Consultation: Management and communication of medicines shortages

The Icon Group and associated parties currently supply medicines to over 50 private and public hospitals where we have on site pharmacies located, over 200 public and private hospitals that receive compounded medicines through our TGA licenced compounding facilities (Slade Health), and through pharmacy services to approximately 90 residential care facilities with over 7000 residents. As such the Icon Group has considerable experience with managing medicine shortages for its patients and client health services across a broad spectrum of medicines use settings.

Icon Group welcomes the TGA's new Protocol for management and communication of medicines shortages and appreciates the opportunity to contribute further considerations from both a pharmacy and health service provider perspective. The organisation also welcomes further involvement in this consultation and any future consultations regarding medicines shortages.

Consultation issue 1: The definition of a medicine shortage

Is the definition of a medicine shortage clear?

Yes

Is the definition of a medicine shortage appropriate, noting that it will be required to be stated in the Therapeutic Goods Act through the proposed amendments?

Yes

Is the proposed scope for covered medicines clear?

Yes

Is the proposed scope for covered medicines appropriate?

Was consideration given to the inclusion of any Special Access Scheme (SAS) items, particularly higher volume/higher clinical impact items, as identified through SAS notifications and applications/approvals data? The nature of items accessed via SAS can include items of high or extreme impact to individual patients.

Consultation issue 2: Reporting obligations

Do you support the suggested timeframes?

Yes, though exemptions may be required in the case of a medicine withdrawal from the market due to safety concerns in accordance with the Uniform Recall Procedure for Therapeutic Goods. Clarification of withdrawal

Do you have an alternative proposal?

No

Do you support the required notification content?

Yes, however clarification is required regarding the following content:

- "Reason for the shortage": What are the drop down menu options?
- "Shortage Type": Current MSII website indicates status (anticipated/current/resolved/discontinued) – is that what is meant by "Shortage Type"? Assume the new website indicate the impact classification (low/med/high/extreme)?
- Is there an expectation that the accuracy of the "Estimated Duration of Shortage" and frequency and timeliness with which this information is updated by Sponsors will improve under the new protocol?

Consultation issue 3: Which products should be on the 'Medicines Watch List' defining an 'extreme' risk shortage

Is the list comprehensive/adequate?

No – further clarification is required regarding of the methodology used to decide on the proposed medicine watch list. Some items in the list have multiple brands available in the Australian market (e.g. ceftriaxone, meropenem) but there are other medicines such as protamine (for reversal of heparin) that have been excluded yet are available from only one Sponsor.

Given there are products with multiple Australian Sponsors, what mechanism will trigger Protocol A as opposed to these medicines undergoing the Protocol B Risk Assessment?

On the basis of Table 1 (P.11), "Extreme" risk medicine shortages appears to include medicines for

- uncommon/rare conditions (< 1 in 1000) where no therapeutic alternatives exist, and
- common conditions (> 1 in 1000) where there is a possible therapeutic alternative (i.e. different active ingredient but comparable pharmacological class or mode of action)

On this basis, the proposed Medicines Watch List seems to take into account epidemiology of medical conditions which medicines may be used to treat but it is unclear if this also includes consideration of the prevalence of surgical procedures which rely on medicines, as there is currently a limited number of key medicines for surgery and anaesthesia included.

It is noted the draft protocol (P.10) discusses a number of medicine classes that will be assessed on a case by case basis – is this meaning for inclusion on the Medicines Watch List or instead meaning they will undergo Protocol B risk assessment in the event of a reported shortage?

Are there other products that would have an extreme or high patient impact if they were to be in short supply?

Icon Group pharmacy staff have noted and support a number of additional medicines suggested in SHPA Specialty Practice forums to support the SHPA submission to this consultation. It is anticipated that medical colleges may also make submissions of medicines relevant to their specialties.

Whilst it is difficult to identify individual medicines given some uncertainty regarding the methodology for the proposed medicines list, the following are some medicines that would seem to meet the requirements for inclusion:

- aciclovir – intravenous and ophthalmic preparations
- amikacin (included in WHO core essential medicines list and currently only one Australian Sponsor)
- protamine (included in WHO core essential medicines list and currently only one Australian Sponsor)

When further considering the categories of antidotes and critical care the absence of neuromuscular blocker reversal agents from the watch list was noted. A shortage of either of these agents could have significant implications for clinical practice. Neostigmine has only two Australian Sponsors whilst sugammadex (indicated for rocuronium and vecuronium reversal only) has a single supplier.

It is noted that oncology medicines have been listed as assessable on case-by case basis as they require individual patient assessment as to whether alternatives are appropriate and switching of the patient is possible. However Table 2 (P.12-13) "Categories of Patient Population Assessment and Ranking" lists as a severe consequence of a medicines shortage "Oncology patients in mid cycle regimen" and WHO list of essential medicines sections 8.2 and 8.3 contains cytotoxic, adjuvant and hormonal antineoplastic agents, including some which currently have one Australian sponsor e.g. rituximab, trastuzumab and established evidence of clinical benefit in certain patient populations.

What would be the best mechanism to add or remove medicines from the list?

Medicines should be considered for addition the list during the ARTG registration process for new chemical entities, and in response to applications made by medical colleges and other professional associations (e.g. SHPA, PSA) which provide evidence supporting a medicine's inclusion on the list.

Suggest also considering a mechanism where a prolonged shortage or discontinuation of a particular agent may require the temporary or permanent addition of other similar items to the Medicines Watch List, under the advice of the Medicines Shortage Action Group. Recent examples which may support this process:

- The clinical significance of fentanyl injections shortage in 2017 was augmented by the pre-existing long term supply constraint with remifentanil. The differences in indications and dosing complicated use of a therapeutic alternative such as alfentanil, and being high potency opioids carries risks of significant adverse patient outcomes if used in error. These concerns were shared by a number of anaesthetists.
- Recent discontinuation of Slow-K and Duro-K tablets due to the lead content exceeding new standards, leaving only one Sponsor for all oral potassium supplementation in Australia whilst the Sponsor for the discontinued products pursues alternative options.

Consultation issue 4: Compliance obligations and potential penalties

Do you support particular options? Why?

As discussed in the consultation's background, Australia is a very small part of the worldwide medicines market. Moreover the relatively low purchase price for many medicines in Australia further contributes to the vulnerability of the Australian market to medicines shortages. Option 1 is insufficient to encourage any material change from the current voluntary reporting situation. Financial penalties must be part of the new medicines shortage scheme and need to be of an amount that is considered material for the Sponsor corporations for it to be an effective incentive.

Which option, or combination of options, do you believe would be the most effective?

A combination of Options 2 and 3 which includes the option to issue infringement notices and penalties but allows scope to impose more severe civil penalties for repeated non-compliance and/or for shortages of extreme impact. Whilst it is hoped that the prospect of substantial penalties may incentivise some international Sponsors to not only ensure prompt notification of shortages but even heighten their prioritisation of maintaining the Australian supply chain and avoiding the shortage altogether, it is also acknowledged that the level of penalty may also act as a deterrent for Sponsors entering or remaining in the Australian market, particularly for smaller Sponsor corporations. Whilst parity with models such as the UK and Canada are under consideration, the difference in those markets must be a consideration of the maximum penalties in Australia.

That being said, it is reasonable to expect that Sponsors understand the indications for their products, the epidemiology and incidence of use (overall market) and their products' market share, and thus be reasonably well informed as to the potential impact on public health in the event of a shortage of their products. Therefore, in the case of medicine shortages with high and extreme impact, failure to disclose anticipated or current shortages in a timely manner to mitigate public health risk could arguably be considered as serious as non-disclosure of known adverse effects of medicines. However it would need to be clear under what circumstances (expected to be rare) that such maximal penalties would apply.

Other considerations for the new Protocol:

1. **Stakeholder Engagement (P.5)**
   Consider elaboration on point 5 by inclusion of the following additional wording (underlined):

   "5. Early and timely engagement with healthcare practitioners is a priority to ensure impacts and recommended mitigation strategies are accurately identified and implemented to minimise impact on patient care. Assessing the potential impacts of a particular shortage will be aided by expertise within medical (colleges and professional organisations) and pharmacy (e.g. SHPA Specialty Practice Groups) bodies."

2. **Expected timeframe for an initial medicine shortage risk assessment should be a maximum 72h (as per pages 13 and 18).**
   - Assessment and Verification/What Dose forms and Strengths are in Shortage? (P.10): "…Partners (sponsors, wholesalers and other stakeholders) will work together with the TGA to determine whether or not supply will meet demand, especially when there is more than one supplier of that molecule/strength/route of administration. *There are currently challenges in obtaining accurate and timely information.*"
     Q: What measures will be implemented to ensure this deadline can be met? The financial penalties apply to delay in initial notification of supply by Sponsors, could there be scope to include subsequent provision of information to enable timely initial risk assessment, and any subsequent updates.
   - Communication with industry sponsors in managing supplies when products are available from multiple sponsors but are in short supply (P.14): "…Some aspects of communication and collaboration described above might be seen as anticompetitive under the Competition and Consumer Act 2010 whether there is a difference if the coordination of such communications is carried out by government rather than by industry. *It would be possible to seek an "authorisation" by formal application to the ACCC for an exemption from anti-competitive dealings provisions*."
     Q: Is such authorisation by formal application likely to contribute to delays in obtaining accurate and timely information to complete the risk assessment within the 72h timeframe? Can mechanisms be implemented to ensure this authorisation process is expedited?

3. **Timely and equitable communication of shortages after initial risk assessment, and management of stock allocations from sponsor(s)**

   The methods of communication are discussed on Page 13 ("Response") and 19 ("TGA (DOH) triages a response to confirmed shortage…"). It is not clear what may be considered a "hospital" shortage versus "community" shortage. Hospitals can be impacted by shortages of medicines that impact on community pharmacies, and conversely community pharmacies can be suppliers to private and public hospitals. It is important to ensure that the communication through public and private health services and all levels of distribution network is both timely and equitable.

   Furthermore, the implementation of stock allocation controls such as those discussed on pages 14 and 23 could be implemented in parallel or immediately prior to the release of communications to safeguard equitable distribution of stock allocations across the country.

4. **TGA and the sponsor coordinate communications about confirmed shortages (P.15 & 16):**
   - Section on Page 15 commencing "For extreme - or high - patient impact shortages, a range of stakeholders will need to work together, to conduct the following steps:…"

     The wording of the last bullet point in this section (as written below) is confusing and requires clarification: "Monitor and respond to shortage status changes and issues that emerge e.g. to follow up with distributors to ensure currency of their information (e.g. follow up from pharmacies)."

     Note: a similarly worded statement is also included in Appendix 2 (Page 20 - second last bullet point): "…To relevant distributors (e.g. CSODs) to ensure currency of their information (e.g. follow up from pharmacies)…"

   - Page 16: consider the following addition of text (as underlined below):
     "…Information about medicine shortages in Australia:
     - why they occur, the types, and how they are managed
     - the different categories of shortages, and what information to expect when a high <u>or extreme</u> impact medicine shortage occurs in Australia "

5. **Appendix 1: Action protocol for management of shortages (P.18)**

   Point 6 "…The outcome of the risk assessment (refer Table 3) will then direct specific response and escalation to the "Medicine Shortage Action Group" (refer Figure 1)…"

   Q: Should the outcome of the risk assessment refer to Table 1? Or Tables 1-3? Table 3 (P.12) outlines substitute medicines or therapeutic alternatives, only part of the risk assessment.

6. **Appendix 2: Coordination approach for notification, management and communication of medicine shortages (P.19) Identifying a shortage – Reporting**

   Consider the addition of the following text (underlined) for consistency of definitions terminology

   "1. Product sponsor confidentially and mandatorily notifies the TGA of:

   - a potential<u>/anticipated</u> shortage to facilitate early investigation with proactive forecasting and management…"