Australian Government

Department of Health

Therapeutic Goods Administration

Management and communication of medicines shortages – proposed implementation approach

Consultation paper

Version 1.0, March 2018

TGA Health Safety Regulation

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Contents

Introduction

Purpose and scope

Purpose

The Government is considering making reporting of all medicines shortages to the TGA by sponsors mandatory from 1 January 2019. Proposed mandatory reporting would be subject to the passage of legislation.

Through consultation to date with the major industry stakeholders involved in managing medicine shortages, and the health care professional groups most affected by medicine shortages, it has been agreed that those medicines shortages classified under a protocol led by the TGA as of 'extreme' or 'high' patient impact will be mandatorily published via the Medicines Shortages Information Initiative (MSII) on the TGA website.

This consultation paper seeks input on a number of matters that will shape how the improvements to the management and communication of medicines shortages are implemented.

Scope

This consultation paper is seeking stakeholder feedback on:

- the definition of a medicine shortage that would trigger mandatory reporting to TGA and subsequent action;
- the medicines in scope for mandatory reporting;
- proposed timing and content of mandatory reports;
- the proposed list of medicines on the 'Medicines Watch List' (a shortage of a product on this list would automatically classify the shortage as of 'extreme' patient impact); and
- compliance obligations and proposed penalties for non-compliance.

Background

Medicine shortages have become an increasing problem in the past few years for a number of reasons. These include the decrease in local Australian manufacture of prescription medicines and the increasingly globalised nature of the supply chains for medicines. This means that even in cases where several products containing the same active ingredient are registered in Australia, they may be made by the same manufacturer. As a result, a manufacturing problem in any facility may simultaneously affect several Australian sponsors.

Many of the medicines that have been in shortage are long-standing generic medicines. Reporting and management of medicine shortages involves all stakeholders - industry, healthcare professionals and State and Territory and Commonwealth governments. The Commonwealth government's role in managing medicine shortages includes having up-to-date and comprehensive information available on medicine shortages, ensuring that this is well-communicated and, where shortages have been identified, to use regulatory measures to enable temporary access to similar foreign-registered medicines.

The MSII was launched in 2014, supported by the MSII Protocol, which sets out how a shortage should be managed by the parties involved. Participation in the MSII is currently voluntary and sponsors provide TGA with information in the form of submitted notifications for publication on the TGA website. These notifications advise health professionals and consumers of current, anticipated and resolved shortages as well as product discontinuations.

However, the MSII has had major failings. Notwithstanding the introduction of the MSII, a significant number of shortages of extreme or high patient impact have not been reported by some sponsors. Instead, the first indication that the TGA received of these medicine shortages has in many cases been from correspondence from members of the community impacted by a shortage and it has been subsequently confirmed after contact with the relevant sponsor. There have also been significant delays in some cases in confirming the existence of a shortage.

Clearly, the reporting of medicines shortages does not in itself prevent the actual shortage occurring. However, timely reporting of all shortages and the timely public communication of those which have a significant clinical impact would enable alternative supplies of the product to be accessed from overseas sources. Also, if a shortage has been notified early the remaining available product in Australia can then be rationed for use in the most serious cases. This also allows relevant groups of health professionals to convene as a matter of urgency to discuss suitable therapeutic alternatives, a critical consideration for ongoing patient care.

Consultations so far

In August 2017, the Minister for Health, the Hon Greg Hunt MP, hosted a meeting of the Medicines Partnership of Australia (MPA) comprising the National Pharmaceutical Services Association, Medicines Australia, Generic and Biosimilar Medicines Association, The Pharmacy Guild, the Pharmaceutical Society of Australia and Australian Self Medication Industry, together with senior departmental officials. At the meeting, it was agreed that a Working Group develop a strategy for better management of prescription medicine and vaccine shortages by the end of 2017. The Australian Medical Association and the Society of Hospital Pharmacists of Australia subsequently joined the Working Group. The Minister asked the Deputy Secretary, Health Products Regulation Group, Department of Health to chair the Working Group.

The Working Group delivered this strategy, and unanimously endorsed a revised MSII Protocol (Attachment A to this paper) that had been jointly developed by the Group, which reflects the proposed changes to reporting and management of medicines shortages. The revised MSII Protocol has also been endorsed by the Chief Executives of the MPA partner organisations.

In January-February 2018, consultations with State and Territory health officials on the proposed new policies and process have occurred. These departments also support the proposed changes to reporting and management of medicines shortages and have unanimously endorsed the revised MSII Protocol, in particular, mandatory notification of medicines shortages and public reporting of those with high or extreme impact on patients.

Enhancements to the reporting and management of medicines shortages

The proposed new MSII Protocol represents a comprehensive set of measures to improve the reporting, management and communication of shortages. In negotiating the new Protocol, peak industry bodies representing the majority of sponsor companies accepted a new requirement for mandatory reporting of all shortages to the TGA on a confidential basis, and only those shortages deemed to be of 'extreme' or 'high' patient impact would be mandatorily published on TGA's website. It would, however, be at TGA's discretion, based on the publicly available

Protocol, whether to deem a shortage as being of 'extreme' or 'high' patient impact. In many cases, such action would be taken following discussions with relevant clinical groups (e.g. infectious disease physicians) or, alternatively, in the cases where an affected medicine was on the Medicines Watch List (which will form an appendix to the Protocol). The industry sponsor would also be consulted.

Those shortages with extreme/high patient impact will be published on a dedicated 'landing page' on the TGA website. This will ensure that the most important shortages are easy to find on the website and that additional communication efforts – which would be undertaken by industry, health care professional organisations, state and territory governments as well as the TGA - can also be directed to these shortages.

Sponsors will continue to be encouraged to publish other shortages to the website on a voluntary basis, and we anticipate that many sponsors will do so. These will be published on the current Medicine Shortages page.

The revised MSII Protocol will also bring Australia into alignment with other major English-speaking countries. Over the past five years, both the USA and Canada have introduced mandatory reporting for some or all medicines. The UK also enacted legislation last year that includes mandatory reporting of medicine shortages and in late 2017 completed a public consultation on a set of proposed regulations for the implementation mandatory reporting of medicine shortages, including details on penalties for non-reporting. We have been advised by the US FDA that introduction of mandatory reporting has led to a three-fold increase in reporting of shortages, and also increased the timeliness of their reporting.

We are consulting on four major issues:

1. The definition of a medicine shortage and the scope of covered medicines.
2. Reporting obligations.
3. Which products should be on the 'Medicines Watch List' defining an 'Extreme' risk shortage.
4. Compliance obligations and potential penalties.

However, we also encourage feedback on any other issues that you may wish to raise from your review of the Protocol document.

Consultation issue 1: The definition of a medicine shortage

It has been agreed that sponsors will be required to report all medicine shortages in confidence to TGA. In order for sponsors to meet this requirement, and for TGA, if necessary, to enforce this requirement, a definition of what constitutes a medicine shortage is required. The proposed definition is below.

A proposed definition of a medicine is also included so it is clear what medicines are in scope. It should be noted that the revised Protocol only applies to medicines on the Australian Register of Therapeutic Goods (ARTG); and does not apply to unapproved medicines that may be accessed via one of TGA's unapproved goods schemes.

For consideration

PROPOSED DEFINITION OF A MEDICINE SHORTAGE:

*A **medicine shortage** covers all instances where a patient's care may need to be revised as a result of:*

(a) the unavailability of a medicine from a sponsor, wholesaler or manufacturer; or
(b) the partial availability of a medicine from the sponsor, wholesaler or manufacturer; or
(c) other constraints on the medicine's availability.

Different types of medicine shortage are defined:

- ***Anticipated medicine shortage** means a medicine shortage that is anticipated to commence at a future date;*
- ***Current medicine shortage** means a medicine shortage that has commenced;*
- ***Resolved medicine shortage** means a medicine is now available because the supply of the medicine is no longer unavailable, partially available, or affected by other constraints;*
- ***Discontinuation** means a decision by a sponsor to permanently cease the supply of a medicine.*

PROPOSED SCOPE FOR MEDICINES IN THIS CONTEXT:

*The kinds of **medicines** intended to be covered for the purposes of the proposed medicine shortage reporting requirements are prescription medicines that are entered on the Australian Register of Therapeutic Goods. However it is also proposed to include a small number of non-prescription medicines. The criteria for inclusion of a non-prescription medicine would be:*

- *The medicine is critical to the ongoing health of the patient (an example would be salbutamol asthma inhalers); and/or*
- *Inclusion of the medicines is critical for public health (an example would be naloxone injections for opioid overdose).*

SOME QUESTIONS TO CONSIDER:

- *Is the definition of a medicine shortage clear? The definition is clear.*
- *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? Whilst the definition is clear, the Act should be modified to ensure that if the medicine affected by the shortage is a PBS listed item, then the non-registered products accessed either through the SAS programme or as a "19A" item then these products should attact the same PBS subsidy as the registered product for the duration of the shortage.*
- *Is the proposed scope for covered medicines clear? Yes*

- *Is the proposed scope for covered medicines appropriate? Yes*

Consultation issue 2: Reporting obligations

Once a medicine shortage has been identified, sponsors will have a duty to report the shortage to TGA. The shortage will need to be reported within a specified time period (see below), in writing to TGA via the MSII portal or e-mail to a designated inbox.

For consideration

SUGGESTED TIMING FOR SPONSORS TO REPORT AN ANTICIPATED OR CURRENT SHORTAGE:

*Sponsors must report an **anticipated** or **current medicine shortage**: as soon as practicable after becoming aware of it , or within 2 business days after being contacted by the TGA regarding a report of a shortage of their medicine.*

*Sponsors must report all **resolved shortages** as soon as practicable after it has resolved and within 5 working days of the day the shortage was resolved.*

A medicine is taken to be in shortage once patient care may need to be revised due to unavailability. This is too late. The earlier the notification the more time clinicians have to consider treatment options, including de-prescribing. It also gives more time for the clinicians to discuss treatment options with their patients. This level of communication is essential to minimise the anxiety patient's may experience when they feel that they won't be able to access their medicines.

SUGGESTED TIMING FOR SPONSORS TO REPORT A DISCONTINUATION:

Sponsor must report:

- *12 months prior to the discontinuation, for a discontinuation with an extreme or high impact level;*
- *6 months prior to the discontinuation, for a discontinuation with medium impact level;*
- *3 months prior to the discontinuation, for a discontinuation with low impact level.*

Who will assess the impact level? From a patient perspective, all their medicines are important.

It should be noted that these timeframes are those currently set out in the medicines shortages Interim Business Specifications and Guidance Supplement available in TGA's eBusiness Services (eBS) portal. The long lead times for reporting discontinuations of medicine shortages with extreme or high imact levels are needed because in many cases the sponsor of these medicines may be the sole supplier in Australia. The lead times enable TGA to identify alternative

suppliers of the product for the Australian market, which may include seeking and reviewing an application for registration of the alternative medicine on the ARTG.

REQUIRED CONTENT OF NOTIFICATIONS:

The information required when reporting a medicine shortage includes:

- *Sponsor name and contact details*
- *Product active ingredient and trade name, strength, dose form and ARTG number*
- *Reason for the shortage (selected from a drop-down menu)*
- *Estimated duration of the shortage*
- *Shortage type*
- *Additional supply details about the medicine as appropriate*
- *Information about substitute medicines or therapeutic alternatives as appropriate.*

It should be noted that this is the same content requested of medicines sponsors under the existing voluntary reporting scheme.

SOME QUESTIONS TO CONSIDER:

- *Do you support the suggested timeframes? Do you have an alternative proposal?*

The earlier the notification the more time clinicians have to consider treatment options, including de-prescribing. It also gives more time for the clinicians to discuss treatment options with their patients. This level of communication is essential to minimise the anxiety patient's may experience when they feel that they won't be able to access their medicines.

On Page 4 of this document, the Background comments include mention of the globilisation of drug supply. This is our reality. Therefore, drug shortages experienced in the global community are likely to impact on Australia.

Given this, I would like to see the mandatory reporting of shortages experienced globally of medicines that are either Australian registered or listed products as there is a high probability that this same shortrage will have an impact on the Australian market.

Australia should also be obliged to report all medication shortages experienced here as these shortages are likely to impact on the global market particularly if medicines are accessed through the SAS programme or as S19A items.

The early notification would also provide other suppliers to increase their production of affected medicines where appropriate. This level of co-operation may result in the absence of a true outage (i.e. prestricted to one or two brands rather than all brands). This level of co-operation should be encouraged and rewarded.

Early notification would also allow the healthcare community (suppliers, prescribers, pharmacists) to introduce a managed supply process. This would minimise the risk of individual's stockpiling particular medicines and may result in reduced true stock outage situations.

- *Do you support the required notification content? Yes.*

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

A specific watch list of known critical products would help simplify and speed decision-making when deciding if a medicine shortage has 'extreme' or 'high' patient impact. Only medicines that are included in the ARTG would be considered for the list. A shortage of a medicine on the watch list would automatically prompt TGA to publish a notification provided to us by the medicine sponsor. However, as described in the Protocol there may be some other medicine shortages that on a case-by-case basis could justify publication of a notification on public health grounds. The proposed Medicines Watch List has been derived from a consensus review of existing state hospital Emergency and Life Saving Drug Lists and the WHO's Model List of Essential Medicines that are contained in the ARTG.

For consideration

PROPOSED MEDICINES WATCH LIST: See below.

SOME QUESTIONS TO CONSIDER:

- *Is the list comprehensive/adequate? Medicines without therapeutic alternatives should be included on this list.*

  Consideration must also be given to the impact of a medicine shortages on the alternates used during this shortage. A current example is the non-availability of morphine 5mg ampoules. This shortage has led to an increased demand for morphine 10mg ampoules to the point where this supply line is now under threat.

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

  A patient may argue that all their medications should be on this list.

  e.g. the current, prolonged outage of disulfiram has a huge societal impact. Whilst this drug does not appear on the medicines watch list, the lack of access to this medication has the potential to result in harm to both the patient and the patient's family/support network (increased domestic violence, increased mental health issues, increased risk of road fatalities etc associated with increased alcohol consumption).

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

  Ongoing review by medical experts.

Proposed medicines watch list

Antibiotics, antifungals and antivirals

Amphotericin (IV)

Ampicillin

Azithromycin

Benzathine penicillin

Benzylpenicillin

Caspofungin

Cefepime

Cefotaxime

Ceftazidime

Ceftriaxone

Chloramphenicol (IV)

Ciprofloxacin

Colistin

Daptomycin

Dicloxacillin

Erythromycin (IV)

Flucloxacillin

Ganciclovir

Gentamicin (IV)

Imipenem/cilastatin

Linezolid

Meropenem

Metronidazole (IV)

Piperacillin/tazobactam

Posaconazole

Rifabutin

Rifampicin

Teicoplanin

Tobramycin

Valganciclovr

Vancomycin (IV)

Voriconazole

Antidotes and treatments for poisonings

Activated charcoal

Atropine injection

Desferrioxamine injection

Digoxin specific antibodies

Edetate calcium disodium (EDTA)

Ethanol injection

Flumazenil

Folinic acid (calcium folinate) injection

Fomepizole

Idarucizumab

Methylene blue injection

N- Acetylcysteine injection

Naloxone injection

Pralidoxime injection

Sodium nitrite injection

Sodium thiosulphate injection

Emergency and Critical Care

Adrenaline

Alteplase

Amiodarone

Benztropine injection

Calcium chloride 1 g/10 mL*

Calcium gluconate gel

Calcium gluconate injection

Cyproheptadine

Ephedrine

Glucagon injection

Hydralazine

Icatibant

Intravenous lipid emulsion 20%*

Ketamine

Lignocaine

Noradrenaline

Octreotide

Propofol

Sodium bicarbonate 100 mmol/100 mL*

Tranexamic acid

Vitamin K (IV)

Other

Dantrolene injection

Desmopressin

Enoxaparin

Heparin

Oxytocin

Quinine injection

Rasburicase

* Specific concentrations are included for these products as they are they are used in specific emergency situations.

National immunisation program vaccines

Any vaccine on the NIP that includes the following:

Hepatitis A

Hepatitis B

Diphtheria

Tetanus

Acellular pertussis

Haemophilus influenzae type b (Hib)

Inactivated poliomyelitis (IPV)

Rotavirus

Meningococcal C

Measles

Mumps

Rubella

Varicella (chickenpox)

Human papillomavirus (HPV)

Seasonal influenza

Pneumococcal polysaccharide (23vPPV)

Pneumococcal conjugate (13vPCV)

Herpes zoster (shingles)

Other vaccines that include:

Adult diphtheria and tetanus

Meningococcal B

Meningococcal A

Meningococcal W

Meningococcal Y

Specific Immunoglobulins

CMV immunoglobulin

Rh(D) immunoglobulin

Tetanus immunoglobulin

Zoster immunoglobulin

Rabies immunoglobulin

Rabies vaccine

Hepatitis B immunoglobulin

Anticonvulsants

Phenytoin IV

Diazepam IV

Obstetrics

Ergometrine

Antivenoms

Brown snake antivenom

Death adder antivenom

Sea snake antivenom

Taipan antivenom

Polyvalent snake antivenom

Stone fish antivenom

Box jellyfish antivenom

Tiger snake antivenom

Red back spider antivenom

Black snake antivenom

Funnel web spider antivenom

S3 medicines

Adrenaline injection

Chloramphenicol

Glyceryl trinitrate

Macrogols

Naloxone injection

Salbutamol inhaler

Ulipristal

Consultation issue 4: Compliance obligations and potential penalties

The introduction of mandatory reporting of medicines shortages raises the need for a compliance mechanism – without penalties of some sort for non-compliance, there are no consequences for failure to provide mandatory reports within the required timeframes and the system would revert to the unsuccessful voluntary model that is currently in place.

It is proposed that the compliance obligations and penalties would align with the principles of the TGA's existing compliance framework, and commence 6 months after the introduction of the reporting requirements specified in the proposed Bill to amend the *Therapeutic Goods Act 1989*, to allow time for sponsors to adjust to the new framework. Such an approach attempts to identify sponsors at risk of unintentional or deliberate non-compliance and enable the development of appropriate strategies to prevent non-compliance. We will also undertake regulatory education activities with industry sponsors to raise awareness of compliance obligations and how to meet them.

In most cases, medicine sponsors will be given an opportunity to comply with the requirement in the first instance; and where there is non-compliance we will take enforcement action. TGA will increase the level of action taken where a given sponsor has a history of repeated non-compliance.

However, where a sponsor's first instance of non-compliance is assessed to be particularly serious, then TGA would consider pursuing one of the more substantial penalties from the outset. The potential options are presented in the table below – we seek feedback on which options are most appropriate.

Options	Penalty for non-compliance	Comments
1. Publicly identifying non-compliant sponsors, without additional sanction	Publishing the names of sponsors who do not comply with the mandatory reporting requirements on the TGA website, and potentially in other media.	• The US FDA has a 'name and shame' policy. However, this policy provides much greater incentive for compliance in a US context than it would in Australia due to the large size of the local US pharmaceutical manufacturing industry. Comparatively less prescription pharmaceutical manufacturing is undertaken in Australia.

Options	Penalty for non-compliance	Comments
2. Focus on civil penalties and infringement notices	The issuing of an infringement notice for a contravention in most circumstances (in the amount of up to 60 penalty units for a body corporate), and publication of the notice on the TGA website. The initiation of civil penalty proceedings where there is repeated non-compliance, or where the shortage involves a critical product for patients. This option would also include publishing the names of sponsors who do not comply with the mandatory reporting requirements on the TGA website and potentially in other media. **Background:** A sponsor would be liable for a maximum civil penalty of: • for an individual – 100 penalty units • for a body corporate – 1,000 penalty units. In most cases this may apply as a single amount, but where there is repeated non-compliance, and where the shortage involves multiple entries in the Register, this may apply per entry. A penalty unit is currently $210, so an infringement notice for a body corporate (e.g. a sponsor company) is currently $12,600.	• These penalties are intended to provide an effective incentive to comply with the requirements, without deterring supply. • It would be open to the Secretary to issue an infringement notice under new Part 5A-2 of the *Therapeutic Goods Act 1989*, one of the recently passed amendments. This would enable a sponsor to choose to pay an infringement notice amount as an alternative to having court proceedings brought against the person for the contravention; • New subsection 42YKA(2) of the Act limits the amount payable under an infringement notice that relates to one alleged contravention of the provision to the lesser of: – one-fifth of the maximum penalty that a court could impose on the person for that contravention, and – 12 penalty units where the person is an individual, or 60 penalty units where the person is a body corporate; • A civil penalty is one imposed by courts applying civil, rather than criminal, processes; • It would be open to a court to impose a civil penalty for a lesser amount if it considered it appropriate in the circumstances; • New section 42YCA of the Act would apply (this provides for daily civil penalties for each day of contravention after the day on which the person must take the required action – i.e. in this case reporting the medicine shortage). This would align TGA with the proposed UK approach which applies daily penalties.

Options	Penalty for non-compliance	Comments
3. Substantial civil penalties and criminal offence	Civil penalty for failing to report a medicine shortage: Maximum civil penalty: • for an individual – 3,000 penalty units; and • for a body corporate – 30,000 penalty units. Criminal offence for failing to report a medicine shortage: Penalty: Imprisonment for 12 months or 1,000 penalty units, or both. This option would also include publishing the names of sponsors who do not comply with the mandatory reporting requirements on the TGA website (and potentially in other media), and the issuing of an infringement notice for a contravention in most circumstances (in the amount of up to 60 penalty units for a body corporate), and publication of the notice on the TGA website.	• The maximum amounts for the penalties in this option are equivalent to those imposed under existing sections 29A and 29AA of the TG Act for failing to notify the Secretary of information relating to adverse effects of registered or listed therapeutic goods that a sponsor is aware of. Section 29A creates a criminal offence and under section 29AA the person is liable to a civil penalty for such conduct; • Subsection 4K(2) of the *Crimes Act 1914* would apply (this creates a daily or continuing offence for each day the person is in breach after the day on which the person must take the required action – ie in this case reporting the medicine shortage); • New section 42YCA of the Act would also apply under this option (this provides for daily civil penalties for each day of contravention after the day on which the person must take the required action – ie in this case reporting the medicine shortage); • Where the offender is a body corporate, its executive officers could potentially be personally liable, in accordance with section 54B of the Act; • The maximum amount of the potential civil penalties under this option would be more substantial, and may not be consistent with a regime in which repeated non-compliance is expected to be rare; • The non-reporting of medicine shortages may not be directly analogous to the non-reporting of the adverse effects of medicines, particularly in relation to whether harm to a person is, or may be, directly related to the non-reporting; • Criminal offences may not necessarily be the most effective sanction where the majority of participants in the prescription medicines and vaccines market are body corporates.

Options 2 and 3 are more aligned to Canada's enforcement approach which takes a graduated, risk-based approach, in which available regulatory measures range from public warnings or advisories to investigation and referral for prosecution of an offence, with applicable fines and penalties. The UK is also proposing significant financial penalties for non-reporting of medicine shortages.

For consideration

PROPOSED COMPLIANCE: Three options are presented in the table above.

SOME QUESTIONS TO CONSIDER:

- *Do you support particular options? Why? I support Option 2.*

  Option 1 is too soft. Whilst I like the concept of "name and shame", this should be accompanied by penalties.

  Option 2 is my preferred option. I would like to see additional penalties such as exclusion from the PBS for a defined period introduced where the company is either a repeat offender or non-complier. The financial fine and the PBS exclusion time could be graded according to degree of shortened notification period and/or number of prior infringements.

  Option 3 is too harsh.

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

Option 2 with the modifications as suggested above.

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