Central Administration of Pharmaceutical Care
General Administration For Pharmaceutical References and Leaflets

Egyptian Guidelines for Medical Leaflets of Medicinal Products for Human Use

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Contents

Egyptian Guidelines for Medical Leaflets of Medicinal products for Human use- Version 3

1. Introduction

The guidance in this document applies to the package leaflets of medicinal products for human use authorized nationally.

2. Legal Basis

The legal basis for requiring approval of the package leaflet as a fundamental part of the authorization process for all medicinal products is the ministerial decrees/EDA Chairman decrees relating to medicinal products for human use and other regulating rules, published guidance issued by EDA in addition to related Pharmacology/technical committee decisions.

3. Background

Product package leaflets play a crucial role in the safe and effective use of medicines by both patients and healthcare professionals and act as pillars of information related to medicinal products. Therefore, approval of the package leaflet is a fundamental part of the authorization process for all medicinal products.

Most medicinal products that are authorized by EDA are obliged to have both an Arabic Patient Information Leaflet (PIL) and an English Summary of Product Characteristics (SmPC) with a few exceptions where an Arabic PIL is not required (in accordance with the technical committee decision 12/3/2009 & 25/8/2022), check it in section 5.1 General notes. Both documents must be completed and submitted to EDA as an intrinsic and integral part of the marketing authorization.

The primary purpose of medicinal products package leaflets is the clear identification of the medicine and the conditions for its safe and effective use. Common factors affecting users of medicines information may be summarized under two headings:

• **Content:** Certain items of information are vital for the safe and effective use of the medicine.

• **Format:** The information must be presented in a legible manner that is easily understood by all those involved in the supply and use of the medicine.

Product package leaflets should be prepared in line with the advice available in this guidance. This guidance is intended to assist applicants and marketing authorization holders in developing the package leaflets for medicinal products intended for human use through recommendations on the content of the package leaflets and on the format, which will aid the production of quality information.

4. Definitions

- **Summary of Product Characteristics (SmPC):** the basis of information on how to use the medicinal product safely and effectively and an integral part of the marketing authorization of all medicines. They should be clear, concise, evidence-based, and relevant to healthcare professionals. The SmPC sets out the agreed position of the medicinal product as distilled during the course of the assessment process. As such the content cannot be changed except with the approval of the competent authority.
- **Patient Information Leaflet (PIL):** contains information for the safe and effective use of medicine directed to the patients/public/end-users.
- **Submitted product:** for the purposes of this guideline, this term is used to refer to the product whose leaflet is submitted to the leaflets administration for evaluation and approval.
- **Proposed leaflet:** for the purposes of this guideline, this term is used to refer to the leaflet submitted to the leaflets administration for evaluation and approval.
- **Reference leaflet:** a leaflet approved and marketed by one of the reference countries determined by technical committee decision (31/12/2009 and 16/9/2021) and is used as the source of information for the proposed leaflet. A reference leaflet has to match the proposed leaflet in active ingredient (and salt if it is unavailable use equivalent) strength, dosage form and route of administration.
- **Non-reference leaflet:** is either a leaflet not approved and/ marketed by any reference country's drug regulatory authority or a leaflet that is not matching in active ingredient, strength, dosage form and route of administration with any reference country's drug regulatory authority and the source of information for the proposed leaflet is collected from scientific data on updated, accredited websites.
- **Replacement Leaflet:** An approved leaflet copy that is requested by the company when the originally approved leaflet is lost/accidentally damaged and is issued in place of the missing leaflet.
- **Grace period:** is a period for implementation of updated paper leaflet in accordance with committee decisions.
- **Template:** an approved model for a specific generic to be used as a reference.

5. Requirements for submission

5.1 General Notes

- **The types of requests submitted to leaflets administration are:**
  - **Under registration, re-registration leaflet**
  - **Update**
  - **Warning addition**
  - **Appeal**
  - **Re appeal**
  - **Replacement leaflet**
  - **Variation**
- **An update is triggered based on a safety update and / or MAH request.**
- **The company is committed to submit safety label updates during the validity of the registration license.**
- **Note: A grace period of 6 months until implementation of the updated paper version is allowed as per the pharmacology committee decision on 24-10-2013.**
- **Receipt is to be delivered as hard copy upon receiving the approved leaflet**
- **Cover letter from the company to Leaflets Administration endorsing the product detailed information and the reason for submission.**
- **An Arabic leaflet is not required for the following products (according to technical committee decision 12/3/2009 & 25/8/2022):**
  - **Intravenous Infusions**
  - **Drugs for Malignant diseases & immunosuppression**
  - **General Anesthetics**
  - **Human Immunodeficiency Virus Drugs**
  - **Drugs intended for hospital use only.**
  - **Contrast media**

It is recommended that the submission should be done before any Deadlines by <u>At least Three Months</u>
Correction is acceptable within <u>one month for local products and three months for the imported and under license products</u> of sending the amendments otherwise a new submission will be required

5.2 Required documents based on product registration status

5.2.1 For Under– registration Products

- Receipt
- Cover letter from the company to Leaflets Administration
- Proposed leaflet (SmPC English & PIL Arabic).
  *For cases of exceptions of Arabic leaflet, see above (technical committee decision 12/3/2009 & 25/8/2022).
- Reference leaflet for both (SmPC & PIL) – most updated version
- Accelerated stability
  -Excluded for 820, EDA Chairman decree (450/2023) case 2 track A, B&C and to be submitted immediately after releasing from the responsible department.
- EDA Approved product composition (stability/CADC)
  -Excluded for 820, EDA Chairman decree (450/2023) case 2 track A, B&C (for imported products) and to be submitted immediately after releasing from the responsible department.
- Naming or Layout approval (optional for Export & Tender)
- Action letter
- PV approval
  -requested for 425, 645, EDA Chairman decree (450/2023) case 1&3
  -excluded for export only, EDA Chairman decree (450/2023) case 2)
- Pricing approval
  -Excluded for 820,export only, Tender & Export and EDA Chairman decree (450/2023) case 2)

5.2.2 For under Re-Registered Products

- Receipt
- Cover letter from the company to Leaflets Administration
- Proposed leaflet (SmPC English & PIL Arabic)
  *For cases of exceptions of Arabic leaflet, see above
- Reference leaflet for both (SmPC & PIL) – most updated version
- Approved composition from the authorized department.
- Naming or Layout approval (in case the Arabic name is not written in the registration license)
- Last approved leaflet
- Registration License, Re-registration action letter
- Pv approval required for products following 150 decision.
- Re-Reg stability (depending on the requirements stated in the ministerial decree that the product follows), and in case of safety update may not be submitted.
- If the leaflet approval date is within 5 years and no updates /&warnings are required, it is permissible NOT to submit to leaflet administration, but if it exceeds 5 years the above should be submitted.

5.3 Required Add-On documents

a) When a non-English reference is used:

Accredited medical translation for the reference product leaflet is required. Both the non-English leaflet (original leaflet) and the English leaflet (translated version) must be attached.

b) In case of Scoring for dose:

- Commitment of whither that scoring is functional or non-functional should be submitted.
- Functional scoring: Reference must be a scored tablet product. Additionally, Subdivision Test should be submitted to relevant department.

c) In the case of imported and innovator Products:

- Leaflet attached to legalized Certificate of Pharmaceutical Product (CPP) could be used as the reference (Declared in cover letter) (optional if the CPP-attached leaflet is the most updated).
- If the leaflet is PIL only: A Legalized letter from the country of origin stamped by Egyptian Embassy will be a must, comprising a warrant that the attached leaflet (Patient information leaflet) with the specified Trade Name, generic name, concentration, revision date and version number is marketed and registered in the country of origin, and is to be translated to Arabic language as the patient information leaflet.
  - Declaration template (see annex 3): "We (License Holder), declare that the attached leaflet of (Trade name) and concentration, code (…), revision date (…), version date is currently marketed and registered and most updated in the country of origin (…)"
- Attached copy of the last updated and currently marketed leaflet in the country of origin, Also, the original package leaflet could be attached If available.
- The SmPC should be submitted to be displayed on the EDA website.

d) **For non-English leaflets:** MAH should submit either of the following:

- A legalized Declaration Letter from License Holder that commits that the leaflet is translated according to authorized medical translation on their responsibility in accordance with the translation attached (2 languages: English and Non-English). (Signature & Stamp)

  Or
- Legalized letter from the head office stating that the scientific office is responsible for the translation and the leaflet is translated a medical translation through their scientific office, the medical translation submitted (2 languages: English and Non-English) should be signed and stamped by the scientific office.
- It should be noted that the English SmPC for imported products shall be displayed on the EDA website.

e) In the case of non-reference Products:

- The Cover letter should clarify that the product is non-reference and the available following committee approvals according to the product ministerial decree should be attached
  - Non reference Committee approval
  - Pharmacology committee approval (if applicable)
  - Scientific committee approval
- Clarify the detailed source of scientific data (References, Scientific papers, Books: Martindale, BNF) for each piece of information inside the
- Proposed leaflet document according to the reference used. For e.g. “The proposed dose is according to “reference name”.
- In case of using multiple references, English SmPC to be translated into Arabic (to be approved by the Pharmacology committee).
- In case of using one reference, the English leaflet will be according to SmPC, Arabic Leaflet can be used according to PIL.
- For multivitamins and minerals products a table including the equivalence for the base of each ingredient in the approved composition must be attached

5.4 Special Requirements based upon the type of request

5.4.1 Update

- Cover letter stating the reason of update
- Receipt
- The Last approved leaflet should be submitted as soft PDF copy.
- Track changes between the proposed updated leaflet and previously approved
- Valid EDA documents (ex., registration approval, re-registration approval)

5.4.2 Replacement Leaflet

- Cover letter
- Scanned copy of the approved leaflet
- Receipt

5.4.3 Variation

- Variation approval (and its requirements)
- Last approved leaflet
- Receipt

- Most updated version of Reference leaflet for both (SmPC & PIL)
- Refer to The Third edition of Human Pharmaceuticals Variations Guidelines 2023

***Note:**

Not all variations will require a leaflet reassessment.

- Variations that affect the scientific content of the leaflet should be submitted and reassessed (e.g. Inactive ingredients (especially requiring warning addition), Equivalence, Naming, Tablet scoring, Storage conditions (In use stability)
- For Variations which do not affect the scientific content of the leaflet, MAH should notify the leaflets administration for updating the published leaflet; This can be applied directly without leaflet reassessment) e.g.: Pack (that do not affect storage conditions), Manufacturer and license holder.

5.4.4 Warning Addition

- Warning to be added should be highlighted inside the leaflet
- Last approved leaflet
- Most updated version of Reference leaflet for both (SmPC & PIL)
- Warning Addition request, is triggered and required by the NRA

5.4.5 Appeal

- Cover letter and appeal request endorsing the detailed reason for submitting appeal (in Word format). (should be delivered also as a hard copy within one week of file submission)
- Appeal Receipt.
- Re-appeal Receipt: In case of appeal refusal by the committee and the company requested to resubmit as there are updates requiring redisplay for the committee. إعادة " عرض"
- Track changes / comparison table (optional according to the reason of appeal)
- Attach all documents and requirements **related to the cause for the appeal.**

5.5 Format of Files for submission

- SmPC & PIL must be in one file with the same format and page orientation, in word format. (Not a PDF file).
- Cover letter is submitted as PDF file (signed stamped scan)
- Appeal and any attached comparison table must be in word format.
- Each single approval document must be submitted as a separate PDF file, not combined with other approvals in the same pdf file. However, approval documents PDF files can be collated together as a zip file.

- If the submission includes multiple product concentrations, approvals documents of each concentration should be presented in separate PDF files.
- The title of each file must be clear. Each file name should follow the following convention: “document title + issuance date”, e.g. “Long-term Stability approval 03-01-2022”
  OR “date format ISO 8601: YYYYMMDD + short descriptive document name”, e.g. “20220103 long-term stability approval”

- **Requirements for the format of the proposed leaflet to be assessed:**

Headings	1. HEADINGS (BOLD, CAPITAL LETTERS) (2 single lines before and 1 single line after)
Subheadings	1.1 Subheadings (bold, normal letters) (1 single line before and 1 single line after)
Additional subheadings	Do not use bold or additional numbering, instead use underline or italics or both and be consistent throughout the document, e.g.: Additional subheading Additional subheading *Additional subheading* *Additional subheading*
Font	Font type: Times New Roman Font Size: 12 Font style: Regular Font color: Black
Language	SmPC: English PIL: Arabic *Certified translation is required when the reference is not in the English language.
Other format	The use of column format of the text version of the information in the leaflet submitted for assessment should be avoided whenever possible.

For products with a reference leaflet; The Company should stick to the format of the reference leaflet (considering the reference countries determined by the technical committee as in annex 1 and for Non-reference products (with more than one reference) stick to the enclosed template.

Note: The Package leaflet font should be readable and with clear formatting.

5.6 Submission forms

- The links for the forms used for submitting a new leaflet, leaflet corrections and checking the leaflet status are provided in **annex (2)**.

6. Requirements for content layout

6.1 General notes

A. The main section headings of the leaflet should cover the following:

1. Name of the medicinal product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars
   - 4.1 Therapeutic indications
   - 4.2 Posology and method of administration
   - 4.3 Contraindications
   - 4.4 Special warnings and precautions for use
   - 4.5 Interaction with other medicinal products and other forms of interaction
   - 4.6 Fertility, pregnancy and lactation
   - 4.7 Effects on the ability to drive and use machines
   - 4.8 Undesirable effects
   - 4.9 Overdose
5. Pharmacological properties
   - 5.1 Pharmacodynamics properties
   - 5.2 Pharmacokinetic properties
   - 5.3 Preclinical safety data (optional for innovator products only)
6. Pharmaceutical particulars
   - 6.1 List of excipients
   - 6.2 Incompatibilities
   - 6.3 Shelf life (shelf life addition is Optional except in case of parenteral/suspension/eye drops)
   - 6.4 Special precautions for storage
   - 6.5 Nature and the contents of the container (Optional unless packs with special administration components)
   - 6.6 Special precautions for disposal and other handling
7. License holder

B. The head of the leaflet

- At the head of the leaflet, the following should be provided:
  - Full product identification (trade name, strength, and dosage form)
  - Active ingredient(s), equivalence.

- Additionally, the leaflet for medicinal products subject to Black box addition according to U.S Food and Drug Administration should include a Black box with accordance to the submitted reference
- Additionally, the head of the leaflet for medicinal products subject to additional monitoring according to European guidelines should include a black triangle with the following statement: (technical committee decision dated 29-06-2016)

قرارات اللجنة الفنية لمراقبة الأدوية بجلستها في ٢٠١٦/٠٦/٢٩

*- بالنسبة للمستحضرات التي ورد Black Triangle في نشرتها طبقاً للـEuropean guidelines، يتم إلزامها بمراجعة نشراتها في قسم الفارماكولوجي لتتطابق مع نشرة الـEMA فيما يخص وضع Black Triangle مع إعطاء الشركات مهلة ستة أشهر اعتباراً من تاريخ اللجنة لتوفيق الأوضاع ويتم تطبيق القرار على جميع المستحضرات المستوردة والمصنعة محلياً.

- **For SmPC:**

"▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions."

- For PIL:

"▼يخضع هذا الدواء للمراقبة الإضافية. سوف يسمح ذلك بالتعرف السريع على معلومات الأمان الجديدة. يمكنك المساعدة عن طريق الإبلاغ عن أي آثار جانبية قد تتعرض لها. راجع نهاية القسم 4 من هذه النشرة للتعرف على كيفية الإبلاغ عن الآثار الجانبية."

- For innovators adding a black triangle or not is according to the reference country.

- To determine if the product is subject to additional monitoring, you can refer to the list of medicines under additional monitoring published on the website of the European Medicines Agency and linked in annex (2) or stick to the reference used.
- SmPC should be in English, while PIL should be in Arabic. Certified translation is required when the reference leaflet is in a language other than English.

C. Trade name

- The trade name of the submitted product used in the leaflet text should be based on the naming approval or registration license (the most updated).

- Using any of the following trademark-related symbols "™, ®, ©" next to the product's trade name in the leaflet should be based on a certificate of trademark approval for the product name. (Or if it's an innovator product and the mark is in the reference leaflet) for English name.

D. Strength and dosage form

- The strength and dosage form of the submitted product used in the leaflet text should be based on the box approval matching with stability approval or registration license (the most updated).

E. Qualitative and quantitative composition

- The qualitative and quantitative composition of active ingredients and excipient(s) of the submitted product used in the leaflet text should be based on the approved composition attached to the stability approval, registration license (the most updated) or The Central Administration of Drug Control (previously known as NODCAR).

F. Physical characters

- The physical characters of the submitted product used in the leaflet text should be based on the stability approval or registration license (the most updated).

G. Shelf life and storage conditions

- The shelf life and storage conditions of the submitted product used in the leaflet text should be based on the stability approval or registration license (the most updated).

H. Container/pack

- The container/pack material of the submitted product (Optional) when referred to in the leaflet text should be based on pricing approval and stability approval or registration license (the most updated).
- The number of units of the pack for the submitted product (Optional) when referred to in the leaflet text should be based on the pricing approval or registration license.

I. license holder

- The license holder of the submitted product when referred to in the leaflet text should be based on registration license or box approval or stability approval (the most updated).
- Any variation approvals regarding any of the previous items should be submitted and considered.
- Note: All the submitted documents should be valid, most updated and meeting timelines of ministerial decrees and any regulations from responsible departments.

J. Committee warnings

- Pharmacology and technical committee warnings for the active ingredient (s), inactive ingredient(s), and pharmacotherapeutic class of the submitted product must be included in the proposed leaflet in the relevant section(s). (See annex 2 for links to warnings) received from relevant departments (e.g. PV)
-

- When adding committee warnings, close attention should be paid to the following points:
  - Whether the warning applies to specific dosage forms.
  - Whether the warning applies when exceeding a specific dose threshold.
  - Whether the warning should be added under a specific subsection of the leaflet.
  - Whether the warning must be applied under a specific timeframe.
  - Whether the warning is superseded by a more updated warning/decision.
  - Whether the warning applies to the PIL, SmPC or both.
- The following should be noted for some inactive ingredient's warnings:
  - If Sorbitol is present: calculation is submitted in grams/day
  - If Methyl Paraben is present: calculation is submitted in mg/kg/ day for child and/ or adult.
  - If Propyl Paraben is present: calculation is submitted in mg/kg/ day for child and/ or adult.
  - If Propylene glycol is present: the calculation is submitted in mg/kg /day
  - If Ethanol is present: calculation is submitted in mg per dose

✱ "These should be presented on stamped company forms"

K. Special recommendations in translating PILs to Arabic

- Authorized translation is preferred. In case of no authorized translation is submitted, clear medical translation to Arabic language is required.
- Aim to use simple words of few syllables. Long sentences should not be used. It is better to use a couple of sentences rather than one longer sentence, especially for new information.
- Long paragraphs can confuse readers, particularly where lists of side effects are included. The use of bullet points for such lists is considered more appropriate.
- An active style should be used, instead of passive. For example:
  - "تناول كبسولتين" بدلاً من "ينبغي أخذ كبسوليتن"
  - "يجب عليك..." أفضل من "من الضروري..."
- When telling patients what action to take, reasons should be provided. Instructions should come first, followed by the reasoning, for example:
  - "احذر عند استخدامك X إذا كنت تعاني من الربو، حيث أنه قد يؤدي إلى أزمة تنفسية"
- "Your medicine, this medicine, etc." should be used rather than repeating the name of the product, as long as the context makes clear what is being referred to.
- Abbreviations and acronyms should not usually be used unless these are appropriate. When first used in the text, the meaning should be spelt out in full. Similarly, scientific symbols (e.g. > or <) are not well understood and should not be used.
- Medical terms should be translated into a language that patients can understand. Consistency should be assured in how translations are explained by giving the lay term with a description first and the detailed medical term immediately after. On a case-by-case basis the most appropriate term (lay or medical) may then be used thereafter throughout the leaflet to achieve a readable text.

6.2 Considerations for products with a reference leaflet

- **For Imported products: the SmPC shall be displayed on the EDA website.**
  - The electronically displayed SmPC shall include the scientific data along with the excipients list. The sections that include data that is based on EDA-regulatory approvals (pack, manufacturer and MAH) will be written the same as information in PIL or bear the following sentence "Refer to the product PIL".
  - Inclusion of other data that is based on EDA-regulatory approvals (pack, manufacturer and MAH) in the electronically displayed SmPC shall be optional.
- A reference product must match the submitted product in active ingredient (in the same form e.g. same salt), strength (with the same equivalence), dosage form, route of administration, scoring and diluents and solvents (whenever available for the product) matching with stability approval. Refer to Annex 1 for sources of references.
- The **most updated version** of the proposed reference should be used.
- The reference product must be **authorized and marketed in a one of the reference countries identified technical committee decision (refer to Annex 1).**
- In case of a combined proposed leaflet of multiple product concentrations: a combined reference product leaflet is a must or multiple leaflets from the same reference country but with the same trade name and revision date and endorsing the same content and indication.
- **In the case of parenteral:**
  - Shelf life after and before reconstitution and dilution should be according to the stability approval. In case of reconstitution and dilution: the solvent(s) and diluent(s) and their volume for the submitted product used in the leaflet text should be based on the stability approval which matches the information in the submitted reference.
- **In case of Scoring for dose:** information should be given on whether or not reproducible dividing of the tablets has been shown, according to the stability approval or registration license E.g.:
  - "The tablet can be divided into two equal doses."
  - "The scoring is only to facilitate breaking for ease of swallowing and not to divide into equal doses."
  - "The score line is not intended for breaking the tablet."

  Note: justification should be submitted (refer to section 5.3: Required Add-on documents
- The information content of the proposed leaflet must be **consistent with the reference leaflet.**
- When mentioning trade name, strength, dosage form, composition and physical characters throughout the proposed leaflet text, they should be taken from the relevant EDA-approved documents previously stated and should replace those of the reference product (active ingredient, strength, dosage form and route of administration would be identical anyway).

- When a **boxed warning** is present in the reference leaflet, it **should not** be omitted from the proposed leaflet.
- The trade name from the reference leaflet must be replaced with the submitted product trade name (based on the naming approval or registration license).
- Information referring to a different concentration or dosage form other than the submitted product is to be mentioned in active ingredients not the submitted product's trade name unless there are other concentrations and/or dosage forms (registered/under registration/re-registered) as a line extension of the submitted product.

6.3 Considerations for products without a reference leaflet

- Products without a reference leaflet should adhere to the following content layout." This includes any submitted product without a matching reference product in addition to any submitted product that has a matching reference but for which no leaflet is available on the official websites of all reference regulatory authorities.
- The main section headings should be included. The sub-headings and associated text within the leaflet should only be included if these are relevant for the particular product. For example, if there is no information concerning excipients of known effect this section may be omitted from the leaflets.
- The trade name of the submitted product should be used in the section that identifies the specific product (section 1). When otherwise referring to properties of the active substance(s) rather than those of the product throughout the SmPC text, the name of the active substance should be used.

6.3. A. Summary of Product Characteristics (SmPC): (This template is only as guidance and is not obligatory and for reference products the reference is their guidance)

- **As previously stated, the head of the leaflet should contain full product identification (trade name, strength and dosage form), active ingredient(s) and additional monitoring required (inverted black triangle, black box) if applicable.**

1. NAME OF THE MEDICINAL PRODUCT

- This section includes the trade name (from naming approval or registration license) followed by the strength and dosage form (from box approval or stability approval or registration license).
  - E.g.: "xxx 500 mg film coated tablets."
- However, when otherwise referring to the medicinal product throughout the SmPC text, the strength and the dosage form do not have to be mentioned in the name. The International Non-proprietary Name (INN) or the usual common name of the active substance should be used when referring to properties of the active substance(s) rather than those of the product. The use of pronouns (e.g. "it") or alternative terms (e.g. 'treatment') should be used whenever possible.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

- This section includes the active substance(s) name, strength and equivalent base strengths (when applicable) per dosage unit, per unit volume, or per unit of weight, according to the approved composition attached to the stability approval or registration license.
  - E.g.: "Each 1 ml contains 125 mg Ferrous Sulphate equivalent to 25mg Elemental Iron"
- Additionally, this section includes the excipient(s) with known effect. Excipients with known effect are those excipients known to have a recognized action or effect and are according to pharmacology or technical committee warnings. (see annex 2)
  - E.g.: "Excipients with known effect: Propylene Glycol"
- The following standard statement should be included at the end of the section: "For full list of excipients, see section 6.1".

3. PHARMACEUTICAL FORM

- This section includes the dosage form, according to box approval or stability approval or registration license, as mentioned in section 1.
  - E.g.: "Film coated tablets."
  - E.g.: "Granules in sachets for oral solution."
- After the dosage form, this section includes the physical characters describing the appearance of the product (color, markings, etc.) in a separate paragraph, according to the stability approval or registration license.
  - E.g.: "White to off-white, oval shaped film-coated tablets."
  - E.g.: "Clear colorless solution."

- In the case of tablets designed with a score line, information should be given on whether or not reproducible dividing of the tablets has been shown, according to the stability approval or registration license E.g.:
  - "The tablet can be divided into two equal doses."
  - "The scoring is only to facilitate breaking for ease of swallowing and not to divide into equal doses."
  - "The score line is not intended for breaking the tablet."

  Note: justification should be submitted (refer to section 5.3: Required Add-on documents)
- Full section example:
  - "Film-coated tablets.

  White, oval tablet with a score on one side and plain on the other side. The scoring is only to facilitate breaking for ease of swallowing and not to divide into equal doses."

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- This section includes the indication(s) stated clearly and concisely and should define the target disease or condition distinguishing between treatment (symptomatic, curative or modifying the evolution or progression of the disease), prevention (primary or secondary) and diagnostic indication. When appropriate it should define the target population especially when restrictions to the patient populations apply.
- It should be stated in which age groups the product is indicated.
  - e.g. "X is indicated in adults/neonates/infants/children/adolescents/aged x to y years/months."

4.2 Posology and method of administration

Posology

- In this part, the dose should be specified for each route of administration and for each indication, as appropriate. The dose should be specified for each patient category where appropriate.
- Frequency of dosing should be expressed using time units (e.g. once or twice daily or every 6 hours) and, to avoid confusion, abbreviations e.g. OD or BID should not be used.
- Where appropriate, the following points should be addressed:
  - the maximum recommended single, daily and/or total dose,
  - the need for the dose titration,
  - the normal duration of use and any restrictions on duration and, if relevant, the need for tapering off, or advice on discontinuation,

- advice on action to be taken if one or more dose(s) is (are) missed, or e.g. in case of vomiting (the advice should be as specific as possible, taking into consideration the recommended
- frequency of dosing
- advice on preventive measures to avoid certain adverse drug reactions with cross-reference to section 4.4,
- the intake of the product in relation to drink and food intake, together with a cross-reference to section 4.5 in case of specific interaction e.g. with grapefruit or milk,
- Advice regarding repeat use, with any information on intervals to be observed between courses of treatment, as appropriate.

▪ Dosage adjustments or other posology-related information in specific patient groups should be stated where necessary in additional sub-headings under posology e.g.: elderly population; renal impairment, hepatic impairment, patients with other concomitant disease, overweight patients or other relevant special population.

▪ A specific sub-section 'pediatric population' should be included and the information given should cover all subsets of the pediatric population, using a combination of the possible situations presented below as appropriate.

- If the posology is the same in adults and children, then a statement to this effect is sufficient; the posology does not need to be repeated.
- If there is no indication for the product in some or all subsets of the pediatric population, no posology recommendation can be made, but available information should be summarized using the following standard statements (one or combination of several as appropriate). E.g.:
    - "The safety/efficacy of X in children aged x to y (*or any other relevant subsets e.g. weight, pubertal age, gender*) have not yet been established." + "No data are available" Or "Currently no recommendation on a posology can be made."

"X should not be used in children aged x to y (*or any other relevant subsets e.g. weight, pubertal age, gender)* because of safety/efficacy

- Concern *(concern(s) to be stated) with cross-reference to sections detailing data e.g. 4.8 or 5.1)."*
- "There is no relevant use of X in children aged x to y (*or any other relevant subsets e.g. weight, pubertal age, gender)* in the indication(s) *(specify indication(s))*".
- "X is contraindicated in children aged x to y (*or any other relevant subsets e.g. weight, pubertal age, gender*) in the indication *(specify indication(s))*".

- If there are more appropriate strength(s) and/or dosage form(s) for administration in some or all subsets of the pediatric population (e.g. oral solution for infants), these can be mentioned in section 4.2 of the SmPC of the less appropriate one(s).
    - E.g.: “Other dosage forms/strengths may be more appropriate for administration to this population.”

Method of Administration:

- This section includes the route of administration, relevant instructions for correct administration and use and any special precautions related to the administration of the product by healthcare professionals, the patient or careers.

4.3 Contraindications

- This section includes situations where the medicinal product must not be given for safety reasons, i.e. contraindications. Such circumstances could include a particular clinical diagnosis, concomitant diseases, demographic factors (e.g. gender, age) or predispositions (e.g. metabolic or immunological factors, a particular genotype and prior adverse reactions to the medicine or class of medicines).
- Hypersensitivity to the active substance or to any of the excipients should be included as follows:

– “Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.” should be included.”

- Other medicines or classes of medicine, which must not be used concomitantly or consecutively should be stated, based on either data or strong theoretical reasons. If applicable a cross-reference to section 4.5 should be made.
- Only if pregnancy or breastfeeding is contraindicated, should it be mentioned here. In section 4.6, a cross-reference should be made, and further background information provided.

4.4 Special warnings and precautions for use

- This section should include any pharmacology and technical committee warnings for the active ingredient (s), inactive ingredient(s), and pharmacotherapeutic class of the submitted product. (See annex 2).
- The exact content of this section will be different for each product and the therapeutic conditions it is intended to treat. It is however suggested that the following items be included where relevant to the specific product:

- The conditions, in which the use of the medicinal product could be acceptable, provided that special conditions for use are fulfilled. In particular, specific risk minimization measures requested as part of a Risk Management Plan to ensure safe and effective use should be described in this section.

- E.g. “Liver function should be monitored before initiation of treatment and monthly thereafter”, “Patients should be advised to immediately report any symptoms of depression and/or suicidal ideation”

- Special patient groups that are at increased risk or are the only groups at risk of experiencing product or product class-related adverse reactions (usually serious or common), e.g. elderly, children, patients with renal or hepatic impairment (including the degree of impairment, e.g. mild, moderate or severe). A Cross-reference to section 4.8 on the differential effects in terms of frequency and severity of the specified adverse reaction should be provided.
- Serious adverse reactions to which healthcare professionals need to be alerted, the situations in which these may occur and the action that may be required, e.g. emergency resuscitation.
- If there are particular risks associated with starting the medicinal product (e.g. first dose effects) or stopping it (e.g. rebound, withdrawal effects), these should be mentioned in this section, together with the action required for prevention.
- Any measures that can be taken to identify patients at risk and prevent the occurrence, or detect early the onset or worsening of noxious conditions. If there is a need for awareness of symptoms or signs representing early warning of a serious adverse reaction, a statement should be included.
- Any need for specific clinical or laboratory monitoring should be stated. Recommendations for monitoring should address why, when and how the monitoring should be conducted in clinical practice. If dose reduction or other posology is recommended in such circumstances or conditions, this should be included in section 4.2 and cross-referenced here.

Any particular risk associated with an incorrect route of administration (e.g. necrosis risk with extravasation of intravenous formulation, or

- Neurological consequences of intravenous use instead of intramuscular use), should be presented, with advice on management if possible.
- When the product is indicated in one or more subsets of the pediatric population and there are warnings and precautions for use that are specific to the pediatric population or any subset of the pediatric population, they should be identified under a subheading titled “Pediatric population”. If measures are requested that are specific to the pediatric population for which the product is indicated (e.g. as part of a Risk Management Plan), these measures should be described in this subsection.

- In general, descriptions of warnings and precautions regarding pregnancy and breast-feeding, the ability to drive and use machines, and other aspects of interactions should be dealt with in sections 4.6, 4.7 and 4.5, respectively. However, in specific cases of major clinical importance it might be more appropriate to describe specific precautionary measures in this section, with cross reference to section 4.5, 4.6, or 4.7.

4.5 Interaction with other medicinal products and other forms of interaction

- This section should provide information on potential interactions (whether pharmacodynamic or pharmacokinetic interactions) of the active substances(s) of the medicinal product with other substances, with a particular emphasis on the interactions that result in a recommendation regarding the use of the medicinal product.
- Interaction checkers from Lexicomp, Micromedex, Epocrates, Rx list and Drugs.com may be used for non-reference products only

4.6 Fertility, pregnancy and lactation

- This section includes information on safety and recommendations in pregnancy and lactation. Moreover, the effect on fertility in males if available shall be added.
- For generic products this section is written by the active ingredient.

4.7 Effects on the ability to drive and use machines

- This section includes information on the performance related to driving and road safety or using machines, it should specify whether the medicinal product has a) no or negligible influence b) minor influence, c) moderate influence or d) major influence on these abilities. Other important factors that affect the ability to drive and use machines should be considered if known, e.g. duration of the impairing effect and the development of tolerance or adverse reactions with continued use.

4.8 Undesirable effects

- Bold headings and/or sub-headings should be used to facilitate identification of information on each selected adverse reaction and each relevant special population.
- For generic products, any important information (concerning patient or safety, mentioned in reference data) must be added.

Reporting of suspected adverse reactions

- Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via The Egyptian Pharmaceutical Vigilance Center directly on hotline 15301 or by sending an e-mail to: pv.followup@edaegypt.gov.eg

4.9 Overdose

- This section includes information on acute symptoms and signs and potential sequel of different dose levels of the medicinal product based on all available information including accidental intake or mistakes and their management.

5. PHARMACOLOGICAL PROPERTIES (For generic products this section is written by active ingredient)

5.1 Pharmacodynamics properties

- This section includes information on pharmacotherapeutic group and mechanism of action, for generic products the clinical safety and efficacy section and clinical trial section may be removed.

5.2 Pharmacokinetic properties:

- This section includes information on Absorption, Distribution, Metabolism and Elimination.
- Additional sub-heading(s), such as “Renal impairment”, “Hepatic impairment”, “Elderly”, “Pediatric population” or “Other special populations” (to be specified) and “drug interaction” should be used, where appropriate

5.3 Preclinical safety data

- This section applies to innovator products only.
- This section includes information on any findings in the non-clinical testing that could be of relevance for the prescriber, and which is not already included in other relevant sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- This section includes the name(s) of the excipient(s) according to the approved composition.
- Note: Excipient(s) that evaporate during manufacturing processes (as per the stability approval) are not meant to be listed in the leaflet.

6.2 Incompatibilities

- This section includes information on physical and chemical incompatibilities of the medicinal product with other products with which it is likely to be mixed or co-administered. This is particularly important for medicinal products to be reconstituted and/or diluted before parenteral administration. Significant interaction problems, e.g. sorption of products or product components to syringes, large volume parenteral containers, tubing, in-line filters, administration sets, etc. should be stated.
- Statements concerning the compatibility of the product with other medicinal products or devices should not be included in this section but in section 6.6. Statements concerning pharmacological and chemical/physical incompatibilities with food should be included in section 4.5. If appropriate, the standard statement, ‘Not applicable’, should be included.
- For certain pharmaceutical forms, e.g. parenteral, either of the following standard statements should be included as appropriate:
  - ‘In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.’

- ‘This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.’

6.3 Shelf life (optional except in case of parenteral/suspension/eye drops)

- This section includes information on the shelf life of the medicinal product as packaged for sale and, if appropriate, after dilution or reconstitution or after first opening, according to the stability approval or registration license.
- May be added as “see outer pack”.

6.4 Special precautions for storage

- This section includes information on storage conditions according to the stability approval or registration license.

6.5 Nature and contents of the container (Optional)

- This section includes information on the pack (the container, material of construction of the container, and any other component of the product e.g. measuring spoons), according to the pricing approval or stability approval or registration license. All pack sizes should be listed according to the pack approval or registration license.

6.6 Special precautions for disposal and other handling of the product.

- If there is no special use or handling instructions for the pharmacist or other healthcare professionals, the standard statement, ‘No special requirements.’ should be included.
- In section 4.2, instructions on handling of the product by the doctor, other health personnel, or patient should be included, as well as general information concerning the administration of the product (whether administered by the patient or the health personnel). If instructions for use/handling are needed where the medicinal product has to be prepared before use, e.g. where it must be suspended or diluted, this information has to be given here. For clarity, a cross-reference in section 4.2 to the relevant information in section 6.6 could be included, e.g. “For instructions on dilution of the product before administration, see section 6.6.”

7. LICENSOR INFORMATION

- This section identifies the license holder of the medicinal product according to registration license or box approval or stability approval.

6.3.B. Patient Information Leaflet (PIL):

- **As previously stated, the head of the leaflet should contain full product identification (trade name, strength and dosage form), active ingredient(s) and additional monitoring triangle if applicable, in Arabic language. This should be followed by the following introduction:**

قم بقراءة هذه النشرة بأكملها بحرص قبل أن تبدأ باستخدام هذا الدواء لاحتوائها على معلومات تهمك.

- **احتفظ بهذه النشرة. قد تحتاج لقراءتها مجدداً.**
- **إذا راودتك أي أسئلة أخرى، استشر الطبيب أو الصيدلي.**
- **تم وصف هذا الدواء لك وحدك. لا تقم بإعطائه للآخرين حتى وإن كانت علامات مرضهم مطابقة لأعراضك حيث قد يؤذيهم ذلك.**
- **إذا ظهرت لديك أي آثار جانبية، تحدث مع طبيبك أو الصيدلي. يتضمن ذلك أي آثار جانبية محتملة غير مدرجة في هذه النشرة. انظر القسم 4.**

ماذا تحتوي هذه النشرة؟

1. **ما هو [الاسم التجاري] وفيم يستخدم؟**
2. **ما تحتاج معرفته قبل استخدام [الاسم التجاري]**
3. **كيف تستخدم [الاسم التجاري]؟**
4. **الآثار الجانبية المحتملة**
5. **كيفية تخزين [الاسم التجاري]**
6. **محتويات العبوة ومعلومات أخرى**

6.1 الخصائص الفيزيائية

(N.B Nature and contents of container (description of pack and no of units) is Optional unless packs are with special administration components)

- **The introduction should be followed by the 6 main section headings outlined as follows:**

1. ما هو [الاسم التجاري] وفيم يستخدم؟

- **يحتوي هذا القسم على محتوى المستحضر من المواد الفعالة ومجموعتها الدوائية وغرض الاستخدام.**
  - **مثال: يحتوي X على المادة الفعالة: Y. تنتمي هذه المادة الفعالة إلى المجموعة الدوائية: Z. يستخدم الدواء لـ[غرض الاستخدام].**

2. ما تحتاج معرفته قبل استخدام [الاسم التجاري]

- **يحتوي هذا القسم على معلومات ينبغي على المريض أو قارئ النشرة معرفتها قبل استخدام هذا الدواء وخلال الاستخدام.**
- **يتضمن هذا القسم عنوان فرعي "موانع الاستخدام" المذكورة في الـSmPC (section 4.3) بنفس الترتيب.**

- بالصيغة التالية:

"لا تستخدم [الاسم التجاري] في الحالات التالية:

- ..[موانع الاستخدام]..
- ..[موانع الاستخدام].."

- يتضمن هذا القسم عنوان فرعي "التحذيرات والاحتياطات" المذكورة في الـSmPC (section 4.4)، وعلى الإجراءات التي ينبغي على المريض اتباعها لتقليل الخطر المحتمل. (تشمل أي تحذيرات صادرة عن لجنة الفارماكولوجي أو اللجنة الفنية حول المواد الفعالة أو غير الفعالة أو المجموعة الدوائية للمستحضر.)
  - بالصيغة التالية:

"التحذيرات والاحتياطات

تحدث إلى طبيبك أو الصيدلي قبل استخدام [الاسم التجاري].

- ..[تحذيرات/احتياطات]..
- ..[تحذيرات/احتياطات].."

- يتضمن هذا القسم عنوان فرعي "الأطفال " يحتوي معلومات حول الاستخدام في تلك الفئات:
  - إذا كان الدواء يستخدم في الأطفال: يحتوي هذا الجزء على التحذيرات والاحتياطات المخصصة لهذه الفئة عند ذكر ذلك في section 4.4 من الـSmPC. بالصيغة التالية:

"الاطفال والمراهقون

..[التحذيرات والاحتياطات المخصصة لهذه الفئة].."

  - إذا كان الدواء لا يستخدم في الأطفال: يشار إلى ذلك بالطريقة التالية:

"الاطفال والمراهقون

لا تعطِ هذا الدواء لـ[..الفئة العمرية التي يمنع استخدام الدواء بها..]. [..سبب منع الاستخدام..]."

- يتضمن هذا القسم عنوان فرعي "الأدوية الأخرى و[الاسم التجاري]" يحتوي معلومات حول التداخلات الدوائية مع المستحضرات الأخرى المذكورة في الـSmPC (section 4.5).
  - يبدأ هذا الجزء بعبارة "أخبر طبيبك أو الصيدلي إذا كنت تستخدم أو استخدمت مؤخرًا أو قد تستخدم أي أدوية أخرى".
  - ينبغي الإشارة للمستحضرات الأخرى بإسم المجموعة الدوائية إلا في حالة حدوث التداخل مع مادة فعالة واحدة في المجموعة.
  - يشمل هذا الجزء الأدوية التي لا يجب استعمالها مع هذا الدواء والأدوية التي تتطلب بعض الاحتياطات عند استعمالها مع هذا الدواء (مثل تعديل جرعة الدواء).
  - مثال:

"الأدوية الأخرى و[الاسم التجاري]

أخبر طبيبك أو الصيدلي إذا كنت تستخدم أو استخدمت مؤخرًا أو قد تستخدم أي أدوية أخرى.

- لا تستخدم هذا الدواء مع [اسم المادة الفعالة التي لا يجب استخدامها مع هذا الدواء]، الذي يستخدم [داعي استخدام الدواء المتداخل]، [سبب منع الاستخدام]."

- ..[التداخلات الدوائية]..
- ..[التداخلات الدوائية]..

- يتضمن هذا القسم عنوان فرعي " الحمل والرضاعة والخصوبة" يحتوي معلومات حول الحمل والرضاعة والخصوبة ينبغي معرفتها قبل استخدام الدواء طبقاً للمعلومات المذكورة في الـSmPC (section 4.6).

- يتضمن هذا القسم عنوان فرعي "القيادة وتشغيل الآلات" يحتوي معلومات حول أي احتياطات ينبغي اتخاذها بخصوص القيادة وتشغيل الآلات طبقاً للمعلومات المذكورة في الـSmPC (section 4.7). ينبغي أن يشار إلى سبب النهي عن القيادة أو تشغيل الآلات، وما إذا كان ينبغي على المريض استشارة الطبيب بهذا الشأن.

3. كيف تستخدم [الاسم التجاري]؟

- يبدأ هذا القسم بعبارة " استخدم هذا الدواء تماماً كما تصف هذه النشرة أو كما يخبرك الطبيب أو الصيدلي. استشر طبيبك إذا كنت غير متأكد.".
- يحتوي هذا القسم على معلومات حول أقصى جرعة منفردة و/أو يومية و/أو كاملة.
- يحتوي هذا القسم على الجرعة الموصى بها. كما يمكن أن يحدد الوقت المناسب لاستخدام الدواء.

(على أن يتفق ذلك مع الجرعة المذكورة بال SmPC)

- يمكن أن يحتوي هذا القسم على عدة عناوين فرعية في حالة اختلاف الجرعة بناءً على دواعي الاستخدام أو الفئة المستهدفة (مثل المسنين، مرضى الكبد، مرضى الكلى).
- يتضمن هذا القسم عنوان فرعي "الأطفال " يحتوي تعليمات الاستخدام الخاصة بكل فئة عمرية بوضوح إذا كان الدواء يستخدم لفئات عمرية مختلفة بجرعة مختلفة أو طريقة استخدام مختلفة أو وتيرة استخدام مختلفة أو مدة علاج مختلفة. وإذا كانت هناك تركيزات و/أو أشكال صيدلانية أكثر ملاءمة للاستخدام في بعض أو كل الفئات العمرية من الأطفال (مثل شراب للرضع)، فيجب ذكر ذلك. مثال: "قد تكون الأشكال الأخرى من هذا الدواء مناسبة أكثر للاستخدام في الأطفال، اسأل الطبيب أو الصيدلي."

يتضمن هذا القسم عنوان فرعي " طريقة الاستخدام" يحتوي إرشادات حول طريقة الاستخدام السليمة للدواء. على سبيل المثال: "لا تبتلع" ، "لا تمضغ" ، "رج جيدًا قبل الاستخدام". من المفيد ذكر أسباب إدراج مثل هذه العبارات، على سبيل المثال "لا تكسر أو تسحق القرص. إذا قمت بذلك،

- فهناك خطر من تناول جرعة زائدة لأن هذا الدواء سيتم امتصاصه في جسمك بسرعة كبيرة " ," بالنسبة للاقراص القابلة للتقسيم يتم توضيح كيفية أخذ القرص و الجرعة"
- عندما ينطبق ذلك، يجب أن توصف تقنية فتح العبوات المقاومة للأطفال والعبوات الأخرى التي سيتم فتحها بطريقة غير معتادة.
- عندما ينطبق ذلك، يجب توضيح ما إذا كان يجب تناول الدواء مع الطعام ، أثناء / قبل الوجبات ، أو تحديد ما إذا كان الطعام / الوجبات ليس لها تأثير، وما إلى ذلك.
- ينبغي تحديد مدة العلاج (بناءً على SmPC section 4.7) عندما يكون ذلك مناسباً، ينبغي أن تضاف بيانات حول:
  - المدة المعتادة للعلاج.
  - المدة القصوى للعلاج.
  - الفترات بدون علاج.

- الحالات التي يجب فيها حصر مدة العلاج.

- يتضمن هذا القسم عنوان فرعي "إذا نسيت أن تأخذ (الاسم التجاري)" يحتوي تعليمات توضح للمرضى ما يجب عليهم فعله عند استخدام الدواء بشكل غير المنتظم، على سبيل المثال: إذا كانت المعلومات متوفرة ، فحاول تضمين معلومات عن الفاصل الزمني الأقصى الذي يمكن خلاله أخذ الجرعة الفائتة فيه وفقًا لقسم SmPC 4.2.
  - مثال: "لا تتناول جرعة مضاعفة لتعويض الجرعة المنسية."

- يتضمن هذا القسم عنوان فرعي "إذا توقفت عن أخذ (الاسم التجاري)" يحتوي على أعراض الانسحاب (إن وُجِدَت) وكيفية تقليلها وفقًا لقسم SmPC 4.2 و/أو ايضاح العواقب المحتملة عند وقف العلاج قبل الانتهاء من خطة العلاج والحاجة إلى سؤال الطبيب المعالج أو الصيدلي أو الممرض قبل ذلك (عند الحاجة).

- ينتهي هذا القسم بعبارة: "إذا كان لديك أي أسئلة أخرى حول استخدام هذا الدواء، اسأل طبيبك أو الصيدلي أو الممرض."

4. الآثار الجانبية المحتملة

- يبدأ هذا القسم بعبارة: "مثل جميع الأدوية ، يمكن أن يسبب هذا الدواء أعراضاً جانبية على الرغم من عدم حدوثها للجميع".

- يتم البدء بأخطر الآثار الجانبية التي يجب إدراجها بشكل بارز أولاً مع تعليمات واضحة للمرضى حول الإجراء الذي يجب اتخاذه. (على سبيل المثال ، التوقف عن تناول الدواء و / أو طلب المشورة الطبية العاجلة. قد يكون استخدام الكلمات "على الفور" أو "فورًا" مفيدًا في هذا السياق).

- المشورة الطبية العاجلة. قد يكون استخدام الكلمات "على الفور" أو "فورًا" مفيدًا في هذا السياق).

- ثم يتم إدراج جميع الآثار الجانبية الأخرى مرتبة حسب التكرارية وبدءًا بأكثرها شيوعًا (دون تكرار أخطرها المذكورة أعلاه).

- في كل قسم مذكور أعلاه، يجب ترتيب الآثار الجانبية حسب معدل تكرارها. يوصى باستخدام مصطلحات التكرارية التالي:
  - شائعة جدا: قد تحدث لدى أكثر من 1 من كل 10 أشخاص
  - شائعة: قد تحدث لدى ما يصل إلى 1 من كل 10 أشخاص
  - غير شائعة: قد تحدث لدى ما يصل إلى 1 من كل 100 شخص
  - نادرة: قد تحدث لدى ما يصل إلى 1 من كل 1000 شخص
  - نادرة جدا: قد تحدث لدى ما يصل إلى 1 من بين 10000 شخص
  - غير معروفة: لا يمكن تقدير معدل تكرار حدوثها من البيانات المتاحة

- عندما يكون معدل التكرار غير معروف يمكن تقسيم الأعراض على حسب أجزاء الجسم على سبيل المثال الجلد والمعدة والأمعاء، مما يسهل الاستيعاب.

- **إذا كان ذلك منطبقاً (تماشـيًا مع المعلومات الواردة في القسـم 4.8 من SmPC)، ينبغي وجود قسـم فرعي يوضـح أي اختلافات ذات أهمية إكلينيكية في الآثار الجانبية بين أي فئة من الأطفال مقارنةً بفئات أخرى أو بالبالغين.**

- **ينتهي هذا القسم كالتالي:**

"الإبلاغ عن الآثار الجانبية

إذا ظهرت لديك أي آثار جانبية، تحدث إلى الطبيب أو الصيدلي أو الممرض. يشمل ذلك أي آثار جانبية محتملة غير مذكورة في هذه النشرة. يمكنك أيضًا الإبلاغ عن الآثار الجانبية لمركز اليقظة الصيدلية المصري مباشرةً عبر الخط الساخن 15301 أو عن طريق إرسال بريد إلكتروني إلى: pv.followup@edaegypt.gov.eg

يمكنك المساعدة في توفير المزيد من المعلومات حول سلامة هذا الدواء من خلال الإبلاغ عن الآثار الجانبية."

5. كيفية تخزين [الاسم التجاري]

- **يتضمن العبارة التالية: "يُحفَظ الدواء بعيدًا عن أنظار ومتناول أيدي الأطفال."**

تاريخ الصلاحية:

- **يتضمن تاريخ انتهاء الصلاحية (optional) وشروط التخزين طبقاً لموافقة الثبات أو اخطار التسجيل.**

ويمكن كتابتها " انظر العبوة الخارجية (فيما عدا الحقن و المعلق و القطرات)"

6. محتويات العبوة ومعلومات أخرى

- **يتضمن بيان بجميع المكونات الفعالة وغير الفعالة.**

- **يجب ذكر اسم وكم المواد الفعالة أما المواد غير الفعالة فيكتفى بذكر اسمها. ويكون ذلك طبقاً لموافقة بيان التركيب. مثال:**
  - **"المادة (المواد) الفعالة هي X**

يحتوي كل [شكل صيدلي أو حجم معين] على ..... مجم من X".

المواد غير الفعالة هي A,B,C..."

- **الخصائص الفيزيائية: يتضمن هذا القسم الخصائص الفيزيائية التي تصف شكل المنتج (اللون و وما إلى ذلك) في فقرة منفصلة ، وفقًا لموافقة الثبات/إخطار التسجيل.**

- **يتضـمن عنوان فرعي "حالات التعارض وتعليمات الاسـتخدام والتعامل" حول أي تعارضـات مع الدواء وعلى فترة الصلاحية خلال الاستعمال/بعد الفتح طبقاً لموافقة الثبات.**

- **يتضـــمن عنوان فرعي " محتوى العبوة "حول العبوة/العبوات المتحوية على الدواء طبقاً لموافقة العبوة أو اخطار التسجيل.**

- **تنتهي النشـرة باسـم حامل الإخطار كما هو مذكور في إخطار التسـجيل أو موافقة صـندوق المثائل أو موافقة الثبات بحسب حالة المستحضر.**

7. Annexes

Annex (1): Sources of leaflet references and list of reference countries

Annex (2): Essential links

Annex (3): Declaration letters templates

Annex (4): SmPC template (as guidance for non-reference products)

Annex (1): Sources of leaflet references and list of reference countries

One of the following sources can be used as reference for the leaflet:

1. **Leaflet of Innovator Product in the Egyptian Market:**

- **Generic Products shall refer to valid leaflets of innovator products in the Egyptian market (According to Technical Committee Decision 7/3/ 2013)**

١- بالنسبة للمستحضرات المستوردة: يتم الموافقة على النشرة كما هي متداولة ببلد المنشأ.
٢- بالنسبة للمستحضرات المحلية: يتم إعداد النشرة مع الاسترشاد بنشرة المستحضر الـ Innovator المتداول بالسوق المصري ، وبالنسبة للمستحضرات المحلية التي ليس لها مستحضرات مرجعية متداولة بالسوق المصري يتم إعداد النشرة استرشاداً بالنشرة المرجعية المنشورة على أحد المواقع العلمية أو بالمراجع العلمية.

وفي جميع الحالات يجب إرفاق نشرة عربية PIL موجهة للمريض.

قررت لجنة الفنية بجلستها فى 2020/12/3 و جاء قرار اللجنة كالتالى:

تعديل قرار اللجنة الفنية لمراقبة الأدوية بجلستها في 2013/03/07 ليصبح: "بالنسبة للمستحضرات المستوردة: السماح باستخدام نشرة معتمدة من بلد مرجعي بشرط أن يكون مسجل ومتداول به المستحضر مع الالتزام بتطبيق القواعد والقرارت الخاصة بالتحذيرات ".

- An Innovator Product is the one which was first authorized for marketing as a patent drug.
- If an innovator in the Egyptian market is not available, or a valid updated innovator leaflet is not available, refer to;

2. **Template:**

- Companies are permitted to request a template of previously approved leaflet of another generic product from the leaflet s administration.
- If the previously mentioned options are not available, refer to;

3. **Leaflet from one of the Reference Countries regulatory authority:**

قررت اللجنة الفنية لمراقبة الأدوية بجلستها في 2021/9/16 بناء على ما تم عرضه،

الموافقة على اعتماد معايير اختيار الدول المرجعية تماشياً مع المعايير الخاصة بمنظمة الصحة العالمية مع الاحتفاظ وعدم التغيير أو الإضافة لقائمة الدول السابق اعتمادها من قبل اللجنة الفنية (22 دولة مرجعية) فى 1995/11/28، 1998/7/28 ، و 2009/12/31 وهي كالآتي: (استراليا – النمسا – بلجيكا – كندا – الدانمارك - ألمانيا الإتحادية – فنلندا – فرنسا – ايسلندا – إيرلندا – لوكسمبورج – هولندا - نيوزيلندا – النرويج – السويد – سويسرا – المملكة المتحدة – الولايات المتحدة- اليابان -ايطاليا - البرتغال – اسبانيا).

Reference	Link
USA (FDA)	**https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm**
European Medicines Agency (EMA)	**https://www.ema.europa.eu/en/medicines/ema_group_types/ema_medicine**
UK (MHRA)	**For MHRA website: https://products.mhra.gov.uk/** **For EMC website: https://www.medicines.org.uk/emc/**
Canada (Health canada)	**https://health-products.canada.ca/dpd-bdpp/index-eng.jsp**
Australia (TGA)	**https://www.ebs.tga.gov.au/**
Ireland (HPRA)	**http://www.hpra.ie/homepage/medicines**
New Zealand	**Search engine for products:** **https://www.medsafe.govt.nz/regulatory/DbSearch.asp** **Search engine for leaflets:** **https://www.medsafe.govt.nz/Medicines/infoSearch.asp**
Japan (PMDA)	**https://www.info.pmda.go.jp/psearch/html/menu_tenpu_base.html** **Search engine for prescription drugs:** **https://www.pmda.go.jp/PmdaSearch/iyakuSearch/** **Search engine for OTC drugs:** **https://www.pmda.go.jp/PmdaSearch/otcSearch/**
France	**http://agence-prd.ansm.sante.fr/php/ecodex/index.php**
Belgium	**Database of SmPCs and PILs:** **https://bijsluiters.fagg-afmps.be/?localeValue=en** **Database of authorized medicinal products for human use:** **https://www.afmps.be/fr/items/banque_donnees**
Germany	**https://www.pharmnet-bund.de/dynamic/en/drug-information-system/index.html**
Finland	**https://www.fimea.fi/web/en/databases_and_registeries/fimeaweb**
Norway	**https://www.legemiddelsok.no/**
Switzerland	**https://www.swissmedic.ch/swissmedic/de/home/services/arzneimittelinformationen.html or https://www.swissmedicinfo.ch/**
Austria	**https://aspregister.basg.gv.at/aspregister/faces/aspregister.jspx** ***http://www.ages.at/***
Netherlands	**https://www.geneesmiddeleninformatiebank.nl/ords/f?p=111:1:0::NO:RP,1:P0_DOMAIN,P0_LANG:H,NL**
Portugal	**https://extranet.infarmed.pt/INFOMED-fo/**

Sweden	**https://www.lakemedelsverket.se/sv/sok-lakemedelsfakta**
Iceland	**https://www.serlyfjaskra.is/**
Spain	**https://cima.aemps.es/cima/publico/home.html**
Italy	**https://farmaci.agenziafarmaco.gov.it/bancadatifarmaci/cerca-per-principio-attivo**
Denmark	**https://laegemiddelstyrelsen.dk/en/sideeffects/find-medicines/**
Luxembourg	**https://sante.public.lu/fr/support/recherche/index.php?q=Liste+des+m%C3%A9dicaments+%C3%A0+usage+humain**

قررت اللجنة الفنية بجلستها فى 2202/08/25 :

1- الموافقة علي المقترح المقدم من ادارة النشرات بتعديل قرار اللجنة الفنية في 2013/3/7 ليصبح :

يتم إعداد النشرة الخاصة بالمستحضرات المتداولة محلياً إسترشادا بالنشرة المرجعية المنشورة على أحد المواقع الخاصة بالهيئات الصحية المختلفة أو إسترشاداً بنشرة المستحضر الأصيل الـ(innovator).

2- بالنسبة للمحاليل في حالة طلب الشركة عدم عمل نشرة فانه يتم وضع التحذيرات التي يتم تقريرها من قبل لجنة الفارماكولوجي علي الـــ outer label بدون نشرة وبالنسبة للصقات المستوردة والمحلية الـــ OTC يتم وضع جميع التحذيرات علي الـــ outer label بدون نشرة.

For non-reference products the following options may be referred to or any accredited updated references in addition to data (If any) from previous reference countries:

- Martindale
- British National Formulary (BNF)
- Physician Desk Reference

Annex (2): Essential links:

- Pharmacology committee warnings (contained in the submission form, however the link is available throughout all days not only during submission time)
  https://forms.gle/dx5c8LJWbv1P8fw27

- Technical committee warnings and inactive ingredients warnings
  https://bit.ly/3liFviC

- Leaflet Submission link (for New applications)
  https://forms.gle/dx5c8LJWbv1P8fw27

- Leaflet Corrections link (for amendments required to be fulfilled for previously submitted application)
  https://forms.gle/ENHLxpYXacHCKxwP7

- Link to check leaflet status
  https://docs.google.com/spreadsheets/d/1SEX2GJuFXkIwd_3EZpc1N6gxuq9BK0ixBhd2As0_FIc/edit?usp=sharing

- Link to leaflet inquiry form
  https://bit.ly/2ZKoK8i

- List of additional monitoring
  https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/medicines-under-additional-monitoring/list-medicines-under-additional-monitoring

Annex (3): Declaration letter templates

A. Declaration letter template regarding reference and translation

• We (License Holder), declare that the attached leaflet of (Trade name) and concentration, code (…), revision date (…), version date is the being marketed and registered in the country of origin (…)

• And for non-English leaflets, a Legalized letter from the head office abroad stating that the scientific office is responsible for the translation (Attached 2 languages) and the leaflet is translated medical translation through their scientific office.

A declaration from the scientific office: We commit that the medical leaflet is translated according to authorized medical translation on our responsibility in accordance with the translation attached. (Signature & Stamp)

B. Declaration letter template regarding the authenticity of submitted documents

- We…….. Declare that the submitted documents are authentic, correct and the versions are the latest issued by EDA.

Annex (4): SmPC template (as guidance for non-reference products)

1. **Name of the medicinal product**
2. **Qualitative and quantitative composition**
3. **Pharmaceutical form**
4. **Clinical particulars**
   - **3.1 Therapeutic indications**
   - **3.2 Posology and method of administration**
   - **3.3 Contraindications**
   - **3.4 Special warnings and precautions for use**
   - **3.5 Interaction with other medicinal products and other forms of interaction**
   - **3.6 Fertility, pregnancy and lactation**
   - **3.7 Effects on ability to drive and use machines**
   - **3.8 Undesirable effects**
   - **3.9 Overdose**
5. **Pharmacological properties**
   - **5.1 Pharmacodynamic properties**
   - **5.2 Pharmacokinetic properties**
   - **5.3 Preclinical safety data (optional for innovator products only)**
6. **Pharmaceutical particulars**
   - **6.1 List of excipients**
   - **6.2 Incompatibilities**
   - **6.3 Shelf life (shelf life addition is Optional except in case of parenteral/suspension/eye drops)**
   - **6.4 Special precautions for storage**
   - **6.5 Nature and contents of container (Optional unless packs with special administration components)**
   - **6.6 Special precautions for disposal and other handling**
7. **License holder**

Reference:
https://www.ema.europa.eu/en/documents/template-form/mutual-recognition-decentralised-referral-product-information-template-version-42_en.docx