Further Public Submissions on the Proposed Amendments to the Poisons Standard

Notice under subsections 42ZCZL of the Therapeutic Goods Regulations 1990 (the Regulations)

A delegate of the Secretary to the Department of Health publishes herein all valid public submissions made in response to the invitation for public submission on the interim decisions regarding the proposed amendments to the Poisons Standard (commonly referred to as the Standard for *the Uniform Scheduling of Medicines and Poisons* - SUSMP). These submissions were considered by the Medicines Delegate.

In accordance with the requirements of subsection 42ZCZL of the Regulations these submissions have had confidential information removed.

Material claimed to be commercial-in-confidence was considered against the guidelines for the use and release of confidential information set out in Chapter 6 of the Scheduling Policy Framework for Medicines and Chemicals (SPF), issued by the National Coordinating Committee on Therapeutic Goods. The SPF is accessible atwww.tga.gov.au/industry/scheduling-spf.htm.

Discrete submissions have been grouped by substance.

List of Submissions

Substance	**Total number of public submissions**
Diclofenac	1 submission
Naproxen	3 submissions

[redacted]

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601
via email: SMP@health.gov.au

June 12th, 2014

To the Secretary,

RE: Comments on the Delegate's Interim Decision, May 2014 - Dermal Diclofenac

[redacted] provides the following comments on the Delegate's Interim Decision published on 29 May 2014 regarding the scheduling of dermal diclofenac.

Current scheduling status

In Australia, dermal diclofenac 1% or less is unscheduled, while >1% and up to 4% diclofenac is Schedule 2, as are transdermal preparations of 140 mg or less. When indicated for use in the treatment of solar keratosis, dermal diclofenac is Schedule 4.

In New Zealand, diclofenac in preparations for external use, other than for the treatment of solar keratosis, is classified as General Sale. At its 47th meeting in May 2012, the New Zealand Medicine Classification Committee (MCC) considered harmonising with the Australian classification for dermal preparations containing >1% and up to 4% diclofenac. The MCC concluded that there was not sufficient data to support a claim that products containing diclofenac at concentrations up to 4% posed a sufficient risk to public health to warrant reclassification from General Sale to Pharmacy Only.

Proposal for Trans-Tasman Harmonisation

It is proposed to exempt dermal preparations containing up to and including 2% diclofenac from scheduling, except when indicated for the treatment of solar keratosis, which should remain as a Schedule 4 item. This would achieve harmonisation with the New Zealand classification for 2% dermal diclofenac.

A non-harmonised approach to scheduling results in different labelling requirements in Australia and New Zealand for the same product. Low volumes for New Zealand means that it is often not commercially viable to launch products with specific New Zealand labelling.

As published on the Medsafe website (http://www.medsafe.govt.nz/profs/class/harmon.asp, last revised 16 August 2013) the following general principles were recommended by the Working Party on the Trans-Tasman Harmonisation of the Schedules between Australia and New Zealand and

[redacted]

accepted by the Australian Advisory Committee on Medicines Scheduling and the New Zealand Medicine Classification Committee:

1. For both countries there should be
   - equivalent scheduling for drugs and poisons
   - equivalent general exemptions from scheduling
   - a common set of definitions and scheduling criteria and guidelines
   - consistent interpretation of scheduling criteria
   - common nomenclature for drugs and poisons
   - within the schedules, common descriptions for generic drug and poison classes or any other general classification
   - harmonisation of labelling and packaging harmonisation of safety directions, warning statements and first-aid instructions.

2. Where differences in scheduling of a drug or poison currently exist between New Zealand and Australia, the following principles should apply
   - the classification should be reassessed using the common set of definitions and scheduling criteria with a view to achieving a common outcome
   - the underlying principle is to harmonise on the less restrictive schedule while giving due consideration to public health and safety issues and/or specific jurisdictional needs.

3. The process of harmonisation of drug and poisons scheduling should recognise the wider regulatory requirements of other agencies and any complexities should not be exacerbated by harmonisation of schedules.

The proposal to exempt 2% dermal diclofenac from scheduling is thus consistent with the Trans-Tasman Harmonisation intent to harmonise to the lowest schedule.

The Delegate's Interim Decision

The Delegate's Interim Decision is that the current scheduling of diclofenac remains appropriate. Please see below our comments in relation to the delegate's reasons:

Delegate's reasons	[redacted] comments
Formulation has not been available for wider community use.	Topical NSAIDs for pain relief have been available for many years, are widely available without prescription, are used extensively, and evidence for their use is considered adequate[1]. [redacted] In Australia, 1% diclofenac gel has been supplied as an unscheduled medicine since late 2000 without any safety issues. Since 2011, many countries have launched 2% diclofenac gel as an over-the-counter medicine (refer to Appendix 1 of original scheduling application for list of international registration and launch dates).
Lack of evidence of safety from the wider use in the community.	The safety profile of 1% diclofenac gel is well-established and is supported by extensive use in the wider community (see above). 2% diclofenac gel has been developed to achieve efficacious pain relief with fewer applications compared to the 1% gel. While the currently available 1% gel is applied 3-4 times a day, the 2% gel only requires twice daily application. Thus the quantity of diclofenac applied per day is the same for the 2 products.

[redacted]

	With similar daily systemic exposure and risk-benefit profile as the pre-existing 1% gel (refer to original scheduling application for discussion on toxicity studies, post-marketing data and systemic exposure), [redacted] contends that the evidence of safety from the wider use in the community for 1% gel is supportive of the safety for 2% gel.
Different dosing regimen from the current product, therefore access from a pharmacist is appropriate.	The only difference in the dosing regimen of the current 1% diclofenac gel and the 2% diclofenac gel is the frequency of daily application: 1% diclofenac gel is applied 3-4 times a day, while the 2% gel only requires twice daily application. The 2% gel has a more simplified regimen that is intended to improve compliance and convenience. The recommended number of applications is made very clear on the product label and leaflet: • The front panel on the carton clearly states 'Apply once every 12 hours' • The back panel on the carton clearly states 'Rub gently into the affected area 2 times daily (preferably morning and evening)' and 'Do not exceed the recommended dose' • The leaflet clearly states 'Apply the gel 2 times a day (preferably morning and evening). The gel provides lasting pain relief of up to 12 hours.' Further, the product name contains '12 Hourly', which serves to reinforce the point-of-difference with the current product by highlighting the frequency of application.

Comparison to other unscheduled substances

It is noted that the following anti-inflammatory substances are exempted from scheduling:

- Ibuprofen in preparations for dermal use (no strength specified in Poison Schedule, currently there is a 5% gel on the market)
- Ibuprofen for oral use in divided preparations each containing ≤200 mg in packs of ≤25 units

With demonstrated tolerability and low systemic absorption, 2% dermal diclofenac is not expected to have increased risks compared to any of the above products.

Request for reconsideration of interim decision

We request reconsideration of the interim decision. Exemption of 2% dermal diclofenac from scheduling is consistent with the Trans-Tasman Harmonisation intent to harmonise to the lowest schedule. The systemic exposure from 2% dermal diclofenac with twice daily application is comparable to that of 1% dermal diclofenac applied four times daily.

Yours sincerely,

[redacted]

References

1. Derry S, Moore RA, Rabbie R. Topical NSAIDs for chronic musculoskeletal pain in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 9. Art. No.: CD007400. DOI: 10.1002/14651858.CD007400.pub2.

[redacted]

The Pharmacy Guild of Australia

Advisory Committee for Medicines Scheduling

Further comment for the ACMS- reasons for scheduling delegate's interim decision May 2014

12 June 2014

Contact person:

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BESTPRACTICE CERTIFICATION ISO9001 QUALITY MANAGEMENT SYSTEM

Comments on Interim Decision for Naproxen

The Pharmacy Guild of Australia welcomes the opportunity to provide comment on the interim decision regarding the scheduling of naproxen considered at the March 2014 of the Advisory Committee on Medicines Scheduling. We note the interim decision outlined by the ACMS was for a new Schedule 3 entry be created for naproxen in a modified release dosage form of 600 mg or less of naproxen per dosage unit in packs of 16 or less dosage units when labeled not for the treatment of children under 12 years of age.

Consistent with our pre-meeting submission, we support this decision.

In light of this scheduling decision, the Guild reiterates that consideration should also be given to listing naproxen on Appendix H.

The Guild believes listing naproxen on Appendix H would increase consumer awareness of therapeutic products available without a prescription and encourage consumers to seek advice by a pharmacist. We believe this proposal if adopted will lead to consumers being better informed and the role of community pharmacists in primary healthcare delivery will be enhanced.

We note that diclofenac, another non-steroidal anti-inflammatory medicine which has similar pharmacological properties and risk profile has been listed on Appendix H since August 2001. As outlined in the committee report at the time, the decision to list diclofenac on Appendix H was based on the following the reasons:

- long history of safe use;
- well characterised adverse effects; and
- increasing consumer awareness of the range of over-the-counter NSAIDS that are available[1]

Owing to the broad similarities between naproxen and diclofenac, we believe these factors are equally pertinent to this proposal.

The Guild's support for this consideration is on the basis that any consumer awareness messages related to naproxen emphasise the essential (mandatory) role of pharmacists in the supply of Schedule 3 medicines and recommend consumers consult with their pharmacists to determine if naproxen is appropriate for them.

Conclusion

The Guild supports the ACMS' interim decision to create a new Schedule 3 entry naproxen. In addition, consideration should also be given to listing naproxen on Appendix H to better inform consumers regarding products that available without a prescription and encourage advice to seek counseling by a pharmacist. Naproxen also has broadly similar pharmacological properties to diclofenac which has been listed on Appendix H for over 10 years.

[1] National Drugs and Poisons Schedule Committee Record of Reasons 32nd Meeting 21-23 August 2001, 26

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12 June 2014

The Secretary
Medicines and Poisons Scheduling Secretariat (MDP88)
GPO Box 9848
CANBERRA ACT 2601

Dear Sir/Madam,

Re: Submission on the proposed new Schedule 3 entry "Naproxen in a modified release dosage form of 600 mg or less of naproxen per dosage unit in packs of 16 or less dosage units when not labelled for the treatment of children under 12 years of age"

We refer to the notice inviting public comment under Regulation 42ZCZP of the Therapeutic Goods Regulations 1990. Thank you very much for the opportunity to provide comment on the interim decision and reasons.

Bayer has addressed all matters mentioned in section 52E of the Therapeutic Goods Act 1989 in the original submission and maintains that Schedule 2 is appropriate given that:

- naproxen has been shown to be safe and efficacious when used for the treatment of mild to moderate pain in adults and children over 12 years. These ailments are common and self-limiting, readily identifiable or diagnosed by the consumer and can be managed without medical intervention.

- the modified release preparation would make dosing easier for patients, especially those with persistent mild to moderate pain.

- the use of the modified release preparation is substantially safe for short term treatment and the potential for harm from inappropriate use is low.

- there is no evidence to date that naproxen at the proposed dosage level can produce dependence, misuse, abuse or be used illicitly.

- the risks associated with the use of naproxen treatment are no greater than other analgesics like ibuprofen, diclofenac or paracetamol. The risk profile of naproxen and other NSAIDs are well defined with identifiable risk factors. These risks have been

effectively managed via appropriate packaging and labelling as is currently done for other S2 NSAIDs.

Although Bayer does not concur with the delegate's interim decision, Bayer believes that if the interim decision is to be finalised, inclusion in Appendix H of the Standard for Uniform Scheduling of Medicines and Poisons (SUSMP) is appropriate. In accordance with the National Co-ordinating Committee on Therapeutic Goods (NCCTG) guidelines, the following criteria for Appendix H listing are discussed for consideration:

- ***The potential public health benefit***

  The efficacy and safety profile of naproxen when administered at low doses of up to 600 mg per day for the short term treatment of minor aches and pain e.g. aches and pain of the joints and muscles as a result of arthritis, injuries, colds and flu and headaches are well-documented and is comparable to other currently available OTC analgesics. These aspects of naproxen were presented under 52E(1)(a) – Risks and benefits and 52E(1)(c) – The toxicity of the substance.

  Naproxen in a modified release dosage form of 600 mg or less of naproxen per dosage unit is suitable for these minor pain conditions and were discussed under 52E(1)(b) – *Purposes for which a substance is to be used and the extent of use of a substance and* 52E(1)(d) – *Dosage, formulation, labelling, packaging and presentation.*

  Naproxen in a modified release dosage form of 600 mg offers consumers greater compliance and the convenience of once-a-day dosing as all the other available OTC analgesics require 4-8 hourly dosing.

  Currently, diclofenac is the only analgesic substance listed in Appendix H. All of the other S3 analgesics are opioid based. Advertising would increase consumer awareness of a new product that may provide a useful alternative and encourage consumers to consult with their pharmacist regarding their pain conditions and if the new dosage form is an appropriate treatment. This will help to expand the professional role of pharmacists in the delivery of primary healthcare by counselling, increasing appropriate access to medicines and referrals to GPs in a timely manner to avoid delay in the treatment of more serious conditions.

- ***The likelihood of advertising of the substance leading to inappropriate patterns of medication use***

  There is no evidence to date to suggest inappropriate patterns of medication use as discussed in the original application under 52E(1)(e) – Potential for abuse of the

substance. Hence it is unlikely advertising of naproxen would lead to inappropriate use.

- ***The wider regulatory system through both the Therapeutic Goods Advertising Code Council and the therapeutic goods registration process;***

  Naproxen in a modified release dosage form of 600 mg or less of naproxen per dosage unit will be a registered OTC product. Bayer will ensure that all advertising to consumers and healthcare professionals is compliant with the Therapeutic Goods Advertising Code.

- ***The provisions of the Therapeutic Goods Advertising Code (TGAC) that apply to all brand advertisements, specifically the provisions on:***
  - ***the Objects of the Code, Clause 1; Compliance and Application, Clause 3; and Principles, Clause 4;***
  - ***the representations listed in Part 1 of Appendix 6 that are prohibited under Regulation 6(1)(a) and item 1, Part 1, Schedule 2, Therapeutic Goods Regulations;***
  - ***the restricted representations listed in Part 2 of Appendix 6;***

  Bayer understands the requirements of the TGAC that apply to all brand advertisements and specifically S3 medicines, including Clause 7(1)(a) to (e) relating to analgesics.

  It is mandatory for all advertisements, which includes TV, radio, mainstream newspapers and magazines, cinema and public display e.g. billboards, posters, public transport directed to consumers to be formally approved by industry associations, such as the Australian Self Medication Industry (ASMI) which has been delegated with the authority to approve advertising by the Commonwealth Department of Health and Ageing.

- ***Whether the application may result in the advertising of goods for an indication other than those included in the Australian Register of Therapeutic Goods (see the note below on how this is an offence under Section 22(5) of the Therapeutic Goods Act 1989);***

  Bayer understands and undertakes that the advertising will be limited to the indications approved or included in the Australian Register of Therapeutic Goods.

- ***The responsibility of pharmacists to be actively involved in the supply of substance(s) included in Schedule 3 of SUSDP*** *(now SUSMP);*

  Being an S3 medicine, Bayer will work with and assist stakeholders to produce a treatment protocol to assist pharmacists in the supply of naproxen.

Consumers will need to go back to pharmacies to get their next supply and pharmacists should be able to counsel and monitor the correct use and safety of the product.

- ***Available consumer medicine information;***

  The Therapeutic Goods Regulations 1990 requires that all S3 medicines are supplied with a Consumer Medicine Information.

- ***The level of patient education necessary to ensure correct use;***

  Bayer will engage with the professional pharmacy associations to develop patient and pharmacy education materials necessary to ensure correct use.

- ***The desire of consumers to manage their own medication; and The requirement under Clause 6.2(e) of the TGAC to include words to the effect of:***

  - ***"Your pharmacist's advice is required"***

    in all advertisements for therapeutic goods containing Schedule 3 substances that are listed in Appendix H of the SUSDP*(now SUSMP).*

  Bayer will ensure that the statement "Your pharmacist's advice is required" will be included in all advertisements on the Naproxen S3 product.

In summary, Bayer requests the delegate to consider inclusion of naproxen in Appendix H if the interim decision is to be finalised.

Yours sincerely,

[redacted]

Evelyn Yeoh
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Bayer Consumer Care

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12th June 2014

The Secretary
Scheduling Secretariat
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Canberra ACT 2601

Dear Sir or Madam,

Notice inviting public submissions under Reg 42ZCZP of the Therapeutic Goods Regulations 1990 Delegate's Interim decisions and reasons for decisions for scheduling proposals referred to the March 2014 meeting of the ACMS (ACMS#11) - Item 1.2 Naproxen

We refer to the notice inviting public comment under Regulation 42ZCZP of the Therapeutic Goods Regulations and would like to provide comment on the scheduling proposals for naproxen (item 1.2) that was referred to the March 2014 meeting of the ACMS (ACMS#11).

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 the delegate's interim decisions and reasons for decisions. We wish to address relevant matters under section 52E of the Therapeutic Goods Act 1989, as applicable to the delegate's interim decision on the scheduling of naproxen.

ASMI accepts the delegate's interim decision for a new schedule 3 entry for naproxen when in a modified release dosage form of 600mg or less per dosage unit in packs of 16 or less dosage units when labelled not for the treatment of children under 12 years of age. ASMI also supports the requirement for the current Appendix F warnings for naproxen, which are comparable to the warnings in RASML, although there are some slight differences. It should be noted that RASML (2008) already contains an entry for naproxen when included in a schedule to the SUSMP.

The reasons provided by the delegate for recommending a schedule 3 entry are:

- That the naproxen ER (extended release) formulation has not been available for use previously, therefore safety within the community has not been demonstrated
- That the pharmacist's advice is required to prevent inappropriate use for transient pain (for which shorter acting alternatives may be more suitable) and to provide advice on the once-a-day dosing regimen.

ASMI believes that these reasons are valid and that the product meets the criteria for a schedule 3 medicine. However, well designed consumer focussed labelling can also assist consumers to use the product appropriately and help differentiate between currently available non-steroidal anti-inflammatory medicines and the new once a day formulation, as well as provide additional information to assist with safe use.

Appendix H

A key decision subsequent to a Schedule 3 entry for a medicine is the ability to advertise to consumers, i.e. Appendix H.

Since the sponsor originally requested a Schedule 2 entry, ASMI understands that the sponsor did not submit an application for Appendix H listing. It is a concern that an Appendix H application may now require an additional application to the Scheduling Committee, with the resulting delay as the application proceeds through another two rounds of public consultation.

ASMI requests that the delegate may wish to consider either:

(i) an Appendix H listing application for this entry for naproxen as a "delegate-only" decision; or

(ii) to provide the sponsor with the option of the shortened "delegate initiated" time frame to submit information in accordance with the Schedule 3 advertising guidelines, to justify an Appendix H entry.

Increased consumer awareness of an alternative option for pain relief, in a once per day dosage form may be important to consumers. The requirement for pharmacist intervention and counselling prior to supply will ensure that consumers are advised on how to use the product appropriately.

Conclusion

Naproxen has a long history of use in Australia as a Schedule 2 medicine. It has a well-documented safety profile, consistent with other non-steroidal anti-inflammatory medicines and low potential for abuse or misuse. The convenience and lower daily dose of the extended release formulation can provide an additional, useful alternative pain relief product for consumers. Availability in the pharmacy environment offers consumers easy accessibility to pharmacists' professional advice.

ASMI therefore supports the proposal for the Schedule 3 entry for naproxen to allow for a modified release product as described above. ASMI also believes that consideration ought to be given to either a favourable "delegate only" Appendix H decision, or to allowing the sponsor to submit an Appendix H application via the "delegate-only" timeframes. ASMI believes that there are benefits in allowing consumer awareness of new Schedule 3 medicines that may provide a useful alternative for consumers and supports a favourable consideration of an Appendix H entry.

Yours sincerely,

[redacted]

QUM Manager