Guideline

Central Administration of Pharmaceutical Care
General Administration of Drug Utilization and Pharmacy Practice

Guides for Classification as Non-Prescription Medicinal Products (OTC)

2021

Code: EDREX: GU.CAP.care.001
Version No:1
Issue Date: 2021
Effective

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1. Introduction

Over-the-counter (Non-Prescription) drug products play an increasingly vital role in health care system. Self-medication has been widely used by patient for the control of symptoms and minor ailments.

The purpose of the present guidelines is to set criteria by which drug regulatory authority can assess the suitability of medicinal products for use in self-medication.

2. Definition of non-prescription medicinal products

Those which do not require a medical prescription and which are sold primarily with the intention that they will be used by consumers on their own initiative and responsibility, when they consider such a use appropriate. The term "over the-counter (OTC) medicines' is widely used to describe this class of product.

3. Scope of the guidelines

This guideline addresses the criteria for assessment of safety and efficacy of self-medication products; it also provides an overview of the regulatory and administrative requirements for classification of a product as an OTC. The guide applies to medicinal products for human use.

4. General Principles

1. Self- medication by non-prescription drugs should be for symptoms and minor ailments.
2. It is critical to have a fully detailed and patient friendly label.
3. Health care professionals should play a basic role in providing information and awareness about self- medication and the rational use of medicines.
4. Generally, in advertising and promotion the use of self- medication should be consistent with the approved insert.
5. Self-medication is not appropriate and a health care professional should be contacted in the following situations:

- Persisting symptoms.
- Condition worsening.
- Severe pain.
- One or more medicines tried without success.
- Experience of unwanted effects.
- Serious psychological problems like anxiety, unease,depression, lethargy, agitation or hyper-excitability.

6. Consultation of health care professionals should be paid during pregnancy or breastfeeding or when the ailment concerns babies and infants.

5. Approaches to assess of a product as Over the Counter (OTC)

The general rule is that drug benefit should outweigh the risks; classification as an OTC should be based on medical and scientific data on safety and efficacy of the compound and rationality in terms of public health.

5.1.Safety Profile

5.1.1. Correct use

Drug not likely to present a danger either directly or indirectly, even when used correctly, if utilized without medical supervision.

- <u>Direct danger:</u>
  <u>OTC Drug should have:</u>
  - Low general toxicity and no relevant reproductive toxicity, genotoxic or carcinogenic properties.
  - Low risk of an adverse reaction -serious type- in thegeneral population.
  - Very low risk of serious type B reactions (non-doserelated “Bizarre”, it is uncommon, not related to a pharmacological action of a drug &

unpredictable.

- No interactions with commonly used medicines whichcan produce serious adverse reactions.
- It may be desirable to avoid certain types of excipient, where they are known to affect certain patient groupsadversely.

- Indirect danger:

  OTC Drug should possess the following characters:

  - Does not mask serious diseases, nor delay the diagnosis and treatment of a condition that requires medical care.
  - Wide Use doesn't increase risk of resistance or cause drug usefulness compromise.
  - The possibility of preventive action should be taken into consideration whenever any of the previous dangers is identified. Package leaflet and or label warnings may be necessary to prevent treatment from “masking” the development of a serious disorder. Therefore, such warnings should indicate a time limit beyond which, if symptoms persist, medical advice should be sought. Medicinal products not subject to a medical prescription should be approved primarily for short term treatment, e.g. when the possibility of “masking” could occur.

5.1.2. Incorrect use (Misuse)

- Health practitioners are not needed for the rational use of the drug.
- A medicinal product should be deemed unsuitable for OTC status if there is a high incidence of conditions listed as contraindications, precautions or warnings, or a high rate of usage of interacting drugs in the population, in case of patients likely to use the medicine.
- It is important that the consequences of use should not represent high

danger to health, if the patient uses the product where it is not indicated, uses it for a longer period than recommended, exceeds the recommended dose or fails to heed warnings or contraindications.

- Potential for drug misuse and abuse is low (ex: doesn't generate tolerance or dependency).
- Medicinal products shall be subject to reverse switch to medical prescription when they are frequently and to a very wide extent used incorrectly and as a result are likely to present a direct or indirect danger to human health.

5.2.Appropriateness for self-care/assessment

- Drugs used for symptoms or conditions that can be assessed by the patient.
- Generally, such indications are widely experienced symptoms or disorders that are readily recognizable by ordinary consumers or that are initially diagnosed by a doctor and are often self-limiting in nature i.e. collaborative care.
- An OTC medicinal product should not require physician's supervision for monitoring during therapy. The patient should be capable of self-monitoring therapy and natural course of the condition, the duration of symptoms and their reoccurrence and consequences.
- The following aspects are considered:

I. Provision of reliable and consistent relief of symptoms
II. Its potential risks in comparison with prescription drugs that are commonly used in the same patientgroup
III. Its mode of action and pharmacokinetics
IV. Drug/Drug & Drug Disease Interactions
V. Risks in specific patient groups, for example in elderly people, during

pregnancy and lactation, and in patients with impaired liver or kidney function

VI. contraindications

VII. The existence of other dosage forms of the same active ingredient that have already been approved for OTC.

5.3. Experience

Medicinal products supported to be available over the counterwhen:

- The use of the product has been sufficiently extensive or in a broad range of people with a wide variety of concomitant diseases, concomitant drugs and risk factors for adverse events “wide therapeutic range”, this enables the detection of relatively rare but serious adverse effects, and sometimes the detection of an increased frequency of particular adverse events.
- A favorable index of safety and efficacy through the data from Egyptian committee warning or decisions (Pharmacovigilance, Pharmacology, Technical committee...etc.) are taken into consideration.
- Experience in other reference countries, which have sufficient post marketing surveillance are also taken into account

5.4. Consideration of one or more specific routes of administration, dosage forms and formulations

Since no active therapeutic substance is likely to be idealin every way, it will usually be necessary to consider which specific presentations or formulations might be best suited to self-medication, since these can affect the medicinal product's safety, efficacy and suitability in such use.

- Route:

  Oral or topical preparations will generally be suitable means that it can be administered in a manner not requiring technical expertise, assistance or

patient training, but injections will usually not suitable for self- medication.

- Dosage:
  Restricting the maximum single dose or maximum daily dose may protect against danger when the medicinal product is used either correctly or incorrectly while retaining efficacy.

- Dosage strength:
  - For Pediatric: specific dosage strengths suitable for pediatrics use are preferable.
  - For Adult: consideration should be given to the need for several strengths, and this should be balanced against any problem that may be encountered in selected proper dose.
- Dosage schedule:
  The recommended duration of treatment should prevent unnecessary prolonged use. If the symptoms fail to respond adequately or persist, medical attention/consultation is necessary.
- Packing material and form:
  Medicinal products should have a container which as far as possible prevents children gaining access to the medicine if they get hold of the container.

5.5.Patient information

- Drugs that can be adequately labeled.
- The way in which the OTC medicinal product is used, is likely to differ from the way the same product is used when available only on prescription. The

written information (package leaflet and label) must contribute effectively to safe and effective use of the medicine.

- The correct use of the medicine should be clearly explained in the information and should be sufficient so that it substitutes for the absence of medical supervision.
- Contraindications, interactions, warnings and precautions need to be clearly described and prominently presented in the leaflet. The written information supplied with the medicine, in addition to the supervision of the pharmacist when applicable, should be adequate to guard against a risk of using the product where it is contraindicated or unsafe.
- The leaflet and the label should describe the situations where the product should not be used, in at least as much detail and prominence as to when it may be used and in accordance with the summary of product characteristics.
- The product information (package leaflet, label & advertising) should recommend the appropriate action to take if the medicine does not have the desired effect or cause an adverse effect. E.g. consulting a doctor or a pharmacist within the time stated in the label/package leaflet.

Abbreviations

- OTC: Over the counter
- POM: prescription only medicine
- PIL: patient information leaflet
- SmPC: summary of product characteristics
- MAH: marketing authorization holder

References

- EMA guideline on changing the classification for the supply of a medicinal product for human use.
- Directive 2001/83/EC of the European parliament and of the council of 6 November 2001 on the community code relating to medicinal products for human use.
- Directive 2004/27/EC of the European parliament and of the council of 31 march 2004 amending directive 2001/83/EC on the community code relating to medicinal products for human Use.
- WHO guidelines for regulatory assessment of medicinal
- products for use in self-medication.
- European Commission Guidelines on changing the classification for the supply of a medicinal product for human use January 2006
- https://www.accessdata.fda.gov
- Working Group on drug Classification Definition and Criteria to apply to OTC Drugs by Pan American Health Organization, Regional Office of WHO and Pan American Network for Drug Regulatory Harmonization March 2005
- Guide to Reclassification (Switching) of Legal Supply Status for Human Medicinal Products by Health Products Regulatory Authority in Ireland February 2019
- WHO Guidelines for the regulatory assessment of medicinal products for use in self-medication2000,https://apps.who.int/iris/handle/10665/66154

Annex I: Workflow for Submission

Objective

Demonstrate the regulatory pathway to be followed bymarketing authorization applicants (MAA) and marketing authorization holders (MAH) to be granted an approval for theclassification of supply of a medicinal product for human useas a medicinal product not subject to medical prescription,known as Over-The-Counter (OTC).

Process

- Marketing authorization applicants who seek to classify a medicinal product as Over-The-Counter shall be required to submit the required documents (annex2،3) via online submission to scientific evidence and referencesadministration for **fees 4000 Egyptian Pounds to evaluate company request.**
- Each company is allowed a maximum of 2 applications/month.
- The application shall receive an evaluation **within 45 calendar days from submission,** receipt date and a formal communication should be sent to applying M.A.H in which the product may be deemed **accepted, rejected or in-need of amendments.**

In case of Acceptance

Applicant will receive an approval for classification as an OTCmedicinal product **for fees 4000 Egyptian Pounds.**

In case of Rejection

- A rejected application renders medicinal product classifies as a Prescription-Only Medicine; **Company has the right to appeal within 30 days**.
- Applicants that receive a formal communication of application rejection shall be allowed to re-apply forchanging classification of the medicinal product once again

with new fees **after 6 months from last evaluation**.

In case of amendments

- The applicant will be required to address the requested comments or requirements in order for the application to be re-considered.
- Applicant has to submit requirements **within 60 days**.
- After the applicant submits the application with complete amendments The application either qualifies the medicinal product to be granted an approval for classification as an OTC Medical product or fails to meet the requirements and consequently rendering the medicinal product as a Prescription-Only Medicine, **Company receive an evaluation within 45 calendar days from submitting amendments**.
- Any approved **variation** related to change in theconcentrations equivalences, route of administration, safety profile of the product or indication after being granted the approval to classify as an OTC product:
- Obligates the company to report this change to the scientific evidence and references administration**within 5 working days** for re-evaluation of the medicinal product's classification.
- Failing to report this change qualifies for the revocationof the medicinal product's OTC classification approval.
- On the occasion of renewal of the marketing authorizationor when new facts are brought to their notice, the classification of a medicinal product shall be examined and, as appropriate, amended. These new facts include new information that comes to the Department's attention through post-market activities or a drug submission**.**
- Products will be re-evaluated with the release of the updated OTC list
- Medicines may be reclassified back from OTC to POM if concern arises about safety**.**

- Notices to inform the public and stakeholders of changes to the Non-prescription Drug List will be published on EDA website and **updated every three years.**

Annex II: Checklist of required documents

1	Cover letter
2	Most recent PIL/SmPC approval
3	Any variation approval
4	Any supportive reference documents (from carefully evaluated, authentic, relevant, unbiased, evidence-based, updated sources)
5	Evidence of payment of the required fees 4000 Egyptian pounds
6	Registration License, (if the product is registered)
7	MAH representative delegation letter

Annex III: Application form

❖ Product Information

Trade name	
Registration number(s)	
Active ingredient (s) and strength (s)	
Dosage form & Route of administration	
Approved Pack	
Pharmacotherapeutic group	
Indication(s) from approved SmPC	
Reference country of the product	

❖ Additional Information

Rationale for addition to OTC list	
Symptoms of the condition	

Duration & course of the condition	
Monitoring (special population) & Reasons	
Susceptibility for development of dependence or abuse	

❖ Status in Reference Countries

No of reference countries the product status is OTC	
No of reference countries the product status is POM	

❖ Committee warnings and decisions:

Technical committee warning (ifany)	
Pharmacology committee warning (if any)	
Pharmacovigilance committee warning (if any)	

❖ Declaration

I certify that the information supplied is complete and correct and that no relevant information has been omitted.	
***Name of regulatory affairs manager:**	
***Contact mobile:**	