MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

PATIENT INFORMATION LEAFLETS (PILs)

This guideline is intended to provide recommendations to applicants regarding Patient Information Leaflets. It represents the Medicines Control Council's current thinking on the provision of information to patients regarding the safety, quality and efficacy of medicines. It is not intended as an exclusive approach. Council reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.
Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

Version 2: First version released for publication	May 2004
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Implementation for new applications for registration	With immediate effect
Implementation for registered products and "Old Medicines"	02 February 2015

REGISTRAR OF MEDICINES
MS M HELA

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1 INTRODUCTION

1.1 Legal Framework

In terms of Section 35 (1) (ix) of the Medicines and Related Substances Act, 1965 (Act 101 of 1965, as amended) (hereinafter 'the Act'), the Minister of Health may, in consultation with the Medicines Control Council, make regulations prescribing the information that must be furnished regarding the use of any medicine or Scheduled substance.

Regulation 10 of the Act requires that each package of a medicine shall have a Patient Information Leaflet (PIL) and prescribes the information that must be contained therein. Regulation 10 also requires that a person dispensing or administering a medicine must ensure that a PIL is made available at the point of such dispensing or administration.

1.2 Purpose of this Guideline

This guideline is intended to provide information and guidance to applicants on the format and data requirements of the Medicines Control Council for the preparation and submission of Patient Information Leaflets (PILs) for evaluation. This guideline is also intended to provide information to applicants on the requirements regarding the legibility, format and content of the PIL for use by consumers, once approved.

The primary objective of this guideline is to ensure that the PIL is written in clear and intelligible terms for the patient and is clearly legible. Applicants are requested to follow the format stipulated in this guideline in conjunction with the provisions set out under Regulation 10 of the Act.

2 REQUIREMENTS FOR SUBMISSION

2.1 Format of submission for evaluation

Patient Information Leaflets for evaluation should be typed using double line spacing and should be in English (British). The print quality of the PIL should be clear so as to enable duplication at a later stage for inclusion into various documents, during the evaluation and registration process. The spelling and grammar in the text of the PIL should be checked thoroughly before submission of the application.

2.2 Language

Although PILs should be submitted in English for evaluation purposes, it is currently a regulatory requirement that a PIL should be made available to consumers in English and in at least one other official language. It is the responsibility of the applicant to ensure that a PIL, once approved, has been appropriately translated and the translation validated, prior to being made available to consumers.

2.3 Reference documents to be supplied

Patient Information Leaflets are evaluated in accordance with the information provided in the approved scientific Package Insert. An application to evaluate a PIL for a registered medicinal product would require that the latest approved Package Insert also be submitted. For new medicine applications, the proposed PIL must be submitted at the same time as the proposed Package Insert. In this case, the PIL will be evaluated in conjunction with the proposed Package Insert, for final approval by Council.

Reference to the Package Insert for each statement in the PIL should be included in a broad margin provided on the right hand side of each page for the purpose of evaluation. Reference to the exact page/s in the Package Insert should be included. No references should, however, be included in the finalised, printed PIL.

An electronic copy (MSWord document) of the Package Insert and the PIL should be included on an appropriate electronic storage device.

2.4 Amendments to approved Patient Information Leaflets

After registration of the medicine, the PIL may not be altered without the approval of Council. When an approved Package Insert is submitted to Council for amendment(s), a corresponding proposed amended PIL and previously approved PIL must be submitted simultaneously.

3 LEGIBILITY OF THE PIL

3.1 Print size and type

The information appearing in the PIL to be provided to the consumer should be printed in English (British) and in at least one other official language and in a type having a minimum legibility as defined in Regulation 10 of the Act.

3.2 Syntax

Lengthy sentences (i.e. more than 20 words) should be avoided. Where appropriate, bullet points should be used. A group of bullet points should be introduced with a colon and a single full stop should be placed at the end of the group. A list of bullet points should begin with the uncommon and specific case and end with the common or general case, unless this is inappropriate for the medicine.

For example:

Tell your doctor or pharmacist if you suffer from:

- tuberculosis of the lungs
- any allergies that affect your lungs
- any chronic lung condition.

A minimum number of words should be used in the bullet points and not more than one sentence for each bullet point. There should be no more than nine items where the bullet points are simple and no more than five when these are complex. Abbreviations should be avoided. Pronouns (e.g. 'it') should be used in preference to repeating the name of the medicine, provided the context clarifies what the pronoun refers to.

4 FORMAT OF THE PIL

4.1 Headings

Headings and sub-headings in the PIL and the order of the headings should be in line with the model template (see Section D of this document). Headings and sub-headings should be made conspicuous. More than two levels of headings may impair legibility.

4.2 Content

The information contained in the PIL must be in accordance with the Package Insert for the medicine **but the text must be phrased so that it is readily intelligible for the patient**. Where a specialised term is used, an explanation should be given. Repetition of information can sometimes be avoided by cross-referring to information that is under another heading. Information not relevant to the patient should be omitted.

4.3 Style

An active and direct style should be used, by placing the verb at the beginning of the sentence, for example:

- '*take* one (*1) tablet*' instead of '*1 tablet should be taken*',
- '*you should…*' is better than '*it is recommended…*'
- '*give one (1) medicine measureful...*' where a medicine is clearly indicated for children only

4.3 Style - continued

This principle should be adapted as, for example, in the case of '*If ... then*' instructions, such as: '*If you feel ill, tell your doctor or pharmacist*'.

This guidance on style may not be appropriate in all languages, nor for all medicines (e.g. those which are not self-administered).

Pictograms may be used as an additional measure if they make the message clearer to the patient, but be without any element of a promotional nature.

4.4 Product ranges

There should be a separate PIL for different pharmaceutical forms.

In the event of a medicine falling in two different schedules, a separate package insert should be submitted for each schedule. [Also refer to the Proprietary Names Guideline]

5 MODEL PIL

This section contains a model template for developing a Patient Information Leaflet. Applicants are requested to follow the format stipulated in this section in conjunction with the provisions set out in Regulation 10 of the Act.

Explanatory notes

An example of a model leaflet is presented in this Section, containing headings and text, which should be used together with examples of text formulated in consumer-intelligible language.
For the purpose of explaining this model leaflet, the following tools are used:

- **bold type** for the headings
- normal type for text which is either mandatory or usually relevant and is not a heading
- possible options which applicants should adapt e.g. for the relevant pharmaceutical dosage form, route of administration or population for which the medicine is intended (e.g. the mother of a child) are presented with a slash, e.g. take / give / use / are given / receive / administered
- text included **[*in italics*]** are explanatory notes. When these notes are taken out of the model PIL template, all relevant and mandatory text will remain

In this model all of the headings are numbered. However, for certain medicines, the headings may not all be relevant. In such instances, the corresponding headings should be omitted.

Throughout the text, "X" indicates the (proprietary) name of the medicinal product.

PATIENT INFORMATION LEAFLET

In the case of a complementary medicine the following shall be included:

- a statement identifying the discipline of the medicine: and
- if the medicine has not received registration with the Medicines Control Council the disclaimer "This medicine has not been evaluated by the Medicines Control Council. This medicine is not intended to diagnose, treat, cure or prevent any disease."

SCHEDULING STATUS

[The Scheduling status of the medicine as it appears in the Package Insert]

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

[The proprietary name of the medicinal product (referred to as X throughout this document) and the active ingredient(s) should be stated here in bold, followed by the strength and pharmaceutical form (i.e. as it appears in the Package Insert). This should be followed by the INN or common name of the active substance (as stated in the package insert).]

*[For medicinal products available **only** on prescription]*

Read all of this leaflet carefully before you start taking / using / are given X

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- X has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

*[For medicinal products available **without** a prescription]*

Read all of this leaflet carefully because it contains important information for you

X is available without a doctor's prescription, for you to treat a mild illness. Nevertheless you still need to use X carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Do not share X with any other person.
- Ask your pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve after (number of) days.

1. WHAT X CONTAINS

[Full statement of the active substance(s) and excipient(s)]

[The active substance(s) (expressed qualitatively and quantitatively) and the other ingredients (expressed qualitatively) should be identified using their names as given in the Package Insert and in the language of the text: e.g.]

- The active substance is…
- The other ingredients are… *[These should be listed alphabetically. This should be in lower case, except at the start of a sentence and when it is a registered proprietary name e.g. Colourant®. If a preservative or alcohol (2 % or more) is present, the content of each must be indicated as required for the Package Insert*]

2. WHAT X IS USED FOR

[The pharmacotherapeutic group or type of activity should be stated here using language intelligible to

the patient, followed by the registered indications for use of the medicine, as accepted by Council.]

3. BEFORE YOU TAKE / USE / ARE GIVEN / ADMINISTERED X

Do not take / give / use / You should not be given / administered X:

- if you are hypersensitive (allergic) to (active substance) or any of the other ingredients of X. *[Include reference to residues, excipients, etc, if applicable]*
- if you ..

[Absolute contraindications]

[Information on absolute contraindications, in accordance with the Package Insert, should be provided here in patient-intelligible language. This should include chronic accompanying diseases (e.g. kidney insufficiency, liver insufficiency, diabetes and other metabolic diseases), contraindications due to interactions with other medicinal products, contraindications due to excipients and specified conditions for certain categories of users , e.g. children or the elderly.]

[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.]

[For a medicine which is not self-administered]

Tell your doctor or healthcare professional before being given the injection if:

Take special care / Special care should be taken with X:

- if you ...
- when ...

[Information, in patient-understandable language, on relative contraindications, warnings and appropriate special precautions for use should be provided here. Care must be taken to ensure that complex details are not omitted and that they are expressed in a way that consumers can understand. It is not acceptable to include only the more common or major warnings/special precautions.]

[A special precaution should be presented as implying the action a patient should take, rather than as factual information that describes a medical condition. The influence of the medicine on the patient's behaviour should be described. A differentiation should be made between the influence on cognitive abilities, reactivity and judgment.]

[Examples:]

- If you have asthma (or used to), because X can bring on an attack
- If you are over 60…
- If X is given to children…
- X may make you sleepy

[Also describe cases (if any) in which the consumer should only use X after consultation with a medical practitioner. Include (as appropriate and if not mentioned in the previous section) reference to chronic accompanying diseases (renal insufficiency, liver insufficiency diabetes and other metabolic diseases).]

[Where applicable, provide information on necessary examinations, which may be carried out by the medical practitioner prior to, or during, the therapy, for example tests carried out in order to exclude contraindications. Provide information (if there is any) about important symptoms which may be masked by the medicine or if the medicine influences laboratory values. If relevant, reference should be made here to possibilities for intolerance to various materials (e.g. disposable plastic syringes), which must be used as part of the medicine.]

[Refer to the need for the avoidance of external influences, such as sunlight after the use of phototoxic medicines. Other warnings concerning for example other diseases and the influence of the medicine on behaviour should be described. Statements should also include for example, reference to discolorations of underwear as a result of changes in the colour of urine and stool.]

Taking / Using / Receiving X with food and drink:

Interactions not related to medicinal products should be mentioned here. For example, patients should not consume milk in combination with tetracyclines and no alcohol should be consumed during treatment with benzodiazepines and other central nervous system depressants.]

Pregnancy and Breastfeeding:

[Include information given in the Package Insert, in patient-understandable language. The following additional statement must be included:]

If you are pregnant or breastfeeding your baby ~~while taking / having this medicine,~~ please consult your doctor, pharmacist or other healthcare professional for advice before taking this medicine.

Driving and using machinery:

[Examples of some useful statements:]

- X may make you feel drowsy/sleepy
- Do not drive because X could interfere with your ability to drive safely
- Do not operate any tools or machines

Important information about some of the ingredients of X:

[If appropriate, details of those excipients for which it is important for the safe and effective use of the medicinal product. Information on intolerances to excipients (e.g. lactose monohydrate), including alcohol should be provided. Indicate "sugar free" if applicable.]

Taking / Giving / Using other medicines with X:

[The following statement must be included:]

Always tell your healthcare professional if you are taking any other medicine.
(This includes complementary or traditional medicines.)

~~If you are taking / using other medicines on a regular basis, including complementary or traditional medicines, the use of X with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice.~~

[Describe the effects of other medicinal products on the medicine in question and vice versa. Reference should be made to the intensification/weakening and the prolonging/shortening of effects. This information should be in line with the Package Insert.]

4. HOW TO TAKE / USE / RECEIVE X

Do not share medicines prescribed for you with any other person.

[The following statements should be included, where applicable:]

Always take X exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose is...

*[For medicinal products available **only** with a prescription, a statement such as the following should be included:]*

Your doctor will tell you how long your treatment with X will last. Do not stop treatment early because …

If you have the impression that the effect of X is too strong or too weak, tell your doctor or pharmacist.

*[For medicines available **without** prescription:*

In particular and if at all possible, for medicines available without a prescription, precise statements should be included on the usual duration of the therapy, the maximum duration of the therapy and intervals with no treatment, together with clear guidance on when to consult a doctor.]

[The instructions for proper use and the intended dosage ranges (individual and daily doses separately), as well as the maximum daily dose, the frequency, method, route of administration and the duration of treatment, should be stated if relevant. In addition, it may be necessary to explain the route of administration in consumer-intelligible language.]

[The text should be structured according to indication, age and sex, taking organic disorders into account. Reference should also be made here to a dosage reduction in case of renal insufficiency and/or liver insufficiency.]

[*Instructions should:*

- *be used to tell consumers what to do. They should not be used to justify or explain an action.*
- *be described in a practical manner.*
- *tell consumers how to use the medicine properly.*
- *be positive rather than negative, whenever possible. Negative instructions should only be used when the consumer should avoid specific actions.*
- *be given as separate instructions when the consumer is to carry out two separate actions. Separate actions should not be compressed into a single sentence.*
- *be numbered and put into the exact order that the consumer should follow.*
- *usually be intelligible without explanations, so as not to overburden consumers with information.]*

[*Explanations should be used to expand on the reasons for instructions and not to give further information. Instructions may be presented in italics or other type with explanations in plain type, so as to give consumers a guide as to the significance of the information.]*

[When applicable, there should be descriptions (if useful with illustrations) of opening techniques for child-resistant containers and other containers to be opened in an unusual manner.]

[Some examples of statements that may be included here:]

- *Take the tablets with a sufficient quantity of liquid (e.g. one glass of water)*
- *…one or two tablets (500 to 1 000 mg of paracetamol) three times a day, this means a daily maximum of six tablets (3 000 mg of paracetamol)'*
- *…in the morning, at lunchtime, immediately before meals, with food, after food'*
- *Do not swallow*
- *Do not chew*
- *Shake well before use*
- *Dissolve the effervescent tablet in one glass of water. Then drink the contents of the whole glass'*
- *Take X once a day, every day, at about the same time each day*
- *Taking your tablets at the same time each day will have the best effect on your blood pressure. It will also help you remember when to take the tablets*

- *Allow to reach room temperature before using (e.g. insulins)*

[For medicines not self-administered]

[The route of administration should be included]

[Include]

You will not be expected to give yourself X. It will be given to you by a person who is qualified to do so.

If you take / use / more X than you should:

[Description of signs and symptoms of overdosage that the patient is able to recognize and actions to be taken]

[The following statement must be included:]

In the event of overdosage, consult your doctor or pharmacist. If neither is available, ~~seek help at~~ contact the nearest hospital or poison control centre.

[For medicines not self-administered]

[The following may be acceptable:]

Since a healthcare professional will administer this medicine, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to take / missed a dose of X:

[Provide clear explanations of what should be done following irregular use of the medicinal product, e.g.:]

Do not take / receive a double dose to make up for forgotten individual doses.

Effects when treatment with X is stopped:

[Indicate any effects of interruption or ending treatment early, if applicable. Indicate withdrawal effects when the treatment ends, if applicable]

5. POSSIBLE SIDE EFFECTS

[A description of the side effects should be provided. Begin this section with:]

X can have side effects.

[Describe, if necessary, the actions to be taken. If the patient needs to seek help urgently use the term 'immediately'; for less urgent conditions use the phrase 'as soon as possible'.]

[The following statement must be included:]

Not all side effects reported for X are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.

[The information given on side effects should be in accordance with the Package Insert. Side effects should be subdivided according to seriousness and frequency, or according to symptom type. Wherever possible, for all side effects the frequency with which they occur must be mentioned to allow patients to know the risk. Irrespective of their frequency, very serious, side effects of the medicine should be mentioned first or specially emphasised. This applies in particular to side effects where there is an urgent need to take action.]

[The risk (frequency) of side effects may be presented using the terms "frequent" or "less frequent" if the information is available in the corresponding package insert. Descriptors such as "common", "rare", etc. should not be used.]

[The following is an example of side effects grouped according to seriousness:]

If any of the following happens, stop taking X and tell your doctor immediately or go to the casualty department at your nearest hospital:

- 'swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing',
- 'rash or itching',
- 'fainting',
- 'yellowing of the skin and eyes, also called jaundice'.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to X. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- chest pain,
- angina,
- changes in the way your heart beats, for example, if you notice it beating faster,
- difficulty breathing,
- signs of recurrent infections such as fever or sore throat,
- less urine than is normal for you,

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

- nausea (feeling sick),
- abdominal cramps or stomach pains,
- headache,
- dizziness,
- tiredness,
- light-headedness,
- dry cough,
- muscle cramps,
- flatulence or wind,
- diarrhoea,
- loss of appetite.

[Should there be side effects that occur at the beginning of the treatment and then subside or that only occur after prolonged treatment, these are to be mentioned here. The measures to be taken to remedy or at least alleviate the side effects should be mentioned here, if relevant. If the consumer needs to seek help urgently, use the term 'immediately'. For less urgent conditions use the phrase 'as soon as possible'.]

[Close this section with:]

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF X

[The following statement must be included in this section:]

~~Keep~~ Store all medicines out of ~~the~~ reach ~~and sight~~ of children.

[Where applicable, the following statements may be included:]
[Storage conditions have to concur with that approved in the package insert]

- Store at or below X °C *[Explain ideal storage environment]*
- Store at 2 °C – 8 °C (in a refrigerator)
- Store in a freezer
- Do not refrigerate / freeze [as appropriate]
- Store in the original package / container
- Keep the container in the outer carton
- Keep the container tightly closed
- There are no special storage instructions for this medicine

[An additional short explanation of the storage conditions, in patient-friendly terms, should be included when appropriate, e.g.:]

- Protect from light / moisture
- Do not store in a bathroom
- Do not use after the expiry date stated on the label / carton / bottle

[Where applicable, shelf life after reconstitution, dilution or after first opening the container should be indicated]

[Where appropriate, include a warning against any visible signs of deterioration]

Do not use X if you notice (*description of the visible signs of deterioration*)

[Information on how to dispose of unused medicine, e.g.:]

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF X

[*In accordance with information provided in the Package Insert, include the pharmaceutical form, the number, volume or mass per package unit, pack size and a description of the packaging material, e.g. bottle, blister pack, etc*.]

8. IDENTIFICATION OF X

[*A physical description, e.g. shape, colour, texture, imprint, etc, of the dosage form should be included here in accordance with the Package Insert Information*.]

9. REGISTRATION NUMBER/REFERENCE NUMBER

[As in the Package Insert]

10. NAME AND ADDRESS OF REGISTRATION HOLDER

[As in the Package Insert]

11. DATE OF PUBLICATION

[As in the Package Insert]

UPDATE HISTORY

Date	Reason for update	Version & publication
	In-house working documents	v1
May 2004	First publication released for implementation	v2 May 2004
Sept – Dec 2012	Amendments to sections: A3; A4; B1; B2; C2; C4; Scheduling Status, Proprietary name, Strength and pharmaceutical form; What X contains; Before you take/use/are given X; How to take/use/receive X; Possible side-effects; Deletion of text in sections: B2; C1; C4; D; E	v3 Dec 2012
Dec 2012	Date of implementation	
Dec 2013	Amendment of section 5 in line with Regulations published in Government Notice R.860, GG37032 of 15 Nov 2013	v4 Dec 2013
With immediate effect	Implementation for new applications for registration	
02 February 2015	Implementation for registered products and "Old Medicines"	