

APPENDIX 7 POINTS TO CONSIDER FOR SINGAPORE LABELLING

Labelling refers to any printed or graphic information on the immediate container, outer packaging and any other form of printed material supplied together with the product.

The product labels, PI and/or PIL must be in English. If non-English text is included in the labelling, applicants must provide an official statement to declare that the non-English text is complete, accurate and unbiased information and is consistent with the English text.

Information provided in the labels should be consistent with the information submitted in the application dossier. Any discrepancies should be highlighted and brought to HSA’s attention.

1 OUTER CARTON AND INNER/BLISTER LABELS

The ‘outer carton’ refers to the product packaging in which the immediate packaging is placed, e.g. the carton box containing blister strips. The ‘inner label’ refers to the label that is fixed onto the primary container closure system, e.g. the label affixed to a bottle, vial or ampoule. The ‘blister label’ refers to the foil backing of a blister strip.

In addition to the legal labelling requirements, the following information shall be present on the labelling of the product:

	Parameters	Outer Carton	Inner Label	Blister Label
1.	Product Name	✓	✓	✓
2.	Dosage Form	✓	✓*	NA
3.	Name of Active Substance(s)**	✓	✓	✓
4.	Strength of Active Substance(s)	✓	✓	✓
5.	Batch Number	✓	✓	✓

6.	Manufacturing Date	✓	✓*	NA
7.	Expiry Date	✓	✓	✓
8.	Route of Administration	✓	✓	NA
9.	Storage Condition	✓	✓*	NA
10.	Name & Address (or Logo) of Product Owner and/or Product Registrant	✓	✓*	Name/Logo of Manufacturer/ Product Owner/Product Registrant
11.	Name & Address of Manufacturer***	✓	✓*	NA
12.	Warnings (if applicable)	✓	✓*	NA
13.	Pack Sizes (unit or volume)	✓	✓	NA
14.	Special Labelling (if applicable)	✓	✓*	NA
15.	Name & Content of preservative(s) (if applicable)	✓	✓*	NA

NA Not applicable

* Exempted for small labels such as an ampoule or vial with a nominal volume of 10 ml or less. Other factors may be considered such as the amount of information which needs to appear on the label and the font size necessary to achieve legibility of the information.

** When the active substance is present as a salt, this should be clearly indicated, e.g. “each tablet contains 60mg active substance (as citrate) or each tablet contains 10mg active substance hydrochloride” etc. This statement is optional for inner labels and blisters. However, the name and strength of active ingredient must be indicated on the inner label and blister.

*** The words “Batch released by” instead of “Manufactured by” may be used if the site named is responsible for product release. The name and address of either the manufacturer or the batch releaser should be present.

If the product is supplied without an outer carton, the information that is required on the outer carton should be stated on the inner label.

Information that is required should be printed on the labels and the use of overstickers is generally not allowed. In circumstances where overstickering cannot be avoided, the applicant should consult the relevant HSA officer or email

HSA_TP_Enquiry@hsa.gov.sg. However, redressing (e.g. use of colour stickers) to facilitate product differentiation may be acceptable and the revised product labels should be submitted for registration.

The outer carton labels for products with different strengths, dosage forms, or formulations should be adequately differentiated (e.g. by using different colour schemes) to minimise confusion and medication errors.

Where practicable, the name and strength of the product should appear over each blister pocket or be oriented centrally across the pack. It is important that the particulars remain available to the user up to the point at which the last dose is removed from the blister pack. Often it will not be possible to apply all the information over each blister pocket, consequently where a random display of the information is proposed it should frequently appear across the pack.

The draft artwork, specimen or mock-up of the outer carton and inner/blister labels submitted in the dossier should be consistent with the format, design and colour that are to be printed. Handwritten information on the artwork, specimens, mock-ups or text is not acceptable, with the exception of statements such as “batch number and expiry dates will be printed” or similar.

Email addresses and telephone numbers on the product’s labelling are acceptable, as long as the intent of such inclusions is non-promotional. However, the inclusion of website addresses is generally not allowed.

QR codes or 2D barcodes on the product’s labelling which are intended for logistics control are allowed. However, the inclusion of QR codes or 2D barcodes with links to internet websites or other information sources is not allowed.

2 PACKAGE INSERT (PI)

Package inserts are required for products classified as Prescription Only Medicines.

The PI is regarded as a document that contains information that will ensure the safe and effective use of the therapeutic product. It includes a scientific, objective account of the medicine's usefulness and limitations based on the data submitted in the application dossier. Information in the PI shall be non-promotional in nature.

The following information is required for the PI:

- (a) Brand or Product Name – as indicated in PRISM.
- (b) Name and Strength of Active Substance(s) – the non-proprietary name of each therapeutically active drug substance.
 - When the active substance is present as a salt, this should be clearly indicated, e.g. “each tablet contains 60mg active substance (as citrate) or each tablet contains 10mg active substance hydrochloride” etc.
- (c) Product Description – a description of the relevant physical and chemical characteristics of the drug product and its formulation(s).
 - A description of the appearance of the product (colour, markings etc.) should be given.
 - In cases of tablets designed with a score line, information on the purpose of the score-line should be given, e.g. ‘the score line only serves to facilitate breaking for ease of swallowing and does not divide the tablet into equal half-doses’, or ‘the tablet can be divided into equal halves’.
 - Information on pH and osmolarity should be provided (if applicable).
 - In cases of products to be reconstituted before use, the appearance before reconstitution should be stated. If a diluent/ solvent is part of the therapeutic product, a physical description of diluent/solvent should be stated.
 - A list of excipients contained in the product, which may include preservatives, pH adjuster, excipient mixture (e.g. list of ingredients of film coating, capsule shell, printing ink, flavouring agent, colourants, diluent/solvent, etc.) should be provided.
- (d) Pharmacodynamics/Pharmacokinetics – information to be mentioned in this section include:

- The ATC code, if available;
 - The pharmacokinetic and pharmacological action(s), particularly in humans, of each drug substance;
 - Clinical trial information relating to clinical efficacy and safety; and
 - Relevant pharmacogenetic information from clinical studies with data showing a difference in benefit or risk to a particular genotype or phenotype.
- (e) Indication – the therapeutic indication(s) of the product.
- (f) Recommended Dosage – the information required include, as appropriate:
- Dosing regimen (dose and interval);
 - Information on dose adjustments in special populations, e.g. elderly, children, renal insufficiency, hepatic insufficiency and concomitant disease;
 - Maximum recommended/tolerated daily dose and the maximum dose for an entire course of therapy;
 - Advice relevant for dosage adjustment from monitoring of clinical symptoms and signs and/or laboratory investigations, when appropriate, with cross-references to other sections where appropriate;
 - Other pertinent information, such as relationship to meals and compatibility with other drugs and fluids; and
 - Reference to a dosing regimen for an unregistered product or unapproved indication is not acceptable.
- (g) Mode/Route of Administration – only standard abbreviations should be used. Non-standard or complicated routes of administration should be carefully explained in full to avoid confusion, particularly when the product is made available for self-selection.
- In cases of products for reconstitution, the appearance of the product after reconstitution should be stated. As appropriate, the information on in-use shelf-life after dilution or reconstitution or first opening should be provided in this section or the section “Shelf life”.
- (h) Contraindications – situations where patients should never or generally not be treated with the medicine. In rare cases where the medicine should never be

given, this must be explicitly stated. Information on the presence of residual quantities of potentially allergenic materials used in the manufacturing of the product should be stated.

- (i) Warnings and Precautions – circumstances where caution is required to ensure the safe and efficacious use of the product. Information on the presence of residual quantities of potentially allergenic materials used in the manufacture of the product should be stated. A warning statement on the risks associated with the switching of products (between the biosimilar product and the reference product) during treatment is to be included in the package insert of the biosimilar product.
- (j) Interactions with Other Medicines and Other Forms of Interaction – information on clinically relevant interactions and other potentially serious interactions based on the pharmacology of the medicine.
- (k) Use during Pregnancy/Lactation
- (l) Adverse Effects/Undesirable Effects – provides an indication of severity, clinical importance and frequency, whenever possible. A description of the adverse reaction based on the MedDRA terminology is preferred.
- (m) Overdose and Treatment – symptoms, signs and recommended treatment of overdose or accidental poisoning.
- (n) Incompatibilities (for injections only)
- (o) Storage Condition – if included in the PI, the storage condition must be consistent with that stated on the product label and/or outer carton.
- (p) Shelf Life – if included in the PI, the shelf life must be consistent with that stated on the product label and/or outer carton.
- (q) The information on in-use shelf-life after dilution or reconstitution or first opening should be provided (if applicable).
- (r) Dosage Form or Presentation – this refers to the available dosage form(s), formulation(s), strength(s) and/or pack size(s).
 - All pack sizes should be listed. Reference should be made to the primary container closure system (e.g. glass vials, PVC/Aluminium blister, Alu/Alu blister, HDPE bottle, ampoule, etc.).

- Any other components should be listed (e.g. desiccant, swabs, needles, etc.).
- The primary container closure system of the diluent/solvent provided with the drug product should also be described.
- The statement '*Not all presentations may be available locally*', or equivalent, must be stated if this section includes unregistered presentations.

(s) Name and Address of Manufacturer or Product Owner or Product Registrant

3 PATIENT INFORMATION LEAFLET (PIL)

Patient Information Leaflets (PILs) are required for Pharmacy Only and General Sale List therapeutic products. The PIL must be easily understood and be consistent with the product labels and/or PI, as appropriate. The following information is required in the PIL:

(a) Name of Product – as indicated in PRISM.

(b) Description of Product

- A description of the appearance of the product (colour, markings, etc.) should be given.
- In cases of tablets designed with a score line, information should be given on the purpose of the score-line, e.g. 'the score line only serves to facilitate breaking for ease of swallowing and does not divide the tablet into equal half-doses', the tablet can be divided into equal halves'.
- A list of excipients, which may include preservatives, excipient mixture (e.g. list of ingredients of film coating, capsule shell, printing ink, flavouring agent, colourants, etc.) should be provided.

(c) What is the medicine?

(d) Name and strength of active

- When the active substance is present as a salt, this should be clearly indicated, e.g. “each tablet contains 60mg active substance (as citrate)” or “each tablet contains 10mg active substance hydrochloride”.
- (e) What is this medicine used for?
- (f) How much and how often should you use this medicine?
- (g) When should you not take this medicine?
- (h) Undesirable effects/side effects
- (i) What other medicine or food should be avoided whilst taking this medicine?
- (j) What should you do if you miss a dose?
- (k) How should you keep this medicine?
- (l) Signs & symptoms of overdose
- (m) What to do when you have taken more than the recommended dosage?
- (n) Name/logo of manufacturer/importer/product registrant
- (o) Care that should be taken when taking this medicine?
- (p) When should you consult your doctor?

If the product is sold without a PIL, the information that is required in the PIL must be stated on the outer carton.

REVISION HISTORY

Guidance Version (Publish Date)

TPB-GN-009-000 (uploaded 31 October 2016)