Consumer Healthcare Products Australia

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15 January 2021

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

Sent by email: committees@moh.govt.nz

Dear Sir/Madam,

Re: Objection to Recommendation made at the 65th meeting of the Medicines Classification Committee (MCC) – Item 6.2 Ibuprofen (Nurofen 400mg Double Strength)

Consumer Healthcare Products Australia (CHP) does not support the MCC's recommendation in relation to item 6.2 of the agenda regarding ibuprofen 400mg.).

CHP Australia is the leading voice and industry body for manufacturers and distributors of consumer healthcare products in Australia, which includes non-prescription medicines. 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.

CHP Australia has reviewed the minutes of the 65th meeting and is concerned about the decision that has been made. We therefore respectfully wish to object to the recommendation of the 65th meeting on the following grounds:

- We believe the MCC did not consider all the safety issues appropriately
- We contend that due process did not occur

CHP Australia urges the MCC to reconsider the recommendation in relation to ibuprofen 400mg.

Please contact me if you have any further queries.

Kind regards,

The MCC did not consider the safety issues correctly

The ibuprofen 400mg (Nurofen 400mg) presentation that is the subject of the submission considered at the 65th meeting of the MCC is a double strength preparation of ibuprofen, i.e., a double strength of the ibuprofen 200mg that is currently available as a Pharmacy Medicine and as a General Sale medicine in New Zealand. The recommended daily dose is the same as the recommended maximum daily dose of the currently available ibuprofen 200mg products.

The maximum daily dose of the ibuprofen 200mg products is 1200 mg per day.

The maximum daily dose of the ibuprofen 400mg products is 1200 mg per day.

The precautions and contraindications are the same for both products, as are the indications.

The key difference is that the ibuprofen 400mg tablet is labelled as DOUBLE STRENGTH with very clear instructions that consumers should table one tablet three times a day. This is clearly labelled on the front of pack, as well as the back of pack in order to mitigate the risk of double dosing.

The applicant seeks to reclassify a pack size of 12 dosage units (4 days' supply) as a Pharmacy Medicine.

CHP is very concerned at some apparent misunderstandings in the minutes, especially around the safety and dosing of ibuprofen.

Products are already available as Pharmacy Medicines (and as GSL medicines in smaller packs) at the same maximum daily dose (400 mg three times a day), the key difference being the strength of the dosage form. There is therefore no difference in safety between the ibuprofen 400mg Double Strength and ibuprofen 200mg tablets; the safety profile is exactly the same when taken as directed.

The MCC's comment that *"The Committee discussed the safety and dosing of ibuprofen and highlighted concerns for consumers that may have otherwise used a codeine containing product then replacing these with a non-steroidal medicine, particularly around the elderly*[1]*"* suggests a misinterpretation of some key elements of this submission.

The Medsafe Labelling Statements Database and the Australian Required Advisory Statements for Medicine Labels (RASML) currently require labelling to include contraindication statements in elderly people and in people with various health conditions. Relevant warning statements include:

- Do not use [this product/insert name of product] if you are aged 65 years or over except on doctor's advice.
- Do not use if you have a stomach ulcer.
- Do not use if you have heart failure.

[1] https://www.medsafe.govt.nz/profs/class/Minutes/2016-2020/mccMin27Oct2020.htm

- Do not use if you have asthma except on doctor's advice.
- Do not use if you are allergic to aspirin or ibuprofen except on doctor's advice.
- Do not use if you are allergic to [other] anti-inflammatory medicines.
- Do not exceed the maximum stated dose.
- Do not use for more than a few days at a time except on doctor's advice.
- Do not use with other medicines you are taking regularly except on doctor's advice.
- Consult a healthcare professional before use if you have kidney problems or impaired renal function.
- Do not use at all during the last 3 months of pregnancy.
- Do not use [this product/insert name of the product] if trying to become pregnant, or during the first 6 months of pregnancy, except on doctor's advice.

Australian labelling also requires the statement "Excessive use can be harmful and increase the risk of heart attack, stroke or liver damage."

These label statements are common to both the 200mg ibuprofen as well as the 400mg ibuprofen.

CHP believes that there is no incremental risk with the availability of the ibuprofen 400mg product since consumers are already aware of ibuprofen and especially elderly consumers who are aware if the product is contraindicated for them.

Using the forthcoming reclassification of codeine products in New Zealand as a reason to not support the reclassification is not aligned with the experience following reclassification of codeine in Australia. Consumers who were previously taking codeine generally tended to seek the advice of a doctor or pharmacist to assist with selection of alternative pain relief and there is no evidence that the codeine reclassification has led to any problems with inappropriate use of ibuprofen.

The Australian Delegate recently made a final decision to reschedule ibuprofen 400mg in packs of 12 dosage units to Pharmacy Medicine[2,3], which will take effect on the 1st February 2021. Given the TGA's activities and monitoring of the codeine rescheduling over the past two years or more, it is not likely that rescheduling of ibuprofen 400mg would have been permitted had there been adverse safety signals with other analgesics following on from codeine rescheduling.

The Delegate stated that ibuprofen 400mg, with the pack restricted to 12 dosage units and when labelled with the appropriate warning statements, meets the factors for Pharmacy Medicines. Additionally, the Delegate addressed concerns around the possibility of double dosing due to a possible culture of taking two tablets at once by stating that ibuprofen has a wide therapeutic index and the risk from harm from

[2] https://www.tga.gov.au/book-page/35-ibuprofen
[3] https://www.tga.gov.au/book-page/315-ibuprofen

overdose is minimal. Very large doses of ibuprofen are required for moderate to severe toxicity (>/= 400mg/kg or 28 g for a 70 kg person) and a 400 mg 12-dosage pack contains only 4.8 g ibuprofen. There is unlikely to be any increased safety risk when taken according to directions, noting the availability of 20 g ibuprofen in the 100 pack of 200 mg tabs (with a maximum dose of 1200mg/day) are currently available as a Schedule 2/Pharmacy Medicine. If a consumer took double the recommended dose of the double strength product (i.e., 800 mg/day) they would take a non-toxic dose and consume the supply in 2 days. In addition, the Delegate stated that other "Double Strength" products are already marketed. The concept of "Double Strength" products is therefore not unusual to consumers.

The labelling includes design features to mitigate against risk of double dosing, with front of pack "1 tablet dose" callout and single tablet graphic, as well as clear dosage instructions on the back of pack.

CHP also has concerns with the MCC's statement regarding increased risk for upper GI bleeding and acute kidney injury. We do not agree with this assessment and believe that the concerns regarding upper GI bleeding and acute kidney injury are not consistent with clinical evidence for doses used in over the counter medicines.

A 2020 narrative review reconfirmed that ibuprofen has the lowest risk of GI side effects compared to other NSAIDs and that a meta-analysis of ibuprofen safety found that the frequency of digestive system adverse events was comparable to placebo (12.1% vs. 11.0%, p = 0.420). In addition, the overall frequency of adverse events reported with ibuprofen was numerically the same or lower than that of adverse events for placebo (27.4% vs. 31.7%, p = 0.018)[4].

In relation to acute kidney injury, this is an uncommon adverse event predominantly in patients with pre-existing renal conditions, for whom OTC ibuprofen is contraindicated, and labelling warning statements to this effect are included for all OTC ibuprofen.

In any case, the risks for upper GI bleeding and for acute kidney injury are no different for ibuprofen 400mg compared to currently available ibuprofen 200 mg when taken at recommended dosages by people for whom the medicine is not contraindicated.

As a Pharmacy Medicine, ibuprofen 400mg will be available with supervision from pharmacists and pharmacy assistants, and pharmacist advice is available at all times to assist consumers. Pharmacists as well as pharmacy assistants are well trained to monitor and provide advice on analgesics, it is an integral part of pharmacist's responsibilities on a day-to-day basis.

In summary, CHP believes that the MCC has misrepresented the risks of ibuprofen 400mg, which has the same safety profile as the currently available ibuprofen 200mg tablet when taken at the same maximum daily dose.

[4] Varrassi G, Pergolizzi JV, Dowling P, Paladini A. Ibuprofen Safety at the Golden Anniversary: Are all NSAIDs the Same? A Narrative Review. Adv Ther. 2020;37(1):61-82.

Breach of process

Concerningly, the MCC minutes refer to risks associated "*with the availability of the 400mg strength ibuprofen at general sale versus the consumer benefit*".

The MCC should prepare clear and unambiguous minutes so that there is an accurate record of discussion.

The criteria for Pharmacy Medicines are different to those of GSL medicines and the above statement implies that the MCC has concerns that pharmacist advice will not be available. The proposal was very clearly framed for reclassification as a Pharmacy Medicine, where advice on appropriate choice of analgesics is available to consumers.

We are concerned that there has been an error in process, with the MCC incorrectly assessing the safety of the product as if no pharmacist advice would be available to consumers, which is clearly incorrect.

Conclusion

CHP Australia requests that the MCC reconsider the decision to reject the application for reclassification of ibuprofen 400 mg in a pack of 12 dosage units to Pharmacy Medicine.

The safety profile of the product is the same as that of the currently available ibuprofen 200mg products and the labelling has been designed to reduce risks of double dosing.

CHP Australia is very concerned that the MCC provides very little detail of its discussions and has not recommended reclassification of ibuprofen 400mg to Pharmacy Medicine for reasons that appear to be arbitrary, non-evidence based and which over-state the risks of availability within pharmacy.

We request that the MCC take the opportunity to harmonise the classification of ibuprofen 400mg with Australia, which will be a Pharmacy Medicine in packs containing 12 dosage units from the 1st February 2021. There is no valid reason why the classification should differ, given the similarities in patient groups across both countries and the similarities in labelling and packaging.

HEALTH · HYGIENE · HOME

13 January 2021

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

Dear Sir/Madam,

Re: Reclassification of Ibuprofen 400mg - MCC recommendation following the 65th meeting on 27 October 2020

Reckitt Benckiser respectfully objects to the decision of the MCC that the current classification of ibuprofen 400mg should remain unchanged as a Restricted Medicine. The basis of our objections are:

1. There was a breach of the appropriate process. Our application was to reclassify ibuprofen 400 mg from a Restricted Medicine to a Pharmacy Only medicine. The minutes of the meeting state that the MCC considered the "availability of the 400 mg strength ibuprofen at general sale…". As such it appears a decision has been made in relation a change in scheduling to general sale as opposed to Pharmacy only.
2. The MCC did not consider all the safety issues correctly. This is evident on several counts, including the MCC considered safety in the elderly even though this product is not indicated for OTC use in the elderly (> 65 years) unless it is on doctor's advice. The risk of gastrointestinal bleeding and acute kidney injury is overstated and does not reflect the published evidence. The statement of a "significant potential for harm if a consumer accidently takes twice the recommended dose" is overstated given that this double dose is an approved prescription dose, which is well tolerated, and pack size restriction limits this risk.

We request that the MCC reconsiders its decision and offer the following information to address the issues raised in the minutes to enable this to occur.

Appropriate process

The application was for the reclassification of ibuprofen 400 mg, in packs containing not more than 12 dose units when sold in the manufacturer's original pack labelled for use by adults and children over 12 years of age, from a Restricted Medicine to a Pharmacy Only Medicine. However, based on the published minutes, the MCC considered the classification with respect to availability as a General Sales medicine (see the excerpt below).

> "The Committee considered the comment raised relating to the risks associated with the availability of the 400mg strength ibuprofen at **general sale** [our emphasis] versus the consumer benefit. The Committee agrees that the risks outweigh the consumer access benefit as the usual prescribed adult dose of ibuprofen is two tablets of the 200mg strength. Additionally, the Committee considered that the 400mg ibuprofen single tablet dose is a relatively new presentation to the market at restricted level so it is unlikely that consumers are familiar with it; Therefore the

consumer benefit is minimal when compared to the significant potential for harm if a consumer accidentally takes twice the recommended dose of ibuprofen."

As the General Sales classification enables the sale in retail channels with no access to healthcare professional advice it is understandable that the MCC would desire more in market experience with the double strength 400 mg formulations. However, as a Pharmacy Only medicine, pharmacists are readily available to provide any additional advice when required and we believe the Pharmacy Only classification is appropriate, given that the maximum daily dose is no different to that of ibuprofen 200 mg dose that is currently available as a general sale and Pharmacy only medicine. The 400 mg dose is the most commonly used OTC ibuprofen dose,(1, 2) and the Pharmacy only pack size is limited to 4 days' supply.

This is not just Reckitt Benckiser's position, but it also reflects the final decision of the Australian Advisory Committee on Medicines Scheduling Meeting #31, where an equivalent application was considered, and the decision was to include ibuprofen 400 mg in Schedule 2 as a Pharmacy Only medicine.

Safety considerations

The minutes of the 65th meeting of the MCC provide evidence that safety considerations were not correctly considered. Areas of concern that we respectfully request be reconsidered are as follows:

A. Safety in the elderly
B. Risk of upper gastrointestinal bleeding and acute kidney injury
C. Safety if a consumer accidently takes twice the dose.

A. Safety in the elderly

The "elderly" is commonly defined as people aged 65 years and older. The non-prescription use of ibuprofen has a clear prominent warning statement that prohibit its OTC use in this patient population except on doctor's advice.

- DO NOT USE UNLESS A DOCTOR HAS ADVISED YOU if you are 65 years and older.

This warning statement is the same as it is for regular strength 200 mg ibuprofen as it is for the Nurofen® 400 DOUBLE STRENGTH (400mg ibuprofen).

There is no evidence to suggest that older people do not follow this instruction. Hence, concerns about the elderly being put at risk by replacing codeine-based analgesics with ibuprofen 400 mg is unfounded and the risk is mitigated by existing labelling.

An analysis of the New Zealand Suspected Medicine Adverse Reaction Search (SMARS) database for the period of 1st January 2000 to 25th April 2020 for adverse events reported with oral ibuprofen, identified 49 patients aged 65 years or older who had a suspected adverse event.(3) This represented 13.5% of all patients that had an adverse event over this period and this correlates to the proportion of the elderly population in New Zealand at 14.9% (in 2018).(4) Hence, this data does not signal any excessive risk associated with the real-world use of ibuprofen amongst the elderly in New Zealand (noting that this data does

not distinguish between OTC and prescription use). It also indicates that the current risk management strategies that surround the OTC use of ibuprofen including its availability as a general sale medicine (at the same maximum dose of 1200 mg/day as pertains to the 400 mg double strength tablets) are appropriate and effective.

Published clinical evidence also supports the excellent safety profile of ibuprofen in the elderly. A meta-analysis assessed the incidence of adverse events amongst elderly people, aged 65 years or older (range 65 - 92 years) taking multiple doses of OTC ibuprofen (400 mg three times daily for up to 10 days) for osteoarthritis pain, compared with placebo. This meta-analysis found no statistically-significant difference in the overall incidence of adverse events between ibuprofen and placebo (OR 1.02, 95% CI: 0.66-1.56, P=0.943). The difference was also not statistically significant for 'body as a whole' events (P=0.315), digestive system events (P=0.712), or any individual digestive system event.(5)

Similarly, a randomised placebo-controlled clinical trial of maximal OTC doses of ibuprofen 1200 mg/day for 10 days found no difference in the adverse event rate between ibuprofen and placebo amongst patients who were aged 65 years or older.(6)

In addition, the context of the discussion about risk in the elderly was specific to the situation where elderly consumers are seeking alternative to codeine-based analgesics. In this scenario an alternative analgesic that is expected to be considered by consumers is the fixed dose combination of paracetamol/ibuprofen, such as Maxigesic® which are available as General Sales medicines in New Zealand. With Maxigesic®, elderly consumers will be exposed to a full OTC dose of both paracetamol (4000 mg/day) and ibuprofen (1200 mg/day). This comes with added risk relative to just taking a single ingredient. Hence, in previous MCC deliberations the conclusion must be that this risk to the elderly is outweighed by the benefit of wider access and that the risk is mitigated by appropriate warnings on product labels. We believe the same conclusion should extend to ibuprofen 400 mg allowing classification to be extended to Pharmacy Only medicine.

B. Risk of upper gastrointestinal bleeding and acute kidney injury

The MCC were concerned that the Pharmacy Only access to ibuprofen 400 mg “could lead to issues such as an increased risk for upper gastrointestinal (GI) bleeding and acute kidney injury”.

This concern is not supported by clinical evidence. Clinical data confirms that OTC ibuprofen (1200 mg/day) has a gastrointestinal safety profile comparable to placebo, at least equivalent to paracetamol and better than other NSAIDs including aspirin.

For example, a 2020 narrative review reconfirmed that ibuprofen has the lowest risk of GI side effects compared to other NSAIDs and that a meta-analysis of ibuprofen safety found that the frequency of digestive system adverse events was comparable to placebo (12.1% vs. 11.0%, p = 0.420). In addition, the overall frequency of adverse events reported with ibuprofen was numerically the same or lower than that of adverse events for placebo (27.4% vs. 31.7%, p = 0.018).(7)

The study by Moore 1999,(8) compared up to 7 days use of aspirin, paracetamol (both up to 3000 mg daily) or ibuprofen (up to 1200 mg daily) for the management of pain in 8,633 evaluable patients. This trial confirmed the good safety profile of OTC ibuprofen with:

- Rates of significant adverse events being equivalent for ibuprofen and paracetamol and lower than that for aspirin (ibuprofen 13.7%, paracetamol 14.5%, aspirin 18.7%)
- Total gastrointestinal events (including dyspepsia) and abdominal pain were less frequent with ibuprofen (4 and 2.8%, respectively) than with paracetamol (5.3 and 3.9%) or aspirin (7.1 and 6.8%) [all $p < 0.035$].
- There were no cases of gastrointestinal bleeding or ulcers with ibuprofen use. Noting that there were 4 cases of non-serious gastrointestinal bleeding with paracetamol and 2 with aspirin, and 1 case of peptic ulcer with aspirin.

Similarly, a randomised placebo controlled trial by Doyle 1999(6) compared the safety of maximal OTC dose of ibuprofen 1,200 mg (400 mg three times daily) for 10 consecutive days in 1,246 healthy adults. Note, patients with a positive gastrointestinal history were not excluded from this study. This trial confirmed the good safety profile of OTC ibuprofen with:

- Ibuprofen having an overall lower adverse event rate than placebo, odds ratio 0.71 (95% CI: 0.55-0.90, P = 0.005)
- Ibuprofen having a comparable rate of gastrointestinal adverse events to placebo, odds ratio 1.24 (95% CI: 0.90-1.72, P = 0.187, not statistically significant)
- The frequency of positive stool occult blood tests was comparable between ibuprofen and placebo. Of the 17 of 1,216 subjects that had positive tests, 5 (all in the ibuprofen group) had an underlying non-drug related gastrointestinal condition (e.g. haemorrhoids). 9 of the 12 remaining subjects agreed to further investigations and all patients had no gastrointestinal pathology, including GI ulcers.

The cardiorenal safety of ibuprofen was extensively reviewed and summarised in our submission (Part B, Section 4). This included a summary of the review paper by White, 2018(9). This review assessed the use of ibuprofen in normotensive patients, patients with hypertension, cardiovascular events from clinical trials and from observational databases. One of the findings of this extensive review was that there is little cardiorenal risk when OTC ibuprofen is used as directed.

Acute kidney issues associated with NSAIDs is an uncommon adverse event that is predominately an issue for patients with pre-existing renal issues under conditions of decreased effective circulating volume. Griffin 1998(10) performed a nested case-control study amongst Tennessee Medicaid patients aged 65 years or older (n = 11,698) to assess the association between community acquired acute renal failure and NSAID use. In this study, ibuprofen accounted for 35% of all NSAID use and OTC doses (≤ 1,200 mg) of ibuprofen 31% of all ibuprofen use. This study confirmed the good renal safety of OTC doses of ibuprofen as this use was not associated with any increased risk of acute renal failure; adjusted odds ratio 0.98 (95% CI: 0.58-1.51). It is important to note that the patient cohort in this study is not reflective of the OTC ibuprofen user, but represents a population at high risk of renal complications for whom OTC ibuprofen use is contraindicated without medical advice. For example, compared to the control cohort, patients that experienced acute renal failure were the very old and frail, with a higher proportion of patients aged ≥ 85 years (40% vs 21%) and were residents of aged-care facilities (46% vs 20%). Hence, despite this evaluation being performed in a patient cohort that is not representative of healthier OTC analgesic users, OTC doses of ibuprofen did not elevate the risk of acute kidney injury.

In summary, not only is the evidence that the use of ibuprofen 400 mg at maximal OTC doses is not associated with an increased risk of gastrointestinal bleeding or acute kidney injury, any perceived risk is mitigated by warning statements on the product label that advise against the use of this medication for patients at risk (i.e. not be used by people with stomach ulcers or other stomach disorders, kidney, liver or heart problems). These warning

statements are equivalent to those that listed on regular ibuprofen (200 mg) which has been safely used as a General Sales medicine at the same maximum daily dose for more than a decade in New Zealand.

C. Safety if a consumer accidently takes twice the dose.

The MCC were concerned that "the consumer benefit is minimal when compared to the **significant potential for harm** [our emphasis] if a consumer accidentally takes twice the recommended dose of ibuprofen."

We respectfully disagree with the MCC's assessment of the risk of a double dose posing "significant potential for harm" on multiple grounds and believe that the MCC has made an error in its assessment.

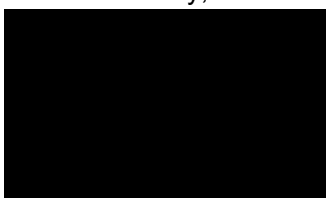
1. Accidentally taking a double dose, 800 mg three times a day, represents an approved therapeutic dose of ibuprofen, that is commonly used in the prescription setting. Hence, it does not represent an unsafe dose, just a higher dose whose long-term use should be under the supervision of a doctor.
2. If a patient were to accidently take a double dose, the Pharmacy Only pack size of 12 tablets means that this accidental use would be limited to TWO days. This two day exposure to an approved and well established dose, does not represent a significant potential for harm.
3. Ibuprofen has a wide therapeutic index and a good safety profile in overdose.(11) In order for ibuprofen to have a harmful effect in overdose one would need to take 100-400 mg/kg for mild effects, and greater than 400 mg/kg for moderate to severe effects.(12) Accidently taking one day's double dose at one time, i.e. 2400 mg would only achieve the problematic 400 mg/kg dose in an infant weighing 6 kg or less. Similarly, if the entire 12 tablets were taken as a single dose the 400 mg/kg dose would only be achieved by a child weighing 12 kg or less. Hence, there is a very large safety margin with ibuprofen 400 mg in packs that contain 12 dose units.
4. Aspirin is available in New Zealand as a General Sales medicine in both a regular strength (300 mg) and extra strength (500 mg) tablets. It is well established that ibuprofen has a superior safety profile to aspirin.(8, 13) Therefore, if the MCC in its previous deliberations has been satisfied that the potential for harm associated with accidently taking a double dose of extra strength aspirin is low and suitable for General Sales classification, then double strength ibuprofen (400 mg) with its wider safety margin relative to aspirin must be considered to have a lower risk of harm in the same scenario and be suitable for Pharmacy Only classification.
5. The potential for dosage confusion is mitigated by multiple design elements on the product packaging, including:
    - The brand name, Nurofen® 400 DOUBLE STRENGTH which clearly calls out that this product has twice the amount of the active ingredient versus regular Nurofen®
    - The 400 mg strength is listed prominently next to ibuprofen directly under the brand name
    - The callout of "1 tablet dose" on front of pack
    - A single tablet is pictured on the Nurofen® 400 DOUBLE STRENGTH pack vs two tablets pictured on the regular Nurofen® formulations
    - The clear dosage instructions on back of pack.
6. Further evidence on the safety of ibuprofen in this scenario can be found in our original submission, Part B, Section 7.

In summary, Reckitt Benckiser believes that the evidence tabled above demonstrates that there are no significant safety concerns regarding the use of ibuprofen 400 mg in either the general population, the elderly or if a double dose is incorrectly taken. There are meaningful benefits to New Zealand consumers having increased access to ibuprofen 400 mg. These include the convenience and desire to take fewer tablets especially amongst people who have difficulty swallowing solid dosage forms and those seeking relief of strong pain. As demonstrated in our application, pharmacists rarely discuss swallowing issues with their customers, hence the current classification does not enable the consumer health benefits of ibuprofen 400 mg to be adequately realised.

We believe that expanding access to a small pack size of ibuprofen 400 mg, limited to 12 dose units or 4 days' supply, represents a balanced approach. It increases access, in a controlled manner, enabling New Zealand consumers to gain more experience with this dosage format and has a positive benefit/risk profile.

Reckitt Benckiser requests that the MCC reconsider its decision and reclassifies ibuprofen 400 mg, in packs containing not more than 12 dose units when sold in the manufacturer's original pack labelled for use by adults and children over 12 years of age, from a Restricted Medicine to a Pharmacy Only Medicine.

Yours sincerely,



Director Regulatory and Medical Affairs ANZ
Reckitt Benckiser (Australia) Pty Limited

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