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10 May 2018

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

Email to: medicines.scheduling@health.gov.au and to: chemicals.scheduling@health.gov.au

Dear Sir or Madam,

Notice inviting public submissions under subsection 42ZCZK/42ZCZL of the *Therapeutic Goods Regulations* 1990. Proposed Amendments to the Poisons Standard to be considered at the ACCS, ACMS and ACCS/ACMS Meetings, June 2018

We refer to the notice inviting public comment under Regulation 42ZCZK/42ZCZL of the *Therapeutic Goods Regulations* and would like to provide comment on three of the scheduling proposals that will be referred to the June 2018 meetings of the ACCS, ACMS and ACCS/ACMS.

ASMI (Australian Self Medication Industry) is the peak body representing companies involved in the manufacture and distribution of consumer health care products (non-prescription medicines) in Australia. ASMI also represents related businesses providing support services to manufacturers, including advertising, public relations, legal, statistical and regulatory consultants.

ASMI appreciates the opportunity to provide public comment in relation to ACCS, ACMS and ACCS/ACMS agenda scheduling proposals. We wish to address relevant matters under section 52E of the *Therapeutic Goods Act* 1989.

Please find enclosed, under cover of this letter, ASMI's comments in relation to the following scheduling proposals that will be considered by the ACCS, ACMS and ACCS/ACMS at the June 2018 meetings:

Budesonide

> *To amend the Schedule 2 entry for budesonide to increase the dose per actuation from 50 to 64 micrograms; and remove the limit of 200 actuations.*

Ibuprofen combined with paracetamol

> *To amend the Schedule 3 entry for paracetamol to allow the Schedule 3 primary pack size, when combined with ibuprofen, to be increased from 30 to 50 dosage units; and amend the Schedule 4 entry to reflect this change.*

Sildenafil

> *To create a new Schedule 3 entry for sildenafil in oral preparations containing 50 mg of sildenafil per dosage unit in packs containing not more than 8 dosage units; to include sildenafil in Appendix H to permit advertising; and to include sildenafil in Appendix M to provide additional controls or supply requirements to allow sildenafil to be supplied by a pharmacist*

Each of these agenda items is presented as a separate attachment.

As an industry representative, ASMI is a key stakeholder in scheduling matters and we are keen to provide further input as required. We look forward to the Delegate's interim decisions and greater detail on the final scheduling proposals.

Please contact me should you require any further clarification relating to this submission.

Yours sincerely,

Steven Scarff
Regulatory and Legal Director

Budesonide (ACMS)

To amend the Schedule 2 entry for budesonide to increase the dose per actuation from 50 to 64 micrograms; and remove the limit of 200 actuations.

Introduction

ASMI supports the proposal to amend the Schedule 2 entry for Budesonide.

The effect of the proposal would be to increase the range of products available to allergic rhinitis sufferers and to remove the upper limit on pack sizes.

ASMI Comment

Budesonide has been available in Australia since 1990 and has been available as an aqueous nasal spray since 2001 for the prophylaxis and treatment of both seasonal allergic rhinitis and perennial allergic rhinitis.

Budesonide has been the subject of numerous clinical studies and the safety and efficacy of the substance are well characterised.

Two strengths of the nasal spray are currently available; 32µg per actuation (S2) and 64µg per actuation (S4). Dosing for the 32µg product is 8 sprays (i.e. 4 sprays per nostril) per day and dosing for the 64µg product is 4 sprays (i.e. 2 sprays per nostril) per day.

The two product strengths therefore provide the same total daily dose of budesonide, but the 64µg product offers a more comfortable and more convenient application. It is to be expected that the less frequent application will lead to better adherence and so to better clinical outcomes.

While having two products on the market for the same indications with different strengths of active might pose some problems for consumers, we believe that consumers will already be comfortable with therapeutic goods being available in different strengths and that the product labelling can be used to effectively differentiate the products.

ASMI understands that 200 actuations corresponds to about 3.5 weeks' usage of the 32µg product (and about 7 weeks' usage of the 64µg product) and that effective long-term management of allergic rhinitis typically involves longer periods of continuous use. The proposal therefore has the potential to improve adherence.

The proposal to remove the actuation limit is also consistent with the schedule 2 entry for the intranasal corticosteroid mometasone (which contains no such upper limit) and with the recent proposal to remove the actuation limit from the Schedule 2 entry for fluticasone. ASMI supports alignment of scheduling entries amongst intranasal corticosteroids.

Scheduling factors

In terms of the scheduling factors for S2 medicines, there is already a Schedule 2 entry for budesonide, the question to be answered now is simply whether adding a higher strength (and a correspondingly lower dose) together with removing an upper limit on the number of actuations

will change the applicability of the factors. In ASMI's view the scheduling factors for S2 medicines will still apply.

In ASMI's view both the 32µg per actuation product and the 64µg per actuation product both meet the scheduling factors for Schedule 2.

Conclusion

ASMI supports the scheduling proposal because it will bring about alignment and consistency between scheduling entries and because it has the potential to improve adherence.

Ibuprofen combined with paracetamol (ACMS)

To amend the Schedule 3 entry for paracetamol to allow the Schedule 3 primary pack size, when combined with ibuprofen, to be increased from 30 to 50 dosage units; and amend the Schedule 4 entry to reflect this change.

Introduction

ASMI supports the proposal to increase the pack size of the Schedule 3 entry from 30 to 50 dosage units. ASMI also continues to support retaining a scheduling cut-off based on the number of dosage units (as opposed to a scheduling cut-off based on a number of days' supply).

Not only will this better reflect the current scheduling principles, but it will be a move towards closer alignment with the New Zealand scheduling of the combination.

The individual components have a long history of use and a well-documented, favourable safety profile.

ASMI Comment

ASMI continues to support retaining a scheduling cut-off based on the number of dosage units (as opposed to a scheduling cut-off based on a number of days' supply), for the following reasons:

- All the other scheduling entries for divided preparations of paracetamol and ibuprofen are based on maximum pack sizes and maximum quantities of active ingredient per tablet or capsule (thereby ensuring consistency of the maximum amount of active per pack). For the sake of this consistency the same approach should be taken here.
- The active ingredient quantities and dosing instructions for the two major combination products are different, so that a 3 day supply of Nuromol is a maximum of 9 tablets and a 3 day supply of Maxigesic is a maximum of 24 tablets. To avoid confusion in the marketplace and to ensure that products in the same schedule contain similar total quantities of active ingredients, the scheduling of the combination should be based on pack size.

Paracetamol 500mg (immediate release) tablets (when labelled with appropriate warnings and dosage instructions) are currently:

- Exempt from scheduling in packs containing not more than 20 tablets,
- Schedule 2 in packs containing between 21 and 100 tablets,
- Not included in Schedule 3.

Ibuprofen 200mg (immediate release) tablets (when labelled with appropriate warnings and dosage instructions) are currently:

- Exempt from scheduling when included in packs containing not more than 25 tablets,
- Schedule 2 in packs containing between 26 and 100 tablets,
- Not included in Schedule 3.

Current policy and scheduling principles for products containing more than one poison[1] states:

> *"If a preparation contains two or more poisons, the provisions relating to each of the Schedules in which those poisons are included apply.*
>
> *Where it is not possible to comply with a provision relating to one of those Schedules and with a provision relating to another of those Schedules, the provision of the more restrictive Schedule applies, unless a contrary intention is indicated in the Schedules or relevant legislation"*

On this basis, ASMI continues to believe that the scheduling of these combination products should be consistent with the scheduling of the individual components, i.e. they should be included in Schedule 2 for packs sizes between 26 and 100 dosage units.

If the upper limit of the Schedule 3 entry for the combination was increased to 50 dosage units as proposed this would mean that the new Schedule 3 upper limit for the combination was still only half of the 100 dosage units already permitted by the Schedule 2 entries for the separate ingredients.

Paracetamol and ibuprofen individually both have a long history of use in Australia, and are well tolerated and have favourable safety profiles. The low risks associated with these ingredients are such that they are unscheduled in small pack sizes.

It is ASMI's position that the low risks individually associated with paracetamol and ibuprofen will similarly be associated with the combination of the two. This view is supported by published studies[2] and by post-marketing data.

ASMI acknowledges that combination products may contribute to unintentional overdose (with consumers taking multiple products containing the same active). However, this issue can be adequately dealt with through product labelling, which is the domain of the regulator, and pharmacist advice at the point of sale.

The labelling of these products contains appropriate warning statements, as per the TGA Medicines Advisory Statement Specifications (MASS 2017) to facilitate appropriate use. Pharmacists are also available at the point of supply to provide advice and referral if needed.

ASMI is unaware of any evidence of dependence, abuse, misuse or illicit use of the combination paracetamol and ibuprofen product. To the contrary, this combination offers an alternative to codeine containing analgesics.

Consumers are familiar with the use of OTC analgesic products to assist them with the short term relief of muscular aches and pains, mild to moderate pain of osteoarthritis, dental pain, headache, migraine etc. These conditions are suitable for short term management by consumers.

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[1] See page vii of the Poisons Standard March 2018 https://www.legislation.gov.au/Details/F2018L00168

[2] De Vries F, Stetakis E, van Staa TP. Concomitant use of ibuprofen and paracetamol and the risk of major clinical safety outcomes. Br J Pharmacol. 2010;70(3):429-38

Harmonisation – New Zealand

ASMI notes that in New Zealand, combination paracetamol and ibuprofen products are Pharmacy Medicines in packs of 21 to 100 tablets / capsules, and suitable for general sale (GSL) in packs of up to 20 tablets / capsules. The New Zealand classification of the combination product is the same as the classification of the separate ingredients.

ASMI supports measures to more closely align Australian schedules with New Zealand and other comparable markets, where there is alignment in scheduling principles.

The marketing history of this combination product in New Zealand adds further support to the safety study referred to above. It would be anticipated that sponsors of these combination products in New Zealand will have post-marketing data that further demonstrates the favourable safety profile of this combination product.

Conclusion

ASMI supports the proposal for amendment of Schedules 3 and 4.

Sildenafil (ACMS)

To create a new Schedule 3 entry for sildenafil in oral preparations containing 50 mg of sildenafil per dosage unit in packs containing not more than 8 dosage units; to include sildenafil in Appendix H to permit advertising; and to include sildenafil in Appendix M to provide additional controls or supply requirements to allow sildenafil to be supplied by a pharmacist

Introduction

ASMI supports the proposal for a new Schedule 3 entry for sildenafil.

ASMI supports the proposals to include sildenafil in Appendix H and in Appendix M.

ASMI Comment – S3

It is well established, that men have greater vulnerability to various health disorders across their lifespan than women, they are also more likely than women to experience serious health problems. These issues arise because Australian men are less likely to seek treatment from a general practitioner or other health professional, and are less likely to have in place the supports and social connections needed when they experience physical and mental health problems. We therefore need initiatives to address the reasons why men are reluctant to engage with GPs, and the consequences of that reluctance, and invest in innovative models of care that overcome these barriers. Health care services need to be flexible and responsive to the complex and unique access needs of men. Increasing men's engagement can be achieved through the provision of novel and flexible health care outreach programs.

A significant proportion of men suffering from ED are not currently seeking professional advice. More convenient access through the pharmacy has the potential to lead men who currently remain untreated into the healthcare system. This has the potential for more frequent conversations with men about the underlying conditions leading to ED and therefore to better health outcomes. It also enables pharmacists to play a vital role in referring men earlier for further discussions with their GP about their health.

Furthermore, there are a growing number of TGA alerts relating to contaminated, adulterated and counterfeit ED products and the men who purchase these products are doing so without the supervision of a healthcare professional. Increased access via pharmacy will provide men with a legitimate product and advice from a pharmacist.

The scheduling proposal meets the scheduling factors for a schedule 3 medicine:

1. **Sildenafil is substantially safe with pharmacist intervention (per Appendix M) to ensure the quality use of the medicine. There may be potential for harm if used inappropriately.** The consumer can identify the symptoms of ED but counselling and verification by a pharmacist is required before use. Consumer consultation with a pharmacist is necessary to reinforce and/or expand on aspects of the safe use of the medicine.

2. **The use of the medicine is not expected to produce dependency at either the established therapeutic dose or at supratherapeutic doses. Where risk of misuse, abuse or illicit use is**

identified, the risk can be minimised through pharmacist-consumer consultation. There has been no evidence of dependence with Sildenafil and it could be argued that the S3 availability of sildenafil will reduce the risks associated with counterfeit and adulterated products.

3. **The risk profile of the medicine is well defined and the risk factors for adverse effects, interactions and contraindications are known, identifiable and manageable by a pharmacist.** Sildenafil has a well-established safety profile

4. **Where the medicine is intended for recurrent or subsequent treatment of a chronic condition, pharmacist intervention is required to monitor safe use of the medicine following recommendation by a medical practitioner or other authorised prescriber**. Appendix M controls will ensure referral to the doctor where necessary.

5. **The use of the medicine at established therapeutic dosage levels may mask the symptoms or delay diagnosis of a serious condition.** ED can be associated with a number of contributing conditions, the Appendix M controls will ensure referral to the doctor where necessary. S3 availability of sildenafil may hasten referral to a doctor.

Sildenafil has been available without a prescription in New Zealand since 2014.

In announcing their approval of the down-scheduling of sildenafil, the UK's MHRA concluded that[3]:

> *Pharmacy availability of Viagra Connect tablets will be of value to men who suffer from erectile dysfunction. Patients can be assessed for suitability by a pharmacist and made aware of the risks, situations where supply is not appropriate, and potential interactions with other drugs.*
>
> *The risks of indirect danger arising from missed diagnosis of underlying disease are minimised through the pharmacist using their professional judgement and the checklist to identify men for whom the product is not suitable and referring them to a doctor.*
>
> *It is also considered that there is a low risk of direct danger and of intentional abuse that will lead to a danger to human health. Furthermore, these low risks are outweighed by the benefits that this route of supply can bring – by bringing a hard-to-reach group into a healthcare environment with the potential to increase early identification of heart disease and also reduce the risks associated with use of counterfeits obtained via the internet.*

<u>ASMI Comment – Appendix H</u>

ASMI believes that raising public awareness of Schedule 3 medicines will deliver a range of benefits – firstly for consumers by increasing awareness of a broader range of therapeutic options; secondly, for pharmacists by promoting their professional role in managing conditions for which Schedule 3 medicines are available.

[3] https://www.gov.uk/government/consultations/proposal-to-make-sildenafil-50mg-film-coated-tablets-available-from-pharmacies

A recent study commissioned by ASMI and conducted by the Centre for Health Economics Research and Evaluation (CHERE), University of Technology Sydney[4] examined the impact of S3 advertising and found the following:

- Advertising raises awareness of therapeutic options and pharmacy services which can result in improved disease management.
- The pharmacist's recommendation had a positive and significant impact on the consumers' choice of preferred product.
- Consumers are comfortable talking to pharmacists about their disease management.
- Advertising is unlikely to drive inappropriate demands for brands.
- Pharmacists showed confidence in handling a direct request from consumers for a particular product, and this was not a significant factor in their recommendations.
- Advertising will not have a significant impact on the recommendations made by pharmacy professionals
- S3 advertising is unlikely to lead to inappropriate use of the medicine.

The TGA Schedule 3 Advertising Guidelines (dated November 2000) refer to the following criteria that should be used when determining suitability of a medicine for inclusion in Appendix H. These include:

- Potential public health benefit
- Likelihood of advertising leading to inappropriate patterns of use
- Provisions relating to the Therapeutic Goods Advertising Code
- Whether the entry may result in advertising of goods for an indication other than those included in the ARTG
- Ability of the consumer to appropriately use through labelling / CMI etc.

ASMI believes that Schedule 3 access to sildenafil fulfils the above criteria.

Re-scheduling alone will not necessarily result in improved access to a medicine and it is important for consumers to be made aware of the non-prescription availability of sildenafil.

Without inclusion of sildenafil in Appendix H, the opportunity to undertake important consumer education initiatives will be severely diminished. Advertising of Schedule 3 sildenafil can encourage more health conversations between consumers and pharmacists, lead to earlier referral to a GP for earlier diagnosis of any potential underlying conditions such as CVD and diabetes, and encourage men to improve their lifestyle and take other positive preventative actions to reduce their risk factors.

As with all Schedule 3 medicines, the labelling of the product is approved by the TGA and a Consumer Medicines Information document will be available from pharmacists in order to assist consumers.

<u>ASMI Comment – Appendix M</u>

ASMI understands that any re-scheduling of sildenafil in Australia would be accompanied by pharmacist training and that pharmacists would be provided with appropriate screening and

[4] https://www.uts.edu.au/sites/default/files/CHERE_report_S3_final.pdf

support tools to ensure Quality Use of Medicines principles were applied and to ensure that referral to a GP occurs where appropriate.

ASMI notes that the concerns from previous ACMS meetings that "additional pharmacist training and use of a specific supply protocol cannot be mandated for the supply of pharmacist-only Schedule 3 medicines" have now been addressed through the establishment of an Appendix M to the Poisons Standard.

ASMI encourages the Committee to take this opportunity to put the new Appendix M to the test.

Conclusion

Sildenafil has a well-established safety profile (it is well tolerated, with adverse events that are mild, transient and easily managed).

Symptoms of ED can be identified by patients and managed by appropriately trained pharmacists with referral to a GP where necessary.

A similar scheduling arrangement to that proposed already exists in New Zealand and the results there have been positive. Additionally, the UK regulator has recently re-classified sildenafil as a Pharmacy Medicine.

ASMI supports the proposal to include sildenafil in Appendix H, and believes that there are benefits for both consumers and pharmacists with increasing awareness of Schedule 3 medicines in general.

ASMI believes that there are potential public health benefits in advertising the Schedule 3 product to consumers.

For these reasons, the scheduling proposal should be supported.