25th October 2023

The Secretary,
Medicines Classification Committee
Medsafe PO Box 5013
Wellington 6145

New Zealand
Sent by email : committees@moh.govt.nz

From:

Consumer Healthcare Products Association Inc.
P O Box 133115
Auckland
New Zealand

Dear Sir/Madam,

Re: Submission on Item 8.2.1 of the Agenda of the Medicines Classification Committee – Decisions by the Secretary to Department of Health and Ageing in Australia (or the Secretary's Delegate).

The Consumer Healthcare Product Association (CHPNZ) (formerly the New Zealand Self-Medication Industry Association Inc (NZSMI) is the national trade association representing importers, manufacturers, marketers and distributors of a wide range of products, generally available "over-the-counter" (OTC) and mainly for use in self-medication by New Zealand consumers. CHPNZ's mission is to promote better health through responsible self-care. This means ensuring that safe and effective self-care products are readily available to all New Zealanders at a reasonable cost. CHPNZ works to encourage responsible use by consumers and an increasing role for cost-effective self-medication products as part of the broad national health strategy. CHPNZ members account for an estimated 85% of OTC paracetamol sales.

We appreciate this opportunity to provide feedback on this upcoming agenda item.

The Current Position

CHPNZ believes:

- General practitioners need the ability to prescribe at current levels for chronic users and these levels should be seen as a maximum, not a target;
- Pharmacists are aware of the risks of paracetamol abuse and misuse and are increasingly being seen by the community as a safe, educated, appropriate source of health information in this space and the current pack sizes are appropriate;
- Retail pharmacy is the appropriate avenue to supply anything but a minimal quantity of paracetamol;
- General sales operators are voluntarily managing the sale of excess amounts of paracetamol with either a single pack or two pack restriction monitored at point of sale;

Commentary on Harmonisation with Australia

New Zealand is a small market at the end of a long supply chain and our regulatory processes are becoming an increasing burden on the ability of suppliers to be viable in such a specialised area of commerce.

The effect of having different pack sizes and scheduling for OTC supply of paracetamol between Australia and New Zealand have not been, and may not able to be, quantified, but increased costs will ensue in a differentiated market.

Anecdotally, the benefits of harmonisation are regularly promoted as efficiency, production cost savings, lower cost to consumer and improved access to pharmaceutical products, particularly in the lower-risk SelfCare space.

The Greater Concern

CHPNZ members have experienced numerous changes to scheduling in recent years; many of which have resulted in substantial financial losses. In the case of both Dextromethorphan and Pholcodine product has had to be recalled and dumped.

The size of the paracetamol market is many times larger than both these products combined and the potential for losses is exponentially higher.

CHPNZ suggests that if the MCC was to make any request of Medsafe to investigate a change to scheduling, and there are to be any changes to paracetamol pack sizes and scheduling, then:

- That a two-year time frame for implementation of label and scheduling changes be mandated (one year into wholesale and one year for retail);
- Pack sizes match Australia for both general sale and pharmacy and that;
- Scheduling by way of quantity able to be supplied at general sale, pharmacy and Pharmacist Only, match Australia

CHPNZ appreciates the opportunity to make comments and thanks the committee for their consideration.

Scott Milne
Chief Executive

On behalf of :
Consumer Healthcare Products Association of New Zealand

11 October 2023

The Medicines Classification Committee Secretariat
Medsafe
PO Box 5013
Wellington

Dear Sir/Madam,

Re: Comment on the Medicines classification Committee 71st meeting agenda item 8.2.1 Paracetamol

Reckitt supports the review of the scheduling of paracetamol to address the issues associated with intentional paracetamol overdose. Reckitt is aligned with the need to reduce pack sizes available for purchase to limit stockpiling of paracetamol in the home given this has been identified as the key source of paracetamol in intentional overdose. We believe that any recommendations adopted be evidence-based and implementable. It is also important that any of the options proposed for scheduling changes do not limit self-selection access in grocery to products containing paracetamol.

In brief Reckitt proposes Medsafe aligns with the scheduling of paracetamol in Australia specifically as it relates to pack size restrictions for single ingredient solid dose paracetamol.

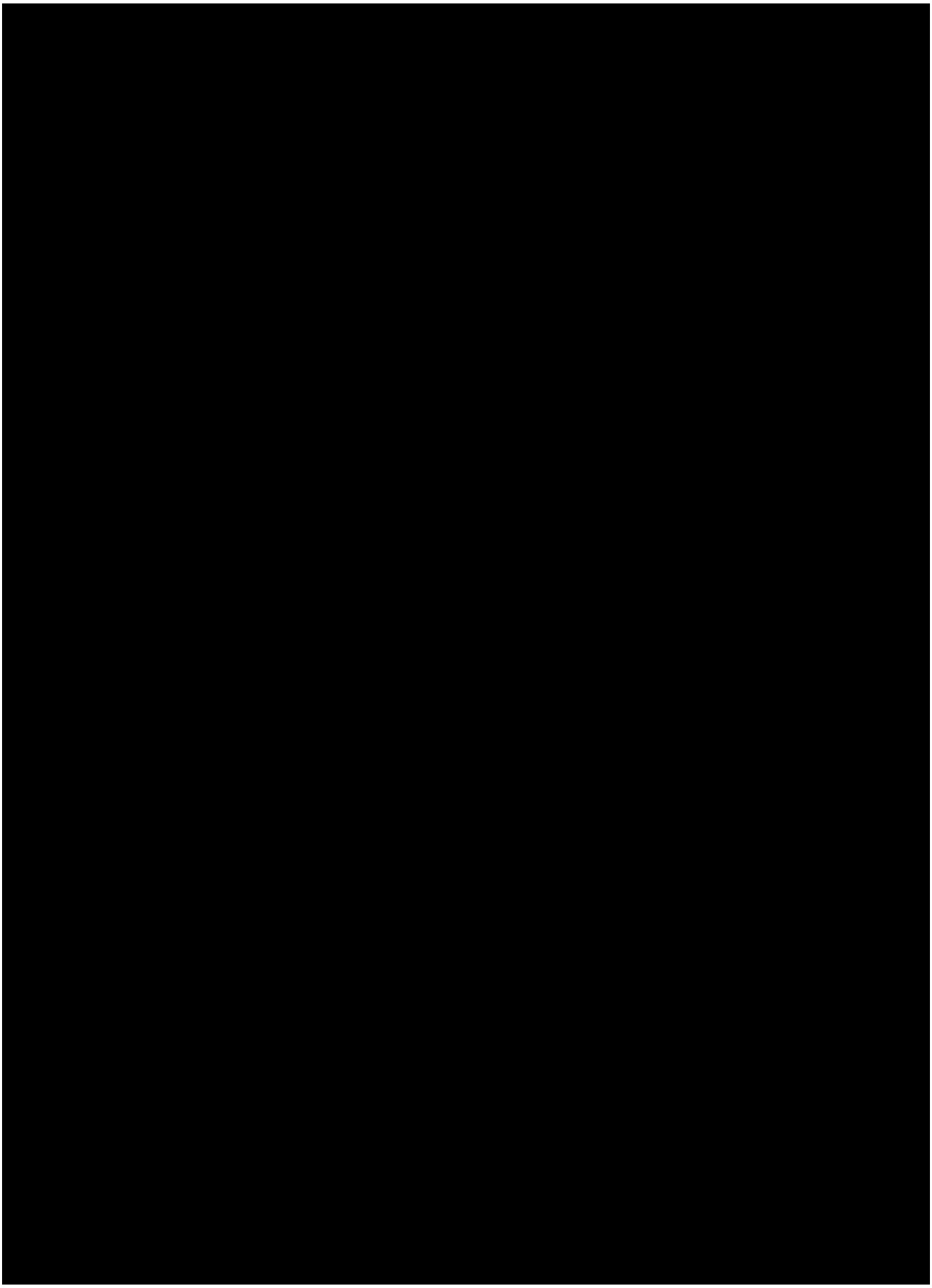
Rationale

Reckitt supports pack size restrictions for single active paracetamol are aligned with those which will be implemented in Australia following the recent decision of the TGA's Scheduling Committee (ACMS). Reckitt's position is that the scheduling of combination analgesics (ibuprofen paracetamol combination), powdered paracetamol and cold and flu preparations containing paracetamol should not be part of a scheduling review as these products are not implicated in overdose situations.

Analysis of the data collected by NZ National Poisons Center over the past 6 years has shown that intentional (2414) and accidental exposure (2476) of single active Paracetamol is **10 times** higher than intentional (136)* and accidental (373)* exposure from paracetamol combination products* available in general sale. As such, it is clear to Reckitt that combinations products are not implicated in overdose situations and consequently any scheduling consideration should be focused on single active solid dose paracetamol.

It's important to note that despite Grocery retailers voluntarily implementing a purchase limit for single active paracetamol in 2020, the rate of intentional overdose with paracetamol has continued to increase (see Figure 1 date from NZ National Poisons Centre).

*The OTC general sale combinations active ingredients included caffeine, phenylephrine, guaifenesin, ibuprofen and unidentified.



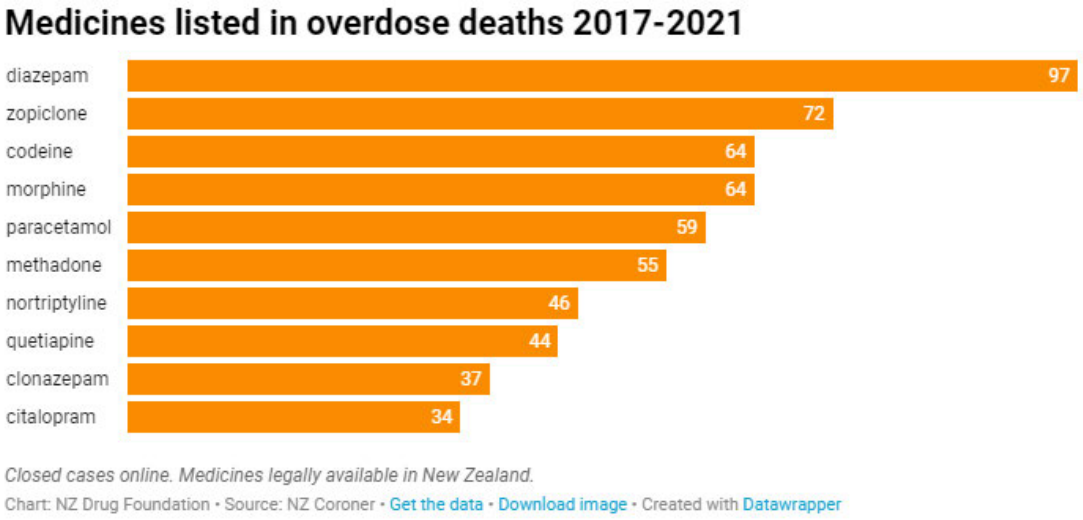
Paracetamol is on the Pharmac schedule as a subsidized medicine. Since the removal of the $5 prescription charges (2023), this is now free for patients who have a prescription (up to a maximum of 300 tablets per prescription). A NZ study investigating the source of paracetamol stock piling in the home has found that prescribed paracetamol is the main source of supply (Kumpula EK, 2020). Given this scenario, any strategy intended to reduce intentional overdose of paracetamol should consider how addressing how paracetamol prescribing habits impact the source of paracetamol in the home and available means for those intending to intentional overdose.

Reckitt proposes that no additional pack size restrictions be applied to paracetamol and ibuprofen combinations as these products are not implicated in overdose situations. Figure details medicines implicated in fatal overdoses in New Zealand. Paracetamol combination products are not in the list of the top 10 medicines implicated in overdose. This further supports Reckitt's view that paracetamol combination products should be excluded from any discussions regarding the scheduling of paracetamol.

Important to note, the cost of these products prohibits their use in overdose situations. The cost of paracetamol combinations products is up to **5 times higher** than single active solid dose paracetamol ($1.99 for 20s paracetamol compared with $10.00 for 20s combination

ibuprofen/paracetamol). In addition, cold and flu products are seasonal and hence purchased as needed during the cold and flu season.

Figure 2: Medicines listed in overdose deaths 2017-2021



In summary, Reckitt is of the view that the scheduling of paracetamol needs to be considered by the MCC, specifically the consideration of implementing pack size restrictions to single active solid dose (tablets and capsules) paracetamol when sold in general sale and in pharmacy front of store (Pharmacy medicine) in line with the decision made by the TGA.

Reckitt believes that pack size of combination products (Paracetamol 500 mg + Ibuprofen 200 mg) should remain the same as these are not implicated in overdose. Data from the NZ Poisons Centre indicates that number of people overdosing on single active paracetamol is 10x higher than with paracetamol combination products. In addition, part of the MCC's review of paracetamol scheduling should include a review of prescribed paracetamol available on Pharmac Schedule. Paracetamol on the schedule is now free further adding to the stockpile of paracetamol in the home. A review of pack sizes for prescription warrants review to minimize the amount of paracetamol in the home.

Yours sincerely

References

At the Heart of the Matter, NZ Drug Foundation. (2022, November 05). Retrieved from Report: Fatal overdoses in Aotearoa 2017 - 2021: https://www.drugfoundation.org.nz/news-media-and-events/overdose-report-2017-2022/

Kumpula EK, N. P. (2020). *Stocks of paracetamol products stored in urban New Zealand households: A cross-sectional study. PloS one, 15(6), e0233806.* Retrieved from https://doi.org/10.1371/journal.pone.0233806

18 October 2023

Medicines Classification Committee Secretary
Medsafe
Wellington

Sent via email to: committees@health.govt.nz

Dear Committee Members,

Re: Green Cross Health submission to the agenda for the 71st meeting of the Medicines Classification Committee

Thank you for the opportunity to comment on the agenda for the 71st meeting of the Medicines Classification Committee.

Green Cross Health represents over 300 Unichem and Life pharmacies across the motu. We continue to be extremely supportive of increasing services and access to medications in an appropriate manner to our communities. Community pharmacies are open extended hours and weekends and for a number of our communities, community pharmacy is the first port of call for care, advice, and treatment.

Green Cross Health would like to comment on:

8. Harmonisation of the New Zealand and Australian Schedules:

8.2 Decisions by the Secretary to Department of Health and Ageing in Australia (or the Secretary's Delegate)

- 8.2.1 Paracetamol

Green Cross Health does not support the proposed change of:

- 20 tablets or capsules to 16 for unscheduled (general sales) products (8 grams per pack)
- 100 tablets or capsules to 50 for schedule 2 (pharmacy-only) products (25 grams per pack)
- limit of 100 tablets/ capsules for schedule 3 (restricted/ pharmacist-only) products (50 grams per pack).

Pharmacy has always provided and continues to provide essential services, and it is the first point of contact when customers and patients require immediate treatment for acute ailments. This has been highlighted even more during the pandemic period and also during the recent Minor Ailment program. Paracetamol is synonymous with pharmacy and is an essential medication that provides valuable means for self-management of minor painful ailments and is an effective antipyretic.

Green Cross Health does not support the proposed scheduling changes, as there is no current evidence that upscheduling the maximum pack sizes for general sales and pharmacy-only products will reduce the incidence of paracetamol abuse or misuse. Restricting the sale of paracetamol to being "Pharmacist Only" for larger packs is strongly opposed, as we believe it will cause barriers for customers obtaining appropriate treatments for acute conditions increasing pressure on GP prescribing and reducing access while offering no data-driven benefit to consumers.

We recognise the TGA recommendations in Australia do not reflect the same concerns as in New Zealand. There are appropriate measures taken to prevent overuse and stockpiling of medications, and education on general sale medication is actively managed within pharmacy for all staff, reducing the potential for misuse. The TGA change was subject to a process conducted in Australia that cannot be compared to what is current in New Zealand and we believe it would be appropriate to establish the appropriate findings in New Zealand first. We request that the supply quantities and scheduling with Paracetamol remain with the current status quo, as there is no evidence presented from Australia that the schedule change has provided a benefit. We request Medsafe base its changes on data-driven findings in New Zealand and Australia before rescheduling and restricting access to Paracetamol which would create unnecessary barriers for customers and patients.

Rachel Newfield
Group Chief Executive Officer

Gemma Buchanan
Commercial Manager Health Service

BAUSCH + LOMB

20 September 2023

Medicines Classification Committee
Medsafe
PO Box 5013
Wellington

Via email – committees@health.govt.nz

RE: Agenda for the Medicines Classification Committee (MCC) 71st meeting - Item 8.2.2 Brimonidine

Dear Sir/Madam,

Thank you for the opportunity to submit comments on the agenda for the 71st meeting of the MCC. Our submission addresses agenda item 8.2.2 regarding brimonidine and the harmonisation of the New Zealand and Australian schedules.

We support the proposed re-scheduling of brimonidine from *prescription medicine* to:

- *Prescription medicine;* except in ophthalmic preparations for adult use containing not more than 0.025% brimonidine.
- *Pharmacy-only medicine;* in ophthalmic preparations for adult use containing not more than 0.025% brimonidine.

Brimonidine tartrate 0.025% (low-dose brimonidine) is an ocular decongestant that is a highly selective α_2-adrenergic receptor agonist. It is used to relieve redness of the eye due to minor eye irritations which can be readily recognised and self-treated by the consumer. As a pharmacy-only medicine, the advice and guidance of a pharmacist is readily available if required. In New Zealand, ocular decongestants currently available as pharmacy-only medicines include naphazoline eye drops and tetrahydrozoline (tetryzoline) eye drops.[1]

An integrated analysis of four clinical trials found that brimonidine tartrate 0.025% significantly reduced ocular redness with no tachyphylaxis, minimal rebound redness and was generally safe and well tolerated.[2] A review of OTC ocular decongestants marketed in the USA found that ocular decongestants with α_1-adrenergic receptor agonist activity can be associated with loss of effectiveness with continued use (i.e., tachyphylaxis) and rebound redness upon treatment discontinuation. In contrast, in the clinical trials of the selective α_2-adrenergic receptor agonist brimonidine 0.025%, tachyphylaxis was not observed, and rebound redness was rarely reported.[3]

The proposed re-scheduling aligns with the classification in comparable overseas countries such as Australia, the USA and Canada. Brimonidine tartrate 0.025% eye drops is currently available as an OTC

[1] Medsafe. Product/Application Search. [Internet; cited 2023 Sep 13]. Available from: https://www.medsafe.govt.nz/regulatory/DbSearch.asp
[2] Ackerman SL, Torkildsen GL, McLaurin E, Vittitow JL. Low-dose brimonidine for relief of ocular redness: integrated analysis of four clinical trials. Clin Exp Optom 2019;102(2):131-139. https://doi.org/10.1111/cxo.12846
[3] Hosten LO, Snyder C. Over-the-Counter Ocular Decongestants in the United States - Mechanisms of Action and Clinical Utility for Management of Ocular Redness. Clin Optom (Auckl) 2020;12:95-105. https://doi.org/10.2147/OPTO.S259398

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medicine in the USA[4] and Canada.[5] In Australia, a new Schedule 2 entry was created for brimonidine from 1 June 2023 (in ophthalmic preparations for adult use containing not more than 0.025% of brimonidine).[6] Alignment with the Australian scheduling may help increase access for New Zealand patients and enhance supply and commercial viability in New Zealand, due to the potential of having shared packs between Australia and New Zealand.

In summary, we support the re-scheduling of low-dose brimonidine from prescription medicine to pharmacy-only medicine. The efficacy and safety studies support the conclusion that low-dose brimonidine is suitable as a pharmacy-only medicine to relieve redness of the eye due to minor eye irritations. The availability in the USA and Canada and the recent re-scheduling in Australia reinforces the suitability and safety of low-dose brimonidine for OTC use in pharmacy.

Yours sincerely,

Regulatory and Medical Affairs ANZ
Bausch & Lomb (NZ) Ltd

[4] U.S. Food and Drug Administration. FDA Approved Drugs Database. [Internet; cited 2023 Sep 13]. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process

[5] Health Canada. Drug Product Database. [Internet; cited 2023 Sep 13]. Available from: https://health-products.canada.ca/dpd-bdpp/

[6] Therapeutic Goods Administration. Notice of final decisions to amend (or not amend) the current Poisons Standard. [Internet]. Canberra: Therapeutic Goods Administration, 2023 [cited 2023 Sep 13]. Available from: https://www.tga.gov.au/sites/default/files/2023-05/notice-of-final-decision-to-amend-or-not-amend-the-current-poisons-standard-acms-40-accs-34-joint-acms-accs-32.pdf

CHP Australia
Advancing Responsible Self-Care

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19 October 2023

The Secretary, Medicines Classification Committee
Medsafe
PO Box 5013
Wellington 6145
New Zealand

Sent by email: committees@moh.govt.nz

Dear Sir/Madam,

Re: Response to public consultation for the Medicines Classification Committee Agenda for 71st meeting, December 2023 – Item 8.2 Paracetamol

Thank you for the opportunity to comment on the agenda for the 71st meeting of the MCC.

Consumer Healthcare Products Australia (CHP Australia) is the leading voice and industry body for manufacturers and distributors of consumer healthcare products in Australia. We strive to advance consumer health through responsible self-care and were previously known as the Australian Self Medication Industry (ASMI). Our key priorities for the industry include improving health literacy, growing the consumer healthcare products industry and increasing access to medicines where appropriate. We work together with our colleagues at the New Zealand Self Medication Industry (NZSMI), especially on matters of common interest between Australia and New Zealand.

CHP Australia would like to provide comment on agenda item 8.2 – paracetamol. We note that paracetamol is included in the agenda in section 8.2 titled '*Decisions by the Secretary to Department of Health and Ageing in Australia*', however it is not included as an agenda item in section 6, '*Submission for reclassification*'.

We are aware that many Australian stakeholders are uncertain and confused as to how this item will be considered at the meeting – specifically, whether the paracetamol agenda item is purely to inform the MCC of the actions taken in Australia and to open discussions on any future plans for consideration of the classification of paracetamol in New Zealand, or whether the MCC will be making a formal decision on re-classification at the December meeting.

The agenda item, as written, does not detail any specific proposal for change to classification of paracetamol in New Zealand. No application has been made, and there is no submission included for stakeholder consideration and comment. For this reason, we are aware that many stakeholders, including members of CHP Australia, have not made a formal submission to Medsafe, believing that the agenda item is only

an initial opportunity for the MCC to discuss the Australian decision, rather than it being a formal proposal for discussion of any immediate change to classification.

CHP Australia would like to request that if the MCC intends to make any change to the paracetamol classification in New Zealand, then any proposed changes to classification should be clearly articulated and should be the subject of a separate application by Medsafe, included as part of the agenda section on 'submissions for reclassification', and discussed at a future meeting where submissions from stakeholders can be considered. The details of any specific proposal for reclassification should be made clear to stakeholders, so that they are given the opportunity to properly engage in an informed discussion about reclassification. The process should be specific, transparent and predictable.

The MCC should also note that in Australia, the decision to change the scheduling of paracetamol will take effect on 1 February 2025. The TGA made a decision (see here), to allow industry a reasonable timeframe for implementation given the large number of affected products and the fact that for some products, re-design and re-tooling will be required and sufficient time ought to be allowed to ensure that supply chains are not disrupted, given that paracetamol is an essential medicine. Any future recommendations by the MCC and Medsafe should take this into consideration, given the potential commercial and supply chain impacts.

In conclusion, CHP Australia members are of the view that there has been confusion on this agenda item, and that it should not be taken to represent a formal reclassification proposal. We are aware that the ambiguous nature of the agenda has led to insufficient stakeholder engagement. If the MCC is of the view that classification changes should be considered, there should be a formal New-Zealand specific proposal together with a clearly worded application, which should be considered at a future meeting (in 2024) and not decided at the 71st meeting to be held in December 2023.

Kind Regards

PHARMACEUTICAL SOCIETY
of New Zealand Incorporated

17 October 2023

Medicines Classification Committee Secretary
Medsafe
PO Box 5013
Wellington 6145
via email: committees@moh.govt.nz

Dear Jessica,

MEDICINES CLASSIFICATION COMMITTEE (MCC)
COMMENTS TO THE 71st MEETING AGENDA December 2023

Thank you for the opportunity to submit comments on the agenda for the 71st meeting of the Medicines Classification Committee.

The Pharmaceutical Society of New Zealand Inc. (the Society) is the professional association representing over 2,500 pharmacists, from all sectors of pharmacy practice. We provide to pharmacists professional support and representation, training for continuing professional development, and assistance to enable them to deliver to all New Zealanders the best pharmaceutical practice and professional services in relation to medicines. The Society focuses on the important role pharmacists have in medicines management and in the safe and quality use of medicines.

Regarding the agenda items for the above meeting of the Medicines Classification Committee, the Pharmaceutical Society would like to note the following comments for consideration:

6.1 Phenol – proposed down scheduling to include provision by podiatrists under certain conditions.
The Society supports the concept of podiatrists having access to phenol under certain conditions.

We are aware that currently, due to previous change in classification, phenol has moved from a medical device to a prescription medicine. This has created some challenges for podiatrists when providing care to their patients.

There is sufficient clinical evidence provided by the applicant to support the use of this treatment for nail chemical matrixectomy.

However, there are currently no products on the New Zealand market that have been consented by Medsafe. As a result until a consented product has been obtained, the only way for a podiatrist to access phenol will be through a medical practitioner prescription.

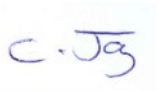
Without a consent product, reclassification will not currently improve access and availability of treatment. This should be addressed at the same time, and we would recommend that any change in classification only occurs if a consented product is available.

The provision of phenol outside a manufacturers packaging creates significant health and safety risks for all involved in handling the product.

We would also like to recommend that perhaps the proposed classification is amended to state: "Prescription except when supplied in a manufacturers original pack by a podiatrist for use in nail ablation" for clarity of purpose.

Thank you for consideration of this submission. I would be happy to discuss any aspect of this further, if required.

Yours sincerely,



Chris Jay
Manager Practice and Policy

PHARMACY GUILD OF NEW ZEALAND

19 October 2023

Medicines Classification Committee Secretary
Medsafe
Wellington

Sent via email to: committees@health.govt.nz

Dear Committee Members,

Re: Agenda for the 71st meeting of the Medicines Classification Committee (MCC)

Thank you for the opportunity to provide feedback on the upcoming MCC agenda items.

The Pharmacy Guild of New Zealand (Inc.) (the Guild) is a national membership organisation representing the majority of community pharmacy owners. We provide leadership on all issues affecting the sector and advocate for the business and professional interests of community pharmacy.

Our feedback covers the following agenda items:

- 6. Submissions for reclassification:
  - 6.1 Phenol – proposed change to prescription classification statement to include provision by podiatrists under certain conditions
- 8. Harmonisation of the New Zealand and Australian Schedules:
  - 8.2.1 Paracetamol
  - 8.2.2 Brimonidine
  - 8.2.3 Fexofenadine
  - 8.2.4 Melatonin
  - 8.2.5 Cetirizine

6.1: Phenol – proposed change to prescription classification statement to include provision by podiatrists under certain conditions (Podiatrist Board of New Zealand and Podiatry New Zealand)

The Guild does not endorse the proposed change to the prescription classification of phenol to include provision by podiatrists under certain conditions for chemical matrixectomy as proposed by the Podiatrist Board of New Zealand (PBNZ) and Podiatry New Zealand. Although the proposed change to prescription classification could potentially simplify access to treatment for patients by podiatrists, their application does not provide any detail and assurance on the controlled provision, storage and custody of a toxic and potentially harmful chemical.

Currently there are no approved products available in New Zealand that would be suitable for a podiatrist to use, including the example that the PBNZ has mentioned in their application, that is, Podopro Swab-It (each ampoule contains between 0.15 – 0.2 ml USP Phenol, which is applied using a swab; ampoules are individually wrapped, pack size of up to 30 units). Therefore, we do not understand how the PBNZ propose to oversee the logistics surrounding such a change and ensuring safe conditions for both the podiatrist and their patients of a toxic and potentially harmful chemical in an enclosed environment.

Keeping in mind the stringent storage and access control requirements that pharmacies must adhere to, we would expect that any podiatrist planning to store phenol for use in chemical matrixectomy would have to adhere to the same requirements and audit processes that pharmacies are currently subject to.

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8.2.1: Harmonisation of the New Zealand and Australian Schedules -Paracetamol

The Guild does not believe that harmonisation of New Zealand with the Australian TGA decision to limit paracetamol pack sizes available for retail sale will result in harm minimisation by reducing the quantity of paracetamol in the home. This is because without a real-time monitoring system, consumers can continue to stockpile paracetamol by visiting multiple stockists.

Paracetamol provides a valuable means for self-management of minor painful ailments and is an effective antipyretic. Even though paracetamol is a commonly used medicine, it has been associated with misuse, self-harm, and suicide attempts due to its ability to cause severe liver toxicity and death, especially in late presentations and high doses. However, a balance needs to be found between meeting a consumer's need for timely and appropriate self-management of pain or fever whilst helping minimise stockpiling in New Zealand households. It is also important that any measures being currently considered for paracetamol do not inadvertently create misinformation pertaining to its well-established safety profile when used as directed on the label.

Given the potential for abuse and the history of harm resulting from paracetamol overuse, the Guild ideally advocates for all sales of paracetamol to be restricted to pharmacies. Pharmacy staff can assess the suitability of paracetamol for individual consumers, provide proper dosing instructions, and monitor usage to ensure it is both safe and effective. This approach not only promotes responsible use but also mitigates the risk of excessive paracetamol consumption, which is of paramount importance in safeguarding public health.

The Guild acknowledges that there might be concerns regarding the potential inaccessibility of paracetamol if it were to be removed from general sales. However, it is important to note that community pharmacies have demonstrated their high accessibility, remaining open seven days a week, often for extended hours.

We believe that, practically speaking, for pack size restrictions in general sales outlets to have the desired outcome of restricting means, it would need to be implemented in conjunction with other purchasing restrictions, otherwise, there is nothing prohibiting multiple packs being purchased. This is particularly the case in supermarkets with the proliferation of 'self-service' checkouts that allow an individual to purchase multiple packs of a medicine without any oversight or involvement of a staff member. Additionally, general retail outlets may offer specials to make it more enticing for consumers to buy multiple packs. It is also not clear if there is the ability to enforce restrictions on the purchase of multiple packs of general sale packs through various retailers and providers, or who will hold responsibility for enforcement and monitoring of non-compliance.

The Guild does not support restriction on purchasing multiple packs of paracetamol through community pharmacy. Pharmacists' ethical responsibilities require them to ensure the safe use of medicines, including paracetamol, purchased from pharmacies. We also believe that it is more difficult for individuals to make multiple purchases or purchases on consecutive days at a community pharmacy due to a more regular workforce that are likely to recognise repeat customers. To support harm minimisation efforts and promote the quality use of medicines, consideration could be given to implementing a requirement for multiple pack purchases in a pharmacy to be reviewed and authorised by a pharmacist.

8.2.2: Harmonisation of the New Zealand and Australian Schedules - Brimonidine

The Guild supports the change in scheduling status for low dose brimonidine (0.025%) to harmonise with the TGA decision in Australia and feel it is a prudent step in ensuring efficient and safe expansion of access to this medicine in New Zealand. This change will allow access to low dose brimonidine (0.025%) for the relief of red eye, itching or irritation, which is easily diagnosed and generally well tolerated with no observed potential of misuse or abuse, which does not cause the same issues of rebound redness and loss of effectiveness seen with the ophthalmic decongestants currently available in New Zealand.

In alignment with the TGA's decision, classifying brimonidine in New Zealand as "*prescription only except when provided by a pharmacist to relieve redness of the eye due to minor eye irritations in ophthalmic preparations for adult use containing not more than 0.025% brimonidine*" acknowledges the specialised knowledge and expertise that pharmacists possess in determining the suitability of this medicine for patients under the supervision of a qualified healthcare provider, ultimately enhancing patient care and ensuring that brimonidine is used safely and effectively for its intended purposes.

As pharmacists are highly trained professionals capable of providing expert guidance on the safe and effective use of medicines for specific indications there should be no requirement for additional training.

8.2.3: Harmonisation of the New Zealand and Australian Schedules - Fexofenadine

The Guild does not believe that harmonising the New Zealand's pack size regulations for fexofenadine with the TGA's recent change in Australia will benefit patient safety.

While the TGA's alteration may reflect their own regulatory approach, we believe the unique healthcare landscape in New Zealand deserves due consideration. The MCC's recommendation, following a comprehensive assessment in October 2020, was made with the paramount aim of patient safety, and proposed that fexofenadine with certain conditions, including a pack size of five dosage units or less, should remain available for general sale in New Zealand.

With fexofenadine being a pregnancy category B2 medicine and having significant adverse effects like torsades de pointes, the potential decision to increase the pack size to 10 dosage units in alignment with the TGA decision may inadvertently encourage individuals to self-administer larger quantities without professional guidance, potentially leading to misuse and safety concerns and should only be available from places where consumers will be able to seek advice from a health professional. New Zealand's current regulations and the MCC's decisions in the past prioritise patient safety and promote safe use of medicines, and any change in this regard should be approached with the same measure of caution.

We would propose the current status quo be preserved, limiting the pack size for fexofenadine for the treatment of seasonal allergic rhinitis in adults and children 12 years of age and over when in tablets containing 180 mg or less of fexofenadine hydrochloride with a maximum daily dose of 180 mg when sold in the manufacturer's original pack available general sale to five dosage units or less and not more than five days' supply via general sale.

8.2.4: Harmonisation of the New Zealand and Australian Schedules - Melatonin

The Guild fully supports the alignment with the TGA's decision in Australia to allow pharmacists to provide melatonin to adults for jet lag and feel this is a crucial step in safeguarding patient safety and ensuring responsible access to this sleep aid. This change would enable professional guidance and support for individuals seeking melatonin for jet lag, thus reducing the risk associated with buying this medicine online from non-regulated sources without oversight or information on safe usage or other alternatives that may be addictive.

By allowing pharmacists to provide melatonin containing 5 mg or less for the treatment of jet lag to adults aged 18 and over, within specific pack size limitations, we can ensure that consumers receive appropriate advice and guidance on its proper use. This pragmatic approach to harmonisation with Australia's regulations considers the best interests of patient safety and well-informed healthcare choices. Pharmacists are well placed to provide consumers with travel advice and solutions before departure and as medicine experts, have a good understanding of the role of melatonin for sleep issues and jet lag, it's potential adverse effects and interactions, and can counsel confidently on this and suitable non-pharmacological strategies for the individual person.

Previous applications for the rescheduling of melatonin have established that this medicine has a good safety profile and noted that the risk of toxicity in acute use of the substance is low. As symptoms of jet lag are transient, e.g., 4-6 days, the treatment of melatonin would therefore be short-term and thus jet lag is a condition suitable for self-management and treatment with melatonin.

Therefore, we suggest the current classification statement in New Zealand is changed to:
Prescription except when supplied in medicines for oral use containing 3mg or less per immediate release dose unit, or 2mg or less per modified release dose unit, when sold in the manufacturers original pack that has received consent from the Minister of Health or the Director General for the treatment of primary insomnia for adults aged 55 years or older for up to 13 weeks, or 5mg immediate release dose unit when sold in quantities up to a maximum of 10 doses in the manufacturers original pack that has received consent from the Minister of Health or the Director General for the treatment of jetlag for adults aged 18 or older by a registered pharmacist.

We also strongly believe that pharmacists are expertly and thoroughly trained and adherent to competency standards as prescribed by the Pharmacy Council of New Zealand to be able to provide melatonin for the treatment of jet lag and would not need to complete any additional qualifications or training to be able to perform the safe and effective provision of this medicine.

8.2.5: Harmonisation of the New Zealand and Australian Schedules - Cetirizine
The Guild does not support the harmonisation of New Zealand's pack size regulations for cetirizine with the TGA's recent decisions in Australia as it does not align with the best interests of patient safety.

While the TGA's rescheduling may reflect their regulatory approach, the context and healthcare landscape in New Zealand should be considered. The recommendation to maintain a five-day supply pack size by the MCC in 2020 was made after thorough evaluation, with patient safety as a paramount concern and should be adequate in providing for the general goals of allergic rhinitis treatment.

The use of cetirizine in pregnancy and breastfeeding is not recommended and consumers need to be able to discuss with a healthcare professional the benefits and potential risks with taking cetirizine in managing allergic rhinitis where medicines, information, advice, and verbal reinforcement can also be provided. While allergic rhinitis is often a self-diagnosed condition it can be commonly confused with a range of other diagnoses, such as a simple cold, a sinus infection, conjunctivitis and serious eye conditions, and thus increasing the general sales level pack size may delay a person seeking advice in a pharmacy and may mean that best practice treatment is similarly delayed, which is not in the best interest of promoting public health. A smaller pack will encourage consumers to seek advice from a pharmacist more regularly than would be the case for a larger pack size.

Amongst other things, the management of allergic rhinitis is varied and the optimal therapeutic choice for an individual patient should be made in consultation with a health professional and provision of other information, such as alternative or additional treatment options, non-pharmacological and/or self-management advice such as avoidance of allergens, use of saline nasal sprays and direct steam inhalation, which play an important role in managing the symptoms.

Cetirizine is more likely to result in sedation and impairment than other non-sedating, similarly effective, antihistamines. Sedation is noted as an adverse effect in most datasheets for cetirizine and consumers need to be advised that there is even a potential low risk with the second-generation antihistamines, which can only be done in consultation with a healthcare professional. Although its sedation effects are dose-related and risks can increase when taken in combination with alcohol and any other medicine that can cause memory impairment and affect psychomotor skills, there is still a higher risk of an adverse outcome in comparison to other antihistamines.

Adherence to the five-day supply in New Zealand serves to ensure that consumers are guided by appropriate dosing instructions and professional guidance, reducing the potential for misuse or unintentional overconsumption. The principle of prioritising patient safety should continue to guide New Zealand's decision-making independently of external harmonisation in this specific case.

Thank you for your consideration of our response. If you have any questions about our feedback, please contact our Senior Advisory Pharmacists, Martin Lowis (martin@pgnz.org.nz, 04 802 8218) or Cathy Martin (cathy@pgnz.org.nz, 04 802 8214).

Yours sincerely,

Nicole Rickman
General Manager – Membership and Professional Services

25 September 2023

The Secretary
Medicines Classification Committee
Medsafe
committees@health.govt.nz

Dear Sir/Madam,

Re: 8.2.4 Melatonin Classification to be assessed at the 71st Medicines Classification Committee meeting

At the 71st meeting of the Medicines Classification Committee the classification of melatonin will be reviewed as a result of the change in scheduling for immediate release melatonin for the treatment of jet lag in Australia.

The TGA has rescheduled immediate release melatonin to allow for pharmacist only provision when containing 5 mg or less of melatonin for the treatment of jet lag in adults aged 18 or over, in a primary pack containing no more than 10 dosage units.

[redacted] supports the Medicines Classification Committee to revise the classification of melatonin in New Zealand in a manner that is consistent with the Pharmacist Only scheduling adopted in Australia. That is to reclassify immediate release melatonin in divided preparations containing 5 mg or less of melatonin in a primary pack containing no more than 10 dosage units when labelled for the treatment of jet lag in adults aged 18 years of over from Prescription Medicine to a Restricted Medicine.

Melatonin is a naturally occurring hormone, which is produced by the brain's pineal gland. It is involved in co-ordinating the body's circadian rhythms or sleep/wake cycle. Melatonin is released by the pineal gland during darkness. Exposure to bright light cuts off melatonin release and the onset of dim light triggers resumption of its release. It has been used therapeutically to re-entrain disturbed circadian rhythms. Exogenous melatonin tends to produce a phase advance when it is taken in the late afternoon or evening before the release of endogenous melatonin.[1, 2] Melatonin is an effective treatment of jet lag[1] primarily due to its clock-resetting effects as well as its dose-related hypnotic activity.[2]

Jet lag is a sleep disorder that results from crossing time zones too rapidly for the circadian clock to keep pace. There is a temporary misalignment between the circadian clock and local time. The circadian clock is slow to reset, so that after several time zones have been crossed, the endogenous signals for sleep and wakefulness do not match the local light–dark and social schedules. The symptoms of jet lag persist until the circadian system is realigned, typically within 4 to 6 days.[1, 2]

Jet lag only occurs after airplane travel across multiple time zones. As such it is a self-diagnosable condition. The symptoms of jet lag are transient and end when the circadian clock has adjusted to the destination time zone. Therefore, there is negligible risk that the non-prescription use of melatonin to manage jet lag will result in any delays in the diagnosis and treatment of a more serious medical condition. Nor is there a risk of long-term treatment with melatonin, as jet lag symptoms last for 4 to 6 days.[1] Hence jet lag is a condition suitable to self-management with pharmacist oversight

Immediate release melatonin is an effective treatment of jet lag

Melatonin is the most extensively studied therapy for the treatment and prevention of jet lag.[1] In addition, 5 mg immediate release melatonin taken once a day at bedtime is the dosage regimen with the most clinical evidence. Ten of the 11 published randomised, placebo controlled melatonin clinical trials have evaluated the effectiveness of the 5 mg dose[3-12] and this dose has been evaluated in 4 of the 8 phase-shift laboratory studies.[13-16] Overall, these studies have established that immediate release 5 mg melatonin is an effective treatment of jet lag and is well-tolerated.[1, 17]

Herxheimer et al, published a Cochrane review to assess the effectiveness of oral melatonin taken in different dosage regimens for alleviating jet lag after air travel across several time zones.[1] The main findings of this review are summarised below.

- Ten clinical trials were included in the Cochrane review and eight of the trials found that melatonin, taken close to the target bedtime at the destination (10 pm to midnight), decreased jet lag from flights crossing five or more time zones. Amongst the two negative studies, there were design issues in the study by Spitzer et al, with a significant proportion of subjects experiencing jet lag at baseline due to the short time period at their destination before the return flight which was used to assess the effect of melatonin.[11] The other apparently negative report (Edwards et al[8]) suggests that melatonin did reduce jet lag in the first three days at the destination, but not later. The analysis of variance of the scores did not however distinguish between the first three days after arrival and the later days, and this may explain how a difference could have been missed.[1]

- Clinically meaningful reductions in the symptoms of jet lag were demonstrated for both eastward travel (4 trials, weighted mean difference in jet lag score was -19.52, 95% CI -28.13 to -10.92 for melatonin versus placebo) and westward travel (2 trials, weighted mean difference in jet lag score was -17.27, 95% CI -27.28 to -7.26 for melatonin versus placebo).[1]

- The number needed to treat is low (NNT = 2) indicating that one in every two patients experience a meaningful benefit.[1]

- Other symptoms of jet lag were assessed across the different placebo-controlled studies. These secondary outcomes also support the use of immediate release melatonin for jet lag. Sleepiness was rated in three trials with all three trials demonstrating significantly less sleepiness (tiredness) with melatonin. Sleep latency was reported in three trials and was shown to be shorter in two of the trials. The third trial which failed to demonstrate a difference in sleepiness used an insensitive assessment tool. Sleep quality was assessed in one trial and was found to be improved with melatonin. Fatigue was assessed in two trials and melatonin increased ‘vigour/activity’ and lessened fatigue compared to placebo in both trials. Recovery was assessed in one trial and faster recovery occurred with melatonin across three measures; number of days for the sleep pattern or energy to normalise and for the disappearance of daytime tiredness.[1]

- The overall conclusions of this Cochrane review were “Melatonin is remarkably effective in preventing or reducing jet lag, and occasional short-term use appears to be safe. It should be recommended to adult travellers flying across five or more time zones, particularly in an easterly direction, and especially if they have experienced jet lag on previous journeys. Travellers crossing 2-4 time zones can also use it if need be.”[1]

A more recently published systematic review by Tortorolo et al,[17] reached comparable conclusions to the Cochrane review. The main finding was that melatonin probably reduces the global symptoms associated with jet lag syndrome in travellers crossing more than five time zones (moderate certainty of evidence). It is not clear whether the use of oral melatonin is associated with adverse effects (nausea, tiredness, drowsiness and headaches). However, no serious adverse effects were reported in any of the participants across the studies. Considering the fact that melatonin is probably a safe intervention the benefits of melatonin use for jet lag probably outweigh the risks. The authors also indicated that the probability of future evidence changing the conclusions of this summary is low due to the certainty of the current evidence.

It is important to recognise that there is limited evidence for doses less than 5 mg. For example, the evidence for 3 mg melatonin is based on three open label clinical trials. These studies demonstrated the effectiveness of immediate release 3 mg melatonin in accelerating the rate of resynchronisation based on the analysis of sleep diaries[18] and plasma melatonin rhythm.[19, 20] However, as the placebo-controlled evidence for melatonin is predominantly based on immediate release 5 mg melatonin, reclassification of melatonin for the treatment of jet lag in New Zealand should reflect this and the reclassification should be for immediate release melatonin 5 mg or less.

In addition, one placebo-controlled clinical trial has assessed the use of modified release melatonin 2 mg in the management of jet lag, Suhner et al.[1, 3] In this study, the 2 mg modified release tablets were compared to 5 mg and 0.5 mg immediate release melatonin as well as placebo. The use of 5 mg immediate release melatonin tablets improved self-rated sleep quality, shortened sleep latency, and reduced fatigue and daytime sleepiness after intercontinental flight. The 0.5 mg immediate release melatonin tablets were almost as effective as the 5 mg dose; with the hypnotic properties of melatonin, sleep quality and sleep latency being greater with the 5 mg dosage. However, the 2 mg modified release tablets were less effective than either of the immediate release tablets. On this issue, the Cochrane review by Herxheimer et al, concluded that “The relative ineffectiveness of 2 mg slow-release melatonin suggests that a short-lived higher peak concentration of melatonin works better.”[1] The reclassification of melatonin for the treatment of jet lag in New Zealand should reflect this evidence and be limited to immediate release formulations.

The use of immediate release melatonin to treat jet lag is well established and consistent with international guidelines

The Australian Therapeutic Guidelines state that “In adults, immediate-release melatonin has evidence of benefit to prevent or reduce jet lag. Melatonin plays a central role in regulating circadian rhythms and can prevent or reduce jet lag in adults flying across 5 or more time zones, but may be useful if crossing more than 2 time zones.” To prevent or reduce jet lag in an adult, consider melatonin immediate-release 0.5 to 5 mg orally, taken on the plane at the bedtime of the final destination; continue for up to 3 subsequent nights.[21]

The British guidelines on the management of circadian rhythm disorders state that there is “solid evidence to support the use of melatonin in jet lag” and that immediate release melatonin should be taken near the desired bedtime.[22]

The American guidelines of circadian rhythm disorders list melatonin as a standard therapy to manage jet lag. Melatonin administered at the appropriate time is indicated to reduce symptoms of jet lag and improve sleep following travel across multiple time zones.[23]

Note that in the American guideline’s “standard” recommendations are defined as “This is a generally accepted patient-care strategy that reflects a high degree of clinical certainty. The

term standard generally implies the use of Level 1 Evidence, which directly addresses the clinical issue, or overwhelming Level 2 Evidence."[23]

Immediate release melatonin is well tolerated

Melatonin is a safe medication. Overall, the published medical literature has not identified any evidence of significant safety risk associated with the use of melatonin.[1, 17, 23]

Drowsiness/sleepiness, headache, and dizziness/disorientation are the most frequently reported adverse effects with the short term use of melatonin to treat jet-lag. Drowsiness, headache, dizziness, and nausea are also the adverse effects reported most frequently when typical clinical doses of melatonin have been taken for periods of several days to several weeks by healthy persons and patients.[24]

Table 1 lists adverse events to melatonin in general that have been reported in clinical trials or spontaneous case reports.[25] As can been seen most adverse events are uncommon or rare.

Table 1: Adverse events reported for melatonin use from clinical trials or spontaneous reports[25]

System Organ Class	**Very Common** (≥ 1/10)	**Common** (≥1/100 to<1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Rare** (≥1/10,000 to <1/1,000)	**Not known:** (cannot be established from the available data)
Blood and lymphatic system disorders				leucopoenia, thrombocytopenia	
Immune system disorders					hypersensitivity reaction
Metabolism and nutrition disorders				hypertriglyceridaemia	hyperglycaemia
Psychiatric disorders			irritability, nervousness, restlessness, abnormal dreams, anxiety	mood altered, aggressive behaviour, disorientation, libido increased	
Nervous system disorders		headache, somnolence	dizziness	syncope (fainting), memory impairment, restless legs syndrome, paraesthesia	
Eye disorders				visual acuity reduced, vision blurred, lacrimation increased	
Cardiac disorders				palpitations	
Vascular disorders			hypertension	hot flushes	
Gastrointestinal disorders			abdominal pain, upper abdominal pain, dyspepsia, oral ulcers, dry mouth, nausea	vomiting, flatulence, salivary hypersecretion, halitosis, gastritis	
Skin and subcutaneous tissue disorders			pruritus, rash, dry skin	nail disorder	tongue oedema, oedema of the oral mucosa

Musculoskeletal and connective tissue disorders				arthritis, muscle spasms	
Renal and urinary disorders			glycosuria, proteinuria	polyuria, haematuria	
Reproductive system and breast disorders				priapism, prostatitis	galactorrhoea
General disorders and administration site conditions			chest pain, malaise	thirst	
Laboratory and other examinations			weight increased	blood electrolytes abnormal	

The toxicity and safety of modified release 2 mg melatonin has been evaluated by Medsafe. Melatonin is generally well tolerated with the rate of adverse events in clinical trials being higher for placebo than melatonin. The Medsafe approved data sheet for modified release melatonin states that administration of daily doses of up to 300 mg of melatonin without causing clinically significant adverse reactions have been reported in the literature.[26]

The Cochrane review also assessed the safety of melatonin in the management of jet lag. Nine of the 10 studies included in the Cochrane review reported symptoms or adverse events, with 3 studies adopting a systematic approach.[1] Suhner et al,[3] found no significant differences in symptoms reported between melatonin and placebo, noting that many of the reports were likely to be symptoms of jet lag and not side effects. A second study by Suhner et al,[4] assessed the use of melatonin alone or in combination with zolpidem. In this study subjects in the zolpidem plus melatonin group felt significantly sleepier in the morning, while the subjects in the melatonin group felt least sleepy. The combination group also felt significantly more confused and more nauseated than all other treatment groups. Ear/ nose/ throat problems were most frequent in melatonin users; pruritus was least frequent in this group. The study by Edwards et al,[8] asked participants to list any minor medical problems, and a disorientating 'rocking' feeling as though they were on a boat one was more frequent with melatonin than placebo (P = 0.036).

Hypnotic effects after melatonin use were reported in 5 of the remaining 6 studies, affecting about 10% of participants. Other side effects reported from these 6 studies included headache or 'heavy head', disorientation, nausea, and gastrointestinal problems. One individual experienced difficulty in swallowing and breathing within 20 minutes of taking the first dose of 0.5 mg melatonin, symptoms which subsided after 45 minutes. This person stopped taking the capsules, and upon later rechallenge the milder symptoms recurred. All adverse events reported in the trials occurred during treatment and were transient.[1]

Overall melatonin is a well-tolerated medicine and short-term use is safe.[1, 17, 23]

Consumer benefits

There are multiple benefits for preventing and treating jet lag and these include:

- Reduced risk of serious misjudgements amongst travellers (especially when travelling for work/business) or with professional dealings.[2]

- Reduced risk of accidents due to daytime fatigue and sleepiness, especially if the traveller is driving a motor vehicle.

- Reduced duration of physical and cognitive impairment that can result in impaired reaction times and decision making times as well as increased risk of making errors.[27]

- Increased capacity to undertake physical and social activity, optimising vacation time.

- Reducing the use of hypnotics (Z-drugs and benzodiazepines) to manage jet lag related insomnia and reducing the risk of adverse effects associated with these medications including amnesia, confusion, dangerous sleep-related behaviours and dependence (addiction).[21]

Increased access to immediate release melatonin to manage jet lag will also improve the safety and quality use of melatonin in the management of jet lag as it will:

- Reduce the use of homeopathic melatonin, which is ineffective and not recommended for use,[21, 28]

- Reduce the use of melatonin sourced from overseas which have been shown to be off variable quality with large variances in melatonin content.[21, 29]

Contraindications and precautions

The Data Sheet for prolonged release melatonin has no contraindications, other than for people with a known hypersensitivity to melatonin or the excipients in the dosage form.[26] There is no evidence to suggest that immediate release melatonin will have any additional contraindications.

The precautions proposed for immediate release melatonin for jet lag in Australia had essentially the same RASML warning statements as applied to modified release 2 mg melatonin. There is no evidence to indicate that the risk profile for immediate release melatonin is different to modified release 2 mg melatonin.

There is no evidence of abuse potential with melatonin and the compound is not a candidate for illicit or recreational use.

Overdose

The Medsafe approved data sheet for modified release melatonin states that administration of daily doses of up to 300 mg of melatonin without causing clinically significant adverse reactions have been reported in the literature.[26] Use of melatonin in a daily dose of 300 mg for 4 months was well-tolerated and did not lead to severe toxicity although it resulted in a decrease in the luteinizing hormone , oestradiol and progesterone.[30]

No cases of overdose were reported in the clinical trials of melatonin for the treatment of jet lag.

A small number of cases of melatonin overdose have been reported (Force 1997 [31], Holliman 1997 [32]) with the main effect being transient sedation. Nevertheless, no severe toxicity has been reported and acute melatonin overdose is not expected to result in any significant clinical toxicity.[33]

Immediate release melatonin for the treatment of jet lag is suitable for classification as a Restricted Medicine

The use of immediate release melatonin in dosages of 5 mg or less in a small pack (≤ 10 dosage units) for the management of jet lag in adults satisfies, and for several aspects exceeds the criteria for a Restricted medicine:

- Melatonin is well tolerated and has a wide therapeutic index. Short term use is substantially safe, is associated with few side effects and there is minimal potential for harm if used inappropriately[1, 33].

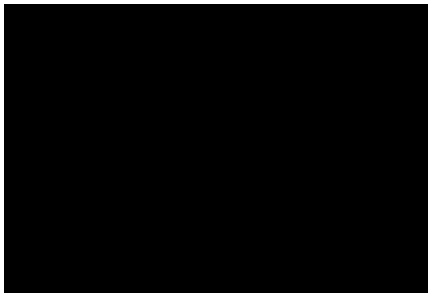
- Melatonin use does not result in dependency or rebound sleep disturbance upon discontinuation.[34]

- The risk profile of melatonin is well defined and the adverse effects, interactions and contraindications are known, identifiable and manageable by a pharmacist.[35]

- Jet lag only occurs after airplane travel across multiple time zones. Jet lag is self-diagnosable and unlike most medical conditions can be anticipated by consumers. The symptoms of jet lag are short-lived ending typically 4 to 6 days after arrival at the new destination.[1] Hence, jet lag is not a chronic condition, and does not require a healthcare professional to aid the diagnosis or monitor ongoing use.

From the information provided above it is clear that jet lag is a self-diagnosable acute condition that is suitable for management with non-prescription melatonin. It is also clear that immediate release melatonin, at doses of 5 mg, is a safe, well-tolerated and effective treatment of jet lag.[1, 17] There are clear and substantial health benefits associated with classifying immediate release melatonin for the management of jet lag as a Restricted Medicine. This classification poses minimal safety risk, which is equivalent or less than that associated with the use of modified release melatonin for the management of insomnia, which is classified as a Restricted Medicine.

Yours sincerely



References

1. Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag. *Cochrane Database Syst Rev*. 2002:CD001520
2. Sack RL. Clinical practice. Jet lag. *N Engl J Med*. 2010;362:440-447
3. Suhner A, Schlagenhauf P, Johnson R, Tschopp A, Steffen R. Comparative study to determine the optimal melatonin dosage form for the alleviation of jet lag. *Chronobiol Int*. 1998;15:655-666
4. Suhner A, Schlagenhauf P, Hofer I, Johnson R, Tschopp A, Steffen R. Effectiveness and tolerability of melatonin and zolpidem for the alleviation of jet lag. *Aviat Space Environ Med*. 2001;72:638-646
5. Pierard C, Beaumont M, Enslen M, Chauffard F, Tan DX, Reiter RJ, et al. Resynchronization of hormonal rhythms after an eastbound flight in humans: Effects of slow-release caffeine and melatonin. *Eur J Appl Physiol*. 2001;85:144-150
6. Beaumont M, Batejat D, Pierard C, Van Beers P, Denis JB, Coste O, et al. Caffeine or melatonin effects on sleep and sleepiness after rapid eastward transmeridian travel. *J Appl Physiol (1985)*. 2004;96:50-58
7. Arendt J, Aldhous M, English MJ, Marks V, Arendt J, Marks M, et al. Some effects of jet-lag and their alleviation melatonin. *Ergonomics*. 1987;30:1379-1393
8. Edwards BJ, Atkinson G, Waterhouse J, Reilly T, Godfrey R, Budgett R. Use of melatonin in recovery from jet-lag following an eastward flight across 10 time-zones. *Ergonomics*. 2000;43:1501-1513
9. Petrie K, Dawson AG, Thompson L, Brook R. A double-blind trial of melatonin as a treatment for jet lag in international cabin crew. *Biol Psychiatry*. 1993;33:526-530
10. Petrie K, Conaglen JV, Thompson L, Chamberlain K. Effect of melatonin on jet lag after long haul flights. *BMJ*. 1989;298:705-707
11. Spitzer RL, Terman M, Williams JB, Terman JS, Malt UF, Singer F, et al. Jet lag: Clinical features, validation of a new syndrome-specific scale, and lack of response to melatonin in a randomized, double-blind trial. *Am J Psychiatry*. 1999;156:1392-1396
12. Nickelsen T, Lang A, Bergau L. The effect of 6-, 9- and 11-hour time shifts on circadian rhythms: Adaptation of sleep parameters and hormonal patterns following the intake of melatonin or placebo. *In: Arendt J, Pevet P editor(s). Advances in Pineal Research.* 1991;5:303-306
13. Deacon S, Arendt J. Adapting to phase shifts, ii. Effects of melatonin and conflicting light treatment. *Physiol Behav*. 1996;59:675-682
14. Burke TM, Markwald RR, Chinoy ED, Snider JA, Bessman SC, Jung CM, et al. Combination of light and melatonin time cues for phase advancing the human circadian clock. *Sleep*. 2013;36:1617-1624
15. Samel A, Wegmann HM, Vejvoda M, Maass H, Gundel A, Schutz M. Influence of melatonin treatment on human circadian rhythmicity before and after a simulated 9-hr time shift. *J Biol Rhythms*. 1991;6:235-248
16. Wyatt JK, Dijk DJ, Ritz-de Cecco A, Ronda JM, Czeisler CA. Sleep-facilitating effect of exogenous melatonin in healthy young men and women is circadian-phase dependent. *Sleep*. 2006;29:609-618
17. Tortorolo F, Farren F, Rada G. Is melatonin useful for jet lag? *Medwave*. 2015;15 Suppl 3:e6343
18. Cardinali DP, Bortman GP, Liotta G, Perez Lloret S, Albornoz LE, Cutrera RA, et al. A multifactorial approach employing melatonin to accelerate resynchronization of sleep-wake cycle after a 12 time-zone westerly transmeridian flight in elite soccer athletes. *J Pineal Res*. 2002;32:41-46

19. Takahashi T, Sasaki M, Itoh H, Ozone M, Yamadera W, Hayshida K, et al. Effect of 3 mg melatonin on jet lag syndrome in an 8-h eastward flight. *Psychiatry Clin Neurosci*. 2000;54:377-378
20. Takahashi T, Sasaki M, Itoh H, Yamadera W, Ozone M, Obuchi K, et al. Melatonin alleviates jet lag symptoms caused by an 11-hour eastward flight. *Psychiatry Clin Neurosci*. 2002;56:301-302
21. Psychotropic Expert Group. Overview of jet lag. *Therapeutic Guidelines Complete*. 2021
22. Wilson S, Anderson K, Baldwin D, Dijk DJ, Espie A, Espie C, et al. British association for psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: An update. *J Psychopharmacol*. 2019;33:923-947
23. Morgenthaler TI, Lee-Chiong T, Alessi C, Friedman L, Aurora RN, Boehlecke B, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An american academy of sleep medicine report. *Sleep*. 2007;30:1445-1459
24. Colonis Pharma Ltd. Melatonin 3 mg film-coated tablets, summary of product characteristics. 2021
25. Melatonin 5 mg summary of product characteristics 2021
26. Circadin (melatonin controlled release 2 mg) data sheet. 2021
27. Anderson J. Exploring the consequences of mobility: Reclaiming jet lag as the state of travel disorientation. . *Mobilities*. 2015;10:1-16
28. Pache D. Melatonin—its role in your life. Part 2: Clinical use of melatonin for sleep. *AJP.com.au*. 2020
29. Grigg-Damberger MM, Ianakieva D. Poor quality control of over-the-counter melatonin: What they say is often not what you get. *J Clin Sleep Med*. 2017;13:163-165
30. Voordouw BC, Euser R, Verdonk RE, Alberda BT, de Jong FH, Drogendijk AC, et al. Melatonin and melatonin-progestin combinations alter pituitary-ovarian function in women and can inhibit ovulation. *J Clin Endocrinol Metab*. 1992;74:108-117
31. Force RW, Hansen L, Bedell M. Psychotic episode after melatonin. *Ann Pharmacother*. 1997;31:1408
32. Holliman BJ, Chyka PA. Problems in assessment of acute melatonin overdose. *South Med J*. 1997;90:451-453
33. HSDB. Melatonin, dwl:02.02.2018.
34. Wade AG, Crawford G, Ford I, McConnachie A, Nir T, Laudon M, et al. Prolonged release melatonin in the treatment of primary insomnia: Evaluation of the age cut-off for short- and long-term response. *Curr Med Res Opin*. 2011;27:87-98
35. Therapeutic Goods Administration. Notice of interim decisions made under regulation 42zczn of the therapeutic goods regulations 1990. *ACMS # 29*. 2020