

**LABELLING AND PACKAGING**

**GUIDELINES**

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# 1. HISTORY

This is the first edition of this document.

# 2. APPLICATION - Guideline for Stakeholders/ Marketing Authorization Holders.

This guideline will be applicable to all prescription and non-prescription drug products as well as drug products of biological origin.

# 3. PURPOSE

* 1. The purpose of this guideline is
     1. To provide guidance on how to ensure that the information on the label and package leaflet is accessible to and can be understood by those who receive it, so that they can use their medicine or ensure its use safely and appropriately.
     2. To help achieve consistency, transparency, clarity, efficiency and high quality in both the content and management of reviews.
     3. This guideline is written to assist applicants and marketing authorization holders when drawing up the label and package leaflet.

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# 4. INTRODUCTION

This guideline is developed in line with Drugs (Labelling and Packing) Rules. 1986. One of the most possible outcomes of inappropriate product label and package has been associated with prescription and medication errors which may occur partly due to look-alike and sound-alike proprietary names, unclear label abbreviations, acronyms, dose designations, and error prone labeling and packaging designs.

This guideline is thus developed in order to provide applicants with clear guidance on naming for their finished drug products in line with acceptable international standards.

# 5. DEFINITION AND ACRONYMS

**Applicant**: The person or company who applies for marketingauthorization of a new medical product or a variation to an existing marketing authorization.

**Application**. The information provided by the applicant to the Authority for evidence-based review and marketing authorization decision.

**Authority**: Drug Regulatory Authority of Pakistan

**Drug**: Drug as defined in Schedule-I of DRAP Act, 2012.

**Act**: Drug Act, 1976

**Finished Drug Product:** A product that has undergone all stages of production, including packaging in its final container and labeling

**Label:** Display of written, printed or graphic matter upon the immediate container or the outside container or wrapper of a drug package**.**

**Labeling:** All labels and other written, printed or graphic matter accompanying any drug.

**Marketing Authorization Holder / Registration Holder:** Any person or legal entity that has received marketing authorization/ registration or licensure to manufacture and/or distribute a medicine. It also refers to a person or legal entity allowed to apply for a change to the marketing authorization or registration. Also referred to as the “manufacturer” or “applicant” in this document if both are same.

**Pharmacopoeial**: Publication mentioned in sub‐clause (ii) of clause (2) of section (3) of drugs Act, 1976 (XXXI of 1976).

**Pharmacopoeial name**: The name of a drug as mentioned in the pharmacopoeia.

**International non‐proprietary name**: The name of drug as recommended by the World Health Organization or such other name as may be notified by the Federal Government in the official gazette

**Transparency**: Defining policies and procedures in writing and publishing the writtendocumentation and giving reasons for decisions to the public.

**Medical products:** include drugs, vaccines, diagnostics and medical devices.

1. **LABELLING AND PACKING INFORMATION**

The definition of label in the *Act* is interpreted to include labels affixed to the container or packaging of the drug, any separate package inserts, product monographs, prescribing information, fact sheets, consumer information/patient medication information (i.e., patient leaflets), patient diaries, or other material containing information specific to the drug product. These separate package labels generated by the manufacturer/sponsor may be included in the packaging or supplied to the consumer at the time of dispensing.

**1. Manner of Labeling:** The following particulars shall appear either in print or in writing in inedible ink in a conspicuous manner on a label of the innermost container of drug and also on the in which such container is packed namely:

(a) The registered name of the drug;

(b) If the registered name is a proprietary name, then immediately following the registered name, the international non‐proprietary name, and if no such non‐proprietary name is known the Pharmacopoeial name or any other name, if any, approved by the registration board for this purpose in conspicuous manner;

(c) The international non‐proprietary name of the pharmacopoeial name of the generic name, and if no such name is known the chemical name of each active ingredient of a drug with weight.

(d) The name and principal place of business of the manufacturer

(e) The drug manufacturing license number.

(f) The drug registration number.

(g) The date of expiry.

(h) Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instructions;

(i) The distinctive batch number date of manufacture and the maximum retail price;

Provided that in the case of a drug packed in a strip of paper or blister or foil or contained in an ampoule of a capacity of not more than two milliliter or in an ampoule containing a sterile suture or ligature and such strip foil blister or ampoule is placed in other package and also in the case of printed collapsible tubes it shall be sufficient to give the information on the outer packing containing such strips, foils, blister or ampoule. Provided further that the registration board may allow relaxation of any of these conditions.

**2. Labelling of Drugs for internal use**: The label of container of a drug meant for internal use, except a Drug contained in a strip or foil or blister or collapsible tube shall in additions to the particulars required to be given under rule 3, bear in a conspicuous manner.

(i) If it contains a substance specified in the schedule the words “to be sold on prescription of a registered medical practitioner only” and;

(ii) If it contains not less than three percent by volume and alcohol a statement giving the quantity of alcohol in terms of average percentage by volume of absolute alcohol in the finished product.

**3. Labelling of parenteral drug:**

* The route of administration (e.g., intravenous, subcutaneous);
* If no preservatives are present, wording such as “Single use. Discard unused portion”;
* If preservatives are present, wording such as “multiple use” as well as wording to explain duration, the conditions of use and the storage after first puncture of the multiple use product (e.g., “use within X hours of first puncture when stored at Y- ZEC”); and
* If dilution is required, the directions for performing the dilution.

**4. Labelling of Drugs of external use only:** The label of a container of ointment, cream, liniment, lotion, antiseptic or any drug for external application shall in addition to the particular required to be given under rule 3, bear in a conspicuous manner :‐ (i) The words “For external use only “ and;

**5. Labelling of physician’s sample:** The label of a container of every drug intended for distribution to the medical profession as free sample shall in addition to the particulars required to be given under these rules bear the words “Physician sample not for Sale” which shall be over printed or stamped. Provided that if the drug is packed in a strip of paper or blister or foil or contained in an ampoule of a capacity of not more than three milliliters or in a collapsible tube, it shall be to label the outer packing only with the said words.

**6. Labelling of Drugs for Government supply:** The label of a container of every drug intended for the supply to any Government agency including an autonomous body or a semi‐Government Agency shall. While complying with the other labelling requirements of these rules, bear the words or mark reading “Government supply” or such other words or mark as may be required by the agency concerned.

**7. Labelling of Drugs for Veterinary use:** The label of a container of drug for veterinary use shall bear in a conspicuous manner the words “For veterinary use only”

**8. Drugs in Pressurized Containers and Flammability:**

Drug products packaged in a disposable metal container designed to release pressurized contents by the use of a manually operated valve must show the cautionary statements, hazard symbols, and signal words.

Drug products packaged in unpressurized containers operated by a manual pump spray device or any other containers that contain flammable ingredients should show a cautionary warning indicating flammable contents and appropriate directions for use (e.g., “Do not use near an open flame”).

**9. Labelling of Special Containers:**

Drug products may be packaged in special containers that are too small to accommodate an

inner label. This inner label may contain further abbreviated labelling, provided there is an outer label that meets all regulatory requirements.

The two types of packages are:

* Multiple-dose packs, such as: blister packs, strips, push-through cards, ampoules, or vials attached by a plastic strip; and
* Single-dose packs, such as: sachets, pouch-type packs, individual dose vials of liquid or pre-packaged syringes.

**10. Safety concerns and other public health concerns in brand names.**

a) The brand name of a medicinal product should not be liable to cause confusion in print, handwriting or speech with the brand name of another medicinal product. When assessing the potential for such confusion, the following aspects are considered:

• The indication(s);

• The patient population(s);

• The pharmaceutical form(s);

• The route(s) of administration;

• The strength(s);

• The setting for prescription, dispensing and use;

b) The brand name of a medicinal product should not convey misleading therapeutic and/or pharmaceutical connotations. This also includes brand names that are similar or allude to the name of pharmaceutical companies if they are thought to be misleading and cause confusion at the level of product information.

c) The brand name of a medicinal product should not be misleading with respect to the composition of the product.

d) The use of qualifiers/abbreviations by letters as part of the brand name should in principle be acceptable on conditions. Qualifiers consisting of a single letter or number(s) are discouraged, because they may be confused with the strength and/or posology of the medicinal product.

e) The brand name should not convey a promotional message with respect to the therapeutic and/or pharmaceutical characteristics and/or the composition of the medicinal product.

f) The brand name should not convey or suggest a spiritual association or be comparative, nor superlative in any way.

g) The brand name should not comprise wholly of initial letters (acronyms) or code numbers nor include punctuation marks.

h) The importance of other elements such as labelling and pack design should be taken into consideration as contributing factors for the safe use of a medicinal product. These aspects should be discussed at the time of the review of mock-ups.

**10.1 Safety Evaluation**

Proposed proprietary name is evaluated for its potential to inadvertently function as a source of error for reasons that are unrelated to the orthographic and phonological similarity to other product names. These situations could occur, for example, when a proposed proprietary name for a multi-ingredient product represents only one of the active ingredients contained in the product; when names suggest a frequency or route of administration inconsistent with the actual product characteristics; or when names look or sound like other medical terms or diagnostic tests or use a standard medical abbreviation in the name. Names with these characteristics may be potentially misleading and cause confusion at any point under the proposed prescribing conditions and lead to medication errors.

To fully assess the safety of proposed proprietary names, it is essential that product characteristics be considered in the overall risk assessment. Product characteristics can act together with the orthographic and phonologic attributes of the proposed proprietary name

(1) to increase the risk of confusion when there is an overlap in product characteristics among two or more products, or

(2) in some instances, to decrease the risk of confusion by helping to differentiate products through dissimilarity.

Typical product characteristics that could lead to confusion with other products, including, but not limited to, the following:

* Established name of the product
* Proposed indication
* Dosage form
* Route of administration
* Strength
* Unit of measure dosage units
* Recommended dose
* Typical quantity or volume
* Frequency of administration
* Product packaging storage conditions
* Patient population
* Prescriber population

Product characteristics are used in the analysis of a proprietary name to anticipate the clinical setting(s) in which the product is likely to be used.

**10.2 Promotional Evaluation**

The promotional review of proposed proprietary names considers whether the name functions to overstate the efficacy, minimize the risk, broaden the indication, or make unsubstantiated superiority claims for the product, or is overly “fanciful” by misleadingly implying unique effectiveness or composition, or is otherwise false or misleading

“The labelling of a drug which contains two or more ingredients may be misleading by reason, among other reasons, of the designation of such drug in such labelling by a name which includes or suggests the name of one or more but not all such ingredients, even though the names of such ingredients are stated elsewhere in the labelling.”

“The employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact, the drug or ingredient is a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name.”

“Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.”

**11. Labelling for Human Prescription Drug and Biological Products — Content and Format**.

**11.1 Basic Dosing Information**

The section must include the following information

• Recommended starting dose, if different from the usual recommended dose

• Usual recommended dose, dosage regimen (e.g., single or divided dose, timing of dosing, primary and booster schedule), and dosage range

• Titration regimen, if there is one (see note below)

• Duration of use, when duration should be limited (e.g., because of lack of data on long-term use and a basis for concern about toxicity associated with longterm use, cumulative toxicity, or tolerance)

• Route(s) of administration

• Duration (or rate) of infusion, if applicable.

NOTE: Similarly, if there are specific dosing instructions for discontinuation of a drug (e.g., a tapering regimen for a drug that has withdrawal effects if abruptly discontinued), those instructions should be described in basic dosing information.

In describing the dosage range and duration, if it is known that a drug provides no additional benefit above a certain dose or beyond a certain duration of use, that dose or duration must be identified. In addition, if it is known that above a certain dose or beyond a certain duration of use, toxicity is increased to an extent that the risk exceeds the benefit, that dose or duration must be identified

**11.2 Important Administration Instructions**

The section should include any specific administration instructions that are important to the safe and effective use of the drug. For example:

• **For complex dosage forms,** the section should describe any important administration instructions (e.g., for sustained release tablets — do not crush tablets or do not chew tablets).

• The section can include discussion of alternative ways to take **solid oral dosage forms** for patients who have difficulty swallowing where there is information adequate to support the recommended alternatives.

• For **parenteral dosage forms**, the section should indicate whether the drug is light sensitive or needs to be filtered before administration and should identify appropriate containers, filters, and tubing (e.g., glass, plastic, polyvinyl chloride (PVC)).

• For **drugs administered intramuscularly or subcutaneously**, the section should indicate, when relevant, the preferred injection site (e.g., gluteal, deltoid, a large muscle). The section should also indicate whether injection site rotation is necessary and, if so, describe the manner of rotation, any special instructions for injection site preparation, and instructions for any specialized devices or other equipment used in the injection process.

• For **drugs administered intravenously**, the section should identify potential infusion reactions and discuss how to manage them (e.g., premedication), and cross-reference any more detailed discussion in the labelling. The section should also identify pertinent restrictions on intravenous administration (e.g., administer via central line only, dilute only with normal saline, avoid intravenous administration methods that risk intra-arterial exposure).

**12. Packing information:**

All finished drug products should be identified by labelling, as required by the national legislation, bearing at least the following information:

1. The name of the drug product;
2. A list of the active ingredients (if applicable, with the international non-proprietary names), showing the amount of each present, and a statement of the net contents, e.g. Number of dosage units, weight or volume;
3. The batch number assigned by the manufacturer;
4. The expiry date in an uncoded form;
5. Any special storage conditions or handling precautions that may be necessary;
6. Directions for use, and warnings and precautions that may be necessary; and
7. The name and address of the manufacturer or the company or the person responsible for placing the product on the market.

**12.1 Storage conditions:**

After the stability of the product has been evaluated, one of the following recommendations as to storage conditions can be prominently indicated on the label:

— store under normal storage conditions;

— store between 2 and 8 °C (under refrigeration, no freezing);

— store below 8 °C (under refrigeration);

— store between -5 and -20 °C (in a freezer);

— store below -18 °C (in a deep freezer).

**12.2 Pack sizes.**

When presenting a range of pack sizes for a medicinal product it is important that the principles of rational use of medicinal products are taken into consideration. The appropriate range of pack sizes should be chosen in accordance with the duration(s) of treatment and in accordance with the posology in the summary of product characteristics, and not in accordance with local traditions or prescription habits. For example, there could be : -

one pack size for a short course of treatment

one pack size for a monthly course of treatment

one pack size for each multiple of the above.

**B) PRODUCT INFORMATION LEAFLETS/PACKING INSERTS**

**13. Distributing Information among Sections**

1. Organizing Information to Avoid Redundancy

Clinical information pertinent to prescribing decisions should be identified, prioritized, and located in the labelling section that most appropriately communicates the type of information. Detailed information about a particular topic should be consolidated in a single labelling section. Other sections of labelling may more briefly describe or refer to the topic, but not repeat the same content or level of detail. For example, information about a drug interaction that rises to the level of a warning will be described in the WARNINGS AND PRECAUTIONS section, with supporting detail in the DRUG INTERACTIONS section and other sections as appropriate (e.g., DOSAGE AND ADMINISTRATION section if a dosage modification is necessary).

1. Using Cross-References

When a topic is discussed in more than one section of labelling, the section containing the most important information relevant to prescribing should typically include a succinct description and should cross-reference sections that contain additional detail. If the detailed information is divided appropriately into more than one section, those sections should cross-reference each other. Cross-references from the more detailed discussion to the less detailed discussion should generally not be necessary (e.g., a succinct BOXED WARNING should reference the fuller discussion of the risk in WARNINGS AND PRECAUTIONS, but the WARNINGS AND PRECAUTIONS section should not refer back to the BOXED WARNING).

**13.1 Highlights**

The purpose of Highlights is to provide immediate access to the information to which practitioners most commonly refer and regard as most important. Highlights also helps guide the practitioner to the section in the Full Prescribing Information (FPI) where details can be obtained about a specific topic. The following information is intended to help applicants develop Highlights.

1. General Principles

Highlights should be a concise, informative summary of crucial prescribing information, not a verbatim repetition of selected material from the Full Prescribing Information, or a repetition of the Contents. Rarely, it may be appropriate to repeat content verbatim from the Full Prescribing Information (e.g., a succinct boxed warning statement or short indication statement), but in most cases, the information should be summarized and presented in an easily accessible format (e.g., bulleted, tabular).

The information in Highlights is derived from the Full Prescribing Information. Selecting the material to include in Highlights requires judgment about the importance of the data in relation to the clinical setting in which the drug is used.

When information about a risk appears in more than one section of the FPI, the information should typically be presented once in Highlights under the most appropriate heading. For example, if a drug interaction is described under Warnings and Precautions in Highlights, it should not be repeated under Drug Interactions in Highlights.

Summarized information should be presented in clear language that is succinct and imparts the most relevant and complete information. For example, under Warnings and Precautions, the statement in Highlights should, as appropriate, identify the risk, its consequences, and the actions to take to prevent or mitigate it. Directive language is preferable, because it conveys explicit information most concisely (e.g., “Discontinue,” as opposed to “You should discontinue”). Each summarized statement should be located under the appropriate Highlights heading and must cross-reference the section(s) or subsection(s) of the Full Prescribing Information that contains more detailed information.

Indications and Usage

Information under the Indications and Usage heading in Highlights must include a concise statement of each of the drug’s indications from the Full Prescribing Information. The information be presented in a bulleted format if multiple indications exist. In some circumstances, it may be appropriate to present the indications with the same wording as in the Full Prescribing Information (e.g., when a product has one indication and the statement in the Full Prescribing Information is sufficiently concise).

If the Full Prescribing Information includes any limitations of use, the presentation in Highlights needs to be clear as to whether the limitation applies to all indications or only certain indications. For a product with limitations of use that are applicable to all of the product’s indications, it is appropriate to list those limitations or concerns together, under an appropriately titled subheading (e.g., Limitations of Use).

If the drug is a member of an established pharmacologic class, the information under Indications and Usage must include the statement “(Drug) is a (name of class) indicated for (indication(s))”. If the drug is not a member of an established pharmacologic class, the applicant should propose one. The NRA will then determine whether to assign a new or existing pharmacologic class to the drug or to omit a pharmacologic class entirely.

Dosage and Administration

Information under the Dosage and Administration heading must contain a concise summary of the recommended dosage regimen (e.g., starting dose, dose range, titration regimens, route of administration), critical differences among population subsets, monitoring recommendations, if any, and other clinically significant clinical pharmacology information that affects dosing recommendations (e.g., dosing adjustments recommended for concomitant therapy, specific populations with coexisting conditions, clinically relevant food effects). A tabular format is recommended to enhance accessibility of information as appropriate (e.g., when there are complex dosage regimens or different dosing regimens for different indications).

Dosage Forms and Strengths

Information under the Dosage Forms and Strengths heading must include all available dosage forms and strengths to assist the prescriber in product selection. If a solid oral dosage form is functionally scored, such information must be included. If a drug product has numerous dosage forms, bulleted subheadings (e.g., capsules, suspension, injection) or tabular presentations are recommended. For some products, including limited information on packaging can facilitate prescribing (e.g., noting that a 0.5% topical cream is available in both 15 g and 30 g tubes). Because of space constraints in Highlights, multiple strengths for a dosage form should be listed on one line (e.g., Tablets: 25 mg, 50 mg, 100 mg, and 200 mg). Descriptors of the product appearance (e.g., tablet color, shape, embossing) that appear in DOSAGE FORMS AND STRENGTHS in the FPI should not appear in Highlights.

Drug Interactions

Information under the Drug Interactions heading must include a concise summary of those drugs (or classes of drugs) or foods that interact or are predicted to interact in clinically significant ways with the subject drug, and practical instructions for preventing or managing the interaction.

Adverse Reactions

For the purpose of prescription drug labelling, it does not include all adverse events observed during use of a drug, only those adverse events for which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event. The applicant should review the ADVERSE REACTIONS section to ensure all events appropriately fall under that section and delete those events unlikely to have been caused by the drug (i.e., usually a lengthy listing commonly referred to as the laundry list). Because such a list is not essential to the safe and effective use of the drug, it should simply be omitted.

**13.2.** **Package inserts for patients (patient information leaflets)**

Product information must help patients and other users to understand the medication. The patient package inserts, together with the label, provides the patient with key information concerning the proper use of the product, potential adverse drug reactions and interactions, storage conditions and the expiry date.

A) Compliance

Packaging and labelling may help to reinforce the instructions given by the physician or the pharmacist, and improve compliance with drug therapy. In this respect, packaging becomes a compliance aid. The design of pharmaceutical packaging should be such that the product can easily be administered in a safe manner to the patient. If the patient feels at ease with the packaging and route of administration, the design of the packaging may become a key factor in increasing compliance. This is also an important factor in clinical trials.

B) Protection of patients

Packaging must not only increase compliance through its design, but must also protect the patient and indicate the integrity of the product. Tamper evident closure system protects against incidental and accidental poisoning. To protect children, several child-resistant closures have been developed.

**References:**

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