Egyptian Drug Authority

C A for Pharmaceutical Care

G A for Pharmaceutical References and Inserts

MEDICAL INSERTS

Submission Guidance

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Preface

Emerging from the keenness of the General Administration of Pharmaceutical References and inserts under the supervision of Dr.Rehab Mehriz for continuous development and fruitful communication with Market Authorization Holders.

Medical Inserts department under the supervision of Dr.Heba Hamdy has the honor to present this submission guidance for medical Inserts endorsing clear and detailed requirements, so as to be a guide for Market authorization holders to ensure optimum submission for inserts.

Special thanks to **Dr.Tamer Essam**, Head of the Egyptian Drug authority, **Dr. Shereen AbdelGAwad** Head of the General Administration of Pharmaceutical Care for continuous support for this document to come to light.

Medical Inserts Submission Process

Submission Link

Wednesday & **Thursday**
(9 am to 1pm)

Initial Assessment (3-5 days)

File Accepted?

No

Mail to company

Correction Link

Fulfilling Requirements

Yes

Main Assessment

Correction

Submission Items

- ✓ **Submission form**
- ✓ **Requirements (general &specific) according to registration status & Type of request**

File Approved?

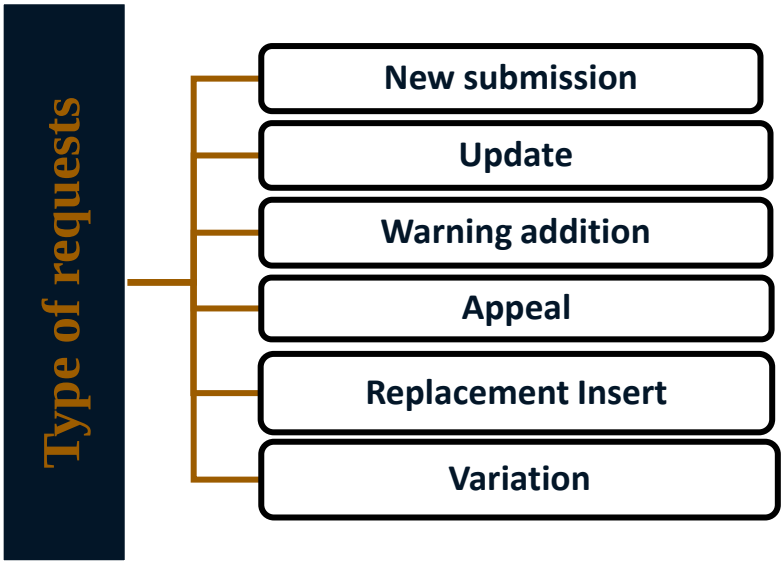
No

Yes

Approved Insert

N.B: You can find status of insert in leaflet status link

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



Requests according to type of registration

Under-Registration	Registered	Tentative to Final	Re-registration
• Under registration • Update • Warning	• Update • Warning • Variation	• Tentative to final • Update • Warning • Variation	• Re-registration • Update • Warning • Variation

General Requirements

For Under– registration Products

- ✓ Cover letter from the company to Inserts department
- ✓ Proposed insert (SPC English & PIL Arabic)
- ✓ Reference for both (SPC & PIL)
- ✓ Action letter
- ✓ Naming or Layout approval (optional for Export & Tender)
- ✓ PV approval (requested for 425, 645 & exclude for export only)
- ✓ Accelerated stability
- ✓ Approved composition stating Active ingredients and Inactive ingredients (Exclude 820)
- ✓ Pricing approval (Exclude 820, Tender & Export)

For Tentative License products

- ✓ Cover letter from the company to Insert Administration.
- ✓ Proposed insert (SPC English & PIL Arabic)
- ✓ Reference for both (SPC & PIL)
- ✓ Tentative License
- ✓ Approved composition stating Active ingredients and Inactive ingredients
- ✓ License Extension (Optional)
- ✓ Naming or Layout approval (in case Arabic name is not written in the registration license)
- ✓ Accelerated stability
- ✓ Last approved insert
- ✓ Transmission letter

General Requirements

For Registered Products

- ✓ Cover letter from the company to Inserts department
- ✓ Proposed insert (SPC English & PIL Arabic)
- ✓ Reference for both (SPC & PIL)
- ✓ Registration License
- ✓ 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

For Products in Re-registration

- ✓ Cover letter from the company to Inserts department
- ✓ Proposed insert (SPC English & PIL Arabic)
- ✓ Reference for both (SPC & PIL)
- ✓ Registration License
- ✓ Re-registration action letter
- ✓ Last approved insert
- ✓ Long Term stability
- ✓ approved composition (Stability/NODCAR)
- ✓ Naming or Layout approval (in case Arabic name is not written in the registration license)

Extra Requirements

For Imported and Innovator Products

- ✓ Insert attached to legalized CPP could be used as the reference (Declared in cover letter) (optional if it 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.

And for non-English inserts,

- ✓ A legalized Declaration Letter from License Holder commit that the leaflet is translated according to authorized medical translation on their responsibility in accordance with the translation attached. (Signature & Stamp)

Or

- ✓ Legalized letter from the head office stating that the scientific office is responsible for the translation and the insert is translated 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.

A declaration letter from the scientific office declares that the letter is to be legalized in 6 month

For Non-reference Products

- ✓ Submit cover letter clarifying that the product is non-reference attaching two of the following (Except 370 only one committee approval)
- ✓ Non reference Committee approval
- ✓ Pharmacology committee approval (if applicable)
- ✓ Scientific committee approval
- ✓ Clarify how the scientific data is collected from
- ✓ (References/ Scientific papers/ Books: Martindale/BNF)
- ✓ English SPC to be translated into Arabic (to be approved by the Pharmacology committee)

Extra Requirements according to the type of request:

Update

- Cover letter stating reason of update
- Receipt (200LE)
- Track changes
- Last approved insert

Variation

- Variation approval
- Last approved insert
- Receipt (200LE) (for valid insert, see below cases require submission

Replacement Insert

- Cover letter
- Copy of the approved insert
- Receipt (500LE)

Warning Addition

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

Appeal

- Cover letter
- Receipt (200LE)
- Track changes / comparison table (optional according to the reason of appeal)

Variation (any change that will reflect in the insert)

Submit

Variations affecting 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

Don't Submit

Variations do not affect the scientific content of the insert e.g.:

1- Inactive ingredients (with no warnings)
2- Shelf life
3- Pack
4- Manufacturer

Apply directly without submission

Assessment of the submitted file

First, you should identify:

- ✓ Type of request
- ✓ Type of registration
- ✓ Requirements according to each type

Maximum Number of inserts per week

- Update Inserts
- Correction Inserts
- Under Reg/ Re-Reg/ Warning addition inserts

Inserts Specifications

1. One Word File (SmPC & PIL) - **Not Pdf file** - in the same format & Orientation.
2. Contains all warnings highlighted (if found any, regarding active & inactive ingredient) and correctly applied in insert in oriented parts.
(Pharmacology committee warnings & Technical committee)
3. Correct Naming of the product as in registration license
(English & Arabic) and in case of under registration products as in Naming approval
4. Dosage form of the product is specified as in stability approval.
5. Active ingredient (s) with its (their) quantity (ies) per unit dose is (are) specified as in the stability approval
6. Good Quality of translation of Arabic insert in case there is no authorized translation

All products have English & Arabic insert unless Arabic insert is excluded:

Arabic Leaflets are not required in the following cases: (according to technical committee 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

SmPC and PIL Specifications

Reference Products

- ✓ Most updated version of the proposed reference
- ✓ Authorized /marketed
- ✓ Download Insert Pdf / direct link to the reference
- ✓ Reference must be equivalent to the product (Same generic – Strength – Dosage form – equivalence and salt)

- ❑ **In case of multiple concentrations in a combined proposed insert:** a combined reference product is a must or multiple ones but the same trade name with same revision date.
- ❑ **In case of parenteral:** diluents and Shelf life after & before reconstitution and dilution in the reference should be similar to that stated in stability approval
- ❑ **In case of Scoring for dose:** Commitment of either that scoring is Functional or non functional should be submitted.
  - **Functional scoring:** Reference is for scored tablet product, Subdivision Test
  - **Non functional scoring:** Reference is for plain tablet product
- ❑ **In case of imported products:**
  - Same requirements as in imported products slide no.7

Non-Reference Products

Assess committee decision according to product ministerial decree

- 296/2009, 425/2015 Ministerial decree under registration products

Scientific committee approval
Pharmacology committee approval (when applicable)

- 425/2015 Ministerial decree re- registration products

Non reference Committee approval
Pharmacology committee approval (when applicable)

- How the scientific data is collected from?

(References/ Scientific papers/ Books: Martindale /BNF)

Attachments

- ✓ Cover letter is a must in word format.
- ✓ Separate pdf files or in a zip file ,each approval paper should be submitted alone not to be combined in one pdf file.
- ✓ Titles must be clear to each file.
- ✓ Registration approvals according to requirements.
- ✓ **In case of translation of Non-English inserts:**

Accredited medical translation for the reference product insert (attached 2 languages: English and Non-English)

- ✓ **In Case of imported product:** see previous requirements of Imported and Innovator Products.

Tips for optimum Appeal

- Appeal request in Word format endorsing the detailed reason for submitting appeal.
- Attach all documents and requirements related to the cause of appeal, such in case of dosing another insert other than that approved by the inserts administration for special situations. For example:
    - Stating the number of insert copies requested to be applied or a period of its application (if available).
    - A complete comparison table in Word format to compare between current and previous insert if available.

Warnings and calculations

- Check Pharmacology committee warnings and Technical committee warnings for active and inactive ingredients

You can find Pharmacology committee warnings via the following link (you can find in submission link):

https://forms.gle/dx5c8LJWbv1P8fw27

Note for some inactive ingredients warnings :

- If Sodium is present: sodium content calculation per dose is submitted
- If Sorbitol is present: calculate content per day, if ≥ 10 g/day highlight the warning
- If Methyl Paraben is present: calculation is submitted per kg/ day for child and/ or adult
- If Propyl Paraben is present: calculation is submitted per kg/ day for child and/ or adult
- If Propylene glycol is present: calculate the content /kg /day Check Pharmacology committee warnings and Technical committee warnings for active and inactive ingredients.

Note: the Pharmacology committee warnings link is available throughout all days not only during submission timing

Annexes:

Insert Submission link: (for New applications) (Endorsing the Pharmacology committee warnings)
https://forms.gle/dx5c8LJWbv1P8fw27

Insert Corrections link: **(for amendments required to be fulfilled for previously submitted application)**
Link is opened on Mondays till Thursdays at 9 a.m. till 1 p.m.
https://forms.gle/ENHLxpYXacHCKxwP7

To Check The Status of Products Click The Following Link:
https://docs.google.com/spreadsheets/d/1SEX2GJuFXkIwd_3EZpc1N6gxuq9BK0ixBhd2As0_FIc/edit?usp=sharing

Declaration letter template

• 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)

Checklist of requirements for medical insert submission

General Requirements for leaflet submission

1	Cover letter
2	Proposed Insert (in Word format (SmPC & PIL)
3	The most Updated reference for both SmPc & PIL
4	EDA approved product composition (stability/NODCAR)
5	Naming approval ,layout or art work (not required for Tender & Export)
6	Checking for Technical & Pharmacology warnings
7	**In case of imported and innovator products:** CPP **In case of imported and innovator products with PIL only:** A Legalized letter from the country of origin stamped from Egyptian Embassy comprising a warrant that the attached leaflet (Patient information leaflet) with the specified Trade Name, generic name, concentration, version 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. **(Template attached in annexes in submission guidance)** **And for non-English inserts,** ✓ A legalized Declaration Letter from License Holder commit that the leaflet is translated according to authorized medical translation on their responsibility in accordance with the translation attached. (Signature & Stamp) Or ✓ Legalized letter from the head office stating that the scientific office is responsible for the translation and the insert is translated 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. A declaration letter from the scientific office declares that the letter is to be legalized within 6 months
8	**In case of Non referenced product:** Committee approval (s)
9	**In case of non-English reference:** Authorized Translation of the Reference
For products under registration:	
1	Action letter (Ministerial Decree)
2	Naming (not required in case of: tender & export)
3	Accelerated Stability (not required in case of: 820)
4	Pricing (not required in case of: 820, tender & export, Export only)
5	PV for 425 & 645
6	**In case of 820:** Naming approval & action letter.

For Tentative to final products:	
1	Tentative license
2	Transmission letter
3	last approved insert
4	Accelerated Stability
5	License Extension (Optional)
6	Naming or Layout approval (in case Arabic name is not written in the registration license)
For registered products:	
1	Last approved insert
2	Valid Registration License
3	Naming or Layout approval (in case Arabic name is not written in the registration license)
For re-registration products:	
1	Last approved insert
2	Registration License
3	Re-registration action letter
4	Long term Stability
5	Naming or Layout approval (in case Arabic name is not written in the registration license)

Requirements for leaflet update:

1	Receipt: 200 L.E
2	Tracked Change
3	Last approved inserts

For warning addition:

1	Warning to be added highlighted inside the insert
2	Last approved insert

For variation:

1	Variation approval
2	Receipt:200 L.E (for valid insert)
3	Last approved insert

For appeals:

1	Receipt:200 L.E
2	Cover letter in Word format
3	Where applicable, a comparison table (in Word format) between the two inserts the appeal is submitted for.
4	Relevant documents to the raised issue.

In case of Replacement insert:

1	Receipt: (500.l.E)
2	Copy of last approved leaflet