Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Updates to medicine labelling rules

Public consultation on proposed changes to TGO 91 and TGO 92 to support medicine safety

Version 1.0, May 2024

Confidentiality
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Overview

Purpose

The Therapeutic Goods Administration (TGA) is seeking feedback on proposed changes to the rules for Australian medicine labels.

Medicines entered in the Australian Register of Therapeutic Goods (ARTG) for supply in Australia must comply with the requirements for labels set out in:

- Therapeutic Goods Order No. 91 - Standard for labels of prescription and related medicines (TGO 91)
- Therapeutic Goods Order No. 92 - Standard for labels of non-prescription medicines (TGO 92).

TGO 91 and TGO 92 were implemented in 2016 with a four-year transition period that ended on 31 August 2020. These new rules helped to make important information easier to find on medicine labels.

Certain aspects of these labelling rules need further improvements to help medicines be used correctly and safely. We want to know if you think the rules we are proposing will support medicine safety.

Scope

This consultation is about 3 medicine safety related matters identified as needing action before we review the labelling rules more broadly.

We will conduct further public consultation about more improvements to labelling rules in the future as part of a 'sunsetting' review. Most legislative instruments are automatically repealed 10 years after commencement under the *Legislation Act 2003*. This automatic repeal is called 'sunsetting' and helps to make sure legislative instruments stay up to date. TGO 91 and TGO 92 are due to sunset on 1 October 2026 which gives an opportunity to review and update requirements to help make sure the instruments are still fit for purpose.

Have your say

We are seeking your views on proposed changes to medicine labelling rules to address 3 safety related matters.

The aim of the proposed amendments to TGO 91 is to:

- Make sure that quantities of active ingredients in injectable medicines intended for electrolyte replacement are clearly expressed in units important to health professionals (Part 1).
- For medicines for injection administered by healthcare professionals that need some preparation before use, make sure that clear instructions on how to prepare and store these products is available to health professionals in an appropriate format (Part 2). This is to support the recent changes to the Product Information (PI) as a package insert for injectable products.
  - We are particularly seeking feedback from health professionals on a proposal to allow a QR code to link to electronic information instead of a separate package insert where preparation information cannot fit on the label.

The aim of the proposed amendments to TGO 92 is to:

- Improve information on listed medicine labels about large solid oral dosage forms intended to be swallowed whole (Part 3).

We want to know if you think the proposals support the safe and quality use of medicines[1].

Your feedback will help to inform how certain information will be displayed on medicine labels in the future.

We invite you to give your feedback by completing our online survey on the TGA Consultation Hub to answer the questions in the 3 parts of this consultation paper. You are welcome to give us feedback on all parts of this consultation, or only on the parts that are important to you. We will publish responses on the TGA Consultation Hub, unless you request that your response be kept confidential.

Depending on the feedback received on this consultation, we may also seek further feedback from respondents on proposals. If you are happy to be contacted, please let us know in the online survey.

If you have any questions about this consultation, please contact TGA.Scientific@health.gov.au.

Background

Medicine labels

Medicine labels communicate information to health professionals and consumers that is critical to support the correct and safe use of medicines. If it is difficult to identify medicines, or to locate and understand critical information, then medication errors are more likely to occur.

The TGA updated Australian medicine labelling rules in 2016 to help make it easier to find important information. We did this after reviewing requirements in collaboration with stakeholders including medicine sponsors and health professionals.

Changes to medicine labels take time. When we update labelling rules, we allow medicine sponsors time to update labels to support the medicine's availability in the community. New labels usually appear gradually as new stock is distributed, and existing stock is sold.

Labelling that supports the safe and quality use of medicines is part of the intended outcomes of Australia's National Medicines Policy. Quality use of medicines is sometimes explained as the correct use of medicines.[2] Along with medicine safety, it is a National Health Priority. Quality use of medicines includes choosing treatment options, choosing suitable medicines, and using medicines safely and effectively. More information is available in the National Medicines Policy and National Strategy for Quality Use of Medicines.

Rules for medicine labels

Labelling requirements for medicines supplied in Australia are set out in:

- Therapeutic Goods Order No. 91 - Standard for labels of prescription and related medicines (TGO 91)
- Therapeutic Goods Order No. 92 - Standard for labels of non-prescription medicines (TGO 92).

TGO 91 and TGO 92 are standards made under section 10 of the *Therapeutic Goods Act 1989*.

TGO 91 and TGO 92 were implemented in 2016 and replaced Therapeutic Goods Order No. 69 - General requirements for labels for medicines (TGO 69). Medicine sponsors were given 4 years to comply with the new rules. Medicines released for supply from 1 September 2020 had to comply with the rules set out in TGO 91 and TGO 92.

[1] More information about the quality use of medicines is available in Australia's National Medicines Policy and National Strategy for Quality Use of Medicines.
[2] National Medicines Policy - plain language version

Guidance to help support sponsors and manufacturers of medicines to meet TGO 91 and TGO 92 requirements is available on the TGA website. See Medicine labels: Guidance on TGO 91 and TGO 92.

There are some other rules for the labelling and packaging of medicines that we are not seeking feedback on in this consultation such as:

- The Poisons Standard which sets the level of control on the availability of poisons, including rules on certain advertising, labelling and packaging requirements.
- Therapeutic Goods (Medicines - Standard for Serialisation and Data Matrix Codes) (TGO 106) Order 2021 which includes rules about the display of information in data matrix codes on the medicine label.
- The rules for displaying the AUST R, AUST L or AUST L(A) number on a medicine label outlined in the Therapeutic Goods Regulations 1990.

Updating medicine labelling rules

From time to time, we need to update or improve labelling rules to support the correct and safe use of medicines.

Clear medicine labels are an important factor in the safe and quality use of medicines. Developing and updating rules for medicine labels to achieve clear labels across different types of medicines can be complex. Labelling rules need to be well considered to avoid introducing inconsistencies, or unintended risks to medicine safety.

2023 targeted consultation

We carried out targeted consultation in August to September 2023 on priorities for future improvements to medicine labels to support the safe and quality use of medicines. The feedback we received will help us plan and prepare for the 'fit-for-purpose' sunsetting review of TGO 91 and TGO 92.

We also took the opportunity in the targeted consultation to get some comments (on expressing quantities of active ingredients in injectable medicines and large oral dosage forms) to help us develop the proposals included in this consultation paper.

In the targeted consultation, we asked if more matters should be addressed before we start the sunsetting review. We considered all feedback before deciding which matters to address now. There was some feedback asking us to address more matters before the sunsetting review. We are not planning to address all of these suggested matters now because:

- Some matters are large, complex, or involve multiple parts or interrelated issues. Considering and addressing these issues will take a long time and need extensive consultation. We will aim to include these matters in the sunsetting review where possible.
- Considering and addressing more or many matters may delay the safety related changes proposed in this consultation.
- Some matters raised may need new legislation or amendments to legislation outside of TGO 91 and TGO 92.

Thank you to everyone who provided feedback in the targeted consultation. We look forward to receiving your feedback as part of this public consultation.

Proposed changes to labelling rules

The proposed changes to TGO 91, TGO 92 and guidance are outlined in 3 parts:

- Part 1: Expressing quantities of active ingredients in injectable medicines intended for electrolyte replacement in units important to health professionals.
- Part 2: Instructions for preparation of injectable products administered by healthcare professionals.
- Part 3: Improving information on listed medicines about large solid oral dosage forms intended to be swallowed whole.

Part 1: Expressing quantities of active ingredients in injectable medicines intended for electrolyte replacement in units important to health professionals

In this part, we will step you through the current rules for expressing active ingredient quantity on labels for injectable medicines intended for electrolyte replacement. We discuss a range of challenges that need to be carefully considered and form the basis of the proposed changes to TGO 91 and guidance. This is outlined in the following sections:

- Rules for expressing active ingredient quantity in injectable medicines intended for electrolyte replacement
- Considerations for updating labelling rules about units of quantity for injectable medicines intended for electrolyte replacement
- Proposed changes to TGO 91 to align with clinical use of medicines intended for electrolyte replacement
- Proposed updates to guidance to align with clinical practice for medicines intended for electrolyte replacement.

Rules for expressing active ingredient quantity in injectable medicines intended for electrolyte replacement

Potassium[3] and other concentrated electrolytes for injection (magnesium, calcium, and hypertonic sodium chloride) are considered high risk medicines, including by the Australian Commission on Safety and Quality in Health Care (ACSQHC)[4].

In clinical practice in Australia, concentrations and doses of these medicines is often based in millimoles (mmol). However, paragraph 11(2)(f) of TGO 91 requires that the quantity or proportion of the active ingredients for these medicines for injection must be expressed as the 'stated weight' in the total volume of the injection. Medicines greater than 100 millilitres (mL) that are intended for electrolyte replacement are required to express quantity in millimole in the stated volume (in subparagraph 11(2)(f)(ii) of TGO 91), but medicines that are 100 mL or less do not have this requirement.

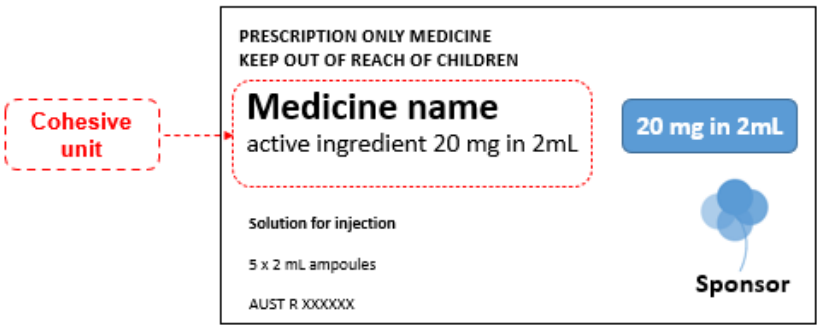
The TGA has been alerted to the potential safety risk of these labelling rules not allowing the clinically relevant unit of quantity to be displayed prominently for some active ingredients. As health care clinicians are most familiar with concentration and doses of these medicines specified in millimole, rather than in grams or milligrams, expression of quantity only in weight may cause confusion and has the potential to lead to medication errors and harm to patients.

[3] High-Risk Medicines - Clinical Excellence Commission (nsw.gov.au)
[4] High risk medicines | Australian Commission on Safety and Quality in Health Care

Medicine sponsors can include quantity in millimoles as extra information on the label for electrolyte medicines that are 100 mL or less, but this is not mandatory. Small label space on some medicines and other important requirements in TGO 91 can limit the ability for sponsors to include non-mandatory information.

For example, subsection 9(3) requires that the name of the medicine, active ingredients and quantity of active ingredients appear as a 'cohesive unit' on the main label[5] without interruption of additional information, except in certain circumstances (Figure 1). This is to help health professionals and consumers to easily identify active ingredients. Therefore, quantity in millimoles is not permitted in the prominent cohesive unit on many labels of medicines intended for electrolyte replacement under TGO 91 (either as the only quantity expression or as an equivalent quantity expression that interrupts the cohesive unit).

Figure 1: Cohesive unit of name of the medicine, active ingredients and quantity of active ingredients[6]



The 'cohesive unit' on a medicine label displaying name of the medicine, active ingredient and quantity of active ingredient without interruption of extra information. This example is the 'main label' of a 'primary pack'[7].

There are other examples of injectable medicines where the clinically relevant unit of active ingredients is not weight. However, many of these are biological medicines, for example, insulin and heparin, which are permitted to express quantity of active ingredients in International Units (IU) because paragraph 11(3) of TGO 91 includes requirements for either weight or potency units. Antibiotic preparations, where potency units are used as a measure of activity, are also permitted to express quantity in International Units (IU), under paragraph 11(2)(g) of TGO 91.

The TGA has been working with individual medicine sponsors of relevant medicines on this safety matter in the interim before a clearer solution is implemented. We encourage medicine sponsors to prominently display millimole concentrations for injectable medicines intended for electrolyte replacement that are routinely prescribed in millimoles. Interim measures have included the TGA approving Section 14 consents to supply medicines that do not comply with certain aspects of the labelling rules but express active ingredients in clinically relevant units. This means that some of these medicines currently in supply may not reflect all the requirements of TGO 91.

[5] 'Main label' is defined in TGO 91 as:
(a) where there are two or more labels or two or more portions of a single label - that label or portion of the label where the name of the medicine is more or most conspicuously shown; or
(b) where the name of the medicine is equally conspicuous on two or more labels or portions of a label – each label or portion.

[6] Please note: Images of medicine labels have been included in this consultation paper to help illustrate considerations for updating rules. Images are examples only. Images may not be to scale and may not satisfy all requirements for all medicine labels.

[7] The 'primary pack' is defined by the *Therapeutic Goods Act 1989* as 'the complete pack in which the goods, or the goods and their container, are to be supplied to consumers'. For more information see 'Should rules be consistent for the label on the container and the primary pack?'

Considerations for updating labelling rules about units of quantity for injectable medicines intended for electrolyte replacement

Updates to the labelling rules and guidance are needed to support standard clinical practice. We want to make sure that quantities of active ingredients are clearly expressed in units important to health professionals on medicine labels. Updates are also needed to give clarity to sponsors of affected medicines for injection to support medicine safety. Potential changes to the labelling rules or guidance need to be carefully considered. We want to continue to support consistency in terminology to describe strength and safe expression of concentrations.

Considerations for updates to labelling rules to address this matter include the below.

Which medicines should new rules be made for?

It is challenging for medicine labelling rules to support consistency but also account for all different types of medicines, including future medicines. There are other regulatory options if rules cannot be made to account for all types of medicines, but these may involve extra fees for the medicine sponsor. For example, if medicines cannot meet the requirements outlined in TGO 91, medicine sponsors can apply for consent to supply medicines that do not comply with a standard under section 14 of the *Therapeutic Goods Act 1989* for individual products.

To make new rules we need to find out the medicines for injection that may need clear expression of active ingredient quantity in millimoles (and where rules do not currently support this).

Electrolytes in injectable medicines with a volume of 100 mL or less include potassium, magnesium, calcium, sodium, phosphate, and chloride. Examples of medicines intended for electrolyte replacement containing these electrolytes include:

- potassium – potassium chloride, potassium acetate, potassium phosphate and ‘potassium dihydrogen phosphate’ medicines
- magnesium – magnesium sulfate, magnesium chloride
- calcium – calcium gluconate, calcium chloride
- sodium – sodium acetate, sodium chloride (including 20% and 23.4% sodium chloride)
- phosphate – sodium phosphate medicines, (potassium phosphate and ‘potassium dihydrogen phosphate’ medicines that also contain the electrolyte potassium).

Where possible, we want to limit new rules to affected medicines where health professionals agree that certain units should be displayed prominently. We also want to focus on developing rules to address issues that have arisen, or for medicines particularly recognised as high risk such as intravenous potassium.[8]

Should all medicines intended for electrolyte replacement be expressed in millimoles in the ‘cohesive unit’?

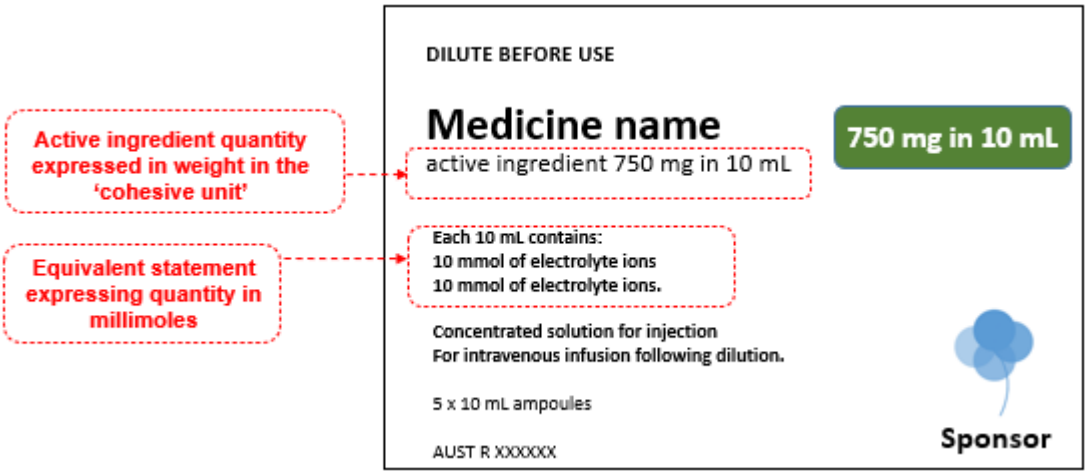
Weight in cohesive unit

While the prescribing and administration of medicines for injection intended for electrolyte replacement is often based in millimoles, there are some medicines where clinical guidelines also refer to quantity in weight or other units. For example, sodium chloride medicines are commonly referred to by the weight-based percentage of sodium chloride (such as ‘sodium chloride 20%’ or ‘23.4%’). There are also some medicines that may be used both for electrolyte replacement and treatment of other conditions. For example, magnesium sulfate may be prescribed in millimoles for treating hypomagnesaemia but prescribed in weight for treating pre-eclampsia.

[8] High-Risk Medicines - Clinical Excellence Commission (nsw.gov.au)

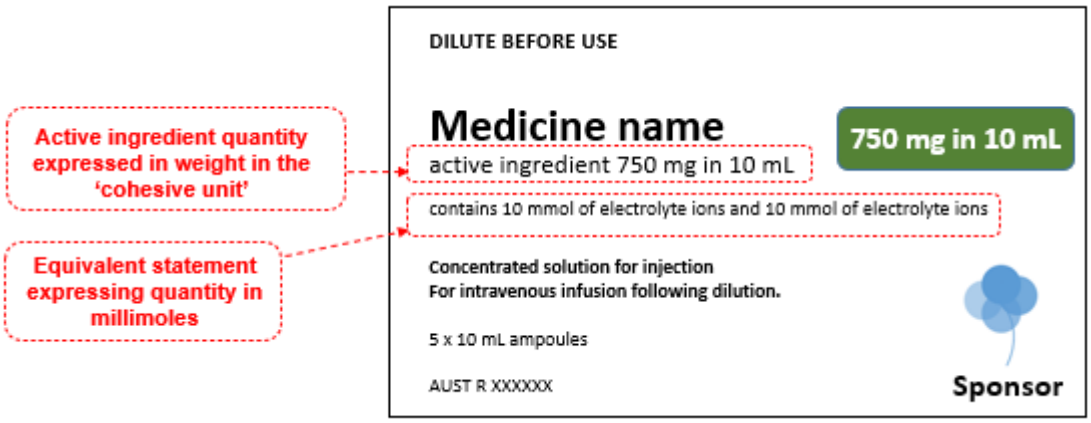
Many medicines intended for electrolyte replacement are currently expressing active ingredients in weight (in the stated volume) in the 'cohesive unit'. Extra information about the equivalent quantity in millimoles (commonly abbreviated as ‘mmol’) is often included in the middle or lower part of the label (for example, like Figure 2A and Figure 2B below). However, this extra information is not mandatory.

Figure 2A: Example 1 of a medicine label expressing quantity of active ingredients in weight, with extra information about quantity in millimoles below the ‘cohesive unit’[6]



Quantity of active ingredient is expressed in weight. A statement to describe the equivalent quantity of electrolytes in millimoles in the stated volume is below the ‘cohesive unit’ as extra information. The equivalent statement is presented below the cohesive unit in a list style stating ‘Each 10 mL contains: 10 mmol of electrolyte ions, 10 mmol of electrolyte ions’. This example is the ‘main label’ of a ‘primary pack’.

Figure 2B: Example 2 of a medicine label expressing quantity of active ingredients in weight, with extra information about quantity in millimoles below the ‘cohesive unit’[6]



Quantity of active ingredient is expressed in weight on a main label of a primary pack. A statement to describe the equivalent quantity of electrolytes in millimoles is below the ‘cohesive unit’ as extra information. The equivalent statement is not directly expressed in the stated volume but is in relation to the stated volume by stating immediately below the cohesive unit ‘contains 10 mmol of electrolyte ions and 10 mmol of electrolyte ions.

For some injectable medicines, health professionals might consider labels displayed like Figure 2A or 2B as satisfactory or appropriate. If so, some current medicine labels may not need to change (where compliant with the requirements of TGO 91). Unnecessary changes to medicine labels can cause confusion and risks not supporting medicine safety. We want to ensure that any changes to medicine

labels (from updating the rules) support medicine safety and provide clarity. We could update rules to make sure sponsors continue to include extra information about quantity in millimoles on the label.

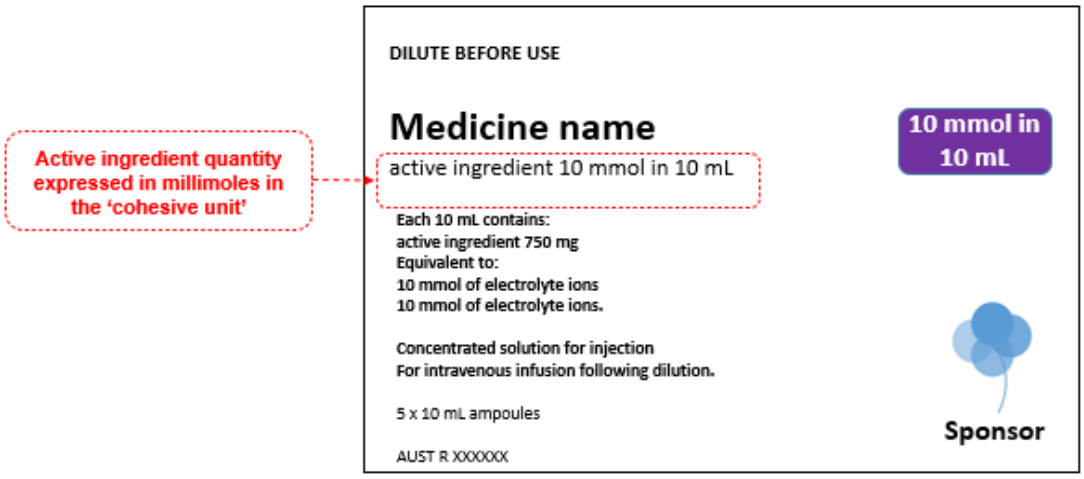
For some medicines, it may be beneficial for the active ingredient to be expressed in weight in the cohesive unit with a clear equivalent statement in millimoles below the cohesive unit (like Figure 2A and 2B). For example, for medicines with multiple types of electrolyte ions of different quantities or multiple active ingredients. Health professionals may also be familiar with active ingredients expressed in this way.

Some medicines refer to the weight-based percentage concentration in the medicine name. In these cases, it could be beneficial for medicines to continue to include the weight in the stated volume somewhere on the label to clearly show the meaning of the percentage. For example, that the medicine be called 'medicine name 50%' because it contains 5 g of the active ingredient in 10 mL[9].

Millimoles in cohesive unit

For some injectable medicines intended for electrolyte replacement, labels presented like Figure 2A or 2B may not be considered suitable by health professionals. Health professionals may want some medicines to have a more prominent display of quantity in millimoles to support medicine safety, for example, potassium chloride. This may include expressing the quantity of active ingredients in millimoles in the cohesive unit (Figure 3).

Figure 3: Example of medicine label expression quantity of active ingredients in millimoles in the 'cohesive unit' (with extra information about quantity in weight and quantity of individual electrolytes below the cohesive unit)[6]



Expressing active ingredients in millimoles in the 'cohesive unit' on the main label of a primary pack. An equivalent statement is included below the cohesive unit. In this example, the equivalent statement is expressed in weight in stated volume and includes quantity of individual electrolytes in millimoles.

Volume of the medicine

Another consideration is the total volume of the electrolyte medicine. For example, some electrolyte medicines with a volume of 100 mL might be supplied as a vial or bottle. Others may be supplied in a flexible bag container like some medicines intended for electrolyte replacement greater than 100 mL that have separate labelling rules for expressing quantity in millimoles. (See Rules for expressing active ingredient quantity in medicines for injection intended for electrolyte replacement and other medicines). We need to consider if the proposed new rules are suitable for the affected

[9] Weight/ volume percentage concentration (w/v%) is calculated by dividing the mass of the solute in grams by volume of solution in millilitres and then multiplying it by 100. For example, 5 g/ 10 mL x 100 = 50%.

medicines with a volume of 100 mL or less. However, we also want to limit changes to the rules before we start the broader sunsetting review. Rules need to be well considered to avoid introducing inconsistencies, or unintended risks to medicine safety.

Should all medicines intended for electrolyte replacement (100 mL or less) be expressed in both millimoles and weight? If so, how?

Health professionals may prefer labels of medicines intended for electrolyte replacement to include quantities of active ingredients in both millimoles and weight to allow for differences in prescribing. This may be especially important for medicines that may be prescribed in different quantity units for different indications (such as magnesium sulfate).

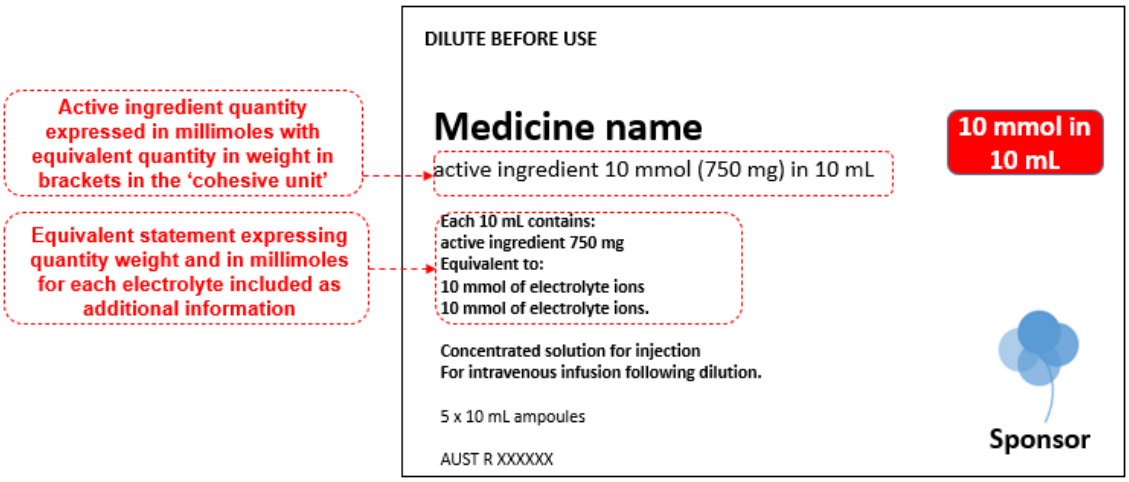
Most respondents who provided feedback on this topic in the 2023 targeted consultation generally supported requiring both the clinically relevant unit and weight on the label. Some respondents specified that they supported both if space allowed on the label. But some respondents preferred only the clinically relevant unit on all labels to support simpler medicine labels or because of concerns that dual units could cause confusion.

If medicines should be expressed in multiple units of quantity, we want to provide clear rules or guidance to medicine sponsors on how this is best displayed to avoid confusion when medicines are selected and administered in clinical practice.

Figure 2A, Figure 2B and Figure 3 (above) give examples of including one unit of quantity in the 'cohesive unit' with an equivalent statement below the cohesive unit. Requiring quantities of active ingredients to be expressed in both millimoles and weight in this way may be difficult on some medicines with limited label space. We need to consider the medicines that might not be able to display both quantities in this way. For these medicines, what is the essential quantity information and how is this best displayed to support medicine safety? For example, is the quantity of potassium chloride in weight essential information for health professionals? If it is, does extra information in the 'cohesive unit', such as an equivalent quantity in brackets, support medicine safety? For example, 'potassium chloride 10 mmol (750 mg) in 10 mL'.

The cohesive unit requirements are intended to help health professionals and consumers to easily identify active ingredients. We need to consider if interrupting the cohesive unit with an equivalent quantity in another unit has the risk of causing confusion. If it is appropriate to interrupt the cohesive unit for certain medicines to support medicine safety, we also need to consider if rules should be consistent across different sized medicines and different types of packaging. See Figure 4 below for an example of an equivalent statement in the cohesive unit. (For more information about considerations for different packaging, see Should rules be consistent for the label on the container and the primary pack?).

Figure 4. Example of label including active ingredient quantity in millimoles with equivalent quantity in weight in brackets in the 'cohesive unit' (with example of continuing to include equivalent statement below the cohesive unit expressing the millimoles of each electrolyte)[6]



Active ingredient expressed in millimoles and weight in the cohesive unit on a medicine label. This is an example of a main label on a primary pack where an equivalent statement would fit below the cohesive unit.

Should rules be consistent for the label on the container and the primary pack (of the same medicine)?

The current rules for expressing quantity of active ingredients in medicines for injection are for the label on both the container and primary pack, and any intermediate packaging.

The 'container' is the packaging that comes into direct contact with the medicine, such as a vial or ampoule. The 'primary pack' is defined by the *Therapeutic Goods Act 1989* as 'the complete pack in which the goods, or the goods and their container, are to be supplied to consumers'. More information about packaging definitions is available at Medicine packaging definitions for sponsors.

The primary pack label is generally larger and may be able to include more information than the container label. But it is important that essential information is included on the container in case it is separated from the primary pack. For example, when a vial is removed from a pack of 5 vials to be administered to a patient.

TGO 91 already includes some allowances for injections with a small capacity. Less information is required on labels of these containers and this information can be presented in smaller text sizes. (This is where the container is enclosed in a primary pack that complies with the full requirements). For more information, see subsection 10(4) and 10(5) of TGO 91 and Medicine labels: Guidance on TGO 91 and TGO 92.

In the 2023 targeted consultation, some respondents stated that weight may not be needed on the container for some of these medicines but that it should be available on the primary pack. Other feedback preferred consistency in how active ingredient quantity is expressed on the container and primary pack of the same medicine.

How do we develop new labelling rules to support consistency of strength information and medication safety?

Rules for expression of strength are intended to provide consistency and minimise risk of errors associated with certain expressions such as ratios and percentages which attract unnecessary calculation. Labels should provide consistent strength information for all medicines containing the same active ingredient. This is important for identifying and selecting medicines. It can also be important for consistency of information in electronic health care systems (for example, in electronic prescribing systems).

A discussed above, different approaches for different medicines intended for electrolyte replacement may be appropriate. See Should all medicines intended for electrolyte replacement be expressed in millimoles in the 'cohesive unit'? An option is to create rules to allow medicine sponsors the choice to express quantity of active ingredients in medicines for electrolyte replacement in either weight or millimoles, to align with clinical practice. But this may not provide clear rules for medicine sponsors and could lead to inconsistent strength information for medicines containing the same active ingredient.

Specific rules for certain active ingredients or types of medicines may be a more appropriate option to support consistency of information on labels and support medicine safety. Rules would need to be well considered and may need to be limited to certain medicines to avoid multiple complex rules and risk of creating inconsistent requirements.

What else needs to be updated if we update the rules for these medicines for injection?

Before we update specific rules about expressing quantities of active ingredients in injectable medicines, we also need to consider if there are other related rules or guidance that will also need to be considered. Examples include:

- Interrelated rules such as the cohesive unit requirements of subsection 9(3) of TGO 91. For more information see Rules for expressing active ingredient quantity in medicines for injection intended for electrolyte replacement and Should all medicines intended for electrolyte replacement (100 mL or less) be expressed in both millimoles and weight?
- Best practice recommendations for potassium for injection or infusion in Medicine labels: Guidance on TGO 91 and TGO 92. These recommendations may need an update to support medicine safety and to align with new proposed rules. For example, the recommendation to also display the strength of potassium for infusion after dilution in millimoles/ litre may not be considered appropriate by health professionals.

Proposed changes to TGO 91 to align with clinical use of medicines intended for electrolyte replacement

Based on the considerations outlined above and the initial feedback we received during the 2023 targeted consultation, we are proposing to amend the TGO 91 rules to support certain medicines to express active ingredients in both millimoles and weight on the label.

For medicines intended for electrolyte replacement with a volume of 100 mL or less, we propose to:

- Require the quantity of potassium chloride to be expressed in millimoles in the total volume of the injection (in the cohesive unit). Also require a statement below the cohesive unit to state the equivalent quantity of potassium chloride in weight, where space permits.
  - For more details see Expressing quantities of potassium chloride in injectable medicines intended for electrolyte replacement with a volume of 100 mL or less below.
- Continue the current requirements for all other active ingredients (those that are not potassium chloride) to be expressed in stated weight in the total volume of the injection in the cohesive unit. But also require a statement below the cohesive unit to state the equivalence in millimoles.
  - For more details see Expressing quantities of other active ingredients in injectable medicines intended for electrolyte replacement with a volume of 100 mL or less below

This proposal will help make sure that quantities of active ingredients are clearly expressed in units important to health professionals on labels of medicines intended for electrolyte replacement, and give clarity to medicine sponsors.

Health professionals are familiar with the abbreviation ‘mmol’ for millimoles on medicine labels. We propose that the unit ‘mmol’ would continue to be considered acceptable for expressing quantity in millimoles under the new proposed rules.

We plan to update Medicine labels: Guidance on TGO 91 and TGO 92 as part of these proposals to give medicine sponsors guidance on the new rules and to help make sure equivalent statements are clear and prominent. See Proposed updates to guidance to align with clinical practice for medicines intended for electrolyte replacement and Appendix A.

In developing these proposals, we considered reasons to change or continue rules for expressing quantity of active ingredients (in the cohesive unit) for several medicines. A summary of these considerations is included in Appendix B.

We are proposing a transition period of 2 years to allow medicine sponsors time to update their labels. This would mean that medicines released for supply 2 years after the rules started would need to follow the new rules. New labels may not appear for some time after this as new stock is distributed and existing stock is sold.

More details about the proposed requirements are included below.

Expressing quantities of potassium chloride in injectable medicines intended for electrolyte replacement with a volume of 100 mL or less

We propose to include the following requirements in TGO 91 for medicines for injection with a volume of 100 mL or less intended for electrolyte replacement containing potassium chloride:

- The quantity or proportion of potassium chloride must be expressed as the number of millimoles in the stated volume of the injection in the container.
- A statement must be included below the cohesive unit on the main label to state the equivalent quantity of potassium chloride in weight (in the stated volume of the injection or in relation to the stated volume of the injection), where space permits.

This would require potassium chloride to be expressed in millimoles in the cohesive unit like in Figure 3. Figure 3 also shows one example of how an equivalent statement below the cohesive unit might be expressed.

We propose that where space does not permit an equivalent statement in weight below the cohesive unit for potassium chloride medicines, that labels do not have to include information about quantity in weight. This would mean that labels of small containers (such as vials or ampoules), for example ‘potassium chloride 10 mmol in 10 mL’, may not include information that this is equivalent to 750 mg.

We want to hear your views on the following questions about this proposal for potassium chloride medicines. In one of the questions, we are seeking your views about interrupting the cohesive unit. For more information on key considerations about this see Should all medicines intended for electrolyte replacement (100 mL or less) be expressed in both millimoles and weight? and Should rules be consistent for the label on the container and the primary pack (of the same medicine)?

Part 1 Consultation questions

1. Do you agree with the proposed new requirements for expressing quantity of potassium chloride in medicines for injection intended for electrolyte replacement with a volume of 100 mL or less? Please explain your answer and let us know if you think the proposed requirements support the safe and quality use of medicines. Please give us feedback on different parts of the proposed rules including:
    a. Requiring the quantity of potassium chloride to be expressed in millimoles in the stated volume of the injection in the cohesive unit. Please note we propose to consider the abbreviated unit ‘mmol’ for millimoles suitable on medicine labels.

b. Requiring an equivalent statement below the cohesive unit, where space permits, to display information about equivalent quantity in weight.
c. Where space does not permit an equivalent statement below the cohesive unit, that information about equivalent quantity in weight is not required on the label. Please tell us your thoughts including:
    i. Do you think the quantity of potassium chloride expressed in weight is essential information on labels of small vials or ampoules?
    ii. If you think the quantity of potassium chloride in weight is essential information, how do you think this information should be displayed on medicines with limited label space? Do you think interrupting the cohesive unit with a brief equivalent statement in weight in brackets (where label space does not permit an equivalent statement to be included below the cohesive unit) supports medicine safety or could cause confusion. An example of interrupting the cohesive unit with equivalent quantity in weight is 'potassium chloride 10 mmol (750 mg) in 10 mL'.
    iii. If you think that interrupting the quantity of potassium chloride in millimoles with the equivalent quantity in weight in brackets (where space does not permit an equivalent statement below the cohesive unit) supports medicine safety, do you think the primary pack should also include quantity in weight in brackets in the cohesive unit to align with a container?

Expressing quantities of other active ingredients in injectable medicines intended for electrolyte replacement with a volume of 100 mL or less

We propose that active ingredients in medicines intended for electrolyte replacement with a volume of 100 mL or less (that are not potassium chloride) would continue to be required to be expressed in weight in stated volume in the cohesive unit according to TGO 91.

We also propose to include the following new requirement in TGO 91 for medicines for injection with a volume of 100 mL or less intended for electrolyte replacement (where the active ingredients are not potassium chloride);

- A statement must be included below the cohesive unit on the main label to state the equivalent quantity of the active ingredients in millimoles (in the stated volume of the injection or in relation to the stated volume of the injection).

This would require the quantity of active ingredients to be expressed like that in Figure 2A or 2B, with an equivalent statement below the cohesive unit.

We propose that this new requirement would not include the statement 'where space permits'. We propose that the quantity of the active ingredients in these medicines must always be included in both weight and millimoles (in stated volume) on labels. This is to make sure information about quantity in millimoles is always included on the label. It is also to support circumstances where both quantity in weight and millimoles can be clinically important (for example, for magnesium sulfate). We also want to align with current labels of these medicines where possible and appropriate.

This proposal is consistent with the current cohesive unit requirements in 9(3) of TGO 91. This means that for many labels of medicines intended for electrolyte replacement, an equivalent quantity in millimoles would continue to not be permitted to interrupt the cohesive unit. We welcome your feedback on this.

We propose the equivalent statements like in Figure 2A and 2B would both be suitable. Therefore, the requirement should be either in the stated volume or clearly in relation to the stated volume. For example, the statement in Figure 2B states 'contains 10 mmol of electrolyte ions and 10 mmol of electrolyte ions'. It does not directly include the stated volume but as it is immediately after 'active ingredient 750 mg in 10 mL', it may be interpreted as being in the stated volume.

Part 1 Consultation questions continued

2. Do you agree with the proposed requirements for expressing quantity of active ingredients in medicines for injection intended for electrolyte replacement with a volume of 100 mL or less (that are not potassium chloride). Please explain your answer and let us know if you think the proposed requirements support the safe and quality use of medicines. Please give us feedback on different parts of the rules including:
    a. Continuing to require the quantity of active ingredients in these medicines to be expressed in weight in the stated volume of the injection in the cohesive unit. In your feedback, please let us know if you do not agree with our considerations included in Appendix B. Please let us know if you think other medicines intended for electrolyte replacement with a volume of 100 mL or less should have been considered.
    b. Requiring an equivalent statement in millimoles in stated volume below the cohesive unit for these medicines. Please note we propose to consider the abbreviated unit 'mmol' for millimoles suitable on medicine labels. Please tell us your thoughts including:
        i. If you agree that equivalent statements like in Figure 2A and 2B would both be suitable and if the statement would not need to directly include the stated volume if it was clear that the statement was in relation to the stated volume.
        ii. If you think there would be challenges with meeting these requirements. Please give examples to explain your answer.
        iii. Any feedback you may have on our intention to not make any changes to the current cohesive unit requirements in 9(3) of TGO 91 for these medicines.

3. Do you agree with the proposed transition period of 2 years for the new requirements to allow sponsors time to update medicine labels? Please explain your answer.

Proposed updates to guidance to align with clinical practice for medicines intended for electrolyte replacement

Guidance on proposed new requirements for electrolyte replacement medicines

To help medicine sponsors understand and meet the proposed new requirements, we plan to update Medicine labels: Guidance on TGO 91 and TGO 92.

We propose that guidance on the new requirements will include that equivalent statements should be:

- clear
- prominent
- where possible, immediately below the cohesive unit.

Proposed guidance for medicine sponsors on proposed rules is included in Appendix A.

Part 1 Consultation questions continued

4. Do you think the proposed guidance in Appendix A to support the proposed new requirements is clear and easy to understand? Please explain your answer. Please note, as health professionals are familiar with the abbreviation 'mmol' for millimoles on medicine labels, examples in the guidance are expressed with the unit 'mmol'. For example, 'potassium chloride 10 mmol in 10 mL'. Please let us know if you think that 'mmol' should instead be written in full as 'millimoles' on labels.

Other proposed changes to labelling guidance

We also plan to make other minor changes to Medicine labels: Guidance on TGO 91 and TGO 92 to support the proposed new requirements. This includes changes to the best practice recommendations in '3.4.9 Potassium for injection or infusion'.

In section 3.4.9, we intend to remove the recommendation to also include the strength of potassium in millimoles/ litre as this is inappropriate, especially for small volumes. We do not intend to recommend strength should also be included in millimoles per millilitre (mL). While this could be helpful for calculations in some situations (for example, where there is a need for less than the total vial or ampoule), this could lead to confusion if misread. Most health professionals using these medicines are most familiar with these products in their stated total volume. For example, 'potassium chloride 10 mmol in 10 mL'. Also, there is limited space on many of these medicines. Recommending more information to be included could reduce the readability of essential information. The most important strength or concentration information on the label of these medicines is often considered to be the total quantity in the stated total volume of the container.

Part 1 Consultation questions continued

5. Do you agree with the proposed updates to guidance in Appendix C? Please explain your answer and let us know if you think it supports the safe and quality use of medicines. Please let us know if you have any suggestions to improve this or other sections of the guidance related to expressing quantities of active ingredients in injectable medicines in units important to health professionals.

6. Please tell us if you have any other comments about expressing quantities of active ingredients in injectable medicines in units important to health professionals.

Part 2: Instructions for preparation of injectable products administered by healthcare professionals

In this part, we discuss the recent changes to Product Information (PI) as a package insert and why we are proposing changes to TGO 91 and guidance about providing instructions for preparation. This is outlined in the following sections:

- Removal of Product Information inserts
- Package inserts for providing instructions for preparation and storage information for prepared products

- Accessing instructions for preparation information in different ways
- Proposed changes to rules and guidance for providing instructions for preparation for injectable medicines administered by healthcare professionals.

We are particularly seeking feedback from health professionals on a proposal to allow a QR code to link to electronic instructions for preparation, instead of a separate package insert, where preparation information cannot fit on the label.

Removal of Product Information inserts

From 1 September 2023, injectable products administered by healthcare professionals are not required to come with a printed copy of the Product Information (PI) in the package of the product.

The TGA made this decision following public consultation. Reasons for no longer requiring a hard copy of the PI in these products include:

- Printed PI documents included in products have a risk of becoming out of date and may be missing important safety information. Accessing PI documents online means the latest version is being viewed.
- The electronic PI is accessible through different platforms and devices. Electronic PI documents may allow faster access to the required information.
- Environmental impact of printing PI documents (which may be about 10-35 pages long). The need to include a large document in the carton can also increase package size.

However, some injectable products administered by healthcare professionals may still need to include a package insert to comply with TGO 91.

Package inserts for providing instructions for preparation and storage information for prepared products

Some injectable products require preparation before use such as diluting or reconstituting. Instructions on how to prepare these products (for example, how to dilute concentrated injections and how to reconstitute powders for injection), and store the prepared products, need to be available to health professionals to make sure products are correctly prepared and stored. This is important to ensure the safety and efficacy of these medicines.

Paragraph 8(1)(l) of TGO 91 explains the requirements for medicine labels when the medicine needs preparation before use. If there is not enough space on the label, the instructions for preparation can be included in a package insert in the primary pack[10] of the medicine, if there is a statement on the label to say the instructions are in an insert.[11]

Subsection 8(1) of TGO 91 states:

Subject to the qualifications and requirements specified in sections 9 and 10 below, the labels of a medicine must include:

And paragraph 8(1)(l) states:

if the medicine requires some preparation, such as dissolving, suspending, diluting or reconstituting before use - instructions for its preparation and, where relevant, a statement of the conditions of storage and the maximum period of storage between preparation and use, except where:

[10] The 'primary pack' is defined by the *Therapeutic Goods Act 1989* as 'the complete pack in which the goods, or the goods and their container, are to be supplied to consumers'.
[11] Note: Preparation steps are not required on injections in small or very small containers in some circumstances but are recommended to be included where possible. See 2.2.3 Injections in Medicine labels: Guidance on TGO 91 and TGO 92 and subsections 10(4) and 10(5) of TGO 91.

(i) there is insufficient space on either the label of the container or the primary pack, or both, to include this information; and

(ii) this information is set out in a package insert provided in the primary pack of the medicine; and

(iii) a statement is included on whichever label on the container, or the primary pack, or both, that does not set out the information itself, that those instructions are set out in the package insert;

In many cases for injectables administered by healthcare professionals, instructions for preparation and storage information as required by paragraph 8(1)(l) was included in the PI to allow for a single package insert.

Guidance is available on the TGA website for medicine sponsors of injectables administered by healthcare professionals about ensuring compliance after removing the product information insert. It includes the option of replacing the PI document with a new package insert to provide the instructions for preparation where there is not enough room on the label. The guidance provides a suggested package insert template for providing instructions for preparation, conditions of storage, and the maximum period of storage between preparation and use. Some improvements to the guidance or template may be needed to give more clarity to medicine sponsors.

Product Information (PI) documents are written by the pharmaceutical company responsible for the medicines and have been approved by the TGA. They are required to include certain information and for the information to be formatted in a certain way. However, package inserts for providing instructions for preparation are not required to be set out in a certain way. The package insert template is not mandatory. This could lead to instructions for preparation package inserts not being consistent and make it difficult for health professionals to easily locate certain information. Making a package insert template mandatory could be considered. But this may not be needed if medicine sponsors are following the guidance (where relevant and appropriate for the medicine), and if the guidance and template are clear and easy to understand. It is important that information in the package insert is consistent with information in the approved PI and is clear for health professionals.

Accessing instructions for preparation information in different ways

Some medicine sponsors would like to be able to include a Quick Response (QR) code linking to the approved PI document to satisfy the requirement for providing instructions for preparation where these instructions cannot fit on the label, instead of providing a package insert. If this was permitted, health professionals preparing medicines, including nurses, would not have the option of viewing instructions for preparation in the packaging for some medicines (where it doesn't fit on the label). Health professionals would need to do one of the following to access instructions for preparation:

- scan the QR code on the label to access instructions for preparation in the electronic PI
- access the electronic PI in another way
- use other appropriate hardcopy or electronic medicine information resources.

Information about viewing PI documents can be found on the TGA website. Where available, links to PI pdf documents can also be found for medicines through the ARTG search.

Health professionals may already access instructions for preparation in these other ways instead of looking at the label or printed PI or package insert for some medicines. However, there could be some health care settings in Australia that have barriers to accessing electronic PIs or other sources of medicine information where medicines are being administered. We want to hear if this is a current concern.

Benefits for allowing a QR code instead of a package insert for instructions for preparation include reducing the environmental impact from printing documents. Printed instructions for preparation might be discarded without reading, especially for medicines that are commonly used or familiar to health

professionals. Sustainability is a fundamental principle of the National Medicines Policy and reducing waste in health care is part of National Health and Climate Strategy. Changes to TGO 91 to support QR codes instead of package inserts, might help to realise some of the intended benefits of removing the need for a printed PI in injectable medicines administered by healthcare professionals (see Removal of Product Information inserts above).

QR codes are currently permitted on medicine labels, for example, to give consumers information about the medicine. However, QR codes currently should not be used to replace important information that must be on the label, except in limited circumstances where permitted under TGO 91 or TGO 92. For more information about QR codes on labels, see Medicine labels: Guidance on TGO 91 and TGO 92 and Standard for serialisation and data matrix codes on medicines: Guidance for TGO 106.

Proposed changes to rules and guidance for providing instructions for preparation for injectable medicines administered by healthcare professionals

We are proposing changes to:

- Help make sure that clear and consistent instructions are available on how to prepare injectable medicines administered by healthcare professionals that require some preparation before use (in the appropriate format).
- Clarify medicine labelling rules for medicine sponsors where instructions for preparations are needed and where the condition of registration to require a printed copy of the PI was removed.

We want to know if you think a QR code on the label linking to instructions for preparation information in a PI document without a printed package insert would be sufficient to support the safe use of injectable medicines administered by healthcare professionals. We particularly want to hear from health professionals and if there are health care settings in Australia that have barriers to accessing electronic PIs when administering medicines and how this is managed.

Proposed updates to package insert template to provide instructions for preparation and storage information for prepared products

We are planning to update guidance and the package insert template to give further clarity to sponsors of injectable medicines administered by healthcare professionals.

We intend to provide more information to medicines sponsors about what is expected to be included in the instructions for preparation package insert. Proposed updates to the package insert template can be found in Appendix D. We are not proposing to make the template mandatory at this time.

We also plan to update Medicine labels: Guidance on TGO 91 and TGO 92 to clarify that the instructions for preparation package inserts should:

- Be legible and limited to only one page where possible, unless there are multiple or complex preparation steps.
- Be consistent with the information about preparation before use that is included in the approved PI.
- Where there are multiple presentations[12] of the medicine available, (for example, multiple strengths or concentrations) be either:
  - specific to the product presentation

[12] 'Presentation' is defined by the *Therapeutic Goods Act 1989* as 'the way in which the goods are presented for supply, and includes matters relating to the name of the goods, the labelling and packaging of the goods and any advertising or other informational material associated with the goods'.

– ensure instructions for each presentation of the medicine are clear and easy to identify.

For more information about proposed updates to the labelling guidance see Proposal to allow QR code linking to electronic preparation instructions below.

Part 2 Consultation questions

7. Do you think the proposed updated package insert template (Appendix D) for providing instructions for preparation for injectable medicines administered by healthcare professionals (where instructions cannot fit on the label) is clear and easy to understand? Please explain your answer and let us know your suggestions to improve the template.

Proposal to allow QR code linking to electronic instructions for preparation in electronic Product Information instead of a printed package insert

We are also considering allowing QR codes on labels that link to electronic information as an option for providing instruction for preparation instead of a package insert where preparation information cannot fit on the label. This would be limited to injectable medicines administered by healthcare professionals.

If this is supported, we propose to amend TGO 91 to allow the option of a QR code or a package insert where instructions for preparation cannot fit on the label for healthcare administered injectable products.

We also propose to require the following:

- The QR code must link to the current approved copy of the PI.
- A statement must be included on the label close to the QR code to state its purpose. For example, 'Please scan this code for the Product Information and instructions on how to prepare this medicine.

We plan to provide guidance for medicine sponsors about these requirements in Medicine labels: Guidance on TGO 91 and TGO 92. Proposed guidance about QR codes and to support Proposed updates to package insert template to provide instructions for preparation is included in Appendix E.

Part 2 Consultation questions continued

8. Do you think a QR code on the label linking to electronic instructions for preparation information in an electronic Product Information document (instead of a printed package insert where the instructions for preparation cannot fit on the label) for injectable medicines administered by healthcare professionals would be sufficient to support the safe and quality use of these medicines? Please explain your answer and tell us if there are any health care settings in Australia where injectable medicines are being administered that have barriers to accessing electronic PIs or other sources of medicine information, and how this is managed. If you do not think a QR code is sufficient, please tell us what conditions you think could be put in place to support medicine safety if QR codes were permitted for providing instructions for preparation. For example, are there certain types of medicines that should not be allowed to have a QR code instead of a package insert.

9. Do you agree with the proposed amendments to TGO 91 to allow a QR code (linking to electronic instructions for preparation information in an electronic

Product Information document) or a printed package insert for injectable medicines administered by healthcare professionals (where instructions for preparation cannot fit on the label). Please explain your answer.

10. Do you think the proposed guidance about providing instructions for preparation for injectable medicines administered by healthcare professionals (Appendix E) is clear and easy to understand? Please note this guidance includes information about both:
    a. Providing instructions for preparation as a package insert.
    b. Proposed changes to TGO 91 to allow a QR code instead of a package insert.

    Please explain your answer and let us know your suggestions to improve the proposed guidance. Please also let us know if you have any suggestions to improve related information on the TGA website in ensuring compliance after removing the product information insert.

11. Please tell us if you have any other comments about instructions for preparation for injectable medicines administered by healthcare professionals.

Part 3: Improving information on listed medicines about large solid oral dosage forms intended to be swallowed whole

Risks from large dosage forms and current guidance

The size and shape of a dosage form can present a choking hazard and impact on the safety of a medicine. The TGA continues to receive serious choking related adverse event reports for large oral dosage forms, some of which led to hospitalisation and sadly one case had a fatal outcome.

There are no legislated limits on the size of solid oral dosage forms for medicines in Australia. There are also no general labelling requirements for warnings or information about size for large dosage forms. However we have included best practice recommendations for the size of discrete dosage forms in the Guidance for TGO 101: Standard for tablets, capsules and pills. This document refers to FDA Guidance[13] which recommends that the largest dimension of a tablet or capsule (including 'liquid fill capsules'), should not exceed 22 millimetres (mm) and that capsules should not exceed a standard 00 size[14]. The Guidance for TGO 101 further states that sponsors should consider the following aspects to minimise the risk of choking hazards from dosage units:

- size

[13] The latest revision to this guideline was published in October 2022 Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules (fda.gov) [accessed 20 March 2024]. While this document is directed at generic medicines that may differ physically from originator medicines, its purpose is to address the physical characteristics of a medicine that could impact patient safety, including difficulty swallowing and associated risks, as well as patient compliance. The principles described in the FDA Guidance are therefore relevant to all tablets and capsules.

[14] An early draft version of the FDA Guidance included an attachment that listed standard hard capsule sizes. This attachment provided dimensions for size '00' capsules as 23.3mm (length) x 8.53mm (external diameter). The final version did not include this table, however online websites that supply capsules confirm these dimensions appear to be consistent across suppliers for size '00' capsules.

- shape
- use of coating materials and
- the intended patient population[15].

These documents provide a useful guide for industry when developing a new medicine and are a measure of safety when assessing the risks presented by large dosage units. However, these documents are guidance only and it is not a legal requirement to follow their recommendations. There are many listed medicine dosage units on the market that exceed the recommended limits in the FDA Guidance.

The TGA has been addressing the risks from large dosage units on a product-by-product basis in response to adverse event reports. We have required label warnings and images on certain products that are in the form of large dosage units that have been involved in choking related adverse events. However, the risk applies to all large solid oral dosage forms that are intended to be swallowed whole. Our approach of taking regulatory action on individual products has limited reach as it relies on adverse event reporting and doesn't extend to all large dosage units on the market.

Therefore, we consider that broader regulatory action is needed for all listed medicines in the form of large dosage units that are intended to be swallowed whole to reduce risks of choking and other serious adverse events. We are proposing new labelling requirements in TGO 92 to address these risks.

We may consider further regulatory changes in future if the new labelling requirements are not enough to address the identified risks. This could include limits on the size of dosage forms.

Proposed new labelling rules for listed medicines that are large oral dosage forms

The TGA is proposing to amend TGO 92 to give consumers more information about large oral dosage forms when purchasing and taking listed medicines. We are doing this by proposing that dosage forms that are larger than a certain size will need to show more information on the label. This includes information about the size of the dosage units and certain instructions on how to take them.

We are proposing a transition period of 2 years to allow medicine sponsors time to update their labels.

Types of medicines that will need labelling information if they are a large dosage form

Most of the choking-related adverse event reports we have received that relate to large oral dosage units involved listed medicines.

Listed medicines are widely available for self-selection by consumers, including from health food shops, supermarkets, pharmacies and online. They are often taken without medical advice to maintain good health or assist with the management of minor conditions.

Listed medicines can contain many active ingredients or large quantities of an active ingredient to provide one-a-day dosage units. This can lead to dosage units that are large and difficult to swallow which presents a risk of choking and other serious adverse events. In comparison, registered medicines typically contain single or a small number of active ingredients at relatively lower doses than those used in listed medicines, so are less likely to be large dosage forms.

[15] The TGO 101 guidance recommends that sponsors should be particularly mindful of choking risks from solid dosage forms intended for children. Our proposal for new labelling rules for large oral dosage forms does not propose separate or additional requirements for medicines intended for children. We have not identified that the risk of choking for children needs additional safety measures at this time. It is a legal requirement for sponsors to certify their listed medicines are safe for their intended purposes.

Therefore, the proposed changes will apply to listed medicines only at this stage (see Appendix F for more information about why this will only apply to listed medicines and not to registered medicines).

Proposed size thresholds for labelling information

We are proposing that the new requirements will apply to medicines where the size of each dosage unit exceeds the following threshold dimensions:

- Oral tablets and oral dosage forms other than capsules where:
  - the length or largest dimension is greater than 22 mm, or
  - the width, widest dimension or diameter is greater than 9 mm, including round tablets with a diameter greater than 9mm.
- Oral capsules where:
  - the length or largest dimension is greater than 23.3 mm, or
  - the width, widest dimension or diameter is greater than 9 mm.

We have considered available evidence when establishing these proposed thresholds for labelling requirements. However, we need to consider if there is other evidence to support a smaller or larger threshold. As part of this consultation, we are seeking feedback on whether the proposed size thresholds for the new labelling rules should be smaller or larger. Please see Appendix F for more details about the evidence we considered when establishing the proposed threshold size.

Proposed labelling information for large oral dosage forms

We are proposing that for listed medicine oral dosage forms that exceed the size thresholds, the label of the medicine must display:

- a statement to warn consumers that the dosage units are large: 'Warning: large [short name of dosage form]'[16], and
- an image of the dosage unit that is true to size with the words 'actual size', unless at least one entire dosage unit can be seen through the container[17] and primary pack[18] without opening the packaging, and
- in the directions for use, the statement 'Swallow with water'.

This information would be required on the container, intermediate packaging (if any) and primary pack, but would not be required on the front panel where the name of the medicine is most prominently shown (the main label'[19]).

[16] See Section 19 of the Therapeutic Goods (Therapeutic Goods Advertising Code) Instrument 2021) ('the Code') for requirements for health warnings in online advertising.
[17] The 'container' is defined by the *Therapeutic Goods Act 1989* as 'the vessel, bottle, tube, ampoule, syringe, vial, sachet, strip pack, blister pack, wrapper, cover or other similar article that immediately covers the goods, but does not include an article intended for ingestion'.
[18] The 'primary pack' is defined by the *Therapeutic Goods Act 1989* as 'the complete pack in which the goods, or the goods and their container, are to be supplied to consumers'.
[19] TGO 92 states that the 'main label' means:
(a) where there are two or more labels or two or more portions of a single label - that label or portion of the label where the name of the medicine is more or most conspicuously shown; or
(b) where the name of the medicine is equally conspicuous on two or more labels or portions of a label – each label or portion.

Warning statement about large oral dosage forms

We are proposing that the full name of the dosage form will not be required, as the message will be clearer to consumers if it is short. The main message for consumers from the proposed warning statement is that the dosage unit is large, not that it is enteric or modified release. Long dosage form names, such as ‘modified release tablet’ or ‘soft enteric capsule’ within the warning statement could distract from the purpose of the warning. Therefore, we are proposing that the large dosage form warning statement will be required to only include a shortened version of the dosage form name. For example: ‘Warning: large tablet’ or ‘Warning: large pill’. We will update our guidance to medicine sponsors on suitable short dosage form names to use in the warning statement (see Appendix G for proposed guidance). Sponsors should note that the label will still be required to display the name of the dosage form on the main label in accordance with paragraph 9(1)(d) of TGO 92.

We consider the warning statement for large dosage units is still needed even when they can be seen through the container and primary pack. This is because consumers may not notice that the dosage units are too large for them to swallow unless they are warned by a label statement, which will prompt consumers to look through the packaging before selecting the medicine.

Feedback provided during the 2023 targeted consultation suggested that the word ‘warning’ was not required, and that the statement ‘large [dosage unit name]’ was enough. We are concerned that if the word ‘warning’ is not present, consumers might not realise that the intent of the statement is to inform them of a potential choking hazard. We are seeking your feedback, especially from consumers and health professionals, on the importance of the word ‘warning’ to draw attention to the potential risks from the large size of the dosage unit. Please see Appendix F for further discussion on the importance of the word ‘warning’.

Image of large dosage form

We will provide guidance to sponsors on what will be considered acceptable packaging for the container and primary pack to allow at least one entire dosage unit to be seen, which will mean that the image will not be required (see Appendix G for proposed guidance).

We are proposing that if an image is required, it must be positioned next to the large dosage form warning statement. Medicine sponsors will be able to choose where on the label to position these two requirements as long as they are next to each other. We will provide guidance to medicine sponsors about acceptable positioning for the image which will include directly beside, directly above or directly below the statement 'Warning: large [short name of dosage form]’ (see Appendix G for proposed guidance).

We will provide guidance to sponsors about the image of the dosage unit, especially for dosage forms that are odd shapes (see Appendix G for proposed guidance). The image must accurately show the size of the dosage unit to allow consumers to decide if they can safely swallow it before purchasing the medicine. Most dosage forms are symmetrical so the size can be easily shown in a two-dimensional image. However, some dosage forms are odd shapes that are not symmetrical, so the size may be difficult to show on the label. For dosage units that are not symmetrical, the image should show the dimension that exceeds the size threshold. If both length and width dimensions exceed the size threshold, the image should show the longest dimension, with the width shown as accurately as possible.

One suggestion during the targeted consultation proposed that an image of the dosage unit is not needed on the label if the dimensions of the dosage unit (length and width in mm) are stated. We are concerned that the dimensions in mm might not be clear enough for all consumers to accurately picture the size, especially in a retail setting with no access to a ruler. An image makes it easier for consumers to think about whether they feel comfortable to swallow a dosage unit of that size. We are seeking your feedback, especially from consumers, on the importance of an image on the label or whether dimensions in mm are enough to allow consumers to picture the size in a retail setting. Please see Appendix F where this is also discussed.

Swallow with water directions

We consider the statement to 'Swallow with water' should be in the directions for use section on the label, as this part of the label is most likely to be read by consumers before taking the medicine. Please see Appendix F for further details on why we think instructions for use to swallow with water are important. We are seeking your feedback, especially from consumers and health professionals, on whether slightly different directions should be allowed as an option, such as 'Take with liquid'.

Which large dosage forms will be required to display label information

We are proposing that listed medicines that are in the following solid oral dosage forms and that exceed size thresholds will be required to display the new information:

- capsule
- capsule soft enteric
- capsule, enteric
- capsule, hard
- capsule, modified release
- capsule, soft
- pills,
- tablet,
- tablet, enteric coated
- tablet, film coated
- tablet, gelatin coated
- tablet, modified release
- tablet, multilayer
- tablet, sugar coated
- tablet, uncoated

The following dosage forms do not usually include instructions to swallow whole, however in some cases consumers could still attempt to swallow them whole. Therefore, we are proposing that listed medicines that are of the following solid oral dosage forms and that exceed size thresholds will also be required to display the new information, unless the directions for use on the label are clear enough that if followed will not result in the dosage unit being swallowed whole:

- lozenge
- pastille
- tablet, chewable
- tablet, dispersible
- tablet, effervescent
- tablet, orally disintegrating
- tablet, soluble

- gum, chewing[20].

We will provide guidance about this for medicine sponsors, including examples of instructions that would likely preclude swallowing whole or those that might not. For example, a chewable tablet with label directions that 'tablets may be sucked, chewed or swallowed' includes swallowing whole, so the labelling requirements for dosage units above the threshold size would apply. We recommend that listed medicines in the above dosage forms should include instructions in the directions for use: 'Do not swallow whole' (see Appendix G for proposed guidance).

Other ways to address risks from large solid oral dosage forms

The TGA intends to provide educational material for consumers on safer swallowing techniques through online forums (for example as a web statement and on social media). We also encourage sponsors to provide educational material for consumers on their websites about safer swallowing techniques for their medicines that are in the form of large dosage units.

Main considerations and stakeholder engagement

We considered several key issues when developing the proposals for new labelling rules.

We also sought feedback from several stakeholders on this matter. This included the Advisory Committee on Complementary Medicines (ACCM) and certain medicine sponsors during individual product investigations. It also included industry, professional bodies, government, and others during the 2023 targeted consultation on priorities for future improvements to medicine labels. We considered advice, comments and proposals provided by stakeholders from these consultation activities when we developed the proposed amendments to labelling rules.

The main issues and stakeholder feedback that were considered are explained in more detail in Appendix F.

Consultation questions – Improving information on listed medicines about large solid oral dosage forms intended to be swallowed whole

Part 3 Questions

12. Do you agree that the proposed dosage unit size thresholds for the labelling requirements are set at the right size? Please explain your answer. If you do not think the proposed size thresholds are set at the right size, do you think they should be smaller or larger than what we have proposed? Please ensure you read Appendix F and provide evidence to support your proposal.

13. Is the word 'Warning' needed as part of the proposed label statement to alert consumers that a dosage unit is large and presents a risk? Please explain your answer. Please ensure you read Appendix F and submit evidence to support your proposal.

14. Please tell us if you have any other comments about the proposed required warning statement.

15. For large oral dosage forms, should alternatives to the directions 'Swallow with water' be allowed if they have a similar meaning? For example: 'Take with fluid'. Please explain your answer. If you think similar directions should be allowed, do

[20] Dosage units in the form of chewing gum.

you think there should be a list of acceptable directions that sponsors can choose from to display on the label? Please see Appendix F for further discussion about this.

16. For large dosage forms, would dimensions of the dosage unit in millimetres (mm) in place of an 'actual size' image on the label be enough to inform consumers about size if dosage units can't be seen through the packaging? Please explain your answer. Please refer to Appendix F for further discussion about this.

17. Do you think the proposed guidance in Appendix G to support the proposed new requirements for large dosage forms is clear and easy to understand? Please explain your answer.

18. Please tell us if you have any other comments about the proposed new labelling requirements for large solid oral dosage forms intended to be swallowed whole.

Next steps

We will consider all feedback received before deciding on changes to TGO 91 and TGO 92.

We will publish your response on the TGA Consultation Hub, unless you specifically request that your response be kept confidential.

We will inform stakeholders about any changes to medicine labelling rules.

If you have any questions about this consultation, please email TGA.Scientific@health.gov.au.

Appendixes

Appendix A: Expressing quantities of active ingredients in units important to health professionals – Proposed new guidance

We propose to add the following information to section '2.23 Injections' of the Medicine labels: Guidance on TGO 91 and TGO 92 guidance. Other proposed updates to guidance related to expressing quantities of active ingredients are included in Appendix E.

Expressing the quantity or proportion of active ingredients

Requirements for the expression of the quantity of active ingredients is included in section 11 of the Orders. There are different requirements for some types of injectable medicines including the below.

Medicines intended for electrolyte replacement with a volume of 100 mL or less

There are specific requirements on how you must express the quantity or proportion of active ingredients in injectable medicines intended for electrolyte replacement with a volume of 100 mL or less.

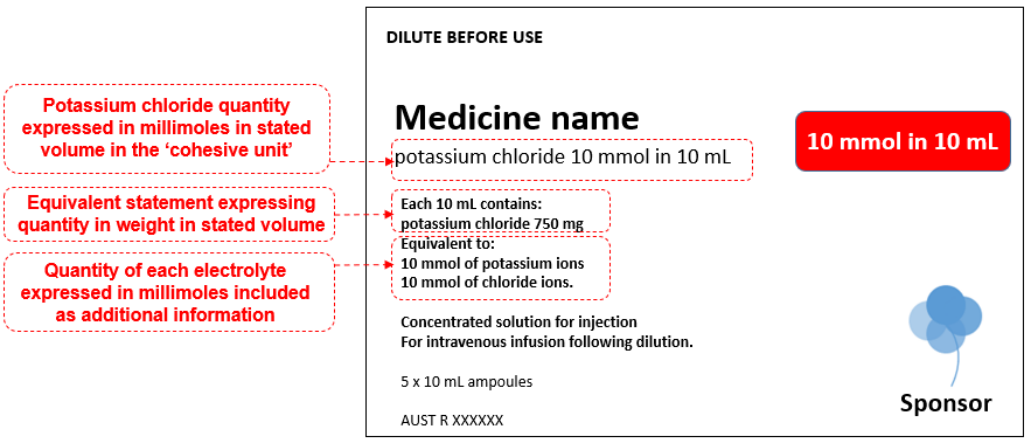
The abbreviated unit 'mmol' for millimoles can be used when expressing quantity in millimoles.

Potassium chloride

For potassium chloride injectable medicines with a volume of 100 mL or less:

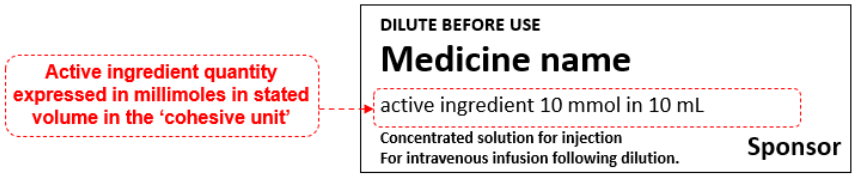
- The quantity or proportion of potassium chloride must be expressed as the number of millimoles in the stated volume of the injection in the container.
- A statement must be included below the cohesive unit (of the medicine name and name and quantity of each active ingredient) to state the equivalent quantity of potassium chloride in weight (in the stated volume of the injection or in relation to the stated volume of the injection), where space permits.

Example: Expressing quantity of potassium chloride in medicines intended for electrolyte replacement with a volume of 100 mL or less



Example of a main label on a primary pack expressing quantity of potassium chloride in millimoles in stated volume. An equivalent statement is included below the cohesive unit to also show the equivalent quantity in weight in stated volume. This is an example only. This image may not be to scale and may not satisfy all the requirements and recommendations for potassium chloride medicines.

Example: Expressing quantity of potassium chloride in medicines intended for electrolyte replacement with a volume of 100 mL or less where label space does not permit an equivalent statement below the cohesive unit



Example of a main label on a container expressing quantity of potassium chloride in millimoles in stated volume. An equivalent statement is not included below the cohesive unit because of limited label space. This is an example only. This image may not be to scale and may not satisfy all the requirements and recommendations for potassium chloride medicines.

There are also recommendations to uniquely identify injectable potassium medicines in 3.4.9 Potassium for injection or infusion.

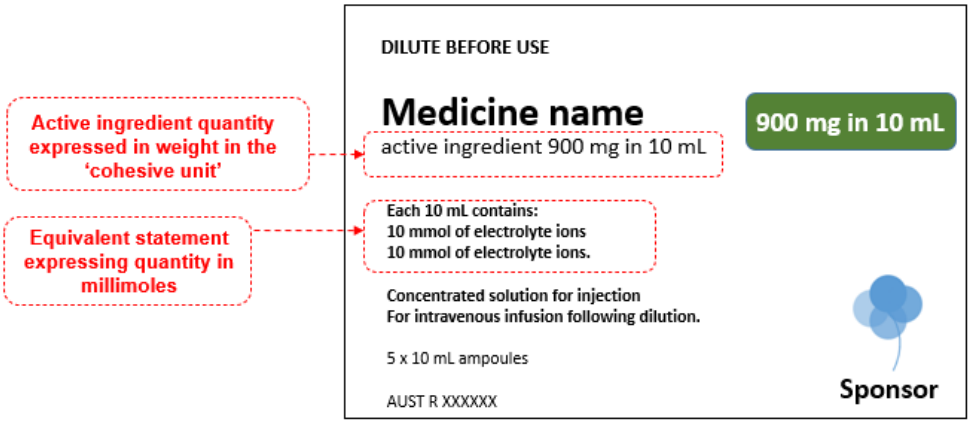
Other medicines

For medicines intended for electrolyte replacement with a volume of 100 mL or less (that are not potassium chloride):

- The quantity or proportion of the active ingredients must be expressed as the stated weight in the stated volume of the injection in the container.
- A statement must be included below the cohesive unit to state the equivalent quantity of the active ingredients in millimoles (in the stated volume of the injection or in relation to the stated volume of the injection).

An equivalent statement is always required for these medicines on the primary pack and the container.

Example: Expressing quantity of an active ingredient (that is not potassium chloride) in medicines intended for electrolyte replacement with a volume of 100 mL or less



Example of a main label on a primary pack expressing quantity of an active ingredient in weight in stated volume. An equivalent statement is included below the cohesive unit to also show the equivalent quantity in millimoles in stated volume. This is an example only. This image may not be to scale and may not satisfy all the requirements and recommendations for potassium chloride medicines.

Appendix B: Expressing quantities of active ingredients in units important to health professionals – Considerations for medicines intended for electrolyte replacement

In developing the proposals for medicines intended for electrolyte replacement (100 mL or less), we considered reasons for continuing or changing rules for expressing quantity for several active ingredients. The outcome of this consideration is summarised in the below tables. Note, we considered reasons with the plan to also require an equivalent statement below the cohesive unit.

Table 1: Active ingredients in injectable medicines intended for electrolyte replacement (100 mL or less) where we propose to continue to require quantity of active ingredients to be expressed in stated weight in stated volume in the cohesive unit.

Active ingredients[21]	Proposed required unit of quantity in cohesive unit	Proposed required unit of quantity for equivalent statement below cohesive unit	Reasons to continue requiring stated weight in stated volume as unit of quantity in the cohesive unit
calcium chloride	Weight in stated volume For example, 'calcium chloride 1 g in 10 mL'.	Millimoles in stated volume For example, 'Each 10 mL contains *x* mmol of calcium ions and *y* mmol of chloride ions.'	These medicines are commonly referred to by the weight-based percentage (%w/v) of calcium chloride. Quantity of calcium ions and chloride ions are different and may be more clearly expressed separately below the cohesive unit. Might avoid unnecessary label changes.[22]
calcium gluconate	Weight in stated volume	Millimoles in stated volume	Consistent approach for different calcium medicines intended for electrolyte replacement (100 mL or less).
magnesium chloride	Weight in stated volume	Millimoles in stated volume	Quantity of magnesium ions and chloride ions are different and might be more clearly expressed separately below the cohesive unit.
magnesium sulfate	Weight in stated volume	Millimoles in stated volume	Prescribed in different units of quantity for different indications. Sometimes referred to by weight-based percentage of magnesium sulfate.

[21] Including hydration states of these active ingredients (for example magnesium sulfate heptahydrate).
[22] Note, this reason may apply to all active ingredients in Table 1 so will not be repeated unless there are additional related reasons.

Active ingredients[21]	Proposed required unit of quantity in cohesive unit	Proposed required unit of quantity for equivalent statement below cohesive unit	Reasons to continue requiring stated weight in stated volume as unit of quantity in the cohesive unit
potassium acetate	Weight in stated volume	Millimoles in stated volume	While it is important for potassium chloride to be expressed in millimoles in stated volume in the cohesive unit, potassium acetate may not be as commonly used. Continuing expression in weight in stated volume might avoid unnecessary changes.
potassium phosphate (including monobasic potassium phosphate and dibasic potassium phosphate)	Weight in stated volume	Millimoles in stated volume	These products may contain multiple electrolyte ions of different quantities. It may be clearer to include quantity in millimoles in the equivalent statement below the cohesive unit. These medicines sometimes include multiple active ingredients. It may be clearer to display total electrolyte ions in an equivalent statement below the cohesive unit.
sodium acetate	Weight in stated volume	Millimoles in stated volume	Consistent approach for different medicines containing sodium for electrolyte replacement.
sodium chloride	Weight in stated volume	Millimoles in stated volume	Medicines commonly referred to by weight-based percentage of sodium chloride.
sodium phosphate (including dibasic sodium dodecahydrate)	Weight in stated volume	Millimoles in stated volume	These medicines sometimes contain multiple active ingredients. It may be clearer to display total electrolyte ions in an equivalent statement below the cohesive unit.

Active ingredients where we propose that quantity should continue to be expressed in weight in stated volume for injectable medicines intended for electrolyte replacement (with a volume of 100 mL or less).

Table 2: Active ingredients in injectable medicines intended for electrolyte replacement (100 mL or less) where we propose to require quantity of active ingredients to be expressed in millimoles in stated volume in the cohesive unit.

Active ingredients[23]	Proposed required unit of quantity in cohesive unit	Proposed unit of quantity for equivalent statement below cohesive unit	Reasons to require millimoles in stated volume as unit of quantity in the cohesive unit
potassium chloride	Millimoles in stated volume	Weight in stated volume	Aligns with clinical practice. Important for medicine safety. Some of these medicines have limited label space. Note: Current labels on medicines in supply might express potassium chloride in different ways. Some labels may not necessarily meet the current rules of TGO 91. Labels may include prominent expression in millimoles to support medicine safety.

Active ingredients where we propose that quantity should be required to be expressed in millimoles in stated volume for injectable medicines intended for electrolyte replacement (with a volume of 100 mL or less).

[23] Including hydration states of these active ingredients (for example magnesium sulfate heptahydrate).

Appendix C: Expressing quantities of active ingredients in units important to health professionals – Other proposed updates to guidance

We propose to update section 3.49 of Medicine labels: Guidance on TGO 91 and TGO 92 with the following edits. Proposed additions are included in **bold** font. Text with strikethrough (for example, ~~text~~) is proposed to be removed).

3.4.9 Potassium for injection or infusion

We recommend that you package all concentrated potassium medicines for injection or infusion in a manner that uniquely identifies them. **Clear differentiation of injectable potassium medicines from other medicines and intravenous fluids is recommended to help mitigate some of the risks associated with the use of these medicines.**

Medicines for injection or infusion after dilution

For medicines that are for injection or infusion after dilution that contain potassium, best practice is:

- for ampoules, include a black block of colour on the 'twist off' tab at the top of the ampoule
- for ampoules, label the end with 'KCl', or equivalent, in large lettering
- for vials, the cap of the vial should have a black 'twist off' seal
- clearly label the containers as 'Potassium Chloride' or the relevant salt
- include the instruction 'dilute before use'
- display the strength prominently as ~~both~~ total content in millimoles **in the stated total volume (for example, 10 mmol in 10 mL)** ~~and strength in millimoles/litre~~.

Premixed bags

For premixed bags containing potassium, we recommend:

- use only red lettering for labelling
- write 'Potassium' in letters vertically on the left hand side of the panel as well as horizontally, both in the largest font used on the label
- display the words 'Potassium chloride' (or equivalent) in large letters on the label
- display the strength prominently as ~~both~~ total content in millimoles **in the stated total volume (for example, 40 mmol in 500 mL)** ~~and strength in millimoles/litre next to the word 'Potassium'~~
- provide a clear space at least equivalent to the maximum font size around main description and key information (such as diluent and volume).

Appendix D: Proposed updated instructions for preparation package insert template

INSTRUCTIONS FOR PREPARATION PACKAGE INSERT – Trade name (active ingredient) dosage form strength(s) or concentration(s) ARTG number

Note 1: ' Trade name (active ingredient)' should be consistent with the title of the approved PI. Dosage form and strength or concentration and ARTG number is recommended to be included in the title, especially where the package insert is specific to one product presentation.

NAME OF THE MEDICINE

Name of the therapeutically active ingredient that is accepted for inclusion in the Australian Approved Names List. Or, in the case of a fixed dose combination or composite pack containing multiple therapeutically active ingredients, the 'approved name' of each therapeutically active ingredient.

Note 2: 'Name of the medicine' in the package insert is the same as the 'name of the medicine' included in Section 1 of the Form for providing product information. This may be different to 'name of the medicine' defined in the standard for medicine labelling. See Therapeutic Goods Orders.

DOSAGE FORM

Dosage form as described on the label of the medicine.

METHOD OF PREPARATION

Include instructions for preparation before use specific to the use of the medicine under relevant subheadings (for example, 'Reconstitution', 'Dilution').

Note 3: Include specific information from Section 4.2 of the Form for providing product information about the type and volume of fluids for relevant preparation steps, for example, for reconstituting a powder for injection medicine. Include information about compatible fluids for diluting the medicine where relevant.

Note 4: Include all relevant instructions or steps. For example, where relevant, 'shake until all the drug is dissolved.'

Note 5: Include the concentration and appearance of the reconstituted solution.

Note 6: Include relevant precautions when preparing the medicine and describe the actions the health professional should take. For example, 'Visually inspect the solution for particles prior to administration. If particles are observed, discard the drug solution.

Note 7: Where relevant, include information such as 'This product/ The content of each ampoule is for single use on one occasion in one patient only. Discard any residue.'

Note 8: Ensure instructions are specific to the presentation of the medicine. Where there are multiple presentations of the medicine available and you want to include instructions for each presentation in one package insert, ensure instructions are clear and the instructions for each presentation is easy to identify.

STORAGE CONDITIONS AFTER PREPARATION

A statement of the conditions of storage and the maximum period of storage between preparation and use.

Note 9: If multiple preparation steps are involved, for example reconstitution and dilution, specify the storage conditions for the reconstituted and diluted product.

SPONSOR

Name

Address

AUSTRALIA

Phone: 1800 123 456

Email: customer.service@sponsor.com

VERSION/DATE OF REVISION

Version 1.0 – dated DAY/MONTH/YEAR

Appendix E: Instructions for preparation – Proposed guidance to support proposed TGO 91 changes

Proposed draft guidance to be included in 'Injections requiring preparation before use' in section 2.2.3 of Medicine labels: Guidance on TGO 91 and TGO 92 is included below.

Injections administered by healthcare professionals

Injections administered by healthcare professionals also have the option to use a QR code on the label to link to preparation steps. Where preparation steps cannot fit on the label, these medicines must include instructions for preparation in either of the following ways.

- A package insert included in the primary pack of the medicine.
- A QR code on the label linking to the current approved version of the Product Information.

A statement must be included on the label stating where the instructions for preparation can be found. For example:

- 'Please see package insert for instructions on how to prepare this medicine.'
- 'Please scan this code for the Product Information and for instructions on how to prepare this medicine.'
- 'Please scan this code for instructions on how to prepare this medicine in the Product Information.'

A package insert can be a printed copy of the approved Product Information or an Instructions for preparation package insert. A recommended template for an instructions for preparation package insert is available at ensuring compliance after removing the product information insert. The package insert should:

- Be legible.
- Limited to only one page where possible unless there are multiple or complex preparation steps.
- Be consistent with the information about preparation before use that is included in the approved PI.

A package insert should be specific to the presentation of the medicine. If there are multiple presentations of the medicine and you wish to include preparation steps for each presentation in one package insert, ensure instructions are clear and that it is easy to identify the instructions relevant to the presentation.

The QR code must link to the current approved version of the Product Information. The QR code may:

- Link directly to the PI document (which must be up-to-date and consistent with the most recent approved PI document). We prefer you to link to the PI available from the TGA Business Services (TBS) website.
- Direct the user to a company website if the website is acceptable (see section 3.1.11 Acceptable web addresses in this guidance) and complies with all advertising restrictions.

Appendix F: Large solid oral dosage forms – Considerations for proposed new labelling rules

Which medicines should have new rules for large dosage forms?

The TGA considers that addressing the risk of choking and other serious adverse events from large dosage units is a priority for listed medicines. Some stakeholders have suggested we should not limit the requirements to listed medicines and should apply them to all medicine types. Analysis of Australian adverse events reported to the TGA shows that of the 326 reports related to medicines with 4 or more choking-related reports each, 88% (288/326) involved listed medicines[24].

Australian adverse event data held by the TGA shows that the types of listed medicines involved in choking-related cases are mostly one of the following four types:

- Glucosamine/chondroitin
- Fish/krill oils/omega 3
- Calcium with vitamin D3
- Multi-vitamin/minerals.

Table 3 shows the types of listed medicine formulations involved in 10 or more choking-related adverse event reports.

Table 3. Formulations of listed medicine products involved in 10 or more choking-related cases[25]

Formulation	Number of choking-related cases
docosahexaenoic acid; eicosapentaenoic acid; omega-3 marine triglycerides	106
bovine sodium chondroitin sulfate; glucosamine sulfate sodium chloride	49
omega-3 marine triglycerides	25
glucosamine hydrochloride	23
calcium carbonate; colecalciferol	21
Euphausia superba oil	13
multi-vitamin / mineral formulation	11

Formulations with 10 or more choking-related cases reported to the TGA shows they fall into one of four types: Glucosamine/chondroitin (‘bovine sodium chondroitin sulfate; glucosamine sulfate sodium chloride’, ‘glucosamine hydrochloride’), Fish/krill oils/omega 3 (‘docosahexaenoic acid; eicosapentaenoic acid; omega-3 marine triglycerides’, ‘omega-3 marine triglycerides’, ‘euphausia superba oil’ [Krill oil]), Calcium with vitamin D3 (‘calcium carbonate; colecalciferol’ [Vitamin D3]), Multi-vitamin/minerals.

[24] Date of data retrieval: 19 February 2024. Reaction terms: choking, choking sensation, foreign body in throat, product size issue. Sole suspected medicines only. Medicines were excluded if they were not solid oral dosage forms intended to be swallowed whole, or if the medicine name was not specified and could relate to dosage forms that are not solid or oral. Medicine names with 4 or more reports each were then selected. Of the cases involving registered medicines, 53% (20/38) were for Clozapine containing medicines, and most of these were not directly related to medicine administration but were events that occurred due to other factors. If these cases are excluded, 94% cases (287/306) involved listed medicines.

[25] Search details: 8 February 2024, sole suspected medicines only, reaction terms: choking, choking sensation, foreign body in throat, product size issue, complementary medicine (CM) type: all, generic names with >10 cases.

These formulations are often large dosage units to achieve one-a-day doses or need a large volume of active ingredient to align with supporting evidence. These formulations are also commonly indicated to relieve symptoms of arthritis, to maintain heart health, to maintain bone health and to promote healthy ageing, all of which include older people in the target population.

Older consumers are particularly at risk of choking on large oral dosage forms because of the higher rates of dysphagia (difficulty swallowing) and other issues that have an impact on swallowing for older adults. This can include normal physiological changes that result in a decline in swallowing functions with age[26, 27, 28].

Most choking related cases reported to the TGA did not include information about the age of the consumer. However, of the reports that included age (83 cases), most cases involved consumers aged 65 years and over (66% [55/83])[29]. See Table 4.

Table 4. Age of consumers in Australian cases reported to the TGA.

Age group	Number of reports
Infant	1
Child	2
18-14 years of age	6
45-64 years of age	19
65-74 years of age	15
75 years of age and over	40
Unknown	349

The number of choking related cases reported to the TGA for each age group (where age was reported) shows that most reports involved consumers 65 years and over, while the highest number of reports of any group was for 75 years of age and over.

Data in other jurisdictions also identified that a higher proportion of reports of swallowing problems for dietary supplements involved older consumers. A literature report published in 2019 from the United States Food and Drug Administration (US FDA) reported on data from the Center for Food Safety and Applied Nutrition Adverse Event Reporting System (CAERS)[27]. This report noted that of the 64.5% reports of swallowing problems that included age data, 76.8% involved adults aged 65 years or older. Seven of the 10 products that accounted for the majority (76.4%) of swallowing problem reports were multivitamins marketed to older adults or calcium supplemen**Error! Bookmark not defined.**s.

Data from a US study on hospital admissions due to dietary supplements reported that 37.6% of all supplement-related emergency department visits that occurred in adults aged 65 or older were because of choking or pill induced dysphagia[30]. This further highlights that dietary supplements present a risk of choking-related adverse events especially in older people.

[26] Fields J, Go JT, Schulze KS. Pill Properties that Cause Dysphagia and Treatment Failure. Curr Ther Res Clin Exp. 2015 Aug 20;77: 79-82 [accessed 20 March 2024].
[27] Punzalan, C., et al. Swallowing problems and dietary supplements: data from US Food and drug administration adverse event reports, 2006– 2015. Ann Intern Med. 2019 Nov 19;171(10):771-773 [accessed 20 March 2024].
[28] The United States Food and Drug Administration (US FDA) document Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules - Guidance for Industry ('the FDA Guidance' October 2022 [accessed 20 March 2024].
[29] Search details: 20 February 2024, sole suspected medicines only, reaction terms: choking, choking sensation, foreign body in throat, product size issue, CM type: all.
[30] Geller, AI., et al. Emergency Department Visits for Adverse Events Related to Dietary Supplements. N Engl J Med. 2015 Oct 15;373(16):1531-40 [accessed 20 March 2024].

Under the regulatory framework in Australia, listed medicines are not individually evaluated by the TGA for quality, safety, and efficacy before they are included in the Australian Register of Therapeutic Goods ('the Register') and supplied in the marketplace. In Australia, listed medicines are regulated as low risk medicines and can only use low level indications appropriate for self-selection and self-administration by the general public. This means they cannot claim to treat serious conditions. When considering the risk-benefit profile of listed medicines (that is, that the risks from the medicine do not outweigh any benefits), benefits are generally limited to the self-treatment of minor conditions that require no or minimal medical advice. Therefore, any risks must also be sufficiently low. This also applies to assessed listed medicines, which are evaluated by the TGA before they are included in the Register and supplied in Australia. Although assessed listed medicines can be for slightly higher risk uses once they have been evaluated by us, they must still be safe for consumers to self-treat and cannot claim to treat serious medical issues.

In comparison, registered medicines can be for the treatment of serious conditions that require medical advice and supervision, so their availability is often restricted. Registered medicines are fully evaluated before they are included in the Register. This also means that the risk- benefit profile will allow for a greater level of risk in some cases due to important (often lifesaving) benefits, often with close medical monitoring. It is usual practice for risks and benefits of registered medicines to be considered by medical professionals or pharmacists when prescribing or dispensing medicines to individuals.

Although registered medicines dosage units are usually smaller in size than many listed medicines, there are a small number of registered medicines available for self-selection and treatment that can also contain a large number or volume of active ingredients in the form of large dosage units. For example, registered complementary medicines and some over the counter (OTC) medicines. These can also present an unacceptable risk of choking and other serious adverse events. However, the number of choking related adverse events reported to the TGA for registered complementary or OTC medicines is very low (1.5% [5/326][24]). The TGA will continue to take regulatory action on individual medicines to address risks from large dosage units when needed.

Therefore, the proposed labelling requirements will apply only to listed medicines at this stage. The TGA may consider extending the same labelling requirements to registered medicines as part of future updates to the labelling order(s).

What size dosage units will require new labelling information?

The TGA has considered available evidence to support size thresholds including published literature and adverse event data. Consultation respondents are welcome to provide any extra evidence to support different size thresholds for the labelling requirements.

Of the choking-related reports received by the TGA where the medicine sponsor provided details of dosage unit dimensions:

- 86% (139/161) of reports for tablets involved dosage units that were either >22 mm in length and/or >9 mm wide,
  - of these 6% (9/139) involved round tablets with a diameter >9 mm.
- 92% (46/50) of reports for capsules involved dosage units that were either >23.3 mm and/or >9 mm wide.

Although the FDA Guidance makes recommendations on the largest dimension of tablets and capsules, there are no specific recommendations on width. However, the FDA Guidance states that longer oesophageal transit times have been observed for 11 mm round tablets and 14 mm x 9 mm oval tablets compared to 8mm round tablets. The FDA Guidance also states that tablets and capsules that have a larger cross-sectional area (for example, tablets that are rounder) would generally be more difficult to swallow than tablets or capsules of the same volume but with smaller cross-sectional areas.

The small size of the lower throat presents a particular risk point at which large dosage units could become lodged (depth 5.6 - 5.8 mm and width 18 mm [low retropalatal oropharynx anteroposterior and laterolateral])[31].

Adverse event data further supports that width of dosage units is an important contributor to choking risk. The TGA's adverse event data shows that of the reports for which size data was provided:

- 32% (22/69) serious[32] and 5% (5/92) non-serious[33] reports involved tablets ≤22 mm but that were wider than 9 mm,
- 17% (4/24) serious and 19% (5/26) non-serious reports involved capsules ≤23.3 mm in length that were wider than 9 mm,
- Notably only one serious report (and no non-serious reports) involved a long dosage unit (>23.3 mm capsule) that was <9 mm wide[34]. See Table 5.

Table 5. Dosage unit data for choking-related adverse events (AEs) reported to TGA Australia

Dosage form and size	Number of serious[32] AEs (% total serious for dosage form)	Number of non-serious[33]AEs (% total non-serious for dosage form)
Tablets (total)	**69**	**92**
tablet length >22 mm, width >9 mm	36 (52)	76 (83)
tablet length >22 mm, width ≤9 mm	0 (0)	0 (0)
tablet length ≤22 mm, width >9 mm	22 (32)	5 (5)
tablet length ≤22 mm, width ≤9 mm	11 (16)	11 (12)
Capsules (total)	**24**	**26**

[31] Daniel MM, et al. Pharyngeal dimensions in healthy men and women. Clinics (Sao Paulo). 2007 Feb;62(1):5-10 [accessed 20 March 2024].
[32] Data retrieval date: 19 February 2024. Serious reaction terms were 'choking' or 'foreign body in throat'. For pharmacovigilance purposes in Australia, reactions included on the European Medicines Agency (EMA) Important medical event (IME) list are considered medically significant and therefore serious. Australian sponsors are expected to treat reactions included on the IME list as serious and report in accordance with expedited timeframes for serious reports. The reaction terms choking and foreign body in throat are both included on the IME list (the globally recognised adverse event coding dictionary (MedDRA) codes adverse events reported as 'medicine stuck in throat' as 'foreign body in throat'). Only cases with confirmed AUST L numbers with reported size data were considered.
[33] Data retrieval date: 19 February 2024. Non-serious reaction terms were choking sensation or product size issue, or one or more of the following where narratives referred to dosage unit size being too large: dysphagia, foreign body, foreign body in respiratory tract, odynophagia, oesophageal discomfort, oesophageal irritation, oesophageal obstruction, oesophageal pain, oesophageal perforation, oesophageal rupture, oesophageal ulcer, oropharyngeal discomfort, oropharyngeal pain, product complaint, product dosage form issue, product physical issue, product shape issue, product use complaint, product use issue. Only cases with confirmed AUST L numbers with reported size data were considered.
[34] Analysis of dosage unit sizes was limited as the Register does not hold dosage unit size data for listed medicines, therefore we have no records of the most common dosage unit sizes for listed medicines on the market. Size data was limited to information provided to the TGA during adverse event investigations.

Dosage form and size	Number of serious[32] AEs (% total serious for dosage form)	Number of non-serious[33]AEs (% total non-serious for dosage form)
capsule length >23.3 mm, width >9 mm	18 (75)	19 (73)
capsule length >23.3 mm, width ≤9 mm	1 (4)	0 (0)
capsule length ≤23.3 mm, width >9 mm	4 (17)	5 (19)
capsule length ≤23.3 mm, width ≤9 mm	1* (4)	2* (8)
Total (tablets and capsules)	**93**	**118**

*some reports involved a hard capsule size 00 reported as 23-23.6 mm long, or a hard capsule size 0 reported as 21-21.8 mm long, with no width provided. These cases were classified as length ≤23.3 mm, width ≤9 mm as capsule size 0 is generally 21.6-21.7 mm (closed length) and 7.64 mm (external diameter), while capsule size 00 is generally 23.3 mm (closed length) x 8.53 mm (external diameter).

Size data for dosage units involved in serious and non-serious choking-related AEs reported to the TGA shows the majority exceeded the proposed size thresholds for labelling requirements for tablets and capsules.

The US FDA CAERS report identified 10 dietary supplements that accounted for 76.4% reports of swallowing problems, all of which were less than 22 mm in length, however 8 (80%) had a width >9 mm[27]**Error! Bookmark not defined.**. It is possible that supplements in the US are more commonly less than 22mm if US supplement sponsors have voluntarily followed FDA Guidance that maximum length should not exceed 22mm.

A survey of general practice patients in Germany provided the average dimensions of dosage forms that did and did not cause swallowing difficulties[35]. The average length, width or diameter of the dosage forms that caused difficulties that were significantly[36] larger than those that did not cause difficulties are summarised in Table 6 below:

Table 6. Dosage unit dimensions that did and did not cause swallowing difficulties[35].

Dosage unit shape and dimension	Mean of tablets and capsules that caused difficulties (mm)	Mean of tablets and capsules that did not caused difficulties (mm)
round: diameter	8.7 ± 2.0	8.1 ± 1.7
oval: length	15.0 ± 4.4	13.2 ± 3.3
oval: width	7.4 ± 1.8	6.6 ± 1.4
oblong: length	16.7 ± 4.0	13.3 ± 4.7
oblong: width	7.3 ± 1.6	6.2 ± 2.0
hard capsules: length	19.0 ± 2.0	17.5 ± 2.8
hard capsules: diameter	6.8 ± 1.4	6.4 ± 1.2

Dimensions of dosage units that did and did not cause swallowing difficulties show that those that caused difficulties were smaller than the proposed size thresholds for labelling requirements.

[35] Schiele JT, et al. Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms. Eur J Clin Pharmacol. 2013 Apr;69(4):937-48 [accessed 20 March 2024].
[36] Only the values that reported statistical significance are reproduced here.

This indicates that dosage units far smaller than the proposed thresholds for label requirements can still cause swallowing difficulties. Therefore, the proposed thresholds may not be small enough.

Feedback from an industry stakeholder proposed that labelling requirements should only apply if either the length *and* width exceeds proposed thresholds. However as demonstrated by the evidence presented above, this would not adequately address risks from dosage units that are not long but significantly wide. Other feedback stated that a width threshold of 9 mm was too small and would result in the new labelling information being required for a large proportion of listed medicines on the market.

Considering the available evidence including adverse event data, dosage unit width/diameter is a contributing factor to the risk of choking/serious adverse events even where dosage length remains below proposed labelling thresholds. Australian adverse event data where size dimensions were reported showed that 17% (27/161) of reports for tablets and 18% (9/50) of reports for capsules involved dosage units below the proposed length threshold for labelling requirements but that were above the 9 mm width threshold.

Authors of the survey of general practice patients in Germany commented that swallowing difficulties were only slightly more frequent with oval tablets even though their length was almost twice the diameter of round tablets. They also commented that although capsules (hard and soft) were up to 25% longer than oblong tablets the prevalence of swallowing difficulties was only 10% higher for capsules. Authors noted that tablets and capsules will rotate during swallowing to pass through the oesophageal sphincter with the lowest possible resistance, and that a more important determinant of smooth passage should be the minimal cross-sectional area rather than the largest diameter (that is, dimension) of solid oral dosage forms[35]. This further supports that a threshold for labelling requirements on length alone is not sufficient to address risks for wide dosage units.

Therefore, the TGA considers that labelling information should be required where dosage units exceed width/diameter thresholds regardless of length. Based on available adverse event data, a width/diameter threshold of > 9mm appears appropriate for the proposed labelling requirements.

Should the size threshold for labelling requirements be different for soft capsules?

Some of the feedback from industry stakeholders to the TGA in response to the August 2023 targeted consultation suggested that soft capsules (also known as softgels) should be subject to different (larger) limits than tablets and hard capsules. Respondents stated that this was because their shape and texture can make them easier to swallow. Respondents provided a range of proposed labelling thresholds, such as length 26 mm, width 10.5 mm, or length 27 mm (all widths), while one industry respondent suggested there should be no labelling requirements at all for soft capsules.

The size of soft gel capsules is usually categorised by manufacturers in terms of volume, referred to as ‘minims’, rather than length and width. Some of the consultation feedback proposed that thresholds for labelling requirements for soft capsules should be in terms of minims and should only apply when above 26 minims. This is not considered an effective risk mitigation option. The TGA is aware of soft capsules as low as 15 minims that are more than 24 mm long and 18 minims soft capsules that are more than 26 mm long. We are also aware of soft capsules that are as low as 10 minims that are less than 22 mm in length with a width greater than 9 mm. Where minim data was provided for soft capsules involved in Australian choking-related adverse event reports, 53% (17/32) serious cases and 96% (47/49) non-serious cases involved soft capsules that were less than 26 minims.

Although industry stakeholders have referred to soft capsules being easier to swallow and a preferred dosage unit for consumers, to date no convincing evidence has been provided to support that soft capsules should be subject to larger size thresholds for the labelling requirements.

There are very limited studies available that directly compare the number of swallowing problem reports for soft capsules with other types of dosage units. The survey of general practice patients in Germany reported that:

'*hard gelatin capsules, soft gelatin capsules and oblong tablets caused problems almost twice as often as tablets with irregular shapes, nearly 1.6 times more frequently than round tablets, and about 1.2 times more often than oval tablets*'[35].

Although this study found no statistically significant difference in the size of soft capsules that caused swallowing problems compared to those that did not, it also noted that the absolute number of dosage forms was lowest for soft gelatin capsules. Therefore, the analysis was possibly underpowered to achieve statistical significance when comparing the size of soft capsules that caused problems with soft capsules that did not.

The US FDA CAERS study did not directly report on types of dosage units, however further information was located online that referred to the CAERS data used for the FDA study[37]. This stated that the 10 dietary supplements that accounted for the majority of reports of swallowing problems were all tablets, with authors commenting that no deaths were attributable to soft gel capsules[37]. Notwithstanding, the same authors indicated that softgels were the 2nd highest dosage form precipitating adverse events after tablets (coated and uncoated). They also stated that 31% consumers preferred tablets/caplets, 19% preferred capsules, while only 11% preferred softgels.

A published survey report carried out in the US found that 50% of survey respondents preferred capsules, while 49% preferred tablets, with reasons for the latter being that capsules are sticky and dissolve too easily[26]. The survey of general practice patients in Germany reported that of those with swallowing difficulties, the preferred dosage form was round tablets (34.1%), although the preference for tablets vs capsules was similar, with only slightly higher preference for tablets[35].

Some of the feedback received from industry during the targeted consultation referred to a thesis paper on oral medication dose forms and patient factors that included a consumer survey. The thesis paper reported that 44% of surveyed respondents felt confident in their ability to swallow a larger (26.2 mm long) soft gel capsule than caplets of a smaller size[38]. However, this indicates that 56% were not confident. Further, a comparison between participants with swallowing difficulties and those without and their confidence to swallow the larger soft gel capsule was not provided. A later published paper based on the same survey reported that only 51% of participants with swallowing difficulties believed they could swallow a hard capsules size 000 (26.1 mm in length). Authors further summarised that '*Those with current medication swallowing difficulties felt significantly less confident to swallow larger size capsules (size 000 and 00), though most of them were able to swallow a size 00 capsule with water when requested to during the study*'[39]. Of note was that the age range of participants in this study was 19-66 years, median 36 years (no mean reported). Therefore, the study findings have limited relevance to people over the age of 66, which comprise a significant proportion of the target population in Australia for many listed medicines with large dosage units.

TGA's adverse event data shows that swallowing risks apply across dosage unit types and that more reports were for soft capsules than other dosage forms. Table 3 above shows that most adverse event reports were for fish/krill oil/omega-3 medicines[40], which are usually always in the form of soft capsules, while the remaining 3 formulation types involved in 10 or more reports are usually in the form of tablets.

The TGA also notes that there were no separate recommendations for soft capsules made in the FDA Guidance, and that the recommended largest dimension limit of 22mm also applies to liquid fill capsules, which includes soft capsules. The TGA's proposal provides a slightly larger threshold for the

[37] Kerins, MJ (2020). Physical / Mechanical hazard: swallowing. Procter and Gamble Company (https://crnusa.org/sites/default/files/RAC%20attachments/kerins_SwallowingPresentationPresOnly_CRN.pdf [accessed 21 March 2024]).
[38] Radhakrishnan, C. (2016). Oral medication dose form alteration: patient factors and the effect of adding thickened fluids. *PhD Thesis, School of Pharmacy, The University of Queensland* [accessed 21 March 2024].
[39] Radhakrishnan, C. et al. A Difficult Pill to Swallow: An Investigation of the Factors Associated with Medication Swallowing Difficulties. Patient Prefer Adherence. 2021 Jan 11;15:29-40.
[40] Docosahexaenoic acid, eicosapentaenoic acid, omega-3 marine triglycerides, Euphausia superba oil

label requirements for soft capsules of 23.3mm to align with standard hard capsule size 00, noting this is not a limit on the permitted dosage unit size, rather a threshold for labelling requirements.

Is the word 'warning' needed for large dosage forms?

We consider the word 'warning' is important to draw consumers' attention to a potential hazard, that is, that the dosage units are large and present a risk of choking and other serious adverse events. This is particularly important for medicines that can be seen through the packaging that will not be required to display an image of the dosage unit. The word 'warning' sends a clear message of a potential problem and will alert consumers to look through the packaging to determine if the size of the dosage unit is something they are able to safely swallow.

The absence of the word 'warning', with only 'large tablet/capsule' could be perceived by some consumers that the medicine is either better value, being larger, or that it contains more active ingredient(s). This could lead to consumers purchasing dosage units just because they are large, and overriding caution where swallowing difficulties exist.

Therefore, the TGA considers the word 'warning' is important. However, one external industry stakeholder considered the word 'warning' could invoke fear and anxiety, which could exacerbate swallowing difficulties in some consumers. This stakeholder therefore considers the word 'warning' is not necessary and could be counterproductive. We do not consider this a compelling argument as the purpose of the warning is to provide information to consumers at the point of purchase. Individuals who experience distress or anxiety at the thought of a large dosage unit triggered by the warning can then choose a more suitable medicine, that is, a smaller dosage unit that does not have the warning.

Nevertheless, we welcome further comments on whether stakeholders consider the word 'warning' is an important part of the message for consumers.

Direction for use to swallow with water for large dosage forms

Studies suggest some consumers attempt to swallow solid dosage units without any water or with not enough water. A survey of general practice patients in Germany reported that only 1.1% of total participants (both with and without swallowing difficulties) took medicines with no food or water, while 23.2% took medicines with just one gulp of water[35]. In a US based survey of 99 patients in clinic waiting rooms, only 55% of participants reported that using plenty of water was a technique they would use for dosage units that were difficult to swallow[26]. This indicates that not all consumers use sufficient water when taking medicines, and many may not think of using water to help swallow large dosage units. Therefore, a prompt in the directions for use on the label will inform consumers of the importance of taking large dosage units with water to decrease risks of choking-related problems.

The TGA had initially proposed the directions for use should include directions to swallow with a glass of water. However, targeted consultation feedback suggested this could be shortened to 'Swallow with water' as it can be expected that most consumers would understand that directions to 'swallow with water' means to take the medicine with enough water to facilitate effective swallowing. There is some evidence that suggests the minimum volume needed to effectively swallow solid oral dosage units is between 40 mL-100 mL[37].

Therefore, the proposed direction for use has been shortened to 'Take with water'. The TGA welcomes further feedback on whether slightly different statements should be allowed (for example: Take with fluid or liquid). If so, we welcome feedback on whether there should be a list of acceptable directions that sponsors can choose from to display on the label.

Would dimensions in millimetres in place of an image be enough to convey risks for large dosage forms?

Some of the consultation feedback proposed that the image of the dosage unit should be optional because of limited space on medicine labels, particularly for some listed medicines that have a large

number of active ingredients that must all be listed on the label. There was one suggestion that the image should be optional if the dimensions of the dosage unit (length and width or diameter in mms) are included on the label as part of the warning statement.

The TGA considers that an image that is true to size is the most effective way to convey the size of a dosage unit to consumers at the point of purchase if dosage units are not visible through the medicine packaging. Consumers could struggle to picture the size of the dosage unit if labels only include the dimensions in mm, particularly in a retail setting with no access to a ruler. Additionally, some consumers may not be familiar with metric units of measure but would understand an image.

Nevertheless we are interested to hear whether public stakeholders consider that dimensions in mm are enough to convey the risks of choking or swallowing difficulties in place of an image for large dosage units.

Other factors that contribute to swallowing risks

The TGA acknowledges that there are many factors that can contribute to difficulties with swallowing medicines such as:

- The shape: Odd shapes, shapes with rough or sharp edges, or wide 'football' shaped dosage units can all present a greater risk.
- Coating: The use of coating materials can help to make it easier to swallow a dosage unit.
- Texture: Soft capsules have a smooth texture that can become slippery when taken with liquid. They can also become sticky and lodge in the throat.
- Physiology: Older people are more likely to have conditions that impact on their ability to swallow. It is unnatural for humans not to chew before swallowing.
- Psychosomatic: Some people experience distress and anxiety at the thought of swallowing anything whole, sometimes because of fears of choking. Fear can cause a physiological response that causes the throat to constrict and the mouth to become dry, which can make the problem worse.

While all of these factors are important when considering the risk for individual consumers, the most consistent risk factor that we identified is the larger size of some dosage units.

Several published surveys have also reported that patients or consumers consider the size of the dosage unit as the main reason for swallowing difficulties when taking medicines[26, 35, 37]. One study reported that 80% of participants would prefer several medium-sized dosage units over large dosage units, with '*virtually every participant'* having a strong aversion to '*extra-large bulky capsules and tablets*'[26]. This supports that consumers should be provided with enough information at the point of purchase to make a choice about which medicines they feel confident to swallow with minimal risk of serious choking related adverse events, with size being the main risk factor of concern for most consumers.

This risk factor can be addressed consistently and relatively easily through clear labelling requirements.

If needed, additional regulatory action can still be taken on any individual medicine to address risk factors that may be unique to a product with a dosage unit that is smaller than the size thresholds for the proposed labelling requirements.

Appendix G: Large solid oral dosage forms – Proposed guidance

We propose to add the following information to Medicine labels: Guidance on TGO 91 and TGO 92. We are proposing that this information will be in a new section in the guidance specifically about the proposed new TGO 92 requirements for listed medicines with large oral dosage forms.

Displaying information on listed medicines about large oral dosage forms

There are specific requirements for listed medicines where the size of each dosage unit exceeds the following dimensions:

- Oral tablets and oral dosage forms other than capsules where:
  - the length or largest dimension is greater than 22 mm, or
  - the width, widest dimension or diameter is greater than 9 mm, including round tablets with a diameter greater than 9mm.
- Oral capsules where:
  - the length or largest dimension is greater than 23.3 mm, or
  - the width, widest dimension or diameter is greater than 9 mm.

For these medicines, the label must display:

- a statement to warn consumers that the dosage units are large in the format 'Warning: large [short name of dosage form]'[41], and
- an image of the dosage unit that is true to size with the words 'actual size', unless at least one entire dosage unit can be seen through the container and primary pack without opening the packaging, and
- in the directions for use, the statement 'Swallow with water'.

Shorter names for dosage forms in the warning statement

The main message for consumers from the warning statement is that the dosage unit is large. Some dosage form names are long and could distract from the purpose of the warning. Therefore, the large dosage form warning statement is required to only include a short version of the dosage form name. The single word that best describes the dosage form is acceptable.

If the warning statement is required, the following dosage forms can state 'Warning: large tablet':

- tablet,
- tablet, enteric coated
- tablet, film coated
- tablet, gelatin coated
- tablet, modified release
- tablet, multilayer

[41] See Section 19 of the Therapeutic Goods (Therapeutic Goods Advertising Code) Instrument 2021) ('the Code') for requirements for health warnings in online advertising.

- tablet, sugar coated
- tablet, uncoated
- tablet, chewable
- tablet, dispersible
- tablet, effervescent
- tablet, orally disintegrating
- tablet, soluble

If the warning statement is required, the following dosage forms can state ‘Warning: large capsule’:

- capsule
- capsule soft enteric
- capsule, enteric
- capsule, hard
- capsule, modified release
- capsule, soft

The names of some dosage forms cannot be shortened. If the warning statement is required for a pill, it must state ‘Warning: large pill’. If a warning statement is required for a pastille, it must state ‘Warning: large pastille’. If a warning statement is required for a lozenge it must state ‘Warning: large lozenge’. If a warning statement is required for chewing gum, it must state ‘Warning: large chewing gum’[42].

Sponsors should note that the label must still display the name of the dosage form on the main label in accordance with paragraph 9(1)(d) of TGO 92.

Packaging that allows at least one entire dosage unit to be seen by consumers without opening

Listed medicines can be packaged in a variety of different ways. Some provide a clear view of the contents inside the packaging while others do not. For dosage forms that exceed the threshold sizes, if at least one entire dosage unit is visible through the packaging, then the label image of a dosage unit is not required.

This includes tinted packaging where a dosage unit can still be seen through the packaging around or through the label, or when viewed through the bottom surface.

It does not include packaging where an opaque label takes up most of the space, for example on a bottle, where a single whole dosage unit cannot be seen when looking through the bottle around the edges of the label and also cannot be seen through the bottom of the bottle.

Positioning of the image and warning statement for large dosage forms

It is important that consumers understand that the reason for an image of a large dosage unit is to warn that it is large and could be difficult for some consumers to swallow. Therefore, it is important that the statement ‘Warning: large [short name of dosage form]’ is next to the image.

[42] This warning would only be required if the directions for use on the label suggest the chewing gum could be swallowed whole.

Therefore, the image (if required) must be positioned next to the large dosage form warning statement. Medicine sponsors can choose where on the label to position these two requirements as long as they are next to each other. For example, the image of the dosage unit can be directly beside, directly above or directly below the statement 'Warning: large [short name of dosage form]'.

Image of large dosage forms

The purpose of the required label image for large dosage forms is to accurately show consumers the size of a dosage unit to allow them to decide if they can safely swallow it before they purchase the medicine.

Most dosage forms are symmetrical so the size can be accurately shown by a two-dimensional image. However, some dosage forms are odd shapes that are not symmetrical, so the size may be difficult to show on the label as a flat image. For dosage forms that are not symmetrical, the image must show the dimension that exceeds the size threshold that results in the requirement for the image. If both length and width dimensions exceed the size threshold, the image must show the largest dimension, with the width shown as accurately as possible. Sponsors can choose to include two images, for example a ‘front’ and a ‘side’ view.

Some medicine containers are curved which could result in an image that is true to size looking slightly smaller when viewed from above on a curved label. However, the slightly smaller appearance from a curved label is not expected to impact on how useful the image is to inform consumers about size. A curved container would need to be held and rotated to read the side or rear label panels, therefore the hand-held rotation of a curved container will correct a slightly smaller static view from above.

Directions for use that preclude swallowing whole for certain dosage forms

The following dosage forms do not usually include instructions to swallow whole, however in some cases consumers could still attempt to swallow them whole. Therefore, listed medicines that are of the following solid oral dosage forms and that exceed size thresholds will also be required to display the new information, unless the directions for use on the label are clear enough that if followed by consumers will not result in the dosage unit being swallowed whole:

- lozenge
- pastille
- tablet, chewable
- tablet, dispersible
- tablet, effervescent
- tablet, orally disintegrating
- tablet, soluble
- gum, chewing.

For example, a chewable tablet with label directions that ‘tablets may be sucked, chewed or swallowed’ includes swallowing whole, so the labelling information for dosage units above the threshold size are required. A chewable tablet with label directions to ‘Chew one tablet daily’ if followed would not result in the dosage unit being swallowed whole, therefore the label is not required to display the labelling information for large dosage units. Lozenges or pastilles with directions to ‘dissolve one [lozenge or pastille] in the mouth’ are also not required to display the labelling information for large dosage units. Chewing gum with label instructions such as ‘Chew gum do not swallow’ are not required to display the labelling information for large dosage units.

It is recommended that listed medicines in the above dosage forms should include instructions in the directions for use: ‘Do not swallow whole’ to remove any doubt for consumers. Where this statement is in the directions for use on the label, the medicine is not required to display the labelling information for large dosage units.

Version history

Version	Description of change	Author	Effective date
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