SHPA submission to TGA consultation regarding Updates to Australian medicine labelling rules to support medicine safety, July 2024

The Society of Hospital Pharmacists of Australia (SHPA) is the national, professional organisation for the 6,100+ Hospital Pharmacists, and their Hospital Pharmacist Intern and Hospital Pharmacy Technician colleagues working across Australia's health system, advocating for their pivotal role improving the safety and quality of medicines use. Embedded in multidisciplinary medical teams and equipped with exceptional medicines management expertise, SHPA members are progressive advocates for clinical excellence, committed to evidence-based practice and passionate about patient care.

SHPA welcomes the opportunity to provide feedback to the consultation regarding updates to Australian medicine labelling to support medicine safety. The changes to labelling rules need to be standardised and easily interpretable to health professionals to enable patient safety. Hospital pharmacist are key figures in medication safety as they have an important role in educating other health care professionals, such as nurses, how to read and interpret medicine labelling to safely administer medicines and prevent patient harm. However, variation in medicine labelling, as portrayed in the consultation, has been a factor in medication administration errors in health care settings.

To provide feedback to this consultation, SHPA has sought expertise from specialist members belonging to SHPA's speciality practice groups of Dispensing and Distribution, Paediatric and Neonatology, Critical Care, Compounding services, Pharmacy Informatics and technology and Medication Safety.

The Society of Hospital Pharmacists of Australia
PO Box 1774 Collingwood Victoria 3066 Australia
(03) 9486 0177 | shpa.org.au | shpa@shpa.org.au | ABN: 54 004 553 806

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

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?
Partially agree.
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.*
Millimoles should be expressed in the stated volume of injection in the cohesive unit to align prescribing practices and recommendations from the Australian Council for Safety and Quality in Health Care.[1] Potassium is a high-risk medication and should be prescribed in millimoles in practice. SHPA recommends labelling to align these requirements to prevent medication errors due to inconsistencies from practice to labelling.
b. Requiring an equivalent statement below the cohesive unit, where space permits, to display information about equivalent quantity in weight.
The statement regarding 'where space permits' should be reviewed. Space on a medicine container and package should not govern medication safety practices. However, to align the current labelling requirements in TGO 91 and to maintain consistency, regardless of space, an equivalent statement below the cohesive unit with equivalent quantity in weight should be considered. It should be emphasised that millimoles is the unit of measure that must be forefront. Given the TGO 91 sets the labelling requirements, consideration to review and refine these requirements is paramount. The need for quantity in weight for certain injectable medicines, such as potassium chloride which always is prescribed in millimoles and is rarely referred to in milligrams in clinical practice, should have more specific requirements which minimise the potential for patient harm. The updates to labelling requirements by the TGA needs to consider the cumulative impact on electronic systems as well. These changes will affect how these injectable medicines are listed in electronic systems and has the potential to cause confusion than preventing harm.
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?*
No. Millimoles must be forefront and prioritised on the labels of small vials and ampoules. By including both millimoles (as the preferred expression of the quantity of potassium chloride) and milligrams in the small vials or ampoules, which would inherently have minimal space, the risk of medication misadventure is high. Additionally, in many healthcare settings, but not limited to, medical centres, aged care and hospital settings all need to provide emergency care as part of a rapid response system. Medicine and equipment

trolleys are an integral component of the rapid response system, and in the medicine trolley there are lifesaving medicines including small vial or ampoule injectable medicine. During an emergency, timely provision of care and medication access is pivotal. Therefore, if a small vial or ampoule contains labelling information that causes confusion it will likely lead to medication errors and increase overall patient harm and risk. These errors could be avoided if medicine labelling for small vials or ampoules contained clear, practice relevant and concise information to aid prompt, safe, administration and decrease patient harm.

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'.*

The quantity in weight is not essential information for potassium chloride and interrupting the cohesive unit with a brief equivalent statement in weight in brackets promotes further inconsistencies and confusion for practitioners. This would not support medication safety.

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?*

Consistency must overarch all labelling requirements such that if the volume of potassium chloride differs, labelling requirements should not be compromised, regardless of space. SHPA does not believe the quantity in weight in brackets in the cohesive unit for potassium chloride supports medication safety, as stated above.

However, IF, TGA considers quantity in weight in brackets in the cohesive unit for potassium chloride, then the primary pack and container should both have the same information for consistency.

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).

Yes.

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.*

To align clinical practice, the quantity of active ingredients should be expressed in weight in the cohesive unit, for the medicines included in Appendix B.

However, certain electrolytes such as calcium are commonly prescribed in millimoles in practice and using the weight in the cohesive unit may cause confusion. SHPA believes the TGA should consider reviewing calcium separately as there are also inconsistencies identified in medicine names listed for calcium injections. Calcium has different salt forms, gluconate and chloride. Some manufacturers have the calcium

chloride proportion as a percentage in the medicine name whilst other manufacturers have the quantity in weight either in the medicine name or cohesive unit which proves inconsistencies.

Sodium bicarbonate is an injectable medicine intended for electrolyte replacement that is not listed in Appendix B. However, the proportion of sodium bicarbonate is generally expressed as a percentage (8.4%) as part of its medicine name and these differences need to be recognised in the updates to the labelling requirements. If sodium bicarbonate is included in Appendix B, it should be noted that millimoles is used routinely used in practice to prescribe this electrolyte not milligrams.

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.

Millimoles (written as mmol) in the stated volume should be in the equivalent statement below, therefore, Figure 2A is more suitable.

SHPA queries the use of the green box which has the active ingredient quantity in weight in the stated volume in larger text. This will draw attention to the quantity expressed in weight and is duplicating information in the cohesive unit. Suggest reviewing the need for the green box which emphasise the quantity of active ingredient.

ii. If you think there would be challenges with meeting these requirements. Please give examples to explain your answer.

The challenges with meeting the requirements will fall on manufacturers strictly abiding to the medicine labelling requirements. However, if medicine labelling is changed, electronic medication management systems and clinical guidelines will need to be updated in a timely manner to reflect these changes and aid prescribing, minimise confusion and inconsistencies without compromising patient care.

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.

No comment.

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

Yes, given adequate educational material and resources are provided in a timely manner.

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.

Yes. Using the abbreviated term for millimoles is appropriate (mmol). As mentioned above, the need for the green box is queried, and SHPA suggests keeping only the cohesive unit and equivalent statement below the cohesive unit.

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.

Partially agree.

- Displaying the strength prominently as total content in millimoles in the stated volume rather than strength in millimoles/L is preferable.
- SHPA queries the use of only red lettering for labelling as it can interfere and impact the sensitivity of scanning product barcodes. Product barcodes should be easy to scan, and red lettering may not be ideal.
- The use of 'KCL' as an abbreviation for potassium chloride is not best practice and does not align with current practice recommendations. As mentioned previously, space should not govern labelling requirements, if need be, the product container should be changed by manufacturers to allow safe prescribing and administration practices that prevent patient harm and uphold safe and quality use of medicines.

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.

The medicine labelling updates should aim to highlight consistent labelling across injectable medicines.

When the updates to medicine labelling requirements are finalised, SHPA suggests TGA provide education to relevant stakeholders including an outline of key changes including before and after images. This will ensure health care professionals have a resource they can refer to if in doubt about a change that has been made and avoid medication misadventure when reading medicine labels.

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

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.
Yes, the proposed updates are reasonable as it contains relevant information to aid safe preparation and administration of injectable medicines. Suggest ensuring all terminology aligns and not to use 'drug' i.e. in the sentence 'shake until all the drug is dissolved', but rather use 'medicine'.
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.
The concept of using a QR code is reasonable and environmentally friendly given the product information (PI) is not utilised as much for drug preparation and administration compared to other national guidelines and electronic references such as SHPA's Australian Injectables Handbook. However, SHPA acknowledge there are situations where a PI will be utilised and there are concerns with using a QR code instead of a PI in clinical settings as outlined below: ▪ To access product information through a QR code an electronic device is required, such as a mobile phone, and the use of personal electronic devices in clinical settings is not recommended in healthcare settings, such as hospitals, where injectable medicines are largely used. This will breach privacy and confidentiality, especially if using personal devices in highly sensitive areas such as a theatre rooms whilst the patient is having surgery or on maternity wards and birthing suites, mainly during emergencies where timely access is key. ▪ The possibility of breaking hygiene requirements is increased by using personal or electronic devices in high-risk settings and the overall feasibility of using a QR code should be reconsidered. ▪ To use a QR code, stable internet connection is essential. Many health services face technological difficulties each week, and if services are required to rely on a QR code to access preparation and administration of injectable medicines this can once again compromise patient care, especially if this information is not readily available in national resources. ▪ Different networks utilise varying levels of technology and devices, and when introducing such change, rural and remote communities need to be acknowledged, as they will face barriers in accessing an electronic PI due to unstable connectivity. ▪ Emergency services, such as ambulances will be impacted by this change. For instance, if ambulance services are required to rely on a QR code to gain access to preparation and administration information for injectable medicines, the risk of patient harm will be increased, and these services should not need to solely rely on electronic devices to access information when timely care is of utmost importance as mentioned above. Technological advances carry challenges,

and the impacts of these challenges need to be carefully considered when making significant changes to accessing medicine administration and preparation information to ensure safe, quality, patient care is upheld.
- Aged care facilities also use injectable medicines, and some facilities are not well equipped with necessary electronic devices and digital resources.
- Some health networks may provide health care workers with electronic devices, whilst some networks may not, which can breed inequitable access to important resources.
- The QR code information must be closely monitored and updated in a timely manner and there should be central accountability for this via the TGA.

The use of QR codes should be viewed as an enhancement to accessing preparation and administration information and not be a replacement for current PI inserts.

Conditions to put in place to support medication safety if using QR codes:

- Critical care areas are dynamic and require high level of expertise and timely care. These areas should have access to a PI, readily available, without any hindrances, such as connection issues from accessing information through a QR code.
- Medications from overseas, such as Section 19A approved and Special Access Scheme (SAS) products won't always have administration information in Australian national guidelines and health care professionals heavily rely on the package insert provided. Therefore, in times when there is no access to the internet, if staff are to rely on QR codes for preparation and administration information, patients may not receive medications due to inability of accessing this information as it is not readily available in national resources.
- There needs to be consistency and a way of distinguishing which medicines will have a QR code instead of a package inserted PI and which ones will not.

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).

Partially agree.

Due to increased confusion with QR codes as listed above, and subsequent increased risk of errors in certain health care settings, a printed package insert is preferable where instructions for preparation cannot fit on the label.

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:

- Providing instructions for preparation as a package insert.
- 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'.

Yes, the information is clear and easy to understand. If these changes occur, the TGA website should have clear education and resources available for healthcare professionals. The information should be easy to navigate and contain images for clarity as mentioned above.
11. Please tell us if you have any other comments about instructions for preparation for injectable medicines administered by healthcare professionals.
Consider seeking stakeholder consultation post implementation in a timely manner to detect any concerns and take appropriate action.

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

12. Do you agree that the proposed dosage unit size thresholds for the labelling requirements are set at the right size? Yes, No, Unsure 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.
No. Patients who have swallowing difficulties can choke on a variety of size formulations and it is not solely due to large oral dosage forms, specifically >22mm in length or largest dimension as stated in the proposal. Restricting the warning statement based on size can be concerning if someone chokes on a smaller dose size and no warning was provided. There are various factors to consider when investigating choking hazards and SHPA agree size is a factor, but it cannot be considered in isolation from other factors. The proposed size for length is considered too large and should be decreased to >17mm based on information provided in table 6 of the consultation and published literature by Punzalan and Fields.[1,2] Table 6 of the consultation document shows that the longest dimensions of tablets/capsules that did not cause an issue was 17.5mm (plus or minus 2.8mm); and 8mm was the widest diameter comfortably swallowed without causing difficulties. The International Dysphagia Diet Standardisation Initiative (IDDSI) use tracheal diameter to recommend food particle sizes that would not occlude the airway. Tracheal diameter for men varies in the literature compared to women, and the lower limit for male tracheal diameter is 13mm and for women is 10mm.[3] Although the consultation document comments on pharyngeal dimensions, the diameter of the cartilage of the larynx that sits above the trachea (airway)and the diameter of the trachea is more important. The consultation mentions the most common listed medicines that have received choking hazard reports, including calcium with vitamin D3, which is predominantly targeted for women, and as mentioned above women have a slightly narrower trachea and this needs to be addressed by reducing the size threshold that is currently proposed.
13. Is the word ‘Warning’ needed as part of the proposed label statement to alert consumers that the 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.
Yes. This statement will uphold medication safety and create awareness amongst consumers through clear communication. Having the warning label will alert consumers to take note of the size of dosage forms prior to administration. SHPA supports and commends the TGA for stating education will be provided to consumers to create awareness about dosage forms and choking hazards as this was suggested in SHPA’s initial submission in 2023.
14. Please tell us if you have any other comments about the proposed required warning statement.
▪ Avoid using the term ‘pill’ and use tablet or capsule instead ▪ Ensure all product information contains information about choking risk and not only communicated through packaging ▪ Consider modified release formulations and how the wording will change to prevent changes to medication pharmacokinetics i.e. ‘do not crush’.

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 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.
▪ Directions should state 'Swallow with water" as it is the safest substance if aspirated. Although 'Swallow with liquid' allows for more options there are safety concerns. ▪ Using an alternative fluid may impact the pharmacokinetics of the medication and the intended effect. ▪ There should be a list of acceptable directions as this encourages uniform guidance. ▪ Taking solid dosage forms whilst upright also aids transit through the oesophagus. ▪ As mentioned above, the TGA will need to consider the slow release and modified release formulations and how directions will be displayed for these dosage forms. ▪ Taking with alternative fluids can also lead to potential drug interactions.
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.
No. Including the dimensions in millimetres on the label will increase the risk of dose and medicine information misinterpretation. Dimensions should not be included on a label if dosage units can't be seen through the packaging, an image is preferable.
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.
Unsure. There is a lot of information in Appendix G and some information was confusing. The comment on page 50 regarding a statement for chewing gum is confusing in this context. As chewing gum is 'chewed' this will change the size of the dosage form. A statement should highlight this dosage form must be chewed prior to swallowing instead.
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.
SHPA suggest consumer and patient feedback is sought for this consultation as they will provide insight into this matter from patient experiences.

If you have any queries or would like to discuss our submission further, please do not hesitate to contact Jerry Yik, Head of Policy and Advocacy on jyik@shpa.org.au.

References

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[2] Punzalan C, Budnitz DS, Chirtel SJ, et al. Swallowing Problems and Dietary Supplements: Data From U.S. Food and Drug Administration Adverse Event Reports, 2006-2015. *Ann Intern Med*. 2019;171(10):771-773. doi:10.7326/M19-0947

[3] Breatnach E, Abbott GC, Fraser RG. Dimensions of the normal human trachea. *AJR Am J Roentgenol*. 1984;142(5):903-906. doi:10.2214/ajr.142.5.903