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

Guideline

GUIDELINE ON
Medical Leaflets of
Medicinal Products for Human Use

Year 2022

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1. Scope

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

2. Legal Basis

The legal basis for requiring approval of the package insert as a fundamental part of the authorization process for all medicinal products is the law No. 127 of 1955 regarding the practice of the profession of pharmacy and ministerial 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 inserts 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 insert 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 technical committee decision 26/3/2009, check it in section 5 Requirement for submission. Both documents must be completed and submitted as an application to EDA before marketing is authorized.

The company is committed to submit safety updates during the validity of the registration license.

An update is triggered based on a safety update and MAH request, for example in case there's an approved variation the affects the scientific content of the insert.

Note: A transition period of 6 months until activation of the updated version is allowed as per pharmacology committee decision in 24-10-2013.

The primary purpose of medicinal products package inserts 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 inserts 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 inserts for medicinal products intended for human use through recommendations on the content of the package inserts 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. They are kept updated throughout the lifecycle of a medicine as new data emerge.
- **Patient Information Leaflet (PIL):** contains information for safe and effective use of medicine directed to the patients/public/end-users.
- **Electronic Product Information (ePI):** product information for authorized medicines (the summary of product characteristics and patient information leaflet) in a -structured format adapted for electronic handling and allows dissemination via the web, e-platforms and print.
- **Submitted product:** for the purposes of this guideline, this term is used to refer to the product whose insert is submitted to the inserts department for evaluation and approval.
- **Proposed insert:** for the purposes of this guideline, this term is used to refer to the insert submitted to the inserts department for evaluation and approval.
- **Reference insert:** an insert approved by a reference country's drug regulatory authority and is used as the source of information for the proposed insert. A reference insert has to match the proposed insert in active ingredient (and salt if it is unavailable use equivalent) strength, dosage form and route of administration.
- **Non-reference insert:** is either an insert not approved by any reference country's drug regulatory authority or an insert 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 insert is collected from scientific data on authorized websites.
- **Replacement Insert:** An approved insert copy that is requested by the company when the originally approved insert is lost/accidentally damaged and is issued in place of the missing insert.
- **Grace period:** is a period for implementation of updated leaflet with accordance to committee decisions.
- **Template:** an approved model for specific generic to be used as a reference.

4.1 General notes

- The types of requests submitted to inserts administration are:
  - new submission
  - insert update
  - warning addition
  - appeal
  - re appeal
  - replacement insert
  - variation
- Receipt is to be delivered as hard copy upon receiving the approved leaflet
- A stamped and signed commitment by the registration manager, endorsing that the submitted documents are authentic, correct, the latest versions issued by EDA.
- Cover letter from the company to Inserts Administration endorsing product detailed information and the reason for submission.
- An Arabic insert is not required for the following products (according to technical committee decision 26/3/2009):
  - Intravenous Infusions
  - Drugs for Malignant diseases & immunosuppression
  - General Anesthetics
  - Human Immunodeficiency Virus Drugs
  - Drugs intended for hospital use only.
  - Contrast media except iodinated contrast media agents

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

4.2 Required documents based on product registration status

5.2.1 For Under– registration Products

- Receipt
- Cover letter from the company to Inserts Administration
- Proposed insert (SmPC English & PIL Arabic).

  *For cases of exceptions of Arabic insert, see above.
- Reference insert for both (SmPC & PIL) – most updated version
- Accelerated stability(excluded for 820)and to be submitted immediately after releasing from competent department.
- Approved composition stating Active ingredients and Inactive ingredients (Excluded for 820) and to be submitted immediately after releasing from competent department
- Naming approval .
- Box Approval
- PV approval (requested for 425, 645& excluded for 820,export only)
- Pricing approval (Excluded for 820,Tender & Export)

5.2.2 For Tentative License products

- If the insert approval date is within 5 years and no updates /&warnings are required, it is permissible NOT to submit to insert administration, but if it exceeds 5 years the following should be submitted.
- Receipt
- Cover letter from the company to Inserts Administration
  - Proposed insert (SmPC English & PIL Arabic)

    *For cases of exceptions of Arabic insert, see above.
  - Reference insert for both (SmPC & PIL) – most updated version
  - Accelerated stability
  - Approved composition stating Active ingredients and Inactive ingredients
  - Naming or Layout approval (in case Arabic name is not written in the registration license)
  - Last approved insert
  - Tentative License
  - License Extension (Optional)
  - Transmission letter

5.2.3 For Registered Products

- Receipt
- Cover letter from the company to Inserts Administration
- Proposed insert (SmPC English & PIL Arabic)
  *For cases of exceptions of Arabic insert, see above.
- Reference insert or both (SmPC & PIL) – most updated version
- Approved composition from authorized department stating Active ingredients and Inactive ingredients
- Naming or Layout approval (in case Arabic name is not written in the registration license)
- Last approved insert
- Registration License

5.2.4 For Products under Re-registration

- If the insert approval date is within 5 years and no updates /&warnings are required, it is permissible NOT to submit to insert administration, but if it exceeds 5 years the following should be submitted
- Receipt
- Cover letter from the company to Inserts Administration
- Proposed insert (SmPC English & PIL Arabic)
  *For cases of exceptions of Arabic insert, see above.
- Reference insert for both (SmPC & PIL) – most updated version
- 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.
- approved composition (Stability/NODCAR)
- Naming or Layout approval (in case Arabic name is not written in the registration license)
- Last approved insert
- Registration License
- Re-registration action letter
- Pv approval required for products following 150 decision.

4.3 Required Add-on documents

a) **When a non-English reference is used:** Accredited medical translation for the reference product insert is required. Both the non-English insert

(original insert) and English insert (translated version) must be attached.

b) **In case of Scoring for dose:** Commitment of either 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.
- Non-functional scoring: matching reference is used

c) In case of imported and innovator Products:

- Insert attached to legalized Certificate of Pharmaceutical Product (CPP) could be used as the reference (Declared in cover letter) (optional if the CPP-attached insert is the most updated).
- If insert is PIL only: A Legalized letter from the country of origin stamped from 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 a 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 EDA website.
- For non-English inserts: 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 insert 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 SmPC for imported products shall be displayed on EDA website.

d) In case of non-reference Products:

- The Cover letter should clarify that the product is non-reference and the available following committee approvals should be attached
  - Non reference Committee approval
  - Pharmacology committee approval (if applicable)
  - Scientific committee approval
- The required committee decisions shall be according to the product ministerial decree:

- 296/2009, 425/2015 Ministerial decree under registration products
  - Scientific committee approval
  - Pharmacology committee approval (if applicable)
- 425/2015 Ministerial decree re- registration products
  - Non reference Committee approval
  - Pharmacology committee approval (if applicable).
- 150/2022 Ministerial decree re- registration products
  - Scientific committee approval

Notes: In case of products registered according to minister decree 370; only one committee approval is required

- Clarify the detailed source of scientific data (References, Scientific papers, Books: Martindale, BNF) for each information inside the proposed insert 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, English insert will be according to SmPC, Arabic Insert 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

4.4 Special Requirements based on the type of request

5.4.1 Update

- Cover letter stating reason of update
- Receipt
- The Last approved insert should be submitted as soft PDF copy.
- Track changes between proposed updated insert and previously approved

Note (the original stamped hard copy issued by EDA should be delivered to insert administration before receiving the approved updated leaflet).

5.4.2 Replacement Insert

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

5.4.3 Variation

- Variation approval (and its requirements if applicable)
- Last approved insert
- Receipt (for valid insert, see below cases require submission

*Not all variations will trigger an insert submission. Only variations that affect the scientific content of the insert should be submitted as follows:

Submit	**Do not Submit**
Variations affecting the scientific content of the insert e.g.:	**Variations do not affect the scientific content of the insert e.g.:**
1- Dosage form 2- Equivalence 3- Inactive ingredients (requires warning addition) 4- Naming 5- Tablet scoring 6- Route of administration 7- Storage conditions (In use stability)	1- Inactive ingredients (with no warnings) 2- Shelf life 3- Pack (that do not affect storage conditions). 4-Manufacturer and license holder **Apply directly without submission**

5.4.4 Warning Addition

- Warning to be added highlighted inside the insert
- Last approved insert

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 of the appeal.

4.5 Format of files for submission

- SmPC & PIL must be in one file with the same format & page orientation, in word format. (Not a PDF file).
  Cover letter must be in word format 2 copies (word and 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 pdfs can be collated together as a zip file.

- If 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 insert 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 English language.**
Other format	**The use of column format of the text version of information in the insert submitted for assessment should be avoided whenever possible.**

For reference products stick to the reference 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.

4.6 Submission forms

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

5. Requirements for content layout

5.1 General notes

A. The main section headings of the insert 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 ability to drive and use machines
   - 4.8 Undesirable effects
   - 4.9 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

B. The head of the insert

- At the head of the insert, the following should be provided:
  - Full product identification (trade name, strength, and dosage form)
  - Active ingredient(s), equivalence.
- Additionally, the insert for medicinal products subject to Black box addition according to U.S Food and Drug Administration should include Black box with accordance to the submitted reference

- Additionally, the head of the insert 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 للEuropean 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 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 website of 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 insert is in a language other than English.

C. Trade name

- The trade name of the submitted product used in the insert 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 insert 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 insert) for English name.

D. Strength and dosage form

- The strength and dosage form of the submitted product used in the insert 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 insert text should be based on the approved composition attached to the stability approval, registration license (the most updated) or The Central Administration of Control (previously known as NODCAR).

F. Physical characters

- The physical characters of the submitted product used in the insert 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 insert 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 insert 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 insert 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 insert 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), pharmacotherapeutic class of the submitted product must be included in the proposed insert in the relevant section(s). (See annex 2 for links to warnings).
- 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 insert.
  - 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: 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 there is no authorized translation, good quality of translation to Arabic language is required.

- Some people may have poor reading skills, and some may have poor health literacy. 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 spelled out in full. Similarly, scientific symbols (e.g. > or <) are not well understood and should not be used.

- Medical terms should be translated into language which 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 insert in order to achieve a readable text.

5.2 Considerations for products with a reference insert

- **For Imported products:** the SmPC shall be displayed on 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 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 reference country**.

- **In case of a combined proposed insert of multiple product concentrations:** a combined reference product insert is a must or multiple inserts but with the same trade name and revision date and endorsing same content and indication.

- **In case of parenteral:**
  - Diluents and solvents and shelf life after & before reconstitution and dilution should be according to the stability approval.
  - In case of reconstitution and dilution: the solvent(s) and diluents and their volume for the submitted product used in the insert text should be based on the stability approval

- **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: requirements for submission)

- The information content of the proposed insert must be **consistent with the reference insert**.

- When mentioning trade name, strength, dosage form, composition and physical characters throughout the proposed insert 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 insert, it should not be omitted from the proposed insert.

- The trade name from the reference insert 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.

5.3 Considerations for products without a reference insert

- Products without a reference insert should adhere to the following content layout." This includes any submitted product without a matching reference product in addition to any submitted product that have a matching reference but for which no insert 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 insert should only be included if these are relevant for the particular product. For example, if there is no information in relation to excipients of known effect this section may be omitted from the inserts.

- 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 a guidance and is not obligatory and for reference products the reference is their guidance)

- As previously stated, head of the insert 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 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: requirements for submission)

- 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 hour) 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 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 'paediatric population' should be included and the information given should cover all subsets of the paediatric 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 paediatric 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(s) *(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, across-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), 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). 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 which 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. Recommendation 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, 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 which 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, 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 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 on 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 Pharmacodynamic 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, 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 which 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 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 insert.

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 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 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 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 are 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.

Patient Information Leaflet (PIL):

- As previously stated, head of the insert 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).

- 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 (تماشيًا مع المعلومات الواردة في القسم 4.8 من SmPC)، ينبغي وجود قسم فرعي يوضح 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) و شروط التخزين طبقاً لموافقة الثبات أو اخطار التسجيل.

و يمكن كتابتها " إنظر 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.

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

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

- تنتهي النشرة باسم **حامل الإخطار** كما هو مذكور في إخطار التسجيل أو موافقة صندوق المثائل أو موافقة الثبات بحسب حالة المستحضر.

Annexes

Annex (1): Sources of references

Annex (2): Essential links

Annex (3): Declaration letters templates

Annex (4): SmPC template

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

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

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

- Generic Products shall refer to valid inserts 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 في 2020/12/3 و جاء قرار اللجنة كالتالي:

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 والقرارات الخاصة بالتحذيرات ".

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

2. **Template:**

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

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

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 (Healthcanada)	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 inserts: 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 2202/8/25 :

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 الـ outer label بدون نشرة وبالنسبة للصقات المستوردة والمحلية الـ OTC يتم وضع جميع التحذيرات علي الـ outer label بدون نشرة.

4. **For non-reference products the following options may be referred to <u>or any accredited updated references in addition to data (If any) from previous reference countries:</u>**

- 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

- **Insert Submission link** (for New applications)

  https://forms.gle/dx5c8LJWbv1P8fw27

- **Insert Corrections link** (for amendments required to be fulfilled for previously submitted application)

  https://forms.gle/ENHLxpYXacHCKxwP7

- **Link to check insert status**

  https://docs.google.com/spreadsheets/d/1SEX2GJuFXkIwd_3EZpc1N6gxuq9BK0ixBhd2As0_FIc/edit?usp=sharing

- **Link to insert 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 is marketed and registered in the country of origin (…)

• **And for non-English inserts,** Legalized letter from the head office abroad stating that the scientific office is responsible for the translation (Attached 2 languages) and the insert 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 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 a guidance for non-reference products)

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 ability to drive and use machines
   - 4.8 Undesirable effects
   - 4.9 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