented in the Reimbursed Medicines List by therapeutic groups according to the NEML 2011 (INN number, including duplication).



At the same time, in the LRM for supportive (long-term) treatment in ambulatory conditions (Section I), the highest share of EMs - 20 INNs would be Cardiovascular Medicines (group 12) with an average compensation rate of 50-70% of the total cost.

Another examined aspect is the registration of the compensated medicines in the National Catalogue of ex-factory manufacturer prices for medicines. As a result, 4 INNs from the LRM (2018) were found not to be included in the National Catalogue of ex-factory manufacturer prices for medicines, but were registered in the NEML 2011 of RM:

- *Beclametazone* (NEML) - the therapeutic group "Medicines for bronchial asthma" (partially compensated medicines, 70%). This group comprises a total of 2 INNs in the LRM, Beclametazone and *Fluticazone*, the first of which does not have the producer price included in the Catalogue, and the latter has the producer price listed in the Catalogue with the doses and pharmaceutical form included in the LRM;
- *Theophylline* (NEML) - therapeutic group "Medicines for bronchial asthma" (100% fully CM). Within this group there are 2 INNs included in the LRM, Salbutamol and Theophylline, the latter of which does not have the manufacturer's price registered in the Catalogue;
- *Fluoxetine* (NEML) - Section II, Chapter 1;
- *Neostigmin Metilsulfat* (NEML) – Section II, Chapter 1.

Through this evaluation, we highlighted that not all the NEML medicines included in the LRM might be accessible to patients because they are not represented in the National Catalogue of ex-factory manufacturer prices for medicines. One of the solutions would be to provide access to the above-mentioned medicines by importing them as non-registered products with the MoHLSP permission, in accordance with the legislation in force. At the same time, the procedure for importing unauthorized medicinal products is triggered by an application to justify the need for such import. If we examine the approval criteria for the import of unauthorized medicinal products, the conditions include the absence of analogues or substitutes on the pharmaceutical market. In the case of the products examined above, Beclametase and Theophylline, we cannot tell whether the regulations for unauthorized import could be applied in the situation described. Also, the lack of a notification/alert system on essential medicines missing on the market does not push for operational decisions to improve access to essential medicines. No information has been found on the NHIC official website to reflect the refusals or limitations in the provision of the medicines in line with the INNs included in the list of compensated medicines on the grounds of their unavailability on the pharmaceutical market.

A barrier to access 4 INNs from the EML is the absence of producer price for these medicines in the National Catalogue of ex-factory manufacturer prices for medicines. Since the producer price is recorded annually in the price catalogue, the issue of access to medicines will be directly linked to the fact that the product has its producer price registered, in addition to the condition of holding the marketing authorization for the medicines. Currently, there are no public reports on the MMDA, NHIC and/or MoHLSP official websites related to the monitoring of essential and compensated medicines flow, including average medicine consumption and medicines unavailability on the pharmaceutical market.