Guidelines

Central Administration for Pharmaceutical Care
General Administration for Regulation of Marketing and Advertising Materials

Prescription Medicine Promotion Guidelines

القواعد الإسترشادية الخاصة بمواد الدعاية للمستحضرات الوصفية

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1. Back ground information

Guidelines for the ethical promotion and education of prescription only medicines and guidelines for proper health and disease awareness in order to support and encourage the improvement of healthcare through rational use of pharmaceutical products & be consistent with international practice.

Vision
Trusted healthcare product communication that promotes optimal health.

Mission
To provide a preclearance review that fosters trustworthy healthcare communications within the regulatory framework.

Values
Integrity, Competency, Credibility, Excellence, Transparency.

Mandate
Marketing Material & Media Monitoring (MM &MM) Department primary role is to ensure that healthcare product communication for prescription products is accurate, balanced evidence-based, and reflects current best practice.

The Role of Marketing Material and Media Monitoring Department:

1. Pre-clearance of:
   A- All electronic and printed promotional materials (directed to HCPs only) undertaken by MAH operating in Egypt for a POM that is intended for human use & have been officially registered.
   B- All printed and electronic Educational (non-promotional) materials.
   C- Reminders in case of violations.

2. Investigation of complaints regarding pharmaceutical products promotional and educational materials and awareness materials.

3. Training courses regarding the MM&MM department guidelines.

Classification of Reviewed Materials:

1. All electronic and printed promotional materials (directed to HCPs only) undertaken by MAH operating in Egypt for a POM that is intended for human use & have been officially registered.
   A- Electronic promotional materials.
   B- Printed promotional materials.

2. All printed and electronic Educational (non-promotional) materials.
   A- Product educational materials (directed to HCPs or distributed to patients through HCPs)
   B- Awareness material about a particular condition or disease directed to patients / public / HCPs).

3. Reminders in case of violations.

2. Definitions

Awareness material
It is concerned with providing information, promoting awareness or educating about health, diseases and their management.

Claim
Any allegations made directly or indirectly in promotional, awareness or educational materials. In many cases, it says something about the promoted drug or what it does. Claims can be made directly by stating, for example, "Brand X treats heartburn." Claims can also be made indirectly by the use of pictures or other graphics. For example: a picture of a playground full of children suggests a claim that the promoted drug treats children.

Educational Material
Means any representation which is intended to provide information about a medical condition or therapy which does not contain specific promotional claims.

Healthcare Professional
Any member of the medical, dental, pharmaceutical or nursing professions.

Patient
A person who has been prescribed a drug product.

Comparative Claim
A statement that compares an identified attribute of one drug product / ingredient to that of another drug product(s) / ingredient(s) in terms of comparability (non-inferiority) or superiority.

Fair Balance
Refers to the presentation of accurate and fair assessment of the risks as well as the benefits of the drug. Fair balance is achieved when the overall presentation of information in the material does not convey a deceptive impression of the drug's risk or benefits.

Indication(s) For Use
Is (are) the therapeutic/diagnostic/prophylactic use(s) defined in the approved leaflet by the MOH.

Ingredient
Refers to the active ingredient(s) & essential inactive ingredient(s).

Observational study
An observational study draws inferences about the possible effect of a treatment on subjects, where the assignment of subjects into a treated group versus a control group is outside the control of the investigator. This is in contrast with experiments, such as randomized controlled trials, where each subject is randomly assigned to a treated group or a control group before the start of the treatment.

Prescription Products
A prescription product requires a physician's authorization to purchase.

Strength
The strength of a drug product tells how much of the active ingredient is present in each dosage.

Promotion
Refer to any activity undertaken, organized or sponsored by a MAH (marketing authorization holder) which is directed at HCPs to promote the prescription, recommendation, supply, administration or consumption of its products through any media.

Promotional Claim
Any statement made by a MAH or MAH's representative, which conveys the positive attributes of a product, which extends beyond a simple non-qualitative or quantitative description of the therapeutic category or approved indication for encouraging the usage of that product. It includes statements concerning efficacy, rate of adverse reactions or other cautionary aspects of the product and comparative information.

Reminder
Trade name reminders are those, which call attention to the name of the product but do not include indications or dosage recommendations for use of the product.

Risk Reduction
Describes the relationship between using a medicinal ingredient and reducing risk of developing a specific disease or abnormal physiological state.

Structure Function
Describes the effect of a medicinal ingredient to support a structure or physiological function in the human body, or a medicinal ingredient's support of an anatomical, physiological, or mental function.

Variation

Type 1: Updating valid approval due to the update of official documents without affecting the approval content.
Type 2: Issuing new approval with new approval number derived from previously approved material.
Type 3: Issuing new approval with new approval number derived from previously approved material having different size& type with the same content. (Section 5.23)

3. Abbreviations

CAPA: Central Administration of Pharmaceutical Affairs
FDA: Food and Drug Administration
HCPs: Healthcare Professionals
INN: International Nonproprietary Name
MAH: Marketing Authorization Holder
MM & MM: Marketing Materials & Media Monitoring
MOH: Ministry of Health
POM: Prescription Only Medicine
WHO: World Health Organization
EPV: Egyptian Pharmacovigilance Center
SPC: Summary of Product Characteristic.

3. Scope

The scope of these guidelines shall cover the following:

(1) All electronic and printed promotional materials (directed to HCPs only) undertaken by MAH operating in Egypt for a POM that is intended for human use & have been officially registered.

A- Electronic Promotional Materials.

- Electronic promotional materials provided /sent to or used for discussion with HCPs.
- Electronic promotional materials must be designed to allow access only to HCPs i.e. appropriate measures must be taken to ensure that the content is secured and not accessible by others.

N.B.

Materials of the external lecturers that are presented in the scientific events sponsored by MAH will not require previous approval taking into consideration that the MAH is responsible for their content and is asked to comply with MM & MM guidelines.

B- Printed Promotional Materials:

- Printed promotional materials provided to or used for discussion with HCPs including detail aids, booklets, block notes, drop cards, flyers, brochures, non-leave behind materials etc.
- Printed promotional materials for display purposes which are used only in scientific communities like conferences, launch events etc., including posters, banners, registration desk, danglers, gates, stands etc.
- Other printed promotional materials.

(2) All Printed and Electronic Educational (Non-promotional) Materials.

A- Product educational materials directed to HCPs or distributed to patients through HCPs. Which are not included in the risk management plan of the product for example: directions for usage of the drug etc.

B- Awareness material about a particular condition or disease directed to patients / public / HCPs.

(3) Reminders

- Reminders do not require previous approval.
- It must follow the guidelines mentioned in Section 9.
- In case of violating the guidelines regarding the regulations of reminders, the MAH will be obliged to submit reminders for previous approvals from the MM & MM department.

The scope of these guidelines does not cover the following:

Guidelines, clinical trials, insert leaflet ... etc. distributed as it is without any minor change in its layout, neither presentation of data nor addition/extraction of any scientific content.

4. General rules for promotional, educational and awareness materials:

5.1. Products subjected to these guidelines are prescription only medicines.
5.2. All pharmaceutical companies including multinational, local etc. must comply with the prescription medicines promotion guidelines. The pharmaceutical companies are encouraged to participate by reporting the violating materials.
5.3. All materials must comply with the locally accepted traditions and religious directions.
5.4. All materials including graphics and other visual representations must conform to generally accepted standards of good taste.
5.5. All material cannot display any violent or offensive statements or visuals or that may have a 'negative effect' upon.-company or patient images for example bloody pictures.
5.6. Ethical promotion criteria are to be complied with, without any direct or indirect offence to competitors or the pharmaceutical industry or medical field in general.
5.7. For prescription products that have a boxed warning included in their approved leaflet, all promotional materials containing any claims must inch:1de the boxed warning.
5.8. All materials should indicate the target audience on the first page/slide for example to healthcare professionals only.
5.9. Any approved material must have the approval number standing alone and displayed prominently on the first page/slide of the material.
5.10. The printed or published materials must be identical to the approved stamped ones.
5.11. A type size of 9 points, with a space between lines of at least 1.5 mm, should be used as a minimum.
5.12. The font proportion should be respected with different size and type, taking into consideration the minimum font allowed as generally, a type size of 9 points, with a space between lines of at least 1.5 mm, should be used as a minimum.

5.13. Prohibition of Promotion on unlicensed product:

POM that does not have a valid registration license must not be educated about nor promoted for medicinal purposes in any material.

5.14. Health authority approval claims:

Claims that the product is FDA, EMA or any health authority approved:

- Must be supported by current evidence.
- Is trade name specific and cannot be generalized to other generic products having the same active ingredient or combination of active ingredients.

5.15. Printed and electronic promotional materials that are directed to HCPs must contain the following requirements:

(1) Trade Name.

(2) The Active Ingredient(s) INN or Generic Name(s) should be placed immediately adjacent to the most prominent display of the name(s) of the product(s), on the first appearance of the product(s) name(s).

(3) Concentration of the active ingredient(s)

In the case of a single strength being promoted, it must be placed immediately adjacent to the most prominent display of the name(s) of the product(s), on the first appearance of the product(s) name(s).

(4) Name of other ingredient(s) known to cause problems.

(5) The promoted dosage form.

(6) Name and Address of MAH and/or scientific office.

(7) References.

MAH has the right to use the insert leaflet as its only reference. In such cases, the insert leaflet will be the only reference mentioned under references title in the promotional material followed by the date of approval of insert.

(8) MM approval number & material invalidation date.

(9) Brief summary summarizing the fair balance of the material:

- Approved therapeutic uses.
  In case of many therapeutic uses, at least the promoted one shall be mentioned.
- Contra-indications.
- Warnings & Precautions.
- Pregnancy, lactation & fertility.
- Very common and common side effects.
- Driving & using machines for example if it affects the driving by causing dizziness or it poses dangerous effect on using machines.

- The following sentences must be mentioned in each material:
  - Always read the full prescribing information.
  - Healthcare professionals are asked to report any suspected adverse reactions to Egyptian pharmacovigilance center (EPV).
  - MOH leaflet approval date.

- Headings must be employed to signal the key fair balance sections & each section heading is underlined and bold.
- Sections must be presented in the form of separate paragraphs
- A space must separate the sections.
- Content may be summarized provided the complete essence is captured.
- There is no need to repeat content which is presented elsewhere in the piece.
- The brief summary section must be stated using a type size not less than 9-point Times New Roman with an interspace of 1.5 mm for printed materials, it must appears on a plain background with text sufficiently. Contrasting for legibility on the same design of the promotional material.
- Those sections apply to trade or scientific non-property name material.
- This information is intended as a reference for HCPs; it is not a substitute for reading the approved leaflet but should convey all the key information from the approved leaflet to be considered before prescribing or supplying the product.
- Where a promotional material is concerning treatment of a particular group of patients, MAH should ensure that the information includes all the relevant leaflet particulars for example, where a product is being promoted for use in children, the particulars should convey all the information in the approved leaflet relevant to that group. This would probably dictate greater detail than it would be required in a promotional material for the same product for treating a more general patient population.

5.16. When an official document(s) of pharmaceutical product having a valid approval has/have been updated, MAH can submit a variation file in case of not affecting the scientific content. Examples of official product documents: approved leaflet, approved pack etc.

5.17. MAH can derive new approvals with new approval number having the same invalidation date of the previously valid approved materials.

5.18. Under-registration products:
Materials of products under registration can be submitted for review only after having the approved leaflet issued from CAPA & the approval will not be delivered to MAH until the valid product registration license has been issued.

5.19. Each submitted file to be reviewed for approval must contain a maximum number of references if number of the references at submission exceeds the maximum allowed number in the fees schedule, each extra reference will require additional fees (see fees schedule in section 11).

5.20. After submission of the file, if an already submitted reference has been rejected, MAH can submit a new reference with additional fees (see fees schedule in section 11). It must be submitted within the time limit allowed for MAH to make the modifications required by the reviewer.

5.21. MM & MM department must be notified previously by any event held by the pharmaceutical companies.

5.22. The approval validation date is up to 3 years, as the following examples:

- Three years at once.
- One year and extended for two years.
- One year extended for another year followed by another extension the year after.

N.B.

The withdrawal of approvals in case any recent data contradict what have been approved in the materials (See fees schedule in section 11).

5.23. In case of changing the color scheme of an approved material, there is no need to submit it for review again while maintaining the basic principles and values as the contrast of colors for legibility, the text must be readable, visual manipulation of colors aren't acceptable etc. (see point 5.14.9).

5.24. One approval may be issued for different sizes and types of materials, taking into consideration the commitment of the companies for the following:
(1) The required sizes and types should be mentioned in advance in the submitted file by the company.
(2) The content should be the same without any extraction nor addition in all types and sizes submitted for approval.
(3) In case of breach of the previous two points, submission of new file(s) is (are) requested.

5.25. Any claim which means any phrase or allegation made in any promotional or non-promotional materials must follow the prescription medicines promotion guidelines.

6. Promotional Materials Guidelines

6.1. Quality standards

A promotional material must:

(1) Compliance with the approved leaflet
This means a promotional material cannot promote a product for use in treating or preventing conditions or illness for which it has not been approved nor can promote a product for use by a patient group not indicated in. For example, a promotional material with an infant for whom the product was not indicated (below the age of 2 years) would violate this provision.

(2) Encouraging rational use
- This might include when a product should be taken, how much should be taken, the route of administration, by whom it should be taken and special precautions.
- A promotional material for a product offering symptomatic relief should not imply that it cures the underlying condition, if it has not mentioned in the approved leaflet.
- A promotional material would not be objective if it failed to refer to any significant limitations that were relevant to the claims made for the product.
- When applicable, where a relative change is quoted, the absolute values should also be given to enable the reader to fully assess the magnitude of the claimed benefit.

(3) Not be misleading
A promotional material must not lead to an incorrect belief of any nature about the product. Unrealistic or inappropriate images can give rise to misleading expectations about the product or the indicated patient population. An example could be the use of a driving image in a promotional material for a product where caution is required over impairment of driving ability.

(4) Not be offensive or traumatizing.
A promotional material should not have unnecessary, exaggerated offensive or traumatizing visual (ex: blood, wounds, etc.)

(5) Not be indecent
A promotional material should not have unnecessary nudity or intimacy.

(6) Represent a "fair balance" between risk and benefits so that, health-care professionals can get complete and accurate information on the product.

(7) Not be vague (ambiguous) and incomplete especially regarding indications, side effects and precautions.

(8) Use the most recent references in the field.

6.2. References

6.2.1. The core of the promotion is the product approved leaflet, the role of any reference is to support what is mentioned in any part of the leaflet information.

6.2.2. For a certain piece of information that is mentioned in the approved leaflet, no contradictions from any reference are to be mentioned in the material.

6.2.3. Any information used to support a claim must include sufficient details and be of adequate quality to allow evaluation of the validity of results and hence the claim.

6.2.4. For articles, only full articles are to be submitted, no abstracts or posters are to be accepted as references.

6.2.5. Data from different references are to be clearly separated, and no collective framing in this case is allowed.

6.2.6. Data from studies made on a particular brand can be used for the generics (using the active ingredient(s) name only) if of same concentration(s), same dosage form(s) & same indication.

6.2.7. Non-clinical studies (ex: in-vitro, ex-vivo, preclinical evidences) are not to be considered except for affinity, selectivity data & claims that cannot be supported by clinical evidence.

- Non-clinical studies are not suitable for efficacy or safety.
- Non-clinical studies may be suitable for mechanism of action, teratogenicity and other toxicities.

6.2.8. Clinical/therapeutic claims must be based on published, well-controlled and/or well-designed studies with clinical significance clearly indicated.

6.2.9. Publication in peer-reviewed journals is usually a good criterion for establishing scientific accuracy.

6.2.10. Pooled data, post-hoc analysis and observational studies are generally regarded as not being high-level evidence to support claims.

6.2.11. The use of post-hoc analyses is acceptable, but must be clearly identified and appropriately qualified.

6.2.12. Papers published in journal supplements are not sufficient evidence to be used as reference support for promotional claims unless it can be demonstrated that the supplement has been subject to accurate peer-review process similar to the attached journal.

6.2.13. Comparative claims of efficacy and safety generally require support of evidence from head to head well designed, adequately controlled, blinded randomized clinical studies. Open-label studies are generally not considered to be a high level of evidence. However, open label studies can be allowed in some cases either including objective or subjective endpoints for e.g., oncology etc.

6.2.14. Safety and efficacy data derived from studies that were not head-to-head are not acceptable support for comparative claims of clinical safety or efficacy.

6.2.15. Comparisons of safety or efficacy of a product or drug ingredient to drug ingredient may be supported by a peer-reviewed, published meta-analysis or systematic review of data from studies in which the conditions of use are consistent with the approved leaflet.

6.2.16. Non-evidence based statements such as those from adverse drug reaction reporting systems or testimonials are not acceptable.

6.2.17. Pharmacoeconomic and quality of life claims must be supported by high-quality studies.

6.2.18. References nomenclature must be written in the following order: authors name, reference title, Journal name, date of publication.

6.2.19. Methodology of the submitted reference including the number of patients, method of administration, indications must be in conformity with the approved leaflet.

6.2.20. References must be stated using as minimum a type size of 9 points, as measured in font "Times New Roman", with a space between lines of at least 1.5 mm for printed materials.

6.2.21. In case of guidelines, the most recent one must be used. In other cases, old references can be used as long as they are consistent and don't contradict the most recent guidelines and approved insert.

6.2.22. Each claim can be supported by one reference only.

6.3. Claims

6.3.1. General

(1) All Claims must be consistent with the approved leaflet, irrespective of the source on which the claims are based.

(2) All information, claims and graphical representations including: charts, graphs and tables provided to HCPs must be current, accurate, complete, balanced, and clear and must not mislead directly, either by implication, or by omission.

(3) All claims must be referred.

(4) Claims that are Out of context or inconsistent with the conclusions of the cited author(s) will not be accepted.

(5) Adaptations of data must be presented in a manner that does not add or subtract from conclusions of the author(s).

(6) Claims from clinical studies must comply with the predetermined primary or secondary end points.

(7) Claims must not imply that a product or an active ingredient has some special merit, quality or property unless this can be substantiated by sufficient evidence.

(8) Exaggerated or non-scientific ambiguous claims, slogans or pictures are prohibited (See section 6.3.11).

(9) Photos and pictures are evaluated as claims and must be proved and relevant without exaggerations, they must conform with the approved indications and limited to the allowed populations (See section 6.3.15).

(11) Statements that claim directly, or indirectly, 100 percent clinical efficacy or safety are not accepted.

(12) The claim preferably should be accompanied by or linked to disclosure of relevant study parameters that would aid the reader in interpreting the data, e.g., patient numbers and p-value or confidence intervals (CI).

(13) Each graph must be followed by the following six items about the methodology and the objective of the reference:
1- Objective of the reference for e.g.: this study aims to evaluate the efficacy etc.
2- Design of the reference for e.g.: double blind, randomized etc.
3- Number= n for e.g.: number of patients.
4- Dose used in the reference consistent with the approved insert.
5- Duration of the study.
6- Significance level: p-value, non-significance etc.

(14) Information that is important for a clear and accurate understanding of a product claim must not be relegated to a footnote. Example - an indication or dosage that is limited or that is restricted to a specific group of patients.

The following are examples of situations where material may breach the guidelines:

- Citation of data previously valid but made obsolete or false by the evaluation of new data.
- Suggestions or representations of uses, dosages, indications or any other aspect of the product Information not approved by the MOH.
- Shortening an approved indication to remove a qualification or limitation to the indication.
- Hiding severe or important adverse drug reactions, warnings, age group limitation or pregnancy limitation ... etc.
- Statements made about a competitor product, particularly negative statements, not balanced with corresponding information about the product being promoted from head-to-head clinical trial.
- Shortening the title of graphical representations reproduced from literature in a manner that alters the original author's meaning.
- Literal or implied claims that a parameter, contraindication, cautionary statement, adverse reaction or limitation on a claim in the Product approved leaflet, is not cause for concern.
- Lack of substantiation of claims not of a medical or scientific nature. It includes information or claims relating to marketing factors such as pricing.

6.3.2. Product Characteristics

6.3.2.1. The promoted product must not be represented as a food .

6.3.2.2. Absence of ingredient statements

A- A promotional material must not include an absence of ingredient claim in a manner that creates an incorrect impression about the promoted product or competitor product(s).

B- Absence of ingredient statements for medicinal and non-medicinal ingredients is acceptable under the following conditions:

Medicinal

1) The statement provides useful and easily identifiable information to the HCPs that aids HCPs medication selection.
2) The absent ingredient would likely be found in a combination product of that type.
3) There is no misleading representation as to the safety and merit of the absent ingredient.

Non-Medicinal

1) The statement provides useful and easily identifiable information to the HCPs to aid in product selection for secondary non-therapeutic attributes such as taste, odour, caloric content, or another meaningful attribute.
2) The statement is accurate.
3) There is no direct or indirect implication that the absent ingredient is medicinal.

6.3.3. Indication / Recommended Use

1) The promotional material must clearly communicate the intended therapeutic use of the product as per its approved leaflet.
2) For treatment of the specified condition where the condition includes a reference to its severity, e.g. mild or moderate, this should be included. Words or illustrations should not suggest that a more serious degree of the condition can be treated.
3) The promotional material must include at least one indication for use of the product

6.3.4. Direction for Use/Dosage and Administration ·

1) A promotional material must not be misleading as to the directions for use/dosage and administration.
2) A promotional material must encourage the correct and proper use of a product; this is a positive obligation.
3) When described or depicted, directions for use/dosage and administration must be consistent with the product's approved leaflet.

6.3.5. Efficacy

1) A promotional material must not be misleading by directly or indirectly exaggerating the degree of relief I benefit to be obtained from use of the promoted product.
2) Efficacy claims are to be specific.
3) High adverse events rate or incidence (if any) accompanying high efficacy in a clinical study are to be clearly mentioned as the efficacy claims obtained from the clinical study.
4) Superiority of certain effect/More efficacy claims are to be from clinically significant results of at least one comparative head-to-head clinical study (See section 6.3.10).
5) When depicted or described, efficacy claims must be consistent with the product's approved leaflet.

6.3.6. Medicinal Vs. Non-medicinal Ingredients

1) Product benefits must not be presented in a manner that is misleading, as to the nature of either the medicinal (therapeutic) or non-medicinal (non-therapeutic) ingredients.
2) Non- medicinal (non-therapeutic) benefit can be directly or indirectly attributed to a non-medicinal (non-therapeutic) ingredient.
3) Non-medicinal (non-therapeutic) product claims such as taste or packaging require support from adequate, unbiased valid reference.

6.3.7. Onset of Action

1) A promotional material must not be misleading as to the time to onset of action of the promoted product.
2) Claims for fast action should be related to a condition where speed of onset is relevant and may not be appropriate for chronic conditions or those not requiring immediate relief. The time scale for which 'fast' claims are appropriate will depend on the clinical indication and the speed of action of other products in the category. It is unlikely that a time to onset of relief of more than 30 minutes would be considered to be 'fast' for a product for relief of an acute condition.
3) When depicted or described, the onset of action must be consistent with the product's approved leaflet, i.e. claims for action within a specific time period are only permitted if contained in the product's approved leaflet.
4) Time to onset of action must not be equated with time to onset of relief, unless clearly specified in the product's approved leaflet.

6.3.8. Duration of Action

1) A promotional material must not be misleading as to the duration of action of the promoted product.
2) For a 24-hour relief claim, data must show clinical effect over the 24-hour period. The product should be for once daily dosing but a once daily dosing interval alone is insufficient to support a 24-hour claim.
3) When described or depicted, the duration of action must be consistent with the product's approved leaflet.
4) Dosing interval must not be equated with duration of action or duration of relief unless supported by the product's approved leaflet.
5) Duration of pharmacological action must not be equated with duration of relief unless supported by the product's approved leaflet.

6.3.9. Duration of Use

1) A promotional material must not be misleading as to the recommended duration of use of the promoted product.
2) When described or depicted, the duration of use must be consistent with the product's approved leaflet. When a product must be used for a specific period of time to obtain the desired effect, this information must be included in the promotion material.
3) Products intended for short term/occasional use must not be represented for long term/chronic use.
4) If the duration of use is unclear in the approved leaflet, the MAH may refer to the summary of product characteristic (SmPC).

6.3.10. Comparative Statements

1) In presenting a comparison, care must be taken to ensure that it properly reflects the body of evidence and does not mislead by distortion, by undue emphasis or in any other way.
2) Comparison of products must be factual, fair and capable of substantiation and referenced to its source; and must not be disparaging.
3) Hanging comparatives - those that merely claim that a product is better, stronger or more widely prescribed etc. must not be used.

4) Comparative claims (related to the therapeutic aspects of drugs) must meet the following principles:

A- Where a claim of comparative efficacy or safety is made, it must not be based on a comparison of product-approved leaflets that does not reflect the general literature, as those leaflets are based on different databases and are not directly comparable.

B- Comparative efficacy or safety must be based on at least 1 head-to-head well designed, adequately controlled, blinded, randomized clinical trial.

C- Where a comparative claim relates to a specific parameter, any claims must be clearly identified as pertaining to that parameter.

D- The claim and its presentation should:

(i) Identify the compared entities (to be mentioned in the same page).

(ii) Not obscure the therapeutic use of the promoted Ingredient(s).

(iii) Not attack the compared drug ingredient(s) in an unreasonable manner.

(iv) Be expressed in terms, language and graphics that can be understood by the intended audience.

E- The accepted level of statistical significance is $p < 0.05$.

F- If comparative data that are not statistically significant are used, such data must comply with the following Conditions:

(i) The lack of significance must be stated explicitly; it is insufficient to state the p-value.

(ii) The data must not be used to generalize or to indicate superiority or inferiority.

G- If comparative data are used where the relevant study does not include a statement of the significance or lack of significance of the comparative data, the lack of a p value must be explicitly stated & no claims are made.

6.3.11. Expressions

A) Exaggerated or all-embracing claims must not be used.

B) It is unacceptable to claim that the product has a unique therapeutic I non-therapeutic formulation or provides a unique therapeutic/ non-therapeutic benefit unless the product is unique in therapeutic or non-therapeutic formulation and effect and it must be supported by evidence of adequate quality.

C) Expressions and statements not allowed to be included in any material include, but are not limited to:

Incomparable; powerful, very limited quantity, amazing guaranteed, pain free, safe, has no side effects, has no toxic hazards or risks of addiction ., 100%, veracious, magic, miraculous, assured success, best product, ideal, famous, granted treatment, trust, smart,..

D) Guarantees of purity, quality or physical characteristics (i.e. guarantees about non-therapeutic attributes) are acceptable if true and supported by evidence of adequate quality.
E) Absolute statements like cures completely certain illness or disease is not accepted.
F) Expressions that mean stability or permanent effect like "Permanent, Eternal, get rid completely" are not accepted.
G) "Fight old age" expression is not accepted, but the expression "helps to fight old age signs" could be used.
H) "Unique, the standard, Pioneer, Original, first, immediate results, most effective, least toxic and all alike expressions are not accepted unless it can be substantiated with evidence of adequate quality.
I) Statements proceeded by without ... are not accepted unless it can be substantiated with evidence of adequate quality.
J) Trade names of products of other companies must not be used.
K) "The": use of the definite article to imply a special merit, quality or property for a product is unacceptable if it cannot be substantiated for example, a claim that a product is 'The analgesic' implies that it is in effect the best, and might not be acceptable.
L) "New": The word 'new' must not be used to describe any product, presentation, or therapeutic indication that has been available for more than 12 months in Egypt since the date of the release of the final three batches confirmed with the report of release of the product in the Egyptian market. The word "new" should be removed from the extended files.

6.3.12. Market share & price claims

Market share and price claims must be based on and referenced to current authoritative data and must not state or imply therapeutic equivalence.

6.3.13. Safety

A) Safety messages given in promotion must comply with the approved leaflet.
B) Promotional material, which states or implies that a product is "safe" is unacceptable.
C) All products have the potential for side effects and no product is completely risk-free as individual patients respond differently to treatment.

For example, the term "placebo-like" in relation to safety or side effects is considered misleading as it implies that there are no associated side effects. By implication, the product could be assumed to be 100% safe, when no product is completely risk-free.

D) Claims that a product is generally well tolerated and claims relating to the overall incidence of side effects versus placebo in clinical trials may be acceptable if supported by at least one clinical trial that aims to assess safety, provided that a misleading impression is not given.

E) Claims that a product has a well-established safety profile must be supported by evidence, 'Well established' should not be confused with 'good'. The terminology well established good, well tolerated etc., and must be used exactly as the reference and not interchangeably.

F) Data from safety studies claiming low incidence of a certain adverse event is to be accompanied by warnings (if any) regarding this certain adverse event & consistent with the incidence mentioned in the approved insert.

G) Promotional material must include a reminder statement giving information on reporting of suspected adverse reactions.

6.3.14. Absence of Side Effect Statements

A) A promotional material must not include a claim for an absence of side effect in a manner that creates an incorrect impression about the promoted product or competitive product(s).

B) Absence of side effect statements is acceptable under the following conditions:

a. Scientific evidence exists to support the statement; e.g. incidence of side effect is compared to placebo consistent with the product's approved Leaflet.

b. The side effect is associated with comparable components of that class.

C) Promotional material should not suggest that a product does not have any side effect or that its safety or efficacy is due to the fact that it is natural.

6.3.15. Pictures

- Photos and pictures are evaluated as claims and must be proved and be relevant without exaggeration.
- Pictures included should be related to the promoted product, to serve its purpose only & consistent with the product approved leaflet.
- Pictures that breach the Egyptian culture and religious teachings are not allowed.
- Pictures should not contradict Egyptian common interest and policies.
- Pictures that show nudity intimacy or sex appeal are not allowed.
- MAHs must confirm their responsibility of photos of individuals in the design.
- Pictures that breach the medical ethics are not allowed.
- Pictures that encourage unhealthy, risky behaviors and habits are not allowed.

6.3.16. Graphics I Schematics I Terminology

A) Graphics, language, schematics, and terminology used to present product features or characteristics must not mislead the HCPs as to the therapeutic merits of the product.

B) Company-generated charts/graphs from one study or combining of graphs from different studies are prohibited.

C) Minimal information on a presented chart should at least be mentioned in the material to determine the quality of the study and the value of its result (this information should be in prominent type size (a minimum of 8 point), this includes:

A. Study design & objective.
B. Dosage.
C. Treatment duration and follow up.
D. Number of subjects involved for each arm of the study.
E. Statistical significance. (if any)
F. Specifications (if any) on race, age of subjects etc.

6.3.17. Statistics

A) Statistics must be presented to accurately report the findings and to help make reliable and valid conclusions.

B) Statistical information should include the level of significance e.g. confidence p-value or non-significance. interval (CT),

C) Materials which present results using relative risk (RR) or relative risk reduction (RRR), must also include an indication of the absolute treatment effect (if applicable). This can be presented as absolute risk reduction (ARR), number needed to treat (NNT) and/or the actual comparative clinical results or rates.

6.3.18. Endorsements / Recommendations / Seals

A) A promotional material should not contain recommendations by scientists or healthcare professionals.

B) MAH should not suggest that their product is “special" or different from or better than other products only because it has been granted a marketing authorization or registration.

C) Combination recommendations, first-line treatment recommendation or any type of recommendations are to be coming from the most recent international guidelines and these claims must clearly state that they are: "according to name of the guideline/the year".

D) Combination recommendations, first-line treatment recommendation or any type recommendations must be stated exactly as it is without any addition nor extraction from the guidelines.

6.3.19. Health / Healthy

A) A promotional material must not be misleading by suggesting that a product may restore, maintain or promote health, unless such claims are included in the product's approved leaflet.

B) A promotional material shall not give the impression that the normal lifestyle requires the use or consumption of a specific product. ·

C) A promotional material must not claim that the use of a certain product is essential for living within modern life pressures.

D) A promotional material should not suggest that certain products use would enhance sportive or educational performance.

E) It is unacceptable to suggest that use of the promoted product is a substitute for good health practices and healthy lifestyle.

F) A promotional material for vitamins should not imply that vitamin supplements:

(1) Are a substitute for good nutrition or a balanced diet.

(2) Are in any way superior to or more beneficial than dietary nutrients or that normal health may be affected by not taking vitamin supplements.

G) Weight management: A promotional material containing claims for weight management, meaning weight loss, measurement reduction, clothing size loss and weight control /maintenance, must have an appropriate balance between the claims and references to healthy energy-controlled diet and physical activity.

6.3.20. Natural, Natural source, Natural action

A) A promotional material must not mislead HCPs to believe that a product is "natural" or "natural source" if it is synthetically derived.

B) Natural: An ingredient can be described as " natural" if it is obtained from a natural source material, is in a form found in nature, and has undergone only the most minimal processing (e.g. drying, grinding, powdering, chopping, Encapsulating). Example: encapsulated powdered garlic.

C) Natural source: An ingredient can be described as "natural source" if it is Obtained via extraction, isolation and/or processing of plant, algal, fungal, Bacterial, or animal material or minerals. Processing can include such steps as boiling and steaming. The ingredient must have the same chemical identity as that in the source material.

D) Ingredients found in nature and undergo chemical modification such as derivatives and salts are considered synthetic and not natural source.

E) Examples: Vitamin E (d-alpha-tocopherol) isolated from soybean is natural source. The derivative, d-alpha-tocopheryl acetate, produced via chemical modification of vitamin E from soybean, is not natural source.

F) Claims that one or several ingredients in a multi-ingredient product are natural/natural source are permissible.
G) Claims about a product, as a whole, being natural/natural source are permissible if this statement is true for all ingredients (medicinal and non-medicinal).
H) A product with ingredient(s) of natural source must not be claimed to be superior (efficacy/safety) because of being natural.
I) A promotional material must not be misleading by claiming that a product acts "naturally" as products, including natural health products, modify the body's physiological processes.

6.3.21. Potent / Potency

A) A promotional material must not be misleading by referring to a product as being "potent" or having a "potent" formulation unless supported by suitable reference and stated exactly as reference.
B) All products contain sufficient medicinal ingredients to be effective as per their approved therapeutic indications.

6.3.22. Power / Strength / Extra strength

A) A promotional material must not be misleading by suggesting that a particular product contains more than sufficient medicinal ingredient to relieve/treat/prevent a particular condition or symptom.
B) A promotional material must not be misleading by suggesting that there is a correlation between the amount of medicinal ingredient and degree of efficacy unless this is part of the approved leaflet.
C) All products are formulated (i.e., contain sufficient medicinal ingredient) to be effective for the condition / symptoms they are designed to relieve/treat/prevent.
D) It is thus appropriate to claim that a product is "effective", "strong enough "for the condition or symptoms it is designed to relieve/treat/prevent. ft is unacceptable to suggest that the product in and of itself, is "strong" or powerful.

6.3.23. Structure Function Claims

A) A promotional material must not mislead HCPs through inappropriate use of a structure function claim.
B) It is unacceptable to make a structure function claim that is inconsistent with a product's approved leaflet.

7. Promotion of products, which are promoted for use during pregnancy:

The following guidance is provided for the promotion of any pharmaceutical product for use during pregnancy to a healthcare professional:

A) Only where there is a specific indication for use in pregnancy m the approved leaflet, pharmaceutical products may be promoted for use in pregnancy.

B) All the information contained in the pregnancy and lactation section of the approved leaflet should be conveyed in the prescribing information in the promotional material.

C) Promotional materials should never state or imply that the promoted pharmaceutical product, or any other medicine, cannot harm the developing fetus. The use of visuals pertaining to the developing fetus is considere9 inappropriate in the promotion of medicines for use in pregnant women.

D) All promotional materials for pharmaceutical products promoted for or providing information on use in pregnancy should include a general warning message appropriate to the medium being used.

An example of appropriate wording is as follows: Care should be taken when prescribing in pregnancy as medicines can affect the fetus.

8. Educational non-promotional materials:

8.1. Product Educational Material:

(1) It is intended for the non-promotional education about a pharmaceutical product(s).
(2) It is either directed to healthcare professionals or provided to healthcare professionals to give to their patients who have been prescribed a particular pharmaceutical product by their doctors.
(3) The content of such material could clarify for example, mechanism of action, dose, timing and method of administration, precautions, special instructions and similar information.
(4) It must contain no promotional claims/visuals.
(5) It must have no comparative claims/visuals regarding a pharmaceutical product.
(6) It must contain no quotes from experts, opinion leaders or patients.
(7) It must be consistent with the approved leaflet for the related pharmaceutical product(s).
(8) It must be in a language appropriate for the intended audience. Confusing medical terms must be avoided in materials provided to healthcare professionals to give to the patients.
(9) The tone of the message must not be presented in a way that unnecessarily causes alarm or misunderstanding in the community.
(10) It does not have to include the pharmaceutical product's approved leaflet.
Examples: - Dosage cards etc.

N.B.

Presence of any promotional claim/visual will necessitate the material to be promotional and to be assessed according to the promotional materials guidelines.

8.2. Awareness Material:

(1) It is intended for raising the awareness about health or a disease condition.
(2) It is either disease awareness materials or health awareness materials
(3) It should cover the key characteristics of the disease, including a balanced overview of the range of therapeutic options available (which may include a range of products/classes and/or alternative treatments such as surgery) in a balanced and fair manner that does not unduly emphasize particular options or the need to seek treatment.
(4) It should not highlight the qualities of a specific pharmaceutical product
(5) It must emphasize a health/disease condition and its recognition rather than on the treatment options.
(6) It must include MAH name (but should not be given prominence).
(7) It must not include any reference to a specific pharmaceutical product(s).
(8) It must be in a language appropriate for the intended audience. Confusing medical terms must be avoided in materials directed to the patients.

(9) It must include a statement directing the patient to seek further information about the condition or treatment options from his/her doctor for materials directed to the patients.

9. Reminder:

Trade name reminders must include the following information:

1. The trade or generic name of the product.
2. And/or MAH name or logo.

Trade name reminders may include the following information:

1. A non-promotional logo or image for example written, printed, or graphic matter containing no representation or suggestion relating to the promoted product.
2. Information relating to quantitative or qualitative ingredient statements.
3. Dosage form.
4. Quantity of package contents.
5. Price.
6. Pack shots are acceptable if no therapeutic claims are visible.

Trade name reminders must not include:

1. Indications or therapeutic category.
2. Promotional claims including promotional tag lines and/or statements (slogan).
3. Recommendations.

10. Complaints

Scope: same as regular scope.

1. Complaints files are received composed of:
   • A cover letter (the form can be found online).
   http://www.eda.mohp.gov.eg/Files/699_complaint%20application%20form.pdf
   • A copy of the promotional material.
2. The MAH will be notified there is a complaint against it, in order to submit all the documents and references required to defend the claims in the material. The complainant name will remain anonymous.
3. The material will be reviewed thoroughly.
4. The material will be submitted for committee review.
6. The complaining party will be notified of the final action within three months.

11. Sanctions

<u>According to ministerial decree 67/2000:</u>

1. Issuing a warning letter to stop the violating material or correct its content within 10 days.
2. Afterwards, withdrawal of the medicine from the market and cancelling its registration license.
3. Finally, Prohibition of re-registration for 1 year from the date of cancellations of its registration license.

Supplementary guidelines can be published in case of any needed clarifications.

12. References

1. Ethical criteria for medicinal drug promotion. WHO
2. The blue guide: advertising and promotion of medicines in UK Third Edition. September 2014
3. Australian code of conduct edition 18. 2015
4. Emirates: http://www.moh.gov.ae/en/Services/Pages/ServiceDescription.aspx.
5. FDA code of federal regulation title 21 part 202 prescription drug advertisements.

Annex (1)

Regulatory guidelines of accepted references

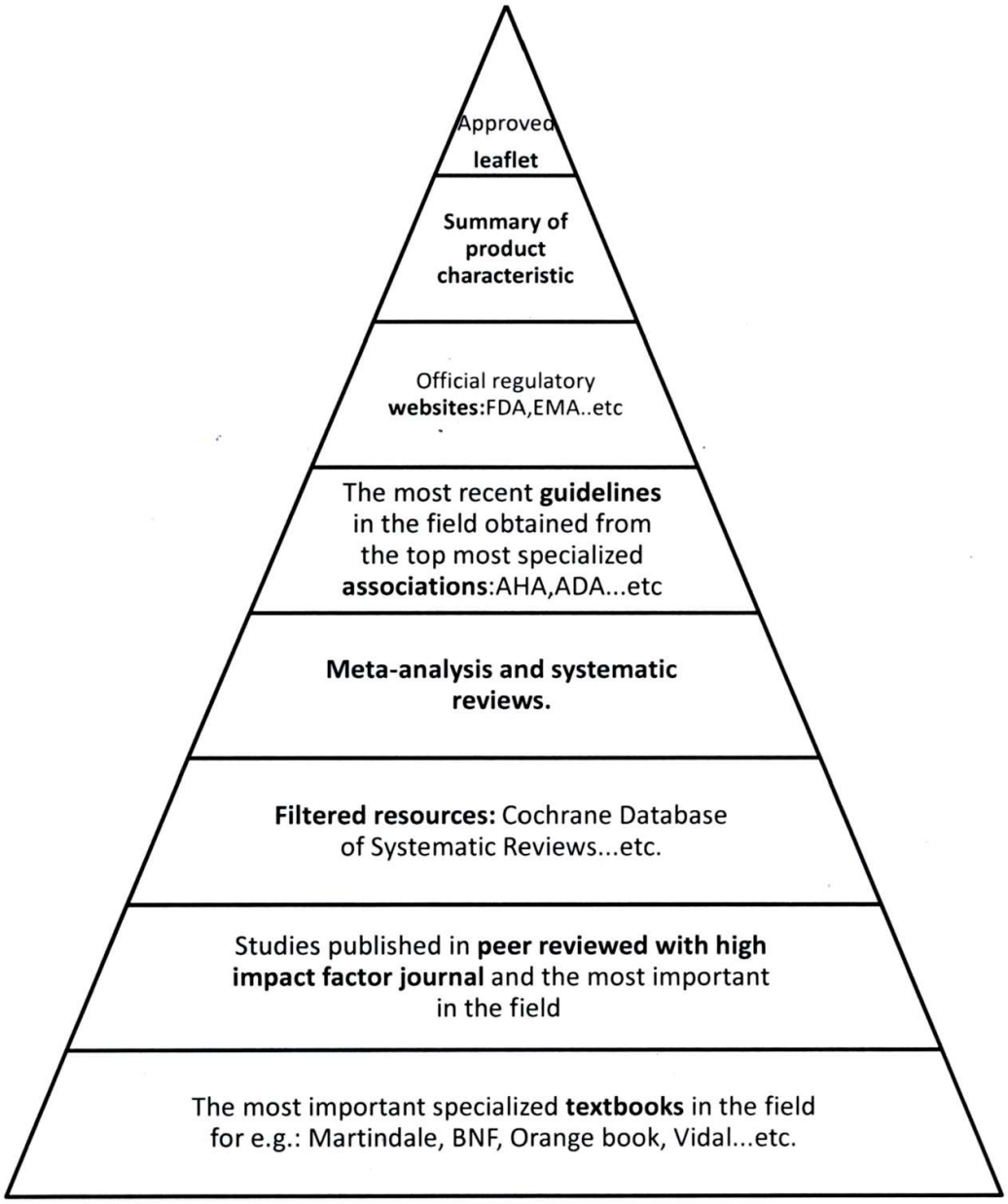
A hierarchy of evidence or levels of evidence is a heuristic used to rank the relative strength of results obtained from scientific research. The following ranking is an example recommended in order to support different claims by the companies. All references must be consistent with the approved insert leaflet:

1- Approved insert leaflet is the only core of any material.
2- Summary of product characteristic consistent with the approved insert from the regulatory authority websites: EMA etc.
3- Official regulatory websites: FDA, EMA, MHRA, TGA, ANSM etc.
4- The most recent guidelines in the field obtained from the top most specialized associations for e.g.: AHA, ADA etc.
5- Meta-analysis and systematic reviews.
6- Filtered resources: Cochrane Database of Systematic Reviews, BMJ Clinical Evidence etc.
7- Studies published in peer reviewed with high impact factor journal and the most important in the field for e.g.:
   - Ca-a cancer journal for clinicians with ~n impact factor: 244.585.
   - New England journal of medicine with an impact factor: 79.258.
   - Lancet with an impact factor: 53.254.
   - Chemical reviews with an impact factor: 52.613.
   - Nature reviews materials with an impact factor: 51.941.
   - Nature reviews drug discovery with an impact factor: 50.167.
   - Jama-journal of the American medical association with an impact factor: 47.66 I.

8- The most important specialized textbooks in the field: Martindale, BNF, Orange book, Vidal, Swiss Drug Compendium, Goodman & Gilman's etc.

N.B.

- All the above-mentioned references can be used only as a support of the approved insert leaflet.
- The impact factor must be checked on yearly basis and a minimum of 2 is accepted. In rare cases, an impact factor less than 2 is accepted such as in rare disease for e.g. Methemoglobinemia.
- For comparative statements, see section 6.3.10.
- Examples of website that can be used in awareness materials: WHO, CDC, mayo clinic, NIH etc.


Approved leaflet
Summary of product characteristic
Official regulatory websites:FDA,EMA..etc
The most recent guidelines in the field obtained from the top most specialized associations:AHA,ADA...etc
Meta-analysis and systematic reviews.
Filtered resources: Cochrane Database of Systematic Reviews...etc.
Studies published in peer reviewed with high impact factor journal and the most important in the field
The most important specialized textbooks in the field for e.g.: Martindale, BNF, Orange book, Vidal...etc.

Abbreviations:

FDA: Food and Drug Administration.
EMA: European Medicines Agency.
MHRA: Medicines and Healthcare products Regulatory Agency.
TGA: Therapeutic Goods Administration.
ANSM: Agence Nationale de Securite du Medicament et des Produits de Sante.
AHA: American heart association.
ADA: American diabetes association.
BNF: British National Formulary.
BMJ: British medical journal.
WHO: World Health Organization.
CDC: Centers for Disease Control and Prevention.
NIH: National Institutes of Health.

Annex (2)

File timeline

Fast Track

• The reviewer pharmacist will submit the comments to the applicant person delegated by the pharmaceutical company for promotional, educational & awareness material according to slides/ pages number:
a) **1-50** slides/pages: **In 6 working days**.
b) **50<** slides/pages: **In 12 working days**.

• After receiving of comments of the reviewed file, the applicant company has 30 working days to submit the amendments.

The approval will be issued as the following:
a) **In 2 working days** from submitting the amendments (for 1-50 slides/pages)
b**) In 4 working days** from submitting the amendments (for 50< slides/pages)

Normal Track

- The reviewer pharmacist will submit the comments to the applicant person delegated by the pharmaceutical company for promotional, educational & awareness material within **21 working days**.
- After receiving of comments of the reviewed file, the applicant company has **30 working days** to submit the amendments.
- The approval will be issued within **7 working days** from submitting the amendments.

Important Notes for normal & fast track files
- If a file enters the committee, the working days to submit the amendments by the company are paused until the committee decision is issued.
- The file will be cancelled automatically, if the allowed time passed without submitting the final copy implying all requested amendments by the reviewer pharmacist.

Extension
- The whole process from submission till approvals/cancellations will take 7 working days.
- The company must submit the original approval so that it can be attached by new approval letter.

Variation Type 1 & 2

• The whole process from submission till approvals/cancellations will take 7 working days as the following:

First Case:

a) The reviewer pharmacist will review the materials within 3 working days.
b) If there are no comments found so the approval will be issued in 2 working days.

Second Case:

a) The reviewer pharmacist will review the materials and submit the comments to the applicant person delegated by the pharmaceutical company within 3 working days.
b) After receiving of comments of the reviewed file, the applicant company has 5 working days to submit the amendments.
c) The approval will be issued in 5 working days from submitting the amendments.

Variation Type 3

For a newly submitted file with only different size/type (of previously approved material)

• The approval can be received in the same day.