12 November 2020

Delegate to the Secretary
Therapeutic Goods Administration
Department of Health
medicines.scheduling@health.gov.au

Dear Delegate,

RE: TGA on the interim decision to amend the current Poisons Standard in relation to nicotine

The Society of Hospital Pharmacists of Australia is the national professional organisation for more than 5,000 pharmacists, pharmacists in training, pharmacy technicians and associates working across Australia's health system. SHPA is committed to facilitating the safe and effective use of medicines, which is the core business of pharmacists, especially in hospitals.

SHPA welcomes the opportunity to provide feedback to the Therapeutic Goods Administration (TGA) on the interim decision in relation to nicotine.

In principle SHPA supports the decision to regulate the use of nicotine as a Schedule 4 substance and its relevant Appendix D listing with the following caveats:

1. Liquid nicotine products should be registered on Australian Register of Therapeutic Goods (ARTG) to ensure safety, efficacy and quality.
2. The Electronic Nicotine Delivery Systems (ENDS) used to administer liquid nicotine must be registered by the TGA as medical devices to ensure their safe use.
3. Imported liquid-nicotine containing products must meet minimum safety and quality standards regarding manufacturing standards, impurities and safety of excipients.
4. Independent Australian clinical guidelines must be developed prior to the implementation date, to support health professionals prescribing and dispensing liquid-nicotine containing products.
5. Child safety must be prioritised through regulatory measures including: regulating flavouring agents, mandating use of child-resistant closures for liquid-nicotine containing products, and maximum volume and concentration limits per liquid nicotine refill container.
6. A one-year post implementation review into the safety and efficacy of liquid-nicotine containing products must be conducted to inform emerging practice in this area.

In addition, SHPA has serious concerns about the difficulty facing hospitals and healthcare services in implementing policy which acknowledges the legal use of these products in healthcare settings.

Given the additional measure that are necessary to ensure appropriate safety, efficacy and quality use of nicotine SHPA believes that the 1 June 2021 proposed implementation date is premature. It does not allow sufficient time for appropriate measures – including those recommended in our submission – to be put in place and ensure the medical and pharmacy workforce are prepared to support the safe provision of liquid-nicotine containing products to consumers for therapeutic purposes.

The attached submission explores SHPA's position and the above caveats in further detail, while highlighting hospital-specific factors for consideration by the Delegate. If you have any queries or would like to discuss our submission further, please do not hesitate to contact Johanna de Wever, General Manager, Advocacy and Leadership on jdewever@shpa.org.au.

Yours sincerely,

K michaels

Kristin Michaels
Chief Executive

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

SHPA submission to TGA's interim decision to amend the current Poisons Standard in relation to nicotine

Position

SHPA supports the TGA's interim decision with the inclusion of several caveats which recognise the significant harm of nicotine, and the complexity of its use as a therapeutic product.

SHPA supports the decision in-principle to regulate nicotine as a Schedule 4 Prescription Only medicine in preparations for human use as an aid in withdrawal from tobacco smoking, excluding in preparations for oromucosal or transdermal administration, or in tobacco prepared and packed for smoking.

SHPA also supports the inclusion of Schedule 4 nicotine preparations in the Appendix D listings, clarifying that all nicotine, other than that excluded from the Poisons Standard, must be prescribed by a medical practitioner for therapeutic use.

SHPA does however recognise that nicotine is harmful and highly addictive, as addictive as heroin and cocaine.[1] It is for this reason that our in-principle support for the decision to regulate the use of nicotine as a Schedule 4 substance, is contingent on satisfying the caveats described below to be considered by the delegate upon formulation of the final decision, to maximise public and clinician confidence and safety in this decision as a public health measure. Additionally, SHPA also would like to highlight the implications of this interim decision for hospitals and hospital pharmacy policies, governance, and practices to be considered by the delegate, which are also discussed in our submission.

Caveats to SHPA's in-principle support of the interim decision

1. Liquid nicotine products should be registered on Australian Register of Therapeutic Goods (ARTG) to ensure safety, efficacy and quality.

   Clinicians must have confidence of the safety, efficacy and quality of the medications which they prescribe and dispense to patients to treat health conditions. One of the main governance structures in Australia regarding the safety, efficacy and quality of the medications, is its regulation by the TGA and having medications listed on the ARTG.

   Providing an ARTG listing for liquid nicotine would give clinicians confidence to prescribe and dispense these products for therapeutic use to patients, as an aid in withdrawal from tobacco smoking. As noted in the notice of the interim decision, this is the same standard applied to existing nicotine replacement products.

   SHPA member feedback indicates there are concerns of incongruence with professional pharmacy practice standards and codes, as well as professional indemnity insurance concerns, if they were placed in a position to dispense unregulated nicotine products to patients. Having all liquid-nicotine containing products ARTG listed would abate these concerns. This process would also provide more consistency between available liquid-nicotine containing products, and clarity on the dose clinicians are providing, given that inhaled substances have wider variability on actual dose delivered. This variability is compounded by the delivery devices used as discussed below.

   As advised by the Committee in the notice of the interim decision, the current pathway for approval to supply products for smoking cessation is available for e-cigarettes containing nicotine. This would be consistent with the requirements for existing nicotine replacement products.

2. The Electronic Nicotine Delivery Systems (ENDS) used to administer liquid nicotine must be registered by the TGA as medical devices to ensure their safe use.

   The device in which a scheduled substance is delivered, must be regulated to ensure a precise and safe dosage is administered to patients. This is even more imperative when the substance is as harmful and

addictive as nicotine. SHPA is concerned that the TGA does not intend to regulate ENDS and believes this position is inconsistent with its role as the regulator.

Failure to regulate ENDS and necessitating patients to source these devices themselves on the global market means prescribers and pharmacists will have no confidence of the accuracy of the treatments they are prescribing and dispensing. As mentioned above, this represents a risk to clinical practice within the bounds of professional pharmacy practice standards and codes that would not breach their professional indemnity insurance.

The TGA has stringent regulations for the delivery of substances that pose significantly less risk to patients than nicotine. For example, the TGA regulates devices used for inhaled medicines, such as budesonide/formoterol delivered via Turbuhaler and Rapihaler devices, and so much so that both the metered and delivered doses require display on the packaging due to their difference. Regulation of these devices ensures a clear understanding of the actual dose delivered via the device.

The treatment of ENDS should be no different to other devices used for inhaled medicines. Medical prescribers and dispensers must have certainty of the maximum dose of liquid nicotine being administered via the different ENDS used by patients and the safety of these devices. SHPA therefore urges the TGA to consider ENDS as medical devices and regulate them accordingly.

3. Imported liquid-nicotine containing products must meet minimum safety and quality standards regarding manufacturing standards, impurities and safety of excipients.

Imported Schedule 4 products must comply with Australian safety and quality standards regarding manufacture, impurities and safety of excipients in-line with other scheduled medications dispensed by pharmacists. SHPA is concerned that the published FAQs supporting the interim decision acknowledges that no specific standards were proposed by the delegate that would require suppliers to ensure that imported liquid-nicotine containing products meets certain standards regarding manufacture, impurities and safety of excipients. Minister Hunt's media release on 'Prescription Nicotine Based Vaping' stated that the Victorian Poisons Centre reported a near doubling of nicotine poisons between 2018 (21 cases) and 2019 (41 cases), largely due to imported products of questionable safety and quality. SHPA believes this position would be inconsistent with the role of the regulator, especially for substances as potentially harmful as liquid-nicotine containing products.

Clinicians need to be confident that the manufacturing, excipients and packaging of liquid-nicotine containing products, meet minimum safety and quality standards, as with any other medication prescribed and dispensed in their practice. It would be reasonable to limit the importation of liquid-nicotine containing products into Australia to countries such as the United Kingdom[2] or New Zealand (in the near future), who have liquid nicotine product safety and quality requirements that align with Australian standards for other Schedule 4 medications.

4. Independent Australian clinical guidelines must be developed prior to the implementation date, to support health professionals prescribing and dispensing liquid-nicotine containing products.

The regulation of liquid-nicotine containing products must be accompanied by the development of independent, reputable clinical guidelines suitable for the Australian setting. Independent clinical guidelines are essential to guide clinicians in providing evidence-based practice. These guidelines are essential in outlining the role of liquid-nicotine containing products in aiding withdrawal from tobacco smoking, noting its place in therapy – given the diversity of nicotine-containing products in Australia – and recommended therapeutic usage. This information will guide health practitioners in their clinical decision making when supporting patients on their quit journey and must be made available to clinicians prior to the implementation of this regulation.

SHPA understands that there exist significant interests in the tobacco industry, and the evidence on e-cigarettes and liquid-containing products is emerging and contested, however this should not prevent

the establishment of clinical guidance – that is updated regularly – to support the delegate's decision. Given the rapid rate in which evidence is being undertaken in this area, these could be living guidelines to dynamically respond to new evidence.

SHPA believes the lessons learnt from medicinal cannabis are broadly applicable to liquid -nicotine containing products, and demonstrates the establishment of clinical guidance is essential. In recent years, the use and regulation of medicinal cannabis had also been controversial with interested parties releasing clinical advice and guidelines, which made it difficult for clinicians to find independent guidance on a potentially risky area of practice. As the TGA and wider Australian government moved to regulate medicinal cannabis products, accompanying this were also evidence and guideline summaries produced by independent bodies and jurisdictional governments to guide practice.

5. Child safety must be prioritised through regulatory measures including: regulating flavouring agents, mandating use of child-resistant closures for liquid-nicotine containing products, maximum volume and concentration limits per liquid nicotine refill container.

It is the delegate's responsibility to priorities the safety of children exposed to liquid-nicotine containing products. Every effort must be made to reduce the risk of children experiencing severe adverse effects and mortality from exposure to these products. This includes the regulation of flavouring agents to ensure they are not highly attractive to children, whilst also mandating child-resistant closures for liquid nicotine containing products. Both these measures will reduce the incidence of accidental child poisoning.

As highlighted in the interim decision, the Therapeutic Goods Order No. 95 – Child restraint packaging requirements for medicines 2017 (TGO 95), only apply to medications on the ARTG. SHPA strongly recommends that liquid-nicotine containing products are placed on the ARTG as noted above, however, regardless of approval status, child resistant containers must be seriously considered by the Delegate in their final decision. Consideration must also be given to restricting the maximum concentration of liquid nicotine per container and maximum size for refill containers permitted for use in Australia, in an attempt to reduce the severity of adverse effects experienced by children who ingest these toxic products.

6. A one-year post implementation review into the safety and efficacy of liquid-nicotine containing products must be conducted to inform emerging practice in this area.

Given the lack of evidence and strong public and professional interest in the regulation of liquid-nicotine containing products, SHPA recommends the TGA undertake a review into the safety and efficacy of these products one-year post implementation of scheduling changes and as required into the future. This would be a similar process to safety and efficacy reviews of high-risk medicines that TGA has conducted over the years, including non-steroidal anti-inflammatory medicines, diclofenac, codeine and cannabidiol.

The aim of a review would be to ascertain whether any further evidence has accrued in relation to the safety and efficacy of liquid-nicotine containing products for smoking cessation since the implementation of the scheduling changes.

SHPA recognises that in regulating liquid-nicotine containing products the delegate seeks to strike a balance between ensuring vaping products are available for adults who smoke tobacco and wish to switch to a less harmful alternative, and ensuring these products are not marketed or sold to young people. However, given the harmful and addictive nature of nicotine, SHPA recommends that the TGA's review should also investigate whether the primary goals of the scheduling decision were indeed achieved, looking at whether there has been an uptake in adults utilising liquid-nicotine containing products to aid their quit attempt, or a reduction in usage among young people.

Implications for hospitals and hospital pharmacy policies, governance, and practices

SHPA members report that Australian hospitals are a significant intervention point for patients who smoke given that those who attend are often critically ill, vulnerable and encouraged to make a smoking cessation attempt. Many people who smoke and happen to be hospitalised with cardiovascular[3,4,5], respiratory or neurological conditions report being prepared and making efforts to quit, as do those who attend emergency departments and attribute their visit to a smoking-related problem.

In response, many hospitals have developed smoking cessation services for inpatients, leveraging critical intervention opportunities to support patients in initiating their quit journey and discharge patients with appropriate smoking cessation medicines.

However, the hospital sector was not consulted in the lead up to this interim decision, therefore hospital specific concerns regarding the regulation of liquid-nicotine containing products have not been considered. For example, nicotine has been associated with high-risk behaviour in hospitals with Hospital and Health Services in Queensland identifying the enforcement of smoking rules as a common contributing factor to occupational violence.[6] Hospitals will be required to develop and implement policies on the use of liquid-nicotine containing products on wards and hospital grounds, which is likely to trigger further workplace safety concerns in hospitals.

Below are some of the hospital-specific considerations SHPA members have noted including, the challenges associated with integration of these products into hospital formularies and electronic medical records (eMRs), and the further complexities caused by the wide variability between jurisdictions and individual hospitals. SHPA members also note various clinical considerations relating to the regulation of liquid-nicotine containing products and their use in Australian hospitals.

Hospital policies regarding smoking on hospital grounds

All hospitals have a ‘no smoking on grounds’ policy. Each hospital would be required to develop new policies to accommodate patients who are prescribed liquid-nicotine containing products prior to hospital admission and visitors who wish to use these products on hospital grounds. A study of all 121 hospitals in the state of North Caroline in the United States found that over 80% of respondents had an existing policy regulating the use of e-cigarettes on hospital grounds, and another 10% intending to establish one.[7]

SHPA believes that if patients are prescribed liquid-nicotine containing products by their primary care prescribers, as with all their regularly prescribed medications, they would expect to be able to continue these therapies as an inpatient upon medication reconciliation. As noted above, nicotine use has historically been a key trigger for violence and high-risk behaviour in some hospitals. Without adequate consideration of these complexities, patients may suffer stress and distress when prevented from using liquid-nicotine containing products on hospital grounds.

Hospital formularies and procurement

The relationship between hospital formularies and liquid-nicotine containing products must be considered prior to the implementation date, so that hospitals can adapt to these changes and avoid distress for patients. Hospital formularies drive prescribing and dispensing practices in hospitals.

Doctors and pharmacists are unable to prescribe and dispense medications that are not on the hospital formulary. Making changes to hospital formularies is a complex process that requires applications with evidence supporting clinical use. Given the lack of evidence surrounding the safety and efficacy of liquid-nicotine containing products, and the fact that they may be non-ARTG listed, it is highly unlikely that these products will be included in hospital formularies. Hospital doctors and pharmacists are unable to prescribe and dispense products that are not on the hospital formulary, without individual patient usage applications to be considered by the Drugs and Therapeutics Committee. This process would be impractical for liquid-nicotine containing products as in most instances, the patients' reason for admission is not related to their nicotine consumption and they would therefore not be approved.

There are also jurisdictional variations in procurement and tender processes, with varying levels of oversight and assistance by the jurisdictional department of health and varying levels of hospital autonomy with procurement practices. Many states also have a single-brand tender for medications, which would mean the lack of regulation of liquid-nicotine containing products would be another significant hurdle for hospitals to supply these medicines.

Electronic medical records and medication charts

The implementation of eMRs across Australian hospitals requires medication to be included on the database for selection and charting on a patient's electronic medication chart. These databases often draw upon Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) and Australian Medicines Terminology (AMT).

If liquid-nicotine containing products are non-ARTG listed, they will not be included in the database, and charting these medicines would then require 'free-text' processes which are inherently less safe for doctors, pharmacists, nurses and patients. This contradicts best practice efforts to minimise medication risk for patients.

Congruence with existing nicotine replacement therapy (NRT) for inpatients

For the reasons discussed above it is unlikely that hospital patients will be permitted to use liquid-nicotine containing products on the wards. In these case medical and pharmacy staff will be required to develop a process for converting liquid nicotine doses to equivalent nicotine replacement therapy (NRT) doses and formulations. However, given there are no clinical guidelines that outline the appropriate conversation, hospitals will need to develop their own clinical processes based largely on trial and error. This is a risky and resource intensive process which requires each hospital to individually rate and review product use.

SHPA believes this should be undertaken in the context of our caveat on the establishment of independent clinical guidelines. These clinical guidelines could be developed centrally by clinician-led organisation for adoption by all hospitals ensuring consistent high-quality treatment for patients.

Education of hospital staff

Given the complexity of the product, its devices and its use in hospital and non-hospital settings, the interim regulation carries significant implications for change in policies and procedures. This will necessitate relevant clinical education in addition to operational changes.

A substantial amount of time will be required to develop educational resources and ensure all hospital staff, clinical and non-clinical such as security guards, are well informed and capable of supporting this transition. Hence, the 1 June 2021 implementation date is unlikely to be feasible. SHPA recommends a delayed implementation date to facilitate a well thought-out out and process driven implementation in Australian hospitals.

Conclusion

Whilst SHPA is supportive of the scheduling of liquid-nicotine containing products, we are unwavering in the caveats discussed in this submission and would appreciate that consideration is given to the hospital-specific challenges noted. SHPA would be happy to further discuss any of the concerns raised in our submission with the TGA to ensure hospitals are prepared and well-supported prior to the implantation of regulated liquid-nicotine containing products in Australia.

Fundamentally, the proposed implementation date is not a realistic time frame to ensure appropriate consideration of points raised in our submission, including the development of comprehensive clinical guidelines, and the necessary upskilling of the medical and pharmacy workforce and all other hospital staff.

References

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