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Gulf Health Council

The GCC Guidance for Presenting the Labeling Information, SPC and PIL

Version 3.1

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What is New in version no. 3.0?

The following table shows the update to the previous version:

Section	Description of change	
General	• Revise the document to comply with the reference. • Transfer all points related to the principles of presenting the information in the SPC, PIL and labeling to the "Templates for SPC, PIL and Labeling information".	
3. Labeling	**<u>Include</u>:** - Datamatrix - Global trade item number - Serial number - Registration number	**<u>Delete</u>:** - Marketing company - Marketing authorization number(s)
4. PIL **5. SPC**	- Include inverted equilateral black triangle for medicinal products require additional monitoring - Update NPC contact information - Delete Pregnancy Categorization	
5. SPC	- Delete black box warning	

What is New in version no. 3.1?

Section	Description of change
3. Labeling	Particulars to appear on the outer packaging and the immediate packaging **<u>Delete</u>** 19. Price Minimum particulars to appear on small immediate packaging units **<u>Delete</u>** 12. Price

Table of Contents

1. INTRODUCTION

1.1. Objective

It is indented to guide applicants on the information required by the Gulf Cooperation Council (GCC) States for:

- Labeling information
- Summary of Product Characteristics (SPC); and
- Patient Information Leaflet (PIL);

1.2. Scope

It is applicable to medicinal products intended for human use.

1.3. Related guidelines

This guidance should be read in conjunction with:

- Tempaltes for Labeling information, SPC and PIL

For Lableing part refer to the following guidlines:

- Guidance for Graphic Design of Medication Packaging
- Drug Barcoding Specifications

2. GENERAL REQUIREMENTS

The SPC is the basis of information for health professionals on how to use the medicinal product safely and effectively. The Patient Information Leaflet (PIL) shall be drawn up in accordance with the SPC.

Applicants should maintain the integrity of each section of the document by only including information in each section, which is relevant to the section heading. However, some issues may

need to be addressed in more than one section and in such situations the individual statements may cross-refer to other sections when these contain relevant additional information.

When submitting a new application for registration, renewal or variation, the information regarding the SPC, PIL and labeling must follow this guidance.

Following the approval of the SPC, PIL and labeling contents, such contents cannot be changed withoute the authority approval (refer to the GCC guidelines for variation requirements).

Applicants are required to submit SPC, PIL and labeling documents in searchable, readable PDF format that is clean from all stamps, watermarks, signatures, headers or footers.

Practical advice on how to draw up SPC, PIL and labeling is provided to applicants in the form of templates refer to “Templates for SPC, PIL, and labeling information”.

3. LABELING

A separate text for outer and inner packaging labeling should be completed per strength and per pharmaceutical form.

The applicant must provide Arabic translation for some labelling information components (see Appendix 1).

Particulars to appear on the outer packaging and the immediate packaging

1. Name of the medicinal product

- A standard packaging box has six faces on which information can be displayed. If it is feasible, display a product description on more than three non opposing faces.
- Use blank space to emphasize critical information such as the medicine name, generic name and strength.

2. Statement of active substance(s)

- Expressed qualitatively and quantitatively per dosage unit or according to the form of administration for a given volume or weight. Where the active substance is present as a salt, this should be clearly indicated.

3. List of excipients

- Express qualitatively those excipients known to have a recognised action or effect. However, if the medicinal product is a parenteral, a topical or an eye preparation or if used for inhalation, all excipients must be stated.

4. Pharmaceutical form and contents

- Contents by weight, by volume or by number of doses or number of units of administration of the medicinal product (e.g. 28 tablets, 100 mL, ...).

For injectable medicine:

- The strength of injectable medicines should be express in quantity /unite volume (mg/ml) e.g. : 5mg/ml.

- Include a representation of the full volume strength , e.g. : total quantity in total volume (mg/ml). This should be emphasized for single-dose containers.
- Display concentration in total quantity/total volume, even if other units of concentration such as percentage and ratios are present e.g. (: 2 %) (20 mg/ml).

5. Method and route(s) of administration

- Method of administration: directions for proper use of the medicinal product, e.g. “Shake well before use”.
- Use positive statements if possible - use “DO” rather than “DO NOT” ,e.g. if the drug given for intravenous , use : (For intravenous infusion) , rather than (NOT for I.M).

6. Special warning that the medicinal product must be stored out of the reach and sight of children

7. Other special warning(s), if necessary

8. Manufacturing and Expiry dates

- Dates should be expressed with the month given as 2 digits or 3 characters and the year as 4 digits. e.g.: 02/2010, Feb 2010.
- Where applicable, the shelf life after reconstitution, dilution or after first opening the container should be included.

9. Special storage conditions

10. Special precautions for disposal of unused medicinal products or waste materials derived from such medicinal products, if appropriate

- E.g. radiopharmaceuticals, cytostatics.
- A reference to any appropriate collection system in place should be included on the outer packaging.

11. Manufacturer name

12. Name and address of the marketing authorisation holder

13. Batch number

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

14. General classification for supply

15. Datamatrix

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

16. Global Trade Item Number (GTIN):

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

17. Serial number

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

18. Registration number

Minimum particulars to appear on blisters or strips

1. Name of the medicinal product
    - The name and strength of the product should be appear over each blister pocket , if the size of the pockets is too small, the information should be repeated in a pattern across the entire strip.
2. Name of the marketing authorisation holder
3. Manufacturing and Expiry dates
    - Dates should be expressed with the month given as 2 digits or pendix characters and the year as 4 digits. e.g.: 02/2010, Feb 2010.
4. Batch number
    - Batch number and Expiry date should be at the end of each blister strip, if technically possible this could be applied to both ends.
5. Other
    - Space permitting, any other information necessary for the correct use and administration of the product can be included here, e.g. calendar days may be included if the product is taken as a single dose and that is packaged in blister strips that comprise multiples of seven.

Minimum particulars to appear on small immediate packaging units

Small immediate packaging units are defined as containers sized up to and including 10 ml. On a case-by-case basis the minimum particulars could also be considered for other containers where it is not be feasible to include all the information. Such exceptional cases have to be justified, discussed and agreed upon with the Authority.

1. Name of the medicinal product and route(s) of administration
2. Method of administration
   - Method of administration: directions for proper use of the medicinal product, e.g. “Shake well before use”.
   - Use positive statements if possible - use “DO” rather than “DO NOT” ,e.g. if the drug given for intravenous , use : (For intravenous infusion) , rather than (NOT for I.M).
   - If full details cannot be included on the immediate packaging itself, a reference to the patient information leaflet should be made, e.g. “Read the patient information leaflet before use”.
3. Manufacturing and Expiry dates
   - Dates should be expressed with the month given as 2 digits or 3 characters and the year as 4 digits. e.g.: 02/2010, Feb 2010.
   - Where applicable, the shelf life after reconstitution, dilution or after first opening the container should be included.
4. Batch number
5. Contents by weight, by volume or by unit

   For injectable medicine:

   - The strength of injectable medicines should be express in quantity /unite volume (mg/ml) e.g. : 5mg/ml.
   - Include a representation of the full volume strength , e.g. : total quantity in total volume (mg/ml). This should be emphasized for single-dose containers.

- Display concentration in total quantity/total volume, even if other units of concentration such as percentage and rations are present e.g. (: 2 %) (20 mg/ml).

6. Special storage conditions

- If drug requires refrigeration , highlight storage conditions.

7. Other

- Space permitting, any other information necessary for the correct use and administration of the product can be included here.

8. Datamatrix

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

9. Global Trade Item Number (GTIN):

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

10. Serial number (SN)

- For more information refer to the "*Drug Barcoding Specifications*" which published in the SFDA website.

11. Registration number

4. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

For submission purpose, applicants may present SPCs for different strengths in one document, clearly indicating with grey-shaded titles the strength or presentation to which alternative text elements refer. However, a separate SPC per strength and per pharmaceutical form, containing all pack-sizes related to the strength and pharmaceutical form concerned will have to be provided by the applicant.

Add the inverted equilateral black triangle at the top of the SPC for medicinal products require additional monitoring (For more information see Appendix 2).

1. Name of the medicinal product

- The (invented) name should be followed by both the strength and the pharmaceutical form.

2. Qualitative and quantitative composition

- Full details of the qualitative and quantitative composition in terms of the active substance(s) and excipients.
- A standard statement should be included at the end of the section, i.e. ‘For a full list of excipients, see section 6.1.

3. Pharmaceutical form

- Full description of the pharmaceutical form should be provided.
- It is recommended that a visual description of the appearance of the product (color, markings, etc.) is given e.g.: ‘Tablet White, circular flat bevelled-edge tablets marked ‘100’ on one side’.
- In case of tablets designed with a score line, information should be given whether or not reproducible dividing of the tablets has been shown.
- Information on pH and osmolarity should be provided, as appropriate.

4. Clinical particulars

4.1 Therapeutic indications

– The indication(s) should be 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.

4.2 Posology and method of administration

– In case of restricted medical prescription start this section by specifying the conditions.

– Instructions for preparation are to be placed under section 6.6 or11, and cross-referenced here.

Posology

– The dosage should be clearly specified for each method/route of administration and for each indication, as appropriate.

– Dose recommendations (e.g. mg, mg/kg, mg/m^2) should be specified per dose interval for each category where appropriate (specify age/weight/body surface area of subsets of the population as 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 and relevant pharmacokinetic data)

- advice on preventive measures to avoid certain adverse drug reactions (e.g. administration of antiemetics),
- the intake of the product in relation to drink and food intake, e.g. with alcohol, grapefruit or milk,
- advice regarding repeat use, with any information on intervals to be observed between courses of treatment, as appropriate,
- interactions requiring specific dose adjustments with cross-reference to other appropriate sections of the SPC, and
- it may also be relevant to recommend not to prematurely discontinue a treatment in case of specific non-serious adverse reaction(s) that are frequent but transient or manageable with dose-titration.

Special populations

– Dosage adjustments or other posology related information on special populations should be presented here, in well-defined sub-sections ordered by importance, e.g. regarding: elderly population; paediatric population; renal impairment; hepatic impairment, patients with a particular genotype; other relevant special population (e.g. patients with other concomitant disease or overweight patients).

Paediatric population

– The specific sub-section ‘paediatric population’ should always 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 product is indicated in the paediatric population, posology recommendations should be given for each of the relevant subsets. The age limits should reflect the benefit-risk assessment of the available documentation for each subset.

– 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.

– Where a product is indicated in children and no adequate paediatric formulation can be developed, detailed instructions on how to obtain an extemporaneous preparation shall be included in section 6.6 with a cross-reference in section 4.2.

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

Method of administration

- The route of administration and concise relevant instruction for correct administration and use should be given here.
- When supportive data are available, information on alternative method(s) to facilitate administration or acceptability should be given as explicitly as possible (e.g. possibility of crushing tablet, cutting tablet or transdermal patch, pulverising tablet, opening capsules, mixing with food, dissolution in drinks – specifying if a proportion of the dose can be given) particularly for administration via feeding tubes.
- For parenteral formulations, information on the rate or speed of injection or infusion should be provided.

4.3 Contraindications

- Situations where the medicinal product must not be given for safety reasons, i.e. contraindications, are the subject of this section. 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). The situations should be unambiguously, comprehensively and clearly outlined. Only if pregnancy or breastfeeding is contraindicated, should it be mentioned here. Hypersensitivity to the active substance or to any of the excipients or residues from the manufacturing process should be included, as well as any contraindication arising from the presence of certain excipients.
- Lack of data alone should not lead to a contraindication. Where for safety reasons, the product should be contraindicated in a specific population, e.g. paediatric or a subset of the paediatric population, it should appear in this section with a cross-reference to the section

giving detailed information on the safety issue. A contraindication in the paediatric population should be listed without a sub-heading.

4.4 Special warnings and precautions for use

- The order of warnings and precautions should be determined by the importance of the safety information provided.
- 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 should be included where relevant to the specific product.
- Information on a specific risk should be given in section 4.4 only when the risk leads to a precaution for use or when healthcare professionals have to be warned of this risk. Patient groups in which use of the medicinal product is contraindicated should be mentioned in section 4.3 only and not to be repeated here.
- The following should be described:
    - 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 minimisation measures requested as part of a Risk Management Plan to ensure safe and effective use should be described in this section. (For example; “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”, “Women of childbearing potential should use contraception”, …).
    - 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), patients having an anaesthesic or patients with cardiac failure (including in this case the NYHA Classification for example). 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 warnings necessary for excipients or residues from the manufacturing process.
- For herbal preparations containing alcohol, information about the ethanol content in the medicinal product should be included in accordance with the Guideline on excipients in the label and package leaflet of medicinal products for human use.
- Any warnings necessary with respect to transmissible agents (e.g. Warning of Transmissible Agents in SPC and Package Leaflets for Plasma-Derived Medicinal Products.
- Subjects or patients with a specific genotype or phenotype might either not respond to the treatment or be at risk of a pronounced pharmacodynamic effect or adverse reaction. These may arise because of non-functioning enzyme alleles, alternative metabolic pathways (governed by specific alleles), or transporter deficiencies. Such situations should be clearly described if known.
- 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.

- In exceptional cases, especially important safety information may be included in bold type within a box.
- Any adverse reactions described in this section or known to result from conditions mentioned here should also be included in section 4.8.
- Specific interference with laboratory tests should be mentioned when appropriate, e.g. Coombs test and Beta-lactams. They should be clearly identified with a subheading, e.g. "Interference with serological testing".
- 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, e.g. contraception measures, or when concomitant use of another medicine is not recommended, and with cross reference to section 4.5, 4.6, or 4.7.

Paediatric population:

- When the product is indicated in one or more subsets of the paediatric population and there are warnings and precautions for use that are specific to the paediatric population or any subset of the paediatric population, they should be identified under this subheading. Any necessary warning or precaution in relation to long-term safety (e.g. on growth, neuro-behavioral development or sexual maturation) or specific monitoring (e.g. growth) in the paediatric population should be described. When long-term safety data are necessary but not yet available, it should be stated in this section. Warnings should be included in case of possible significant or long-lasting impact on children's daily activities, such as learning ability or physical activities, or in case of impact on appetite or sleep pattern.

4.5 Interaction with other medicinal products and other forms of interaction

- This section should provide information on the potential for clinically relevant interactions based on the pharmacodynamic properties and in vivo pharmacokinetic studies of the medicinal product, with a particular emphasis on the interactions, which result in a recommendation regarding the use of this medicinal product. This includes in vivo

interaction results which are important for extrapolating an effect on a marker ('probe') substance to other medicinal products having the same pharmacokinetic property as the marker.

- Interactions affecting the use of this medicinal product should be given first, followed by those interactions resulting in clinically relevant changes on the use of others.
- Interactions referred to in other sections of the SPC should be described here and cross-referenced from other sections.
- The order of presentation should be contraindicated combinations, those where concomitant use is not recommended, followed by others.
- The following information should be given for each clinically relevant interaction:
  - Recommendations: these might be
    - contraindications of concomitant use (cross-refer to section 4.3),
    - concomitant use not recommended (cross-refer to section 4.4), and
    - precautions including dose adjustment (cross-refer to sections 4.2 or 4.4, as appropriate), mentioning specific situations where these may be required.
  - Any clinical manifestations and effects on plasma levels and AUC of parent compounds or active metabolites and/or on laboratory parameters.
  - Mechanism, if known. For example, interaction due to inhibition or induction of cytochrome P450 should be presented as such in this section, with a cross-reference to 5.2 where in vitro results on inhibition or induction potential should be summarised.
- Interactions not studied in vivo but predicted from in vitro studies or deducible from other situations or studies should be described if they result in a change in the use of the medicinal product, cross-referring to sections 4.2 or 4.4.
- This section should mention the duration of interaction when a medicinal product with clinically important interaction (e.g., enzyme inhibitor or inducer) is discontinued. Adjustment of dosing may be required as a result. The implication for the need for a washout period when using medicines consecutively should also be mentioned.
- Information on other relevant interactions such as with herbal medicinal products, food, alcohol, smoking, or pharmacologically active substances not used for medical purpose, should also be given. With regard to pharmacodynamic effects where there is a possibility of a clinically relevant potentiation or a harmful additive effect, this should be stated.

- In vivo results demonstrating an absence of interaction should only be mentioned here if this is of major importance to the prescriber (e.g. in therapeutic area where potentially problematic interactions have been identified such as with anti-retroviral medicines).
- If no interaction studies have been performed, this should be clearly stated.

Additional information on special populations

- If there are patient groups in which the impact of an interaction is more severe, or the magnitude of an interaction is expected to be larger e.g., patients with decreased renal function (in case the parallel pathway is renal excretion), paediatric patients, elderly etc, this information should be given here.
- If interactions with other medicinal products depend on polymorphisms of metabolising enzymes or certain genotypes, this should be stated.

Paediatric population

- Information specific to a subset of the paediatric population should be given here if there is an indication for the particular age group.
- The resulting exposure and clinical consequences of a pharmacokinetic interaction can differ between adults and children, or between older and younger children. Therefore;
    - Any identified treatment recommendations should be given in relation to concomitant use in the paediatric subset(s) (e.g. dose adjustment, extra-monitoring of clinical effect marker/adverse reactions, therapeutic drug monitoring),
    - If the interaction studies have been performed in adults, the statement 'Interaction studies have only been performed in adults' should be included.
    - If the extent of an interaction is known to be similar in a paediatric age group to that in adults, this should be stated.
    - If this is not known, this should also be stated.
- The same applies to pharmacodynamic drug interactions.
- In cases of food interaction leading to a recommendation on co-administration with a meal or specific food, it should be specified whether this is relevant for paediatric use (especially newborns and infants) whose diet is different (100 % milk in newborns).
- Overall, section 4.5 should be presented in the simplest possible way to highlight the interactions resulting in a practical recommendation regarding the use of the medicinal

product. Presentation in a tabulated format may help where interactions are numerous and various, such as with anti-viral products.

4.6 Fertility, Pregnancy and lactation

- Efforts should be made by the Marketing Authorization Applicant or Holder to provide the reasons for the recommendations for use in pregnant or lactating women and in women of childbearing potential. This information is important for the healthcare professionals informing the patient.
- In the overall assessment, all available knowledge should be taken into account, including clinical studies and post-marketing surveillance, pharmacological activity, results from non-clinical studies, and knowledge about compounds within the same class.
- Efforts should be made to update the recommendations for use during pregnancy and lactation on the basis of increasing human experience in exposed pregnancies which eventually supersede the animal data.
- The following should be mentioned:
  - Women of childbearing potential / Contraception in males and females.
  - Pregnancy
  - Breastfeeding
  - Fertility

4.7 Effects on ability to drive and use machines

- On the basis of the pharmacodynamic profile, reported Adverse Reactions and/or specific studies on a relevant target population addressing the performance related to driving or using machines, specify whether the medicinal product has:
  a. no or negligible influence;
  b. minor or moderate influence, or
  c. major influence on these abilities.
- For situation c, special warnings/precautions for use should be mentioned here and also in section 4.4. Effects of the disease itself on these abilities should not be discussed.

4.8 Undesirable effects

4.8.1: adverse reactions:

- This sub-section should include all adverse reactions from clinical trials, post-authorisation safety studies and spontaneous reporting for which, after thorough assessment, a causal relationship between the medicinal product and the adverse event is at least a reasonable possibility, based for example, on their comparative incidence in clinical trials, or on findings from epidemiological studies and/or on an evaluation of causality from individual case reports.
- The content of this sub-section should be justified in the Clinical Overview of the marketing authorization application based upon a best-evidence assessment of all observed adverse events and all facts relevant to the assessment of causality, severity and frequency. This section should be regularly reviewed and, if necessary, updated with the aim to ensure appropriate information to health care professionals on the safety profile of the product. In addition, the whole section could be revised at the renewal of the marketing authorization, where the safety profile of most products is likely to be well established, and thereafter at each of the three-yearly PSUR.
- It is important that the whole section is worded in concise and specific language and does not include information such as claims regarding the absence of specific adverse reactions, comparative frequency statements other than as described below, or statements of general good tolerability such as “well tolerated”, “adverse reactions are normally rare”, etc. Statements on lack of proof of causal association should not be included.
- In order to provide clear and readily accessible information, section 4.8 should be structured according to the following recommendations:

    a. Summary of the safety profile
    b. Tabulated summary of adverse reactions
    c. Description of selected adverse reactions
    d. Paediatric population
    e. Other special population(s)

a. Summary of the safety profile

- The summary of the safety profile should provide information about the most serious and/or most frequently occurring adverse reactions.
- If known, it may be helpful to indicate the timing when adverse reactions occur. For example, in order to prevent early discontinuation of a treatment, it may be important to inform about non-serious adverse reactions that are frequent in the beginning of the treatment but may disappear with its continuation. Another example would be to inform about adverse reaction associated with long-term use. Frequencies of cited adverse reactions should be stated as accurately as possible. This summary of the safety profile should be consistent with the important identified risks mentioned in the Safety Specification of the Risk Management Plan. The information should be consistent with the Table of Adverse Reactions (see section b). Cross-reference should be made to section 4.4 if relevant risk minimization measures have been proposed in that section.
- An example of an acceptable statement is given below:

'At the beginning of the treatment, epigastric pain, nausea, diarrhoea, headache or vertigo may occur; these reactions usually disappear within a few days even if treatment is continued. The most commonly reported adverse reactions during treatment are dizziness and headache, both occurring in approximately 6% of patients. Serious acute liver injury and agranulocytosis may occur rarely (less than 1 case per 1,000 patients)'.

b. Tabulated list of adverse reactions

- A single table (or structured listing) should list all adverse reactions with their respective frequency category. In some cases for common or very common reactions, and when it is necessary for the clarity of the information, frequency figures may be presented in the table.
- Separate tables are acceptable in exceptional cases where the adverse reaction profiles markedly differ depending on the use of the product. For example, it might be the case for a product used for different indications (e.g. an oncology and a non-oncology indication) or at different posologies.

- The table should be introduced with a short paragraph stating the source of the safety database (e.g. from clinical trials, post-authorisation safety studies or spontaneous reporting).
- The table should be presented according to the MedDRA system organ classification. The system organ class (SOC) should be presented in the order shown in the annex. Adverse reactions descriptions should be based on the most suitable representation within the MedDRA terminology. This will usually be at the Preferred Term (PT) Level, although there may be instances where the use of Lowest Term Level or exceptionally group terms, such as High Level Terms may be appropriate. As a general rule, any adverse reactions should be assigned to the most relevant SOC related to the target organ. For example, PT 'Liver function test abnormal' should be assigned to the SOC 'Hepatobiliary disorders' rather than to the SOC 'Investigations'. Within each system organ class, the adverse reactions should be ranked under headings of frequency, most frequent reactions first. Within each frequency grouping, adverse reactions should be presented in the order of decreasing seriousness. The names used to describe each of the frequency groupings should follow standard terms established in each official language using the following convention: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).
- In exceptional cases, if a frequency cannot be estimated from the available data, an additional category frequency 'not known' may be used. In case the expression "Frequency not known" is used, the following text should be added in the list of terms explaining the frequency categories: "not known (cannot be estimated from the available data)". The expressions isolated/single cases/reports should not be used.
- Where additional details about an adverse reaction are described in section c), the reaction concerned should be highlighted, for example with an asterisk, and, "see section c)" should be included as a footnote.

c. Description of selected adverse reactions

- This sub-section should include information characterising specific adverse reaction which may be useful to prevent, assess or manage the occurrence of an adverse reaction in clinical practice.
- This sub-section should include information characterising individual serious and/or frequently occurring adverse reactions, or those where there have been reports of particularly severe cases. The information should provide frequency and may describe for example reversibility, time of onset, severity, duration, mechanism of the reaction (if of clinical relevance), dose relationship, relationship with duration of exposure or risk factors. Measures to be taken to avoid specific adverse reactions or actions to be taken if specific reactions occur should be mentioned under section 4.4 and cross-referenced here.
- Information on the occurrence of withdrawal reactions may be mentioned here with cross-reference to section 4.2 in case of need for tapering off or advice on discontinuation of the product. Mention should be made here of any differences between different dosage forms in respect of adverse reactions.
- In the case of combination products, information should be included in this sub-section pointing out which particular adverse reactions are usually attributable to which active substance of the combination, where known.
- Any adverse reactions resulting directly from an interaction should be mentioned here and cross referenced to section 4.5.
- This sub-section should also inform on adverse reactions with very low frequency or with delayed onset of symptoms which may not have been observed in relation to the product, but which are considered to be related to the same therapeutic, chemical or pharmacological class. The fact that this is a class attribution should be mentioned.
- Any adverse reaction specific to excipients or residues from the manufacturing process should be included.

d. Paediatric population

- A pediatric sub-section should always be included (unless irrelevant).

- The extent and age characteristics of the safety database in children should be described (e.g. from clinical trials or pharmacovigilance data). Uncertainties due to limited experience should be stated. If the observed safety profile is similar in children and adults this could be stated: e.g. “Frequency, type and severity of adverse reactions in children are <expected> to be the same as in adults”. Similarly, it is appropriate to state whether the safety profiles in the different paediatric subsets are similar or not.
- Any clinically relevant differences (i.e. in nature, frequency, seriousness or reversibility of adverse reactions) between the safety profiles in adult and paediatric populations, or in any relevant age groups, should be described and presented by age group. If there is a need for specific monitoring, this should be highlighted by cross-referencing to section 4.4. For clinically relevant differences, a separate table listing such adverse reactions by frequency can be added and presented by relevant age groups if appropriate. If some paediatric adverse reactions are considered common (≥1/100 to <1/10) or very common (≥1/10), the frequencies should be provided in parentheses. In case of major difference with the safety profile in adults, a summary of the safety profile in children could be presented to facilitate the presentation of the information. Available information, from any source scientifically validated, on long-term safety in children (e.g. on growth, mental development and sexual maturation) should also be summarized, whether positive or negative, with cross-reference to section 5.1 if appropriate. Any risk factors such as duration of treatment or period at risk should be specified.
- If relevant, symptoms of neonatal withdrawal should be listed in a separate paragraph with cross reference with 4.6.

e. Other special populations

- This sub-section may include information on any clinically relevant differences (i.e. in nature, frequency, seriousness or reversibility of adverse reactions, or need for monitoring) specifically observed in other special populations such as elderly, patients with renal impairment, patients with hepatic impairment, patients with other diseases or a specific genotype. Cross-reference to other sections such as 4.3, 4.4 or 4.5 may be added as appropriate.

- Adverse reactions may also be related to genetically determined product metabolism. Subjects or patients deficient in the specific enzyme may experience a different rate or severity of adverse reactions. This should be mentioned and where relevant correlated with data from clinical trials.

4.8.2: Clinical Studies Experience (upon request from any regulatory Authority in GCC)

- The presentation of adverse events identified from clinical trials must include a listing of all such adverse events that occurred at or above a specified rate that is appropriate to the drug's safety database.
- The table of adverse events identified from clinical trials should be introduced with a description of the overall clinical trial database from which adverse events data have been drawn, including number of patients, dose, schedule, duration, demographics of the exposed population, designs of the trials in which exposure occurred (e.g., placebo-controlled, active-controlled), and any critical exclusions from the safety database.
- A single adverse event table in the tabulated list of adverse events section will usually be adequate. However, it may be more informative to present data in more than one table for a product used for different indications (e.g. an oncology and a non-oncology indication), posologies, demographic subgroups, study durations, dosing regimens, and types of studies.

4.8.3 Post-marketing Experience (upon request from any regulatory Authority in GCC)

- To help healthcare professionals interpret the significance of data obtained from postmarketing spontaneous reports, this sub-section should be introduced with the following statement:

The following adverse events have been identified during post-approval use of drug X. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Decisions about whether to include an adverse event from spontaneous reports in the SPC are typically based on one or more of the following factors: (1) seriousness of the event, (2) number of reports, or (3) strength of causal relationship to the drug.

- To reports any side effect(s):

  - **Saudi Arabia:**

- The National Pharmacovigilance Centre (NPC):

  - SFDA Call Center: 19999
  - E-mail: npc.drug@sfda.gov.sa
  - Website: https://ade.sfda.gov.sa/

  - **Other GCC States:**

  - Please contact the relevant competent authority.

4.9 Overdose

- Describe acute symptoms and signs and potential sequelae of different dose levels of the medicinal product based on all available information including accidental intake, mistakes and suicide attempts by patients.

- Taking into account all relevant evidence, describe management of overdose in man, e.g. in relation to monitoring or use of specific agonists/antagonists, antidotes or methods to increase elimination of the medicinal product such as dialysis.

Additional information on special populations

- Information specifically observed in special populations such as elderly, patients with renal impairment, patients with hepatic impairment, other concomitant diseases etc.

Paediatric population

- If there are specific paediatric considerations, there should be a sub-section entitled 'paediatric population'. Special mention should be made of those medicinal

products/strength of formulation for which ingestion of only one dose unit by children can cause fatal poisoning.

5. Pharmacological properties

5.1 Pharmacodynamic properties

– Describe the following:

- Pharmacotherapeutic group
- Mechanism of action (if known)
- Pharmacodynamic effects
- Clinical efficacy and safety

Paediatric population

– The results of all pharmacodynamic (clinically relevant) or efficacy studies conducted in children should be presented under this sub-heading.

– Results should be presented by age or relevant subsets.

– When there are data available, but there is no authorised paediatric indication, data should be presented and a cross-reference should always be made to section 4.2 and, as appropriate to 4.3.

5.2 Pharmacokinetic properties

– Pharmacokinetic properties of the active substance(s) relevant for the advised dose, strength and the pharmaceutical formulation marketed should be given in this section. If these are not available, results obtained with other administration routes, other pharmaceutical forms or doses can be given as alternative.

– Basic primary pharmacokinetic parameters, for instance bioavailability, clearance and half-life, should be given as mean values with a measure of variability.

– Pharmacokinetics items, which could be included in this section when relevant, are given below:

a. General introduction, information about whether the medicinal product is a pro-drug or whether there are active metabolites, chirality, solubility etc.

b. General characteristics of the active substance(s) after administration of the medicinal product formulation to be marketed.

- Absorption: complete or incomplete absorption; absolute and/or relative bioavailability; first pass effect; T_{max}; the influence of food; in case of locally applied medicinal product the systemic bioavailability.
- Distribution: plasma protein binding; volume of distribution; tissue and/or plasma concentrations; pronounced multi-compartment behavior.
- Biotransformation: degree of metabolism; which metabolites; activity of metabolites; enzymes involved in metabolism; site of metabolism; results from in vitro interaction studies that indicate whether the new compound can induce/inhibit metabolic enzymes.
- Elimination: elimination half-lives, the total clearance; inter and/or intra-subject variability in total clearance; excretion routes of the unchanged substance and the metabolites.
- Linearity/non-linearity: linearity/non-linearity of the pharmacokinetics of the new compound with respect to dose and/or time; if the pharmacokinetics are nonlinear with respect to dose and/or time, the underlying reason for the non-linearity should be presented.

Additional relevant information should be included here.

c. Characteristics in patients

- Variations with respect to factors such as age, gender, smoking status, polymorphic metabolism and concomitant pathological situations such as renal failure, hepatic insufficiency, including degree of impairment. If this influence on the pharmacokinetics is considered to be clinically relevant, it should be described here in quantitative terms (cross-referral to 4.2 when applicable).

d. Pharmacokinetic/pharmacodynamic relationship(s)

- Relationship between dose/concentration/pharmacokinetic parameter and effect (either true endpoint, validated surrogate endpoint or a side effect).
- Contribution (if any) of metabolite(s) to the effect.

5.3 Preclinical safety data

– The findings of the non-clinical testing should be described in brief and qualitative statements.

– Conclusions on the environmental risk assessment on the product should be included where relevant, with reference to section 6.6.

6. Pharmaceutical particulars

6.1 List of excipients

– A list should be given of the excipients, expressed qualitatively only. All excipients, which are present in the product, should be included, even those present in small amounts, such as printing inks.

– Each to be listed on a separate line according to the different parts of the product.

6.2 Incompatibilities

– Information on physical and chemical incompatibilities of the medicinal product with other products with which it is likely to be mixed or co-administered should be stated. 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 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. parenterals, 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

- Information on the finished product shelf life and on the in-use stability after 1st opening and/or reconstitution/dilution should appear here. Only one overall shelf life for the finished product is to be given even if different components of the product may have a different shelf life (e.g. powder & solvent).

6.4 Special precautions for storage

- General storage conditions of the finished product should appear here, together with a cross-reference to section 6.3 where appropriate.

6.5 Nature and contents of container

- The material of construction of the immediate container should be stated (‘Type I glass vials’, ‘PVC/Aluminum blisters’, ‘HDPE bottles’); and any other component of the product should be listed, e.g. needles, swabs, measuring spoons, inhaler devices, desiccant. The graduation on measuring devices should be explained. The container of any solvent provided with the medicinal product should also be described. Excessive detail, e.g., concerning the color of the stopper, the nature of the heat-seal lacquer, should usually not be included.

  Examples on the text in this section:

  ‘(Volume) ml suspension in a pre-filled syringe (type I glass) with plunger stopper (chlorobutyl rubber) with or without needle in pack sizes of 5 or 10.’

‘HDPE bottle with a child-resistant closure and a silica gel desiccant. Pack-sizes of 30, 60 or 90 filmcoated tablets.’

- All pack sizes must be listed. Pack sizes mentioned should include the number of units, number of doses (for e.g. multi-dose vaccines, inhalers, etc.), total weight or volume of the immediate container, as appropriate, and the number of containers present in any outer carton.

6.6 Special precautions for disposal and other handling

- Include practical instructions for preparation and handling of the product, where applicable, including disposal of the medicinal product, and waste materials derived from the used medicinal product.
- If applicable, e.g. for cytotoxics, the following standard statement should be included, ‘Any unused product or waste material should be disposed of in accordance with local requirements.’
- 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.
- Information on the preparation (e.g. the suspension of a powder for injection, or preparing a dilution) of the medicinal should be included in section 6.6, regardless of who prepares the product (e.g. pharmacist, doctor, other health personnel, patient, parents or carers). In the case of products for reconstitution, the appearance of the product after reconstitution should be stated.
- Statements concerning compatibility of the product with other medicinal products or devices can be given here provided the data have been provided in the dossier.
- In the exceptional cases where a product is indicated in children and where no adequate paediatric formulation can be developed (based on duly justified scientific grounds), information on extemporaneous formulation should appear under a sub-heading “Use in the paediatric population” and should cross-refer to the section 4.2. Detailed instructions for the preparation of the extemporaneous formulation from the appropriate “adult” or other “older children” dosage form and additional information on extemporaneous

formulations for use in younger children shall be provided and, where appropriate, the maximum storage time during which such preparation will conform to its specifications. When necessary, the required packaging material and storage conditions should be stated here.

7. Marketing authorisation holder

8. Date of first Authorisation/ renewal of the authorisation

- Once the Marketing Authorisation has been granted or renewed. Both the date of first authorisation and, if the authorisation has been renewed, the date of the (last) renewal should be stated.

9. Date of revision of the text

10. Dosimetry

- For radiopharmaceuticals, full details of internal radiation dosimetry.

11. Instructions for preparation of radiopharmaceuticals

- For radiopharmaceuticals, additional detailed instructions for extemporaneous preparation and quality control of such preparation and, where appropriate, maximum storage time during which any intermediate preparation such as an eluate or the ready-to-use pharmaceutical will conform to its specifications.

5. PATIENT INFORMATION LEAFLET (PIL)

A separate patient information leaflet should be provided per strength and per pharmaceutical form in cases of different indications for different strengthes and/or dosage forms. However, applicants may present PILs for different strengths in one document for submission process, clearly indicating the strength or presentation to which alternative text elements refer. Where applicants consider to also market a combined package leaflet, a detailed justification for such a combined PIL should be provided in the application at submission. E.g. (Different strenghts have the same indication).

Applicants should justify the use of alternative headings (e.g. by reference to user testing results). For certain medicinal products not all items may be relevant, in this case the corresponding heading should not be included.

It is important that the PIL can easily be tracked for updates and review. Each PIL should be given a reference number along with the date the leaflet was issued and a suitable review date.

Iinverted equilateral black triangle should be added at the top of the PIL for medicinal products require additional monitoring (For more information see appendix 2).

Patient Information Leaflet (PIL)

In this leaflet:

1. What is the product and what it is used for

(Invented) name, active substance(s) and Pharmacotherapeutic group:

- You should first of all include the (invented) name of the medicinal product and the active substance(s) included in it, if necessary, as per section 1 and 2 of the SPC.
- The pharmacotherapeutic group or type of activity as per section 5.1 of the SPC should be stated here using patient understandable language.

Therapeutic indications:

- The therapeutic indications in line with section 4.1 of the SPC should be stated here. It should be stated in which age group the medicine is indicated, specifying the age limits.

Information on the benefits of using this medicine:

- On a case-by-case basis, information on the benefits of the treatment could be included in this section, as long as it is compatible with the SPC, useful for the patient, and to the exclusion of any element of a promotional nature. This could be included under a separate sub-heading, e.g. entitled “How {invented name}works”.

– The information should be depicted in a clear and condensed way. For example, information could relate to:

  - Signs and symptoms of the target disease, in particular for non-prescription medicines, but also for medicines to be taken "on-demand" (e.g. treatment of migraine);
  - The benefit(s) of taking the medicine could be summarised (e.g. "this medicine reduces pain associated with arthritis", "this medicine has been shown to reduce blood sugar, which helps to prevent complications from your diabetes"). This would be particularly important to encourage adherence to the treatment, e.g. for long-term and prevention treatment. Benefit may be described in terms of prevention of disease complications (e.g. anti-diabetic), if established. The timing of the effect may also be described if useful. In any case, information must be compatible with the SPC, in particular section 5.1;
  - Information on the amount of time the medicine usually takes to work may be presented if relevant for the patient (pain-killer, antidepressant, etc).

2. Before you take or use the product

This part should include the following headings:

a. Do not take or use the product

– All contraindications mentioned in section 4.3 of the SPC should be included here in the same order as presented in the SPC. Other precautions and special warnings should be presented in the next section.

– Care must be taken to ensure that complex details are not omitted. It is not acceptable to state only the common or major contraindications. Belief that a patient cannot understand a contraindication is not a reason for omitting it.

b. Take special care with the product

- All warnings and precautions for use included in section 4.4 of the SPC should be provided here (as in the SPC, the order should be in principle determined by the importance of safety information provided) and it should also be made clear for each warning or precaution for use, what action the patient should take to minimise the potential risk.
- Detailed information on warnings and precautions relating to side effects that could occur while a patient is taking the medicine should be presented in section 4 (e.g. symptoms), with an appropriate cross-reference in section 2.
- Warnings relating to interactions, fertility, pregnancy and breast-feeding, the ability to drive and use machines, or excipients should be presented in the relevant subsequent subsections, unless they are of major safety importance (contraindication) in which case they should also be highlighted in the subsection "Do not take/use (inveted name)", above.
- An additional sub-heading could be included for information on additional monitoring tests that the patient will be required to undergo during treatment.
- When the medicine is indicated in children, the warnings and precautions which are specific to this population (and identified as such in section 4.4 of the SPC) should be included under this subheading. Where relevant, parents/carers should also be alerted in this section of potential children/teenager specific warnings included under "driving and using machines".
- If there is no indication in some or all subsets of the paediatric population, information should reflect the paediatric subsection of section 4.2 of the SPC.

c. Taking or using other medicines, herbal or dietary supplements

- Describe the effects of other medicines, herbal or diary supplements on the medicine in question and vice versa as per section 4.5 of the SPC. Refer to other medicines by their pharmacotherapeutic group/type of activity and by their INN(s) (including the lay terms first and the INNs in brackets unless the interaction is only with one active in a class, e.g. "pravastatin (medicine used to lower cholesterol)"), where possible.

- In some cases, where it may be helpful to the patient, you should describe in brief terms the consequence of the interaction. One possibility could be to distinguish the medicine which must not be used with the medicine.
- For those which the combination should be avoided and which the combination would require some precaution (e.g. dose adjustment; in such a case please cross-refer to section 3 of this leaflet). For example, if hormonal oral contraceptives are likely to become ineffective as a result of an interaction, patients should also be advised to use additional forms of contraceptives (e.g. barrier contraceptives).
- Interactions with herbal or alternative therapies should be addressed if mentioned in section 4.5 of the SPC.

d. Taking or using the product with food and drink

- Interactions not related to medicines should be mentioned here if reference is made in section 4.5 of the SPC. For example, patients should not consume milk in combination with tetracyclines and no alcohol should be consumed during treatment with benzodiazepines. This section should not be used to tell patients whether or not their medicine should be taken before, during or after meals as this should only be addressed in section 3 (below), but a cross-reference to section 3 can be included.

e. Fertility, Pregnancy and lactation

- Where the information is significantly different, pregnancy and breast-feeding information can be presented under separate headings.
- Include conclusion summary of the information given in section 4.6 of the SPC.

f. Driving and using machines

- Where there is cautionary advice in section 4.7 of the SPC this should be translated into meaningful colloquial language for the patient.
- MAH should bear in mind that medicines taken by children may need specific advice. For example, regarding road safety, children who may not be old enough to drive may nevertheless cycle.

– The advice should include an explanation as to why the patient is advised not to drive or undertake these tasks, and whether or not they should discuss this with their doctor if they wish to do so.

g. Important information about some of the ingredients of the product

– If appropriate, details of those excipients knowledge of which is important for the safe and effective use of the medicinal product, including relevant warnings for residues from the manufacturing process.

– This subsection should be omitted when the medicine does not contain any excipients of known effect.

3. How to take or use the product

– The following information have to be included:

- Dosage
- Method and/or route(s) of administration
- Frequency of administration

– Additional information might be included here.

- Instructions for proper use
- Duration of treatment

– If you take or use more than you should

- Describe how to recognise if someone has taken an overdose and what to do.

– If you forget to you take or use the product

- Make clear to patients what they should do after irregular use of a product.

– If you stop taking or using product

- Indicate any effects of interrupting or ending the treatment early, if applicable.
- Indicate withdrawal effects when the treatment ends, when necessary.

4. Possible side effects

- Describe the side effects and whenever possible, an estimate of frequency should be provided, expressed in standard category of frequency.
- The section should generally be divided into two sections bearing in mind that there should be sufficient patient-friendly description of the overt clinical signs and symptoms to enable the patient to recognise all side effects which may occur as set out in section 4.8 of the SPC:
    1. The most serious side effects need to be listed prominently first with clear instructions to the patients on what action to take (e.g. to stop taking the medicine and/or seek urgent medical advice. The use of the words “straight away” or “immediately” may be helpful in this context).
    2. Then a list of all other side effects, listed by frequency and starting with the most frequent (without repeating the most serious included above).
- Within each section mentioned above, side effects should be arranged by frequency. The following frequency convention is recommended:
    - Very common: may affect more than 1 in 10 people
    - Common: may affect up to 1 in 10 people
    - Uncommon: may affect up to 1 in 100 people
    - Rare: may affect up to 1 in 1,000 people
    - Very rare: may affect up to 1 in 10,000 people
    - Not known: frequency cannot be estimated from the available data.
- This frequency convention should not appear before the list of side effects as this takes up space and has shown in user testing to be misleading to patients.
- In any case, when expressing the likelihood of side effects it is important to include verbal terms and numerical data, as far as possible. Bear in mind that user testing has

shown that double sided expressions such as “affects more than 1 in 100 but less than 1 in 10” are not well understood and should not be used.

- System organ class listings should not be used. However, patient-friendly terms for parts of the body may be used as headings where the frequency is not known (e.g. for older medicines) in order to break up an otherwise long list, e.g. skin, stomach and gut, etc.

5. How to store the product

- Add directions and warnings related to storing the product (e.g. Keep out of reach of children, Do not use after the expiry date..etc.)

6. Further information

a. What the product contains

- The active substance(s) (expressed qualitatively and quantitatively) and the other ingredients (expressed qualitatively) should be identified.

b. What the product looks like and contents of the pack

- The pharmaceutical form should be stated.
- It is recommended to include a physical description, e.g. shape, colour, texture, imprint, etc. as per section 3 of the SPC.
- All pack sizes for this pharmaceutical form and strength should be detailed here; if appropriate indicate that not all pack sizes may be marketed. A cross-reference to other pharmaceutical forms and strengths may be included.

c. Marketing Authorisation Holder and Manufacturer

d. Leaflet approved date

e. To report any side effect(s):

- **Saudi Arabia:**

- The National Pharmacovigilance Centre (NPC):
  - SFDA Call Center: 19999
  - E-mail: npc.drug@sfda.gov.sa
  - Website: https://ade.sfda.gov.sa/

- **Other GCC States:**

  - Please contact the relevant competent authority.

f. Council of Arab Health Ministers

The following statements issued by the Council of Arab Health Ministers should be printed in the PIL.

This is a Medicament

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers

Union of Arab Pharmacists

g. This patient information leaflet is approved by the Saudi Food and Drug Authority

6. APPENDIXES:

Appendix 1:

Labeling information that are required to be translated into Arabic language (not applicable for medicines used solely in hospitals)

- **المعلومات الواجب ترجمتها على الملصق الخارجي للمستحضر الصيدلاني باللغة العربية**

1. إسم المستحضر التجاري والعلمي وتركيزه
2. الشكل الصيدلاني للمستحضر وحجم العبوة
3. ظروف تخزين المستحضر
4. الشركة الصانعة للمستحضر
5. مالك رخصة التسويق
6. التسعيرة
7. رقم التسجيل

- **المعلومات الواجب ترجمتها على شريط المستحضر الصيدلاني باللغة العربية**

1. إسم المستحضرالتجاري والعلمي وتركيزه

- **المعلومات الواجب ترجمتها على ملصق العبوات الصغيرة (10 مل أو أقل) باللغة العربية**

1. إسم المستحضر التجاري والعلمي وتركيزه
2. ظروف تخزين المستحضر
3. مالك رخصة التسويق
4. التسعيرة
5. رقم التسجيل

Appendix 2:

Inverted Equilateral Black Triangle ▼

Criteria for including a medicinal product in the additional monitoring list

It is mandatory to include the following categories of medicinal products in the additional monitoring list

- Medicinal product authorized that contains a new chemical entity
- Biological medicinal products
- Biosimilar medicinal products
- Products for which a post-authorization safety studies (PASS) was requested at the time of marketing authorization
- Products for which a post-authorization safety studies (PASS) was requested following the grant of marketing authorization
- Registered products that have been granted an approval for a new indication based on phase 2 trials
- Other medicinal product upon request

The initial period of maintenance in the additional monitoring list

The initial period of inclusion in the additional monitoring list is five years.

Rules and responsibilities of the Marketing authorization holder:

- Shall include in the SPC and PIL of their medicinal products subject to additional monitoring the black triangle symbol and the explanatory statement on additional monitoring;
- Shall include information on the status of additional monitoring in any material to be distributed to healthcare professionals and patients and should make all efforts to encourage reporting of adverse reactions, as agreed;

- Shall submit the relevant variation to include/remove the black symbol, the statement, and the explanatory sentence from the SPC and PIL, where applicable.

For more information, please refer to module X in the Good Pharmacovigilance practice (GVP) guideline

REFERENCE

- EudraLex – Volume 2 – Pharmaceutical legislation notice to applicants and regulatory guidelines medicinal products for human use.