Vol. 18(2), pp. 12-16, March 2024
DOI: 10.5897/AJPP2024.5379
Article Number: 99159D371884
ISSN 1996-0816

http://www.academicjournals.org/AJPP

ACADEMIC JOURNALS
expand your knowledge

African Journal of Pharmacy and Pharmacology

Full Length Research Paper

Approval of conventional medicines in Cameroon in 2023: Why do some fail?

Zoa Bindzi Joseph Bertin Alexis[1]*, Etoundi Ada Valérie[2], Minyem Ngombi Afuh Aude Perine[2,3], Tsafack Edmond Elisée[2,4], Khou-kouz Nkoulou Claude Hervé[2], Mballa Magalie Flore[2], Nyangono Ndongo Martin[1,3], Yaba Dana Basil[2] and Nnanga Nga[3]

[1]Department of Pharmaceutical Sciences, Faculty of Medicine and Pharmaceutical Sciences, University of Ebolowa, Sangmélima 599, Cameroon.
[2]Department of Pharmacy, Drugs and Laboratories, Ministry of Public Health, Yaoundé, Cameroon.
[3]Department of Galenics and Pharmaceutical Legislation, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé 3316, Cameroon.
[4]Department of Pharmacotoxicology, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé 3316, Cameroon.

Received 5 January, 2024; Accepted 15 February, 2024

This study focuses on the work of the specialized commission responsible for assessing the conformity of registration files for drugs seeking marketing authorization (MA) in Cameroon during 2023, particularly examining why certain applicants submit noncompliant files for approval. First, the files submitted to the specialized commission in 2023 were listed. The data on the reasons for noncompliance were then compiled, and finally, a statistical analysis was performed. Out of the 768 files assessed by the specialized commission in 2023, only 151 (19.6%) were compliant. Letters of observation (LO) were issued for the remaining 617 participants for the following reasons: Lack of bioequivalence studies (19.6%), incomplete or missing finished product stability data (16.8%), primary and secondary packaging and/or package leaflets in one language (11.3%), missing control section from technical dossiers (11.3%), certificate of analysis missing or not signed (8.4%), absence of information on the quality of the active substance (8.1%), absence of edging (6.4%), expired or uncertified good manufacturing practices (GMP) certificate and/or operating license (5.6%), and absence of a route of administration on the primary and/or secondary packaging (4.8%). The first four reasons alone account for more than 55% of the reasons for noncompliance, highlighting the need for targeted communication to improve the compliance rate. This could serve as a partial solution to the availability of pharmaceutical references and drug shortages in Cameroon.

Key words: registration, marketing authorization, observation letter, *commission spécialisée des médicaments conventionnels*, regulatory assessment.

INTRODUCTION

A medicinal product is defined as "any substance or composition represented as having curative or preventive properties in respect of human or animal diseases, as well as any substance or composition which may be used in or administered to human beings or animals, with a view to making a medical diagnosis or to restoring, correcting or

*Corresponding author. E-mail: 1918093836@qq.com. Tel: +237 692169976. ORCID: 0000-0002-3051-5772.

modifying their physiological functions by exerting a pharmacological, immunological or metabolic action" (CSP, 2022). In response to serious accidents caused by inadequately tested drugs, all industrialized countries have intensified the regulation of drug marketing (de Mazières and Paris, 2004). Before a pharmaceutical specialty can be marketed, it must obtain marketing authorization (MA). Approval refers to the process by which a pharmaceutical regulatory authority grants, renews, extends, or varies an MA. A statutory system of approval is required at the national level as a prerequisite for the marketing of a pharmaceutical product. According to Decree No. 98/405/PM of October 22, 1998, which sets out the conditions for the approval and marketing of pharmaceutical products, any marketing of a drug in the Cameroonian territory must take place after obtaining MA, following an administrative and technical examination by the competent authorities (MINSANTE, 1998).

In 2018, Cameroon's department of pharmacy, drug, and laboratories (DPML) published the "Guide *Pratique* de *Soumission des Dossiers d'homologation des Produits Pharmaceutiques*" (MINSANTE, 2018). This guide contains information ranging from the receipt of applications for approval (granting, renewal, variation, or extension) to the opinion formulated by the "Commission *Nationale du Médicament* (CNM)" and the subsequent decision of the competent authority. Nonetheless, only a few drugs are granted marketing authorization (MA) after evaluation. Once the files for conventional drugs are received by the DPML, they are evaluated by an internal commission and submitted to the "Commission *Spécialisée des Médicaments Conventionnels* (CSMC)" for its opinion. The CSMC comprises sixteen members (medical specialists and pharmacists) appointed by the Minister of Public Health (MSP) and it is convened by the MSP of Cameroon as needed.

The CSMC is responsible for the administrative and technical evaluation of MA files, as well as for the visual analysis of drug samples upon presentation by the DPML's internal commission, following advice from the "National Laboratory for Drug Quality Control and Expertise (LANACOME)." Based on these analyses, the CSMC issues an opinion stating whether the file is compliant or noncompliant. In the latter case, a letter of observation (LO) is generally sent to the applicant. The LO can be defined as the Ministry of Health's administrative response to the applicant for MA in Cameroon. The aim of the present work is to highlight the frequent reasons for drafting a letter of observation to laboratories applying for the granting of marketing authorization after evaluation by the CSMC and the CNM. To this end, the work of the CSMC for the 2023 financial year was examined.

MATERIALS AND METHODS

The type of study is foresight and analytics. The materilas used included the following

1) Minutes of the sessions of the CSMC
2) Conventional drug samples

The study periods was January to December, 2023
The method used was as follows:

1) Inventory of the therapeutic classes submitted to the CSMC for evaluation from January to December 2023;
2) Identify the various reasons for writing a letter of observation over the same period;
3) Compile the data;
4) All the statistical analyses were performed on the compiled data.
5) Rate (%) of most common therapeutic classes;
6) Rate (%) of compliant files;
7) Rate (%) reasons for noncompliance.

The data were compiled using Microsoft Excel 2016 and analyzed using GraphPad Prism 8.0.2.

RESULTS

Most represented therapeutic classes

Seven hundred and sixty-eight conventional drugs were evaluated by the CSMC in 2023. The most frequently encountered therapeutic classes are shown in Figure 1.

Compliant drugs

During 2023, the CSMC held four sessions and 768 conventional medicines were evaluated. Of these, only 19.6%, or 151 products out of 768, received a "compliant or favorable" opinion, as shown in Table 1.

Most common reasons for an LO

During 2023, six hundred and seventeen out of seven hundred and sixty-eight drugs did not have a compliant dossier, and an LO was issued for each of these drugs to the MA applicant laboratory. The most frequent reasons for which this LO was written are listed in Table 2.

DISCUSSION

The registration of a drug in Cameroon can be defined as the process through which the Ministry of Public Health, via the DPML, grants marketing authorization (MA) and approves its use after evaluating its quality, efficacy, and safety (Lexchin, 2008).

The marketing authorization (MA) is the agreement granted to the holder of the exploitation rights for an industrially manufactured drug, allowing it to be marketed. In Cameroon, Article 30 of Decree No. 98/405/PM of October 22, 1998, which outlines the procedures for approving and marketing pharmaceutical products, specifies a period of 18 months, followed by 5 years

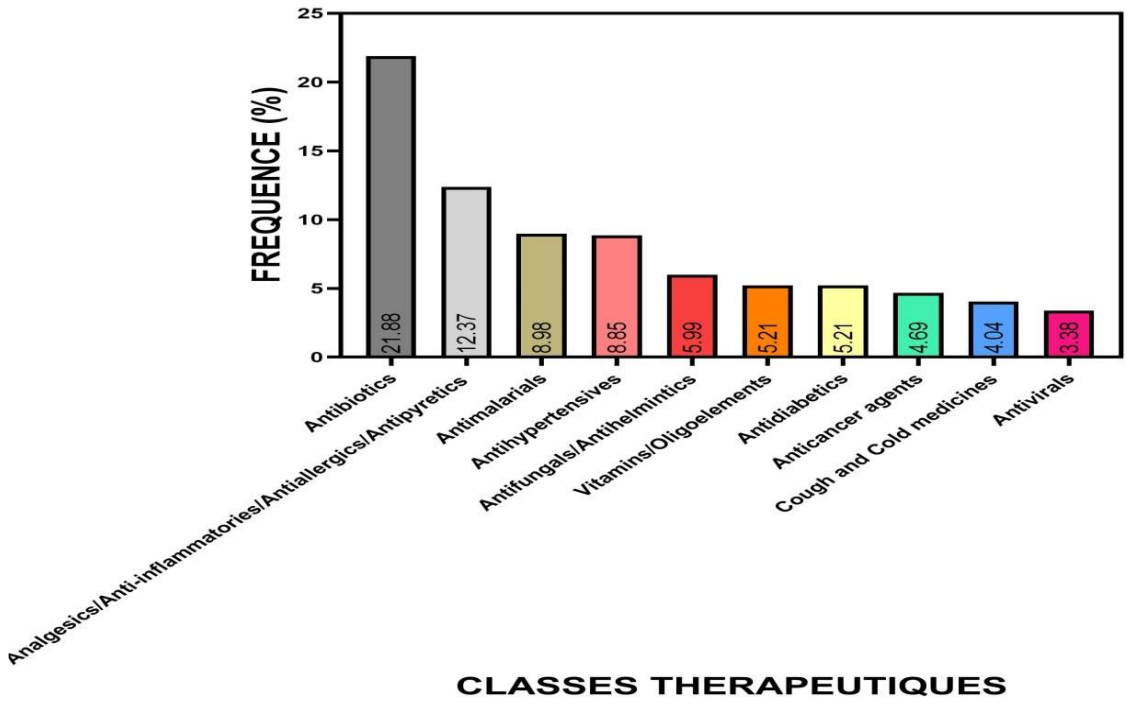

Figure 1. The 10 therapeutic classes most frequently encountered during the evaluation of the registration files in 2023 are as follows, listed in descending order: antibiotics, analgesics/anti-inflammatories/antiallergics/ antipyretics, antimalarials, antihypertensives, antifungals/antihelmintics, vitamins/oligoelements, antidiabetics, anticancer agents, cough and cold medicines, and antivirals.

Table 1. Number and frequency of compliant drugs used in 2023.

2023 sessions	Assent	Total	Frequence (%)
CSMC1	32	183	17.4863388
CSMC2	38	187	20.32085561
CSMC3	64	249	25.70281124
CSMC4	17	149	11.40939597
Total	151	768	19.66145833

Table 2. Frequency of reasons for drafting an LO to MA applicant in 2023.

No.	Reason	Total	Frequence (%)
1	Lack of bioequivalence studies	121	19.61102107
2	Incomplete or missing finished product stability data	104	16.85575365
3	Primary and secondary packaging and/or package leaflets in one language	70	11.3452188
4	Missing control section from technical dossiers (CTD)	70	11.3452188
5	Certificate of analysis missing or not signed	52	8.427876823
6	The absence of information on the quality of the active substance	50	8.103727715
7	The absence of edging	40	6.482982172
8	An expired or uncertified good manufacturing practices (GMP) certificate and/or operating license	35	5.6726094
9	The absence of a route of administration on the primary and/or secondary packaging	30	4.862236629
10	Others	45	7.293354943
	Total	617	100

(MINSANTE, 2013). However, it has been five years since the drafting of Regulation No. 5/13-UEAC-OCEAC-CM-SE-2 on the Harmonization of Approval Procedures for Medicinal Products for Human Use in the CEMAC area (UEAC, 2018). This can be justified by the fact that the Regulation is a mandatory standard that does not require transposition. It directly affects the member states within the community. To obtain marketing authorization, the holder of the right to use a drug must submit a file in a standardized format: the CTD ("common technical document") format. In the CTD format, information is organized into five parts: module 1 contains administrative information; module 2 includes "summaries" of modules 3, 4, and 5; module 3 comprises documents on the chemical (and/or biological) properties of the drug, its manufacture, and control, including stability; module 4 covers preclinical studies; and module 5 encompasses clinical studies (Feroyard, 2014). For a new molecule, we add to the above a description of how the active substance is manufactured (often-based on documents such as the Certificate of Conformity to the European Pharmacopoeia or the Drug Master File, which help to evaluate the substance). For well-established generic medicinal products, the file can be shortened. Clinical studies are replaced by bioequivalence studies. In 2023, 768 MA dossiers were evaluated in Cameroon, 151 of which were compliant, for a compliance rate of 19.6%. This low rate may reflect a lack of knowledge of Cameroon's pharmaceutical regulations on the part of applicant laboratories, particularly with regard to drug registration in Cameroon. This also highlights the need to step up communication on drug registration in Cameroon.

Our focus was to identify the primary reasons for noncompliance or unfavorable outcomes in marketing authorization application files. In 2023, we identified several reasons for this, with the ten main reasons listed in descending order in Table 2. This chapter will specifically address the first four reasons, as they collectively account for over 55% of the non-conformities found in the MA dossier. The primary reason is the lack of bioequivalence studies. It is noteworthy that most of the drugs approved in Cameroon are already off-patent (generic drugs) (Geest, 2017). One of the reasons for this is that Cameroon, as a developing country, prefers medicines with the best quality/price ratio, in line with World Health Organization (WHO) guidelines (World Health Assembly, 2002). Elsewhere, taking into account the purchasing power of potential customers, it is possible that applicants will give priority to their generics, as most of the medicines treating priority diseases in Cameroon have patents that have fallen into the public domain. The second most common reason is that the data on finished product stability studies are incomplete and/or absent. Finished product stability studies are an essential part of marketing authorization, as they ensure that the quality of the product is maintained throughout its shelf life. In this way, the shelf life of a drug can be defined (Pierre-Antoine, 2020). In 2023, 11.35% of the dossiers were noncompliant, with inserts in French, English, Chinese, Arabic, or Spanish only, or bilingual (English-Arabic, French-Arabic, English-Chinese, and Spanish-English). As Cameroon is a bilingual country, packaging and leaflets must be printed in the two official languages, French and English. The authors also had to address issues of poor translation, highlighting the need for these documents to be translated by sworn translators.

The fourth reason pertains to the lack of a control section in the technical file. It encompasses the control of the active substance, excipients, and packaging materials, as well as intermediate controls during manufacture. This fourth reason is equally significant as the previous three, as it encompasses both quality control and quality assurance.

Conclusion

One of the limitations of our discussion was the absence of data on this subject published in other countries, which complicates the expansion of our discussion. The objective of this study was to identify the common reasons why conventional medicines from marketing authorization (MA) applicants fail to obtain MA in Cameroon. In 2023, only 19.6% of drugs submitted to the CSMC had a compliant dossier. The most common reasons for this discrepancy include the absence of bioequivalence studies, incomplete or missing information on the stability of the finished product, unilingual primary and secondary packaging and/or package leaflets, and the lack of a control section in the technical dossier. We believe that if applicants address these four reasons, the compliance rate will significantly increase, as they alone account for more than 50% of the reasons for refusal of marketing authorization. This could represent a significant advancement in the availability of pharmaceutical references in Cameroon and a partial solution to drug shortages.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

ACKNOWLEDGMENT

Our thanks go to His Excellency Dr Manaouda Malachie, Cameroon's Minister of Public Health, and to Dr Ngene Jean Pierre, President of the Specialized Commission on Conventional Medicines.

REFERENCES

CSP (2022). Article L5111-1: Definition du Medicament, Legifrance.

https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000006689867/ (accessed July 5, 2023).
de Mazières C, Paris V (2004). La régulation de l'industrie pharmaceutique. Revue D'économie Financière pp. 241-265.
Feroyard A (2014). Constitution d'un dossier d'autorisation de mise sur le marche d'un médicament à usage humain et ses différentes procédures d'enregistrement en Europe. https://dumas.ccsd.cnrs.fr/dumas-01064013.
Geest S (2017). Van der, Les médicaments sur un marché camerounais, Http://Journals.Openedition.Org/Anthropologiesante. https://doi.org/10.4000/ANTHROPOLOGIESANTE.2450.
Lexchin J (2008). Homologation progressive des médicaments : promesse ou cacophonie ? Healthc. Policy 3:15-20.
MINSANTE (2013). Décret N°98-405/PM dU 22 Oct 1998 Fixant les Modalités d'Homologation et de Mise sur le Marché des Produits Pharmaceutiques, DPML. https://dpml.cm/images/Publications/Decrets/Produits pharmaceutiques/Decret Homologation Medicaments.pdf.
MINSANTE (2018). Guide Pratique de Soumission des Dossiers d'Homologation des Produits Pharmaceutiques, DPML.
MINSANTE (1998). Décret N°98-405/PM dU 22 Oct 1998 Fixant les Modalités d'Homologation et de Mise sur le Marché des Produits Pharmaceutiques, DPML. https://www.juriafrica.com/lex/decret-98-405-pm-22-oct-1998-15906.htm
Pierre-Antoine D (2020). Importance des etudes de stabilite dans le domaine pharmaceutique: qualite, reglementation et processus general, Universite de Lyon. https://bibnum.univ-lyon1.fr/nuxeo/nxfile/default/8cb46375-664a-4936-972a-a4f1f1bafe51/file:content/THph_2020_DURAFOUR_Pierre_Antoine.pdf.
UEAC (2018). Les annexes au Règlement N° 05/13-UEAC-OCEAC-CM-SE-2 portant Référentiel d'Harmonisation des Procédures d'Homologation des Médicaments à usage Humain en Afrique Centrale, OCEAC. https://manualzz.com/doc/5083879/les-annexes-au-règlement-n°05-13-ueac-oceac-cm-se.
World Health Assembly (2002). Ensuring accessibility of essential medicines. WHO-Iris 55:2. https://iris.who.int/handle/10665/78531.