POINTS TO CONSIDER FOR CLASS 2 CTGTP 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 cell, tissue and gene therapy product (CTGTP).

The CTGTP labels, package insert (PI) and/or patient information leaflet (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 LABELS

The 'outer carton' refers to the CTGTP packaging in which the immediate packaging is placed, e.g., the carton box containing vials. The 'inner label' refers to the label that is fixed onto the primary container closure system, e.g., the label affixed to a freezing bag, glass vial or syringe.

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

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

6.	Expiry Date	✓	✓
7.	Route of Administration	✓	✓
8.	In relation to an autologous CTGTP, Unique Patient Identifier and the statement “For autologous use only” or similar wordings	✓	✓
9.	Storage Condition	✓	✓*
10.	Name & Address (or Logo) of Product Owner and/or Product Registrant and/or Manufacturer	✓	✓*
11.	Warnings (if applicable)	✓	✓*
12.	Pack Sizes (unit or volume)	✓	✓
13.	Special Labelling (if applicable)	✓	✓*
14.	Name & Content of Excipients, including preservative(s) (if applicable)	✓	✓*

NA Not applicable

* Exempted for small labels such as a 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 contains cells, the strength should be expressed on the basis of the general term “cells” which in this section is considered to define cells that exert a therapeutic effect.

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

The outer carton labels for CTGTP with different strengths, dosage forms, or formulations should be adequately differentiated (e.g., by using different colour

schemes) to minimise confusion and medication errors.

The draft artwork, specimen or mock-up of the outer carton and inner 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.

Email addresses, website addresses and telephone numbers on the CTGTP's labelling are acceptable, as long as the intent of such inclusions is non-promotional.

2 PACKAGE INSERT (PI)

The PI is regarded as a document that contains information that will ensure the safe and effective use of the CTGTP. It includes a scientific, objective description of the CTGTP's clinical and safety details 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 CTGTP Name.

(b) Name and Strength of Active Substance(s) – the non-proprietary name of each therapeutically active substance.

- When the active substance contains cells, the strength should be expressed on the basis of the general term "cells" which in this section is considered to define cells that exert a therapeutic effect.

(c) CTGTP Description – a description of the relevant physical and chemical characteristics of the CTGTP and its formulation(s).

- A description of the appearance of the CTGTP (colour, free of visible particulate matter, etc.) should be given.
- Information on pH and osmolarity should be provided (if applicable).
- In cases of CTGTPs to be reconstituted before use, the appearance before reconstitution should be stated. If a diluent/ solvent is part of the CTGTP, a physical description of diluent/solvent should be stated.
- A list of excipients contained in the CTGTP, which may include preservatives, cryopreservative, pH adjuster, excipient mixture (e.g., 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 CTGTP;
- 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 CTGTP.

(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 clinical safety management 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 compatibility with other drugs and fluids; and
- Reference to a dosing regimen for an unregistered CTGTP or unapproved indication is <u>not</u> 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.

- In cases of CTGTPs for reconstitution, the appearance of the CTGTP 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 CTGTP. In rare cases where the CTGTP 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 CTGTP should be stated.

(i) Warnings and Precautions – circumstances where caution is required to ensure the safe and efficacious use of the CTGTP. Information on the presence of residual quantities of potentially allergenic materials used in the manufacture of the CTGTP should be stated. Any precaution relating to the disposal of any unused CTGTP or any waste derived from the CTGTP (where appropriate) and any available collection system for the unused CTGTP or waste should be included.

(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 CTGTP.

(k) Use in specific populations - Pregnancy/Lactation/Females and males of reproductive potential/Paediatric use/Geriatric use

(l) Adverse Effects/Undesirable Effects – provides an indication of severity, clinical importance and frequency, whenever possible, of the adverse reactions identified from the clinical trials experience and also during the post approval use (if applicable). A description of the adverse reaction based on the MedDRA terminology is preferred. Immunogenicity data to be included.

(m) Nonclinical safety data/toxicology – Carcinogenesis, Mutagenesis, Impairment of Fertility

(n) Overdose and Treatment – symptoms, signs and recommended treatment of overdose or accidental poisoning.

(o) Incompatibilities (for injections only)

(p) Storage Condition – if included in the PI, the storage condition must be consistent with that stated on the CTGTP label and/or outer carton.

(q) Shelf Life – if included in the PI, the shelf life must be consistent with that stated on the CTGTP label and/or outer carton.

(r) The information on in-use shelf life after dilution or reconstitution or first opening should be provided (if applicable).

(s) 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 vial, syringe, freezing bag, etc.).
- Any other components should be listed (e.g., needles, applicator, catheter etc.).
- The primary container closure system of the diluent/solvent provided with the CTGTP should also be described.
- The statement '*Not all presentations may be available locally*', or equivalent, must be stated if this section includes unregistered presentations.

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

3 PATIENT INFORMATION LEAFLET (PIL)

The PIL is not a mandatory document for Class 2 CTGTP. If PIL is provided, it must be easily understood and be consistent with the CTGTP labels and/or PI, as appropriate. The PIL may include the following information:

(a) Name of CTGTP.

(b) Description of CTGTP

- A description of the appearance of the CTGTP (colour, free of visible particulate matters, etc.) should be given.
- A list of excipients, which may include preservatives, cryopreservative, excipient mixture (e.g., diluent/solvent) should be provided.

(c) What is the CTGTP?

(d) Name and strength of active substance

- When the active substance contains cells, the strength should be expressed on the basis of the general term "cells" which in this section is considered to define cells that exert a therapeutic effect.

(e) What is this CTGTP used for?

(f) How is this CTGTP administered?

(g) What do you need to know before and/or after you are administered this CTGTP?

(h) Possible undesirable effects/side effects

(i) What other medicine or food should be avoided whilst using this CTGTP?

(j) Name/logo of manufacturer/importer/product registrant

(k) When should you consult your doctor?

REVISION HISTORY

Version	Date of publication	Amendment Summary
1	Oct-2024	This document GN-ATPB-1-3 Version 1 replaces the previous document ATPB-GN-007-002 dated March 2024.