Pharmaceutical Solutions
Clinical Research & Regulatory Specialists

09 September 2014

Andrea Kerridge
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Medsafe
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By email: committees@moh.govt.nz

Dear Andrea,

Agenda for the 52nd Meeting of the Medicines Classification Committee

Thank you for the opportunity to submit comments on the Agenda for the 52nd meeting of the Medicines Classification Committee (MCC).

Retail NZ (formerly the New Zealand Retailers' Association) wishes to provide comment on agenda item 6.3 – Paracetamol in combination with Phenylephrine.

With around 5,000 members, Retail NZ is the leading retail trade association with a membership that represents over 65% of retail industry turnover. Members represent a wide variety of retailers, from Kaitaia to Stewart Island, from small independent operators to large national and international chain stores. Retail NZ assists members by providing retail advice, member benefit savings, industry information, education and is the main retail industry group.

Item 6.3 – Paracetamol in combination with Phenylephrine

Retail NZ strongly opposes the submission for reclassification of paracetamol in combination with phenylephrine in packs containing:

- any number of solid dose units containing paracetamol 500 mg in combination with more than 2.5 mg phenylephrine per dose unit from general sale or pharmacy-only medicine to restricted medicine
- any number of sachets of powder containing 1000 mg paracetamol in combination with more than 5 mg phenylephrine per sachet from general sale or pharmacy-only medicine to restricted medicine

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Our general comments:

- The clinical evidence around this claim is currently limited. The findings cited were not fully published or available to the public to allow for the methodology and results to be peer reviewed, and it is also inconclusive whether this finding will have any clinical impact. Therefore more studies should be conducted before any conclusion can be made.

- Since the worldwide introduction of paracetamol and phenyleprine combinations in 2006, there have been no major side effects reported or significant safety concerns. A recent search of the Joint Adverse Event Notification System on products containing paracetamol- phenylephrine hydrochloride in New Zealand and Australia indicated 5 reported cases[1] between 01 January 2000 to 21 May 2014. These events include aggravated condition (2), ineffective drug (1), dyspnoea (1), erythema (1), swollen face (1), anaphylactic reaction (1) and asthma (1).

  There is no indication of any increase in adverse effects with the use of paracetamol and phenyleprine combination products, at the marketed strengths of paracetamol 500mg/phenylephrine hydrochloride 5mg and paracetamol 1000mg/phenylephrine hydrochloride 10mg, since its introduction.

  Due to the General Sale status and wide-use in United Kingdom, we have search on the Medicines and Healthcare Products Regulatory Agency (MHRA)[2] and the Drug Analysis Prints (DAP) for phenylephrine adverse effects. No drug safety updates or other reports regarding safety concerns were found, other than the use of over-the-counter cough and cold medicines in children.

- Warnings are available on packaging advising consumers with high blood pressure and heart problems to seek medical advice from their health care professional before use. Therefore the risk of patients from higher risk groups taking the medication is minimised.

- The pack size available for General Sale is limited to short-term treatment and warning is available on the packaging advising consumers to seek medical advice from their health care professional if symptoms persist. Therefore the risk of unsupervised long-term use is minimised.

- Access to medicine will be severely limited if the combination products are reclassified to Restricted Medicine. The opening hours[3] of pharmacies are limited and so are their reach in rural areas. Until further evidence is available, the availability of these combination products should not be restricted as it will only increase the burden on healthcare costs and limit consumers from obtaining medications quickly and delay access to symptomatic benefit.

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We hope that our comments on this agenda item are helpful and will be taken into consideration during the upcoming 52nd meeting.

Yours sincerely,

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[1] Joint Adverse Event Notification System, Medicine Summary and List of Reports for paracetamol and phenylephrine (accessed on 04 September 2014) http://www.anztpa.org/aen/jaen-entry.aspx

[2] Medicines and Healthcare Products Regulatory Agency (accessed on 04 September 2014) http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/index.htm

[3] Scoop News, New Zealand Retailers Association, Chemist shops have the shortest opening hours, 04 March 2003

Australian Government
Department of Health
Therapeutic Goods Administration

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

Joint Adverse Event Notification System Medicine summary

Both Australian and New Zealand data

You searched for the following **5 medicines** between **01/01/2000 – 21/05/2014**:

- Codral Relief Max Cold & Flu + Decongestant (Phenylephrine Hydrochloride-Paracetamol)
- Not specified (Phenylephrine Hydrochloride-Paracetamol)
- Panadol Sinus PE Night & Day (Phenylephrine Hydrochloride-Paracetamol)
- Robitussin Head, Cold & Sinus (Phenylephrine Hydrochloride-Paracetamol)
- Sinutab PE Sinus & Pain Relief (Phenylephrine Hydrochloride-Paracetamol)

Important information on the Joint Adverse Event Notifications System – medicines

The TGA and Medsafe use adverse event reports to identify when a safety issue may be present. An adverse event report does not mean that the medicine is the cause of the adverse event. If you are experiencing an adverse event, or think you may be experiencing one, please seek advice from a health professional as soon as possible. The TGA and Medsafe strongly advise people taking prescription medicines not to change their medication regime without prior consultation with a health professional.

About the Joint Adverse Event Notification System – medicines

- JAENS - medicines contains information from reports of adverse events that the TGA and Medsafe have received in relation to medicines including vaccines used in Australia and New Zealand.
- JAENS - medicines does not contain all known safety information about a particular medicine. Please do not make an assessment about the safety of a medicine based on the information in the JAENS - medicines.

The medicine safety monitoring program

More information about the JAENS - medicines, the TGA medicines safety monitoring program and the Medsafe medicines safety monitoring program is available at:

- About the JAENS - medicines <http://www.anztpa.org/projects/jaens-limitations.htm>
- TGA medicines safety <http://www.tga.gov.au/safety/information-medicines.htm>
- Medsafe medicines safety <http://www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medicines-Safety-and-Pharmacovigilance.asp>

You are encouraged to report an adverse event suspected of being related to a medicine used in Australia or New Zealand. In Australia, information on how to report is located on the TGA website < http://www.tga.gov.au/safety/problem.htm>. In New Zealand, information on how to report is located on the CARM website <https://nzphvc-01.otago.ac.nz/carm-adr/>

Other useful sources of information on Australian medicines

More information about a medicine is available from the Product Information (PI) < http://www.tga.gov.au/hp/information-medicines-pi.htm> and Consumer Medicine Information (CMI) < http://www.tga.gov.au/consumers/information-medicines-cmi.htm> leaflet or the labelling of the medicine. Australian Public Assessment Report for Prescription Medicines (AusPARs) <http://www.tga.gov.au/industry/pm-auspar.htm> for some prescription medicines, are also available from the TGA website. <http://www.tga.gov.au>
Information on medicines used in Australia is also available from NPS MedicineWise <http://www.nps.org.au/>.

Other useful sources of information on New Zealand medicines

More information about a medicine is available from the Data Sheet < http://www.medsafe.govt.nz/profs/Datasheet/dsform.asp> and Consumer Medicine Information (CMI) < http://www.medsafe.govt.nz/Consumers/cmi/CMIForm.asp> or the labelling of the medicine.

About the release of this information

While reasonable care is taken to ensure that the information is an accurate record of the adverse events reported to the TGA and Medsafe, the TGA and Medsafe do not guarantee or warrant the accuracy, reliability, completeness or

currency of the information or its usefulness in achieving any purpose.
To the fullest extent permitted by law, including but not limited to section 61A of the Therapeutic Goods Act 1989, the TGA and Medsafe will not be liable for any loss, damage, cost or expense incurred in or arising by reason of any person relying on this information.

Results

Number of reports (cases): 5

(Multiple adverse events have been reported for some patients)

Number of cases with a single suspected medicine: 5

(The TGA or CARM think there is a possibility that the medicine caused the adverse event)

Number of cases where death was a reported outcome: 0

(These reports of death may or may not have been a result of taking a medicine)

MedDRA system organ class[i]	MedDRA reaction term[ii]	Number of cases[iii]	Number of cases with a single suspected medicine[iv]	Number of cases where death was a reported outcome[v]
General disorders and administration site conditions	Condition aggravated	2	2	0
General disorders and administration site conditions	Drug ineffective	1	1	0
Respiratory, thoracic and mediastinal disorders	Dyspnoea	1	1	0
Skin and subcutaneous tissue disorders	Erythema	1	1	0
Skin and subcutaneous tissue disorders	Swelling face	1	1	0
Immune system disorders	Anaphylactic reaction	1	1	0
Respiratory, thoracic and mediastinal disorders	Asthma	1	1	0

Footnotes

[i] A description of what, in general terms, was affected by the adverse event, as described by the Medical Dictionary for Regulatory Activities MedDRA (for example 'cardiac disorders')

[ii] A description of the adverse event as defined by MedDRA; these adverse events are grouped by system organ class. You can use the MedlinePlus medical dictionary <http://www.nlm.nih.gov/medlineplus/mplusdictionary.html> to look up terms.

[iii] The number of cases for which each type of adverse event was reported

[iv] Results show where a medicine is the only medicine suspected to be related to the adverse event

[v] These reports of death may or may not have been the result of taking a medicine

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Department of Health
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Joint Adverse Event Notification System
List of reports

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Case number[i]	Report entry date[ii]	Age (yrs)[iii]	Gender[iv]	Medicines reported as being taken[v]	MedDRA reaction terms[vi]
AU00245349	13/10/2008	-	-	• Sinutab PE Sinus & Pain Relief (Phenylephrine Hydrochloride-Paracetamol) - Suspected	• Asthma
AU00274520	21/09/2010	-	F	• Panadol Sinus PE Night & Day (Phenylephrine Hydrochloride-Paracetamol) - Suspected	• Dyspnoea
NZ00098127	01/10/2011	22	M	• Not specified (Phenylephrine Hydrochloride-Paracetamol) - Suspected	• Anaphylactic reaction
AU00302768	27/06/2012	-	M	• Robitussin Head, Cold & Sinus (Phenylephrine Hydrochloride-Paracetamol) - Suspected	• Condition aggravated • Drug ineffective
AU00306409	05/09/2012	-	F	• Codral Relief Max Cold & Flu + Decongestant (Phenylephrine Hydrochloride-Paracetamol) - Suspected	• Condition aggravated • Erythema • Swelling face

Footnotes

[i] A unique alphanumeric code that provides a reference to a particular case. Australian reports have the prefix AU and New Zealand reports have the prefix NZ.

[ii] The date that information from the original report was entered into the system

[iii] Age of patient at time of adverse event, '-' if unknown

[iv] Gender of patient, '-' if unknown

[v] Medicines reported to have been taken by the patient

[vi] A description of the adverse event as defined by the Medical Dictionary for Regulatory Activities (MedDRA). You can use the MedlinePlus medical dictionary <http://www.nlm.nih.gov/medlineplus/mplusdictionary.html> to look up terms.

Chemist shops have the shortest opening hours

Tuesday, 4 March 2003, 3:32 pm
Press Release: NZ Retailers Assoc.

Chemist shops have the shortest opening hours

The current argument for deregulation of pharmacy ownership is about improving the benefits to consumers – which can only be achieved by removing what will be the last retail monopoly in New Zealand, said New Zealand Retailers today.

Chemist shops have some of the shortest operating hours in retail according to information presented to the Health Select Committee by the Association yesterday.

“The survey of chemist shop hours shows why the Ministry of Health and the Government are concerned about people’s access to prescription and pharmacy-only medicines,” said New Zealand Retailers’ Chief Executive John Albertson.

“When you have a monopoly you expect to see short opening hours and high prices and that’s exactly what you get with the current situation, where only pharmacists can own chemist shops.

“When we looked at supermarket opening hours and compared these with chemist shops in the same area we found that supermarkets were open for 101.5 hours per week on average and chemists shops were open 55.1 hour per week on average.

“In some areas the differences were even more marked.

“Chemists have been using fear tactics saying that if their monopoly is ended communities would lose services, but this survey shows that the most likely impact is that access would be improved if supermarkets where able to operate a pharmacy within their supermarket, employing registered pharmacists to dispense prescriptions and provide advice.”

“Under the current regime consumers’ choice is being limited,” said Mr Albertson.

About the Health Professionals’ Competency Assurance Bill At present only a pharmacist can own a chemist shop, with a minimum 75% ownership requirement. The Health Professionals’ Competency Assurance Bill before the House would retain this monopoly (with a minimum 51% ownership requirement), though it would end the only other retail ownership monopoly, which is currently held by optometrists. Optometrists support the ending of their monopoly, while the Pharmacy Guild, which represents chemist shop owners, is fighting to retain chemists’ monopoly.

Ending the monopoly would allow someone other than a pharmacist to own a chemist shop, but would not change who could dispense drugs (that could only be done by a registered pharmacist). If a pharmacy was owned and operated by a supermarket or department store it would be a ‘store within a store’ employing qualified pharmacists. Standards would be assured through the training and registration requirements applying to pharmacists (which are similar to those of other health professionals), and through the requirement that all pharmacies be registered.

Supermarkets vs Chemists

A Review of Opening Hours

Prepared By: John Albertson NZ Retailers Association June 2002

Background

When the new parliament is elected in late July one of the early tasks for the new (or re-appointed) Minister of Health will be to introduce the bill that incoporates the changes to the legislation pertaining to the ownership of chemist shops.

The current minister had had to back off her original position of total deregulation of chemist shop ownership as she lost the support of the National Party and just didn't have the numbers.

The new proportions in Parliament may open the door for a return to the original proposition for full deregulation.

One of the questions that has been asked repeatedly over the last 15 years or so of debate on this issue relates to accessability. If supermarkets, for example, could have in store pharmacies then this will spell the end of the chemist shop as we know it and the consumer will lose out. This has been the catch-cry of those apposed to deregulation.

Objectives of the report

How real is the issue of accessability? If supermarkets and general merchandise department stores could have in store pharmacies would this add to or detract from consumer accessability.

In this report we have analysed the shop opening hours of supermarkets and chemists to test out the various arguments.

Source material

The major supermarket chains (Progressive Enterprises, Woolworths, and the three Foodstuffs companies) were asked to submit their opening hours for each branch/store and the opening hours for the nearest chemist shop. The analysis of this data is attached in detail.

In some instances two supermarkets identified the same chemist shop as the one nearest to them. In a few of these situations the opening hours of the chemist from the two sources differed. Where this occurred the longer opening hours were included in the analysis. That is, the best picture has been painted for the chemists.

The analysis covers:

Number of supermarkets 315

Number of Chemists 336

I would like to thank all of the store managers and owners for their help in gathering the data.

Note: (1) Chemists marked * were nominated by more than one supermarket as Being "the local competition."

The analysis doesn't purport to be an analysis of all chemist shops. It only includes those that are in the proximity of the supermarket.

The analysis covers the supermarket from the 3 major operators only. The 315 store analysed account for

just on 80% of all supermarkets in numeric terms. On a turnover business the % would be considerably higher.

(4) The 342 chemist shops included in the analysis account for about 1/3 of all chemist shops.

Executive summary

As one would expect supermarkets in NZ offer the consumer far greater shopping hours (both in terms of hours per day and number of days) than chemist shops.

Set out below are a number of averages drawn from the accompanying analysis:

Region	Supermarkets			Chemists		
	Number	Average Days Open	Average Hours/ week	Number	Average days open	Average Hours/Week
(a) Northland						
Whangarei	6	7	95.3	6	6.2	53.9
Other Northland Towns *	8	7	88.6	10	5.9	49.4

(* includes Kaikohe, Kerikeri, Warkworth, Orewa, Paihia, Kaitaia)

(b) Auckland						
North Shore	20	7	111.6	21	6.7	61.2
Central/West	41	7	113.3	47	6.5	59.7
South	18	7	103.6	22	6.4	57.0
Total Auckland	79	7	110.6	90	6.5	59.4
(c) Waikato/Bay of Plenty/Poverty Bay						
Tauranga	8	7	94.1	9	6.2	66.6 *
Hamilton	12	7	93.2	14	6.2	56.0
Rotorua	4	7	99.0	4	6.0	51.3
Gisborne	2	7	91.8	2	6.5	48.3
Other Waikato/BOP/PB *	32	7	90.3	35	6.2	49.4

(*Includes Taupo, Otorahanga, Te Awamutu, Ngarawahia, Cambridge, Morrinsville, Matamata, Te Kuiti, Taumarunui, Tokoroa, Putaruru, Paeroa, Papamoa, Katikati, Te Aroha, Te Puke, Waihi, Whakatane, Kawerau, Huntly, Turangi, Thames)

Lower North Island	Supermarkets			Chemists		
	Number	Average days Open	Average Hours/Week	Number	Average Days Open	Average Hours/Week
Palmerston North	6	7	122.5	6	6.3	59.2
Hawkes Bay (Napier/Hastings)	11	7	107.9	9	6.0	52.3
New Plymouth	6	7	119.0	5	6.4	55.7
Wellington/Hutt/ Porirua	31	7	117.0	31	6.4	56.8
Wanganui	4	7	105.0	4	5.8	48.9
Levin	3	7	93.3	2	6.5	55.5
Masterton	4	7	90.1	3	6.7	73.3
Other Lower North Island *	23	7	97.5	19	6.2	49.3

(* Inclues Waikanae, Otaki, Paraparaumu, Fielding, Marton, Hawera, Stratford, Waitara, Ohakune, Wairoa, Waipukurau, Dannevirke, Pahiatua, Carterton)

South Island						
Christchurch	25	7	98.1	27	6.3	56.1
Dunedin	11	7	96.9	11	6.2	53.0

Timaru 4 7 93.9 3 5.7 48.8
Invercargill 7 7 91.7 5 6.2 62.7
Nelson/Stoke/Richmond 6 7 89.5 6 5.8 47.9
Other South Island * 23 7 85.2 35 6.1 50.7
(* Includes Rolleston, Oamaru, Waimate, Gore, Winton, Queenstown, Ashburton, Temuka, Alexandra, Balclutha, Wanaka, Cromwell, Greymouth, Westport, Rangiora, Blenheim, Hokitika.)

Note: * Tauranga – 'Chemists' includes a 24 hour/day emergency chemist which has a material impact on the averages which are based on 9 stores only . Without the inclusion of this outlet the average hours for chemists in Tauranga comes down to 53.9 hours (compared with 66.6 hours shown)

The summary for each area above highlights the vast improvement in accessability that would be provided to consumers by the supermarket sector.

All of the 315 supermarkets operate 7 days/week.

The average hours nationally for the supermarket sector is 101.5 hours/week compared with the closet chemists to each at an overall average of 55.1 hours/week.

That is, the average supermarket offers the consumer nearly double the hours that the closest chemist offers. Thus, for those consumers with access to a supermarket (and virtually all New Zealand homes visit a supermarket at least once week the accessibility to pharmacy products would be vastly enhanced by chemist shop facilities within a supermarket.

Anybody else in the market place (and if one considers the town sizes covered there won't be many places or people outside of the analysis) will be no worse off than they are today.

The defensive argument by the pharmacists is not about accessibility it is about profitibility. Based on the latest Statistics NZ Annual Enterprise Survey the pharmacy sector has the best net profit rate in retail:-

Net Profit % to Sales Chemists 11.1% Supermarkets 2.3% All Retail 4.4%

This is all about patch protection but accessability is not a valid argument to protect his particular patch.

Opening Hours Supermarkets vs chemists

Supermarkets Chemists

Northland Days Hours Days Hours
(1) Whangarei
Onerahi New World 7 84 Onerahi Shopping Centre Pharmacy 6 45.5
Otaika New World 7 89 Otaika Shopping Block Pharmacy 6 48.5
Regent New World 7 98 Kensington Pharmacy (Urgent) 7 86
Tikipunga Countdown 7 91 Tikipunga Pharmacy 6 51
Whangarei Big Fresh * 7 119 Orrs Unichem Pharmacy ** 6 47
Whangarei *Pack N Save 7 91 Sargents Pharmacy 6 45.5

Whangarei Average 7 95.3 6.2 53.9

(2) Kaikohe
Kaikohe New World 7 80 Broadway House Pharmacy 7 56

(3) Kerikeri
Kerikeri New World * 7 83 McGadziens Amcal 6 49.5
Price Chopper, Kerikeri * 7 98 Kerikeri Unichem ** 6 48.5
Average 7 90.5 6 49

(4) Warkworth
Warkworth New World 7 84 Franklin Pharmacy 6 55
Parker & Lee Unichem 6 49

(5) Orewa
Orewa New World * 7 105 Hickey's Pharmacy 6 55
Orewa Twice Guys * 7 84 Orewa Care Chemist ** 7 60.5
Average 7 94.5 6.5 57.8

(6) Paihia
Paihia Woolworths 7 105 Paihia Pharmacy 3 24

(7) Kaitaia
Kaitaia Pak N Save 7 69.5 Shakeltons Pharmacy 7 53.5
Far North Pharmacy 5 42.5
Average 6 48
3) Auckland – North Shore

Supermarkets Chemists

Days Hours Days Hours

Pak n Save Albany 7 87.5 Albany Care Chemist 7 73
3 Guys – Flatbush 7 86 Dawson Rd Pharmacy 7 77.5
Woolworths – Helensville 7 105 Unichem Helensville 6 49.5
Woolworths – Dargaville 7 112 Unichem Kaipara 7 58
Woolworths – Kensington 7 112 Kensington Pharmacy 7 86
Woolworths – Mairangi Bay 7 118 Unichem Mairangi Bay 6 54.5
Woolworths – Milford 7 118 Centre Pharmacy – Milford Mall 7 60.5
Woolworths – Northcote 7 118 Unichem (Harris & Cameron) 6 50
Woolworths – Whangaparoa 7 119 -
Woolworths – Browns Bay 7 118 Commodore Pharmacy 6 54
New World – Browns Bay 7 84 Unichem Browns Bay 7 57.5
New World – Milford 7 99 Unichem Milford 6 52.5
New World – Devonport 7 91 Wigmores Pharmacy 7 61.5
Uncle Toms Unichem 7 67
New World – Takapuna 7 84 Don McKay Pharmacy 6 46
Unichem, Shore City 7 58.5
Countdown – Birkenhead 7 119 Amcal Birkenhead 7 69.5
Foodtown – Birkenhead 7 87.5 Birkdale Pharmacy 6 45.5
Foodtown –Browns Bay 7 119 Browns Bay Med Centre Pharmacy 7 58.5
Foodtown – Glenfield 7 119 Life Pharmacy 7 63
Woolworths – Glenfield 7 168 Life Pharmacy – Glenfield 7 73.5
Foodtown – Takapuna 7 168 Amcal 7 69

Auckland – Central/West

Supermarkets Chemists

Days Hours Days Hours

3 Guys Point Chevelier 7 80.5 Point Chev Dispensary 6 51.5
Highland Park Count Down 7 168 Highland Park Pharmacy 6 57
Royal Oak Pak n Save 7 98 Unichem Royal Oak 7 56.5

Walls & Roache 7 76.5
Mt Albert Pak n Save 7 98 Grant Gillard Pharmacy 6 46.5
Botany Pak n Save 7 87.5 Life Pharmacy 7 58
Botany Pharmacy 7 61.5
Glen Innes Pak n Save 7 91 Nicola Johns Pharmacy 6 51
Cox 7 Day Pharmacy 7 71
Henderson Pak n Save 7 91 Devich Pharmacy 6 50.5
Westgate Pharmacy 7 75.5
Lynfield Countdown 7 168 Lynfield Pharmacy 6 46.5
Henderson Big Fresh 7 91 Amcal West City 7 56
Grey Lynn Woolworths 7 168 Unichem Grey Lynn 7 78
Lynnmall Woolworths 7 168 Unichem – The Pharmacy Shop 7 66.5
Meadowlands Woolworths 7 168 Meadowlands Pharmacy 7 61
Newmarket Woolworths 7 119 Life Pharmacy – Newmarket 7 61.5
Massey Woolworths 7 91 Royal Heights Pharmacy 6 49
Waiheke Island Woolworths 7 98 Ostend Village Pharmacy 5 41.25
Mt Wellington Big Fresh 7 168 Unichem Neils Pharmacy 6 54.75
Hall Ave Price Chopper 7 91 Hall Ave Pharmacy 6 47

Auckland Central/West
Supermarkets Chemists

Auckland Central/West (continued) Days Hours Days Hours

Te Atatu Price Chopper 7 119 Sues Pharmacy 6 48.5
Titirangi New World 7 89 Titirangi Village Pharmacy 6 55
Green Bay New World 7 87.5 Green Bay Pharmacy 6 54
Blockhouse Bay Pharmacy 6 50.5
Victoria Park New World 7 112 -
Eastridge New World 7 98 Eastridge Pharmacy (Mall) 7 70
Remuera New World 7 91 Remuera Life Pharmacy 6 57.5
Remuera Pharmacy 6 50
Botany New World 7 98 Botany Pharmacy * 7 61.5
Panmura New World 7 84 Amcal Panmure 7 74
Westgate Countdown 7 168 Westgate Pharmacy 7 75.5
Blockhouse Bay Foodtown 7 87.5 Allan Spalter Pharmacy 6 51.5
Greenlane Foodtown 7 168 Greenlane Pharmacy 6 51.5
Grey Lynn Foodtown 7 168 West City Pharmacy 6 59
Henderson Foodtown 7 66.5 Unichem Life Pharmacy 7 65.5
Highland Park Foodtown 7 119 Highland Park Pharmacy 6 57
Howick Foodtown 7 91 Amcal Howick Mall Pharmacy 6 52
Kelston Foodtown 7 98 Kelston Pharmacy 7 62
Meadowbank Foodtown 7 119 Amcal Pharmacy 7 60.5
Mt Eden Foodtown 7 168 Amcal Eden Quarter 7 60.5
Pakuranga Foodtown 7 119 Life Pharmacy 7 61.5
St Lukes Foodtown 7 84 Unichem Life Pharmacy 7 66.5
Sunnynook Foodtown 7 87.5 Sunnynook Pharmacy 7 61.5
Te Atatu South Foodtown 7 87.5 All Seasons Pharmacy 7 54
Three Kings Foodtown 7 105 3 Kings Plaza Pharmacy 7 77.5
Lincoln Pak n Save 7 87.5 Lincoln Mall Pharmacy 6 54.5
White Cross Henderson A&E 7 98
Auckland (3)

Supermarkets Chemists

Days Hours Days Hours
Auckland – South
Clendon New World 7 91 Chemist 1 6 51.5
Chemist 2 6 50
Papatoetoe New World 7 91 Robin Garlich Pharmacy 6 49
Angus Graham Pharmacy 6 44
St George St Pharmacy 6 50
Southmall New World 7 98 Southmall Pharmacy 6 48
Papakura New world 7 84 Papakura Pharmacy 7 84
Waiuku New World 7 84 Grahams Pharmacy 7 52
Bakers Pharmacy 7 49.5
Pukekohe Woolworths 7 168 Liddels Pharmacy 6 48
Papakura Woolworths 7 98 Unichem Guys Pharmacy 6 54.5
Manurewa Woolworths 7 105 Unichem Manurewa 6 46
Manukau Pak n Save 7 87.5 Manukau City Centre x2 7 62
Pukekohe Pak n Save 7 87.5 Pukekohe x2 6 53.5
Mangere 3 Guys 7 91 Hunts Pharmacy 6 53
Papakura Countdown 7 168 Papakura Pharmacy 6 50.5
Airport Foodtown 7 168 Forbes Chemist 6 51.5
Mangere Foodtown 7 98 Amcal 6 55
Manukau Foodtown 7 98 Murray Dunn Pharmacy 7 63
Onehunga Foodtown 7 73.5 Unichem Onehunga 7 72
Papatoetoe Foodstown 7 87.5 Hunters Plaza Unichem 7 61
Takanini Foodtown 7 87.5 Takanini Care Chemist 7 107

Waikato/BOP/Poverty Bay
Supermarkets Chemists

Days Hours Days Hours
1) Tauranga
Bayfair Woolworths 7 112 Bayfair Pharmacy * 7 65
Tauranga Big Fresh 7 112 Gregs Pharmacy 5 45
Tauranga Pak n Save 7 87.5 Faulkaus Pharmacy 7 60.5
Brookfield New world 7 91 Brookfield Pharmacy 6 54.5
John Pharmacy (Urgent) 7 168
Mount New World 7 84 Central Parade Pharmacy 6 51.5
Unichem Bayfair * 7 65
Bayfair Countdown 7 91 Bayfair Pharmacy 7 65
Greerton Countdown 7 84 Raceway Chemist 6 48.5
Tauranga Foodtown 7 91 12th Ave Pharmacy 5 41.25

2) Hamilton
Bridge St Woolworths 7 112 Anglesea Clinic 7 108.5
Dinsdale Woolworths 7 112 Trevor Barret Pharmacy * 6 49
Hamilton Big Fresh 7 112 Neville, Kane Pharmacy 7 59.5
Mill St Pak n Save 7 85 Neville O'Kaine Pharmacy 7 59.5
Glenview New World 7 91 Unichem Urlich Ave 6 50.5
Dinsdale New World 7 81.5 Trevor Barrett Pharmacy * 6 49
Geoff Williamson Unichem 5 40
West Hamilton Pharmacy 6 43
Hillcrest New World 7 91 Robertsons Pharmacy 6 54.75
Hillcrest Pharmacy 6 45.5
Heaphy Tce New World 7 77 Fairfield Pharmacy 6 49
Chartwell Pharmacy * 7 65
Chartwell Foodtown 7 94.5 Life Pharmacy 7 59

Hamilton Central Foodtown 7 84 Central Hamilton Pharmacy 7 59.5
Nawton Foodtown 7 87.5 West Hamilton Pharmacy 6 51.5
Clarence Street Pak n Save 7 91 Anglesea Clinic 7 108.5

6) Rotorua
Rotorua Big Fresh * 7 119 Ludgates Pharmacy * 6 49
Rotorua Pak n Save * 7 88
Westend New World 7 91 Westend Pharmacy 5 45
Central Pharmacy 7 63

Waikato/BOP/Poverty Bay

Supermarkets Chemists

Rotorua (continued) Days Hours Days Hours

Rotorua Countdown 7 98 Amcal Pharmacy 6 48

4) Taupo
Taupo Pak n Save 7 86.5 Unichem, Heuheu St 7 56
Main St Pharmacy 7 80.5
Woolworths 7 168 Amcal Wedekinds Pharmacy 6 43

5) Otorohanga
Woolworths 7 105 Trevor Walter Amcal 6 43

6) Te Awamutu
Woolworths 7 105 Marshalls Pharmacy * 6 54
3 Guys 7 80

7) Ngaruawahia
New world 7 71.5 Robertsons Pharmacy 5 41.25
Sherson Pharmacy 5 40

8) Cambridge
New World 7 84 Munro Burgess Amcal * 6 52
Claytons Pharmacy 6 49
Countdown 7 84

9) Morrinsville
New World 7 80 Morrinsville Pharmacy 6 51.5
Countdown 7 86 Unichem Pharmacy * 6 51.5

Waikato/BOP Poverty Bay
Supermarkets Chemists

Days Hours Days Hours
10) Matamata
New World 7 84 Neil McSweeneys Amcal * 6 49.75
Countdown 7 84

11) Te Kuitu
New World 7 72 O'Fee & Bain Pharmacy 7 52

12) Taumarunui
New World 7 76 Clayton & Hayes Pharmacy 7 47.5

13) Tokoroa
New World 7 84 Centre Pharmacy 6 49
Amcal Spectrum * 6 55.5
'Chemist On Duty' 6 6
Countdown 7 84

14) Putaruru
Woolworths 7 105 Heslop Pharmacy 6 45.5

15) Paeroa
Woolworths 7 112 Barry's Pharmacy 7 47.5

16) Papamoa
Woolworths 7 112 Palm Beach Pharmacy 7 68.5

17) Katikati
Woolworths 7 112 Katikati Pharmacy 7 58.5

18) Te Aroha
Price Chopper 7 98 Unichem Logan Packers 7 49

Waikato/BOP Poverty Bay

Supermarkets Chemists

Days Hours Days Hours
19) Te Puke
Price Chopper 7 98 Castle Pharmacy * 6 49.5
New World 7 84 Blacketts pharmacy 6 47

20) Waihi
Price Chopper 7 98 Clarks Pharmacy * 6 46.5
New world 7 77 Barrows Unichem 6 51

21) Whakatane
Price Chopper 7 98 Kope Pharmacy * 6 48
New World 7 75.5 Whakatane Pharmacy 6 48
Unichem Central 6 54
Pak n Save 7 89 Adamsons Pharmacy 6 49

22) Kawerau
New World 7 80.5 Glen Grahams Pharmacy 6 43

23) Huntly
3 Guys 7 75.5 Barry Roberts Pharmacy 5 42.5

24) Gisborne
Woolworths 7 105 Bramwell Pharmacy 7 51
Pak n Save 7 78.5 Sun St Pharmacy 6 45.5

25) Turangi
New World 7 64.5 Amcal Turangi 7 50.5

26) Thames
Pak n Save 7 77.5 Unichem 6 47
Goldfields 7 62.5

Lower North Island

Supermarkets Chemists

Days Hours Days Hours
1) Palmerston North
Broadway Woolworths 7 126 Roses Pharmacy 6 51.5
Palmerston North Woolworths 7 168 Centre Drive Pharmacy 7 56
Palmerston North Pak n Save 7 112 The Chemist – PnS Car Park 7 91
Pioneer Highway New World 7 105 Pioneer Pharmacy 5 44.75
Melodys New World 7 105 Roses Pharmacy 6 51.5
Palmerston North Foodtown 7 119 Balfours Plaza Pharmacy 7 60.5

2) Hawkes Bay (Napier/Hastings)
Napier Big Fresh 7 126 Balmoral Pharmacy * 7 58.5
Write Price Hastings 7 126 Peter Church Pharmacy 6 49.5
Write Price Napier 7 105 Balmoral Pharmacy * 7 58.5
Napier Pak n Save 7 126 Tamatea Pharmacy 6 55
Onekawa New World 7 91 Andrew Spence Pharmacy 6 57.5
McDonalds Taradale New World 7 126 Glen Roberts Pharmacy 6 48.5
Flaxmere New World 7 84 Flaxmere Pharmacy 6 58
Havelock North New World 7 105 Gilmours Pharmacy 6 50
Hastings City New World 7 105 UFS Dispensary 5 43.5
Hastings Coundown 7 98 Richardsons Guardian Pharmacy 6 50.5
Napier Countdown 7 94.5 Balmoral Pharmacy 7 58.5

3) New Plymouth
Weston Woolworths 7 112 CAREfirst.co 6 64
New Plymouth Woolworths 7 168 Chemist #1 6 47
New Plymouth Pak n Save 7 112 Lienise Young Pharmacy 7 60
New Plymouth New World 7 119 Lander & Black Unichem 7 59.5
Merilands New World 7 84 Merilands Pharmacy 6 48

Countdown New Plymouth 7 119 Lander & Black Unichem 7(?) 59.5

Lower North Island
Supermarkets Chemists

Days Hours Days Hours
Wellington/LowerHutt/Porirua
Churchill Drive Woolworths 7 105 Churchill Mall Chemist 7 63
Karori Woolworths 7 105 David Thompson Pharmacy * 6 55.5
Kilbirnie Woolworths 7 168 Kilbirnie Pharmacy 6 49.5
Tawa Woolworths 7 105 Drummonds Pharmacy 6 47.5
Upper Hutt Woolworths 7 126 Hooper Pharmacy 7 54.5
Wainuiomata Woolworths 7 126 Wainuiomata Pharmacy 6 53
Johnsonville Woolworths 7 168 Unichem Johnsonville 7 74
Upper Hutt Pak n Save 7 154 Guppys Pharmacy 7 101.5
Petone Pak n Save 7 154 Collinges Pharmacy 6 45.5
Porirua Pak n Save 7 154 Fa'anois Pharmacy 6 54
Kilbirnie Pak n Save 7 154 Baycourt Pharmacy 6 51
Island Bay New World 7 98 Island Bay Pharmacy 6 44.5
Wellington City New World 7 119 UFS Courtenay Place 6 42
Whitby New World 7 84 Whitby Pharmacy 7 59
Silverstream New World 7 91 Silverstream Pharmacy 6 60
Metro New World (Willis St) 7 112 Unichem Willis St 6 54.5
Hutt City New World 7 105 Life Care Queensgate 7 59.5
Paramata New World 7 91 Mana Pharmacy 6 63.5
Newtown New World 7 112 Amcal Riddiford St 7 59
Porirua New World 7 112 North City Pharmacy 7 63
Thorndon New World 7 98 Thorndon Pharmacy 6 48
Stokes Valley New World 7 91 Ross Cook Amcal 6 52
Naenae New World 7 84 Hillary Court Pharmacy 5 45
Miramar New World 7 93.5 Miramar Healthcare Pharmacy 6 59.5
Karori New World 7 87.5 David Thompson Pharmacy * 6 55.5
Khandallah New World 7 86.5 Khandallah Pharmacy 6 49
Johnsonville Countdown 7 105 Life Pharmacy 7 66
Lower Hutt Countdown 7 168 Amcal Chemist 6 51
Porirua Countdown 7 168 Plaza Pharmacy 7 64
Upper Hutt Countdown 7 98 Queen St Pharmacy 7 55
Lower Hutt foodtown 7 105 Queensgate Unichem 7 61
Lower North Island

Supermarkets Chemists

Days Hours Days Hours
Waikanae
Woolworths 7 119 Guardian Waikanae Pharmacy 6 54

Otaki
Price Chopper 7 98 Otaki Pharmacy 6 51.5
New World 7 91 Hamish Barham Pharmacy 6 49

Paraparaumu
Woolworths 7 126 Unichem, Paraparaumu * 7 59.5
Pak n Save 7 126 Unichem, Paraparaumu * 7 59.5

Levin
Woolworths 7 112 Berrys Pharmacy * 6 52.5
Write Price 7 70 Robyn Yates Unichem 7 58.5
New World 7 98 Berrys Pharmacy * 6 52.5

Fielding
Price Chopper 7 105
Write Price 7 91 Tattons Pharmacy 6 49

Marton
Price Chopper 7 105 Marton Pharmacy 7 49
New World 7 98 Broadway Pharmacy 6 45.5

Wanganui
Woolworths 7 126 Guardian Pharmacy 6 49
Write Price 7 105 Wicksteed Pharmacy 6 56
Gonville New World 7 98 Gonville Pharmacy 6 45.5
Countdown 7 91 Hawkins Pharmacy 5 45

Lower North Island
Supermarkets Chemists

Days Hours Days Hours
Hawera
Price Chopper 7 126 Amcal Hawera * 6 47.25
Write Price 7 74.5 Central Pharmacy 6 48.5
New World 7 105 Amcal * 6 47.25

Stratford
New World 7 84 Moss Rocord & Smith 6 45.5

Waitara
New World 7 84 Peter Budden Unichem 6 50.5

Ohakune
New World 7 77 Ohakune Photo Pharmacy 5 40

Wairoa
Write Price 7 61.5 Wairoa Pharmacy 6 48.5

Waipawa
New World 7 98 Jollys Pharmacy 6 53.5

Waipukurau
Price Chopper 7 126 Amcal * 6 49.5
New world 7 98

Dannevirke
Price Chopper 7 67 Wilsons Pharmacy 7 55.5
New World 7 112 Wards Pharmacy 7 47.5

Pahiatua
New World 7 80.5 Pahiatua Amcal Pharmacy 6 48
Lower North Island

Supermarkets Chemists

Days Hours Days Hours
Masterton
Woolworths 7 105 Southend Pharmacy 7 84
Write Price 7 91 The Chemists * 7 77
Kuripuni New World 7 87.5 McArthurs Pharmacy 6 52
Church St New World 7 77 The Chemists * 7 84

Carterton
New World 7 91 Chisholms Pharmacy 6 45.5

South Island
Supermarkets Chemists

Days Hours Days Hours
Christchurch
Northland Pak n Save 7 98 Northland Mall Chemist 7 66
Riccarton Pak n Save 7 98 Riccarton Mall Chemist 7 67
Moorhouse Ave Pak n Save 7 98 Unichem Moorhouse Ave * 7 71
South City Pharmacy ** 7 61
Ferrymead Woolworths 7 105 Ferrymead Pharmacy 6 48
The Palms Woolworths 7 105 The Palms Unichem 7 60
Moorhouse Ave Big Fresh 7 126 Unichem on Moorhouse * 7 71
Bishopdale Price Chopper 7 91 Bishopdale Pharmacy 6 50.5
New Brighton Price Chopper 7 105 New Brighton Unichem 7 57
Northwood Woolworths 7 105 Redwood Chemist 5 47.5
Bush Inn Woolworths 7 105 Unichem Bush Inn 7 61
South City New World 7 83 South City Pharmacy ** 7 61
Fendalton New World 7 79 Fendalton Mall Pharmacy 6 48
Belfast New World 7 74 Belfast Chemist 6 64.5
Aranui New World 7 80 Aranui Pharmacy 6 50.5
Hornby New world 7 82 Hornby Unichem 7 61
Bishopdale New World 7 80.5 Unichem – Bishopdale 7 63
Amcal – Bishopdale 7 63
Halswell New World 7 81 Unichem – Haslwell 6 50.5
Church Corner Countdown 7 168 Bests Pharmacy 6 51.5
Eastgate Countdown 7 87 Eastgate Pharmacy 7 64
Kaiapoi Countdown 7 91 Kaiapoi Amcal 6 46.75
Northlands Countdown 7 168 Shields Pharmacy 7 74
South Island

Supermarkets Chemists

Christchurch (continued) Days Hours Days Hours

Kaiapoi New World 7 88 Unichem Kaiapoi 6 53
Kaiapoi Independent (1) 6 46.5
Kaiapoi Independent (2) 6 46.5
Redcliffs New World 7 91 Redcliffs Independent 5 50
St Martins New World 7 84 St Martins Independent 6 46.5
Stanmore New World 7 80 Stanmore Independent 5 46.25

Rolleston
New World 7 84 Pharmacy in shopping centre 6 49

Dunedin
Dunedin Pak n Save 7 98 Cameron Wilkie Pharmacy 6 48.5
Anderson Bay Woolworths 7 112 -
Dunedin Big Fresh 7 112 Unichem 7 55.5
Mosgiel Price Chopper 7 84 Taieri Amcal 6 51
Roslyn New World 7 71.5 Roslyn Pharmacy 6 48.5
Mosgiel New World 7 91 Amcal 6 51
Unichem 6 51
Gardens New World 7 78.5 Gardens Pharmacy 6 51.5
Port Chalmers New World 7 73 Vantage Pharmacy 6 45
Centre City New World 7 89 Unichem 7 73.5
Dunedin Central Countdown 7 168 Amcal Octagon 6 56
Mailer St Dunedin Countdown 7 89 Unichem Mornington 6 51.25

Timaru
Pak n Save 7 98 Amcal In the Mall 5 44
Woolworths 7 105 Highfield Pharmacy 6 48
Countdown 7 91 Faulks & Jordon Amcal 6 54.5
New World 7 81.5 Highfield Pharmacy 6 48

South Island
Supermarkets Chemists

Days Hours Days Hours
Oamaru
Woolworths 7 105 Oamaru Pharmacy 7 70
Northside new world 7 84 Northend 5 43
Oamaru New World 7 83 Amcal (Sun –with Drs) 6 45.5

Waimate
New World 7 85 Waimate Pharmacy 6 50.5

Gore
Woolworths 7 105 La Hoods The Chemist 6 48
New World 7 93.5 Unichem 7 47.5
Independent 6 50

Winton
New World 7 69 Winton Chemist 6 46

Queenstown
New World 7 84 Wakatipu Pharmacy 6 52

Invercargill
Pak n Save 7 98 Donna Kerr Pharmacy 7 76.5
Woolworths 7 98 UFS Pharmacy 6 52
Waikiwi Woolworths 7 98 Waikiwi Pharmacy 6 84
Elles Rd New World 7 82.5 Vantage Group 6 52.5
Newfield New World 7 76.5 No Pharmacy
Windsor New World 7 91 Wallaces Pharmacy 6 48.5
Countdown 7 98 Donna Kerr Pharmacy 7 76.5

Ashburton
Countdown 7 91 Wises Pharmacy 6 47.5
New World 7 87 UFS 6 45.5
Unichem 6 55.5

South Island

Supermarkets Chemists

Days Hours Days Hours
Temuka
New World 7 74 Unichem 6 45.5
Amcal 6 45.5

Alexandra
New World 7 81 Budges Pharmacy 6 50
Amcal 6 52.5

Balclutha
New World 7 70.5 Elwyn Bates 6 45.5
Grays Unichem 6 45.5

Wanaka
New World 7 84 Amcal 6 60
Unichem 7 66

Cromwell
New World 7 71.5 Cromwell Pharmacy 6 48.5

Greymouth
New World 7 75 Unichem 6 48
Guild 6 48
Guild 6 48
(plus limited Sunday service)

Westport

New World 7 78 Guild 7 48

Rangiora
New World 7 98 Guardian 6 50
Woolworths 7 105 Unichem 6 + 3 hour roster 52
South Island

Supermarkets Chemists

Days Hours Days Hours
Blenheim
Countdown 7 91 UFS * 6 52.5
New World 7 87.5 Unichem 6 48.5
Amcal 6 51.5
UFS * 6 52.5
Indep (1) 7 63
Indep (2) 6 54

Nelson/Stoke/Richmond
Richmond Pak n Save 7 98 Mall Pharmacy 5 50
Nelson New World 7 80.5 UFS Amcal 6 + 1 hour 50
Motueka New World 7 81 Guardian/Amcal/HealthCare 6 49
Stoke New World 7 81.5 Amcal 6 48
Nelson Big Fresh 7 105 Nelson City Pharmacy 5 40
Nelson Countdown 7 91 US Pharmacy 7 50.5

Hokitika
New World 7 74 Hokitika Pharmacy 6 48.5

Medicines Classification Committee Secretary
Medsafe, Wellington

via email: committees@moh.govt.nz

Dear Sir/Madam

MEDICINES CLASSIFICATION COMMITTEE
SUBMISSIONS TO THE 52nd MEETING AGENDA

Thank you for the opportunity to submit comments on the Agenda for the 52nd meeting of the Medicines Classification Committee.

I would like to comment on the reclassification of Omeprazole 10mg (losec) and the nasal spray Beclomethasone.

For each of these medicines I do not support the reclassification from Pharmacy Only medicine to General sale.

Reasons are as follows:

- The main reason for reclassification as presented by each of these submissions are for improved access and that supermarkets have significantly longer opening hours than pharmacy. This may be true, however there are more pharmacies nationwide than supermarkets, supporting more communities and providing consistent professional advice.

- Beclomethasone Nasal spray is used regularly for chronic and/or seasonal conditions. It can take days for this medicine to be effective for most patients. Therefore is irrelevant to argue that it requires longer hours of trade to provide better access to patients.

- Omeprazole is used for patients that experience regular indigestion/GORD and not commonly acute cases. Patients experiencing these symptoms require intervention to be assessed regularly as they can commonly be mistaken for very serious conditions (Myocardial Infarctions) or maybe caused by other underlying conditions (stomach ulcers, gastric bleeding, medicine interactions/side effects).

- Patients have no access to advice or care at a supermarket for a condition which is chronic and ongoing. Advice that can play a critical role in reducing incidence of the condition without the use of medicines or advice that works synergistically with the medicine for better health outcomes for consumers. E.g. identifying triggers, recommending use of sinus rinses to reduce need for nasal sprays, improving compliance and understanding of the medicine and how it works, identifying cases of incorrect use or other underlying conditions (rebound congestion).

- General sale medicines are extremely poorly regulated and supermarkets have an extremely poor reputation for maintaining any standards around safety of medicines. An example of this is that you can walk into any supermarket in the country and buy as many packs of paracetamol and cough and cold remedies (containing paracetamol) as you like. You can take this through a check out and 10/10 times no one will ever question you, check that you know how to use these medicines safely, or that it is even legal/ethical to sell multiple packets at once. Something needs to change…

- This and all reclassifications should not be taken on a medicine by medicine basis. The larger picture must be taken into account. As we have seen more and more medicines move to general sale. Pharmacy's ability to provide an acute triage service diminishes. This is an invaluable service which benefits all of New Zealand by providing sound advice, care and better health outcomes for minor to moderate ailments. This must not be overlooked or underestimated.

- These submissions regularly use statistics of low reports of misuse and side effects of a medicine in New Zealand and is an identification of how effective Doctors and Pharmacists are at providing medicines safely and appropriately. It is unrealistic to believe that these good statistics will continue for a medicine moved to General Sale.

- Supermarkets do not contribute to providing any safety statistics or monitor medicine misuse or side effects. They provide no easy access for these vital services on an in store basis. This leads to a significant reduction in reporting or identification of misuse.

Please contact me if you require further discussion.

Yours Sincerely,

Sam Appleford MPS

[redacted]

17th September 2014

The Secretary
Medicines Classification Committee
Medsafe
PO Box 5013
Wellington 6145

Dear Sir/Madam

Re: Application for Reclassification – Response
Agenda Item 6.3 for the 52nd Medicines Classification Committee Meeting 21st October 2014
Subject: Paracetamol in combination with Phenylephrine

[redacted] would like to thank the Medicines Classification Committee (MCC) for the opportunity to comment on the proposed rescheduling / reclassification application requests for Paracetamol and Phenylephrine (PE) combination products which result in products that are currently either in pharmacy only or general sale being up-scheduled to restricted medicine (pharmacist supervising the sale).

The proposed amendments to the current scheduling /classification of paracetamol and phenylephrine combination products are:

- **Any number of solid dose units containing paracetamol 500 mg in combination with more than 2.5 mg phenylephrine per dose unit from general sale or pharmacy only medicine to restricted medicine**
- **More than 20 solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit to remain a pharmacy only medicine**
- **20 or less solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit to remain a general sale**
- **Any number of sachets of powder containing 1000 mg paracetamol in combination with more than 5 mg phenylephrine per sachet from general sale or pharmacy only to restricted medicine**
- **More than 10 sachets of powder containing 1000 mg paracetamol in combination with 5 mg phenylephrine or less per sachet to remain pharmacy only**
- **10 or fewer sachets of powder containing 1000 mg paracetamol in combination with 5 mg of phenylephrine or less per sachet to remain in general sale.**

As [redacted] is a member of New Zealand Self Medication Industry Association (NZSMI), their comments and recommendations in relation to the proposed rescheduling of Paracetamol and PE combination products are fully endorsed by [redacted]. To be brief, the particular issues included in NZSMI's submission will not be repeated in the [redacted] submission.

Based on the information available in the public domain, [redacted] also believes that the application for rescheduling is based primarily on one piece of evidence i.e. AFT Pharmaceuticals (New Zealand) published study in the New England Journal of Medicine (NEJM)[1] as Letter to Editor entitled "Increased Phenylephrine Plasma Levels with Administration of Acetaminophen" with a claim "In a combination with Paracetamol, the level of PE is twice of what it should be".

AFT Pharmaceuticals' published letter in NEJM did not provide information on when and where the study was conducted; the precise study design; study analysis; whether or not subjects were taking other concomitant medications.

There are potential concerns regarding the potential biased interest of AFT Pharmaceuticals since they have submitted new applications for their new paracetamol 500mg and phenylephrine 2.5mg combination products to Medsafe and possibly to TGA.

The four new products currently being evaluated by Medsafe[2] are:

a. Maxiclear 2.5 PE Cold and Flu Relief Film Coated tablet, (General Sale)
b. Maxiclear 2.5 PE Cold and Flu Relief Film Coated tablet, (Pharmacy only medicine)
c. Maxiclear 2.5 PE Sinus and Pain Relief Film Coated tablet, (General Sale)
d. Maxiclear 2.5 PE Sinus and Pain Relief Film Coated tablet, (Pharmacy only medicine)

While the details of these products are not in the public domain in Australia, it is possible that the product registration applications may currently be under evaluation by the TGA as well.

New Zealand Media Release

Dr. Stewart Jessamine, Medsafe Group Manager commented on the AFT letter published in NEJM on 20th March 2014 which appeared in NZ Media press releases.[3,4]

In a statement, Dr Jessamine said *"phenylephrine has been used in alone and in combination for many years with no significant safety concerns."*

"A check of the New Zealand and Australian adverse events database does not show that wide use of phenylephrine over the past 14 years has been associated with any significant health problems."

"Finding a potential new interaction is interesting but the most essential thing is to determine whether that interaction is clinically significant, i.e. causes harm."

"At this point in time the Ministry of Health's assessment is that further immediate action on the safety of phenylephrine is not required."

Dr Jessamine said that Medsafe does not see any signs that this product is causing a significant number of side effects or patient harm, adding *"that there was no need for regulators such as Medsafe or the FDA or anyone else to take any action around phenylephrine."*

[redacted] Recommendations

[redacted] does not support the proposal to amend the rescheduling / reclassification of paracetamol plus phenylephrine combination products and believes that the current medicine classification remains appropriate for the following reasons:

- [redacted] believes that the AFT publication which was in a Letter to Editor format lacks important information such as study design, subject enrolment criteria, concomitant medications, sample analysis, data analysis, data repeatability for a meaningful assessment.

  In the application submitted by AFT to NZ Medicines Classification Committee for the 52nd meeting, it includes the *predicted* blood pressure increase for different products containing 5-10mg phenylephrine. It also states that the combination of paracetamol 1000mg plus PE 5mg would be *expected* to result in much higher potential rises in blood pressure for patients with co-existing disease states. There is no evidence that clinical safety or efficacy studies were undertaken.

  There is no evidence to suggest that AFT provided any supportive clinical safety and efficacy studies. Rather it appears AFT relied on the increase in AUC or Cmax to derive a blood pressure range for phenylephrine 10mg and paracetamol 1000mg.

- [redacted] conducted a literature search for all time until 31 July 2014 for drug-drug interaction between phenylephrine and paracetamol. No relevant articles have been retrieved.

- Post-marketing safety database review (with limited data) conducted by [redacted] indicated no evidence to support drug-drug interaction between phenylephrine and paracetamol.

- There is no documented safety issue with the existing products and their current scheduled status. We believe that "up-scheduling" should take place when a public health risk is demonstrated, and the scheduling proposal does not appear to meet this criterion. Recent examples of "up-scheduling"

include pseudoephedrine and codeine containing analgesics; the rationale for this rescheduling application appears to fall far short in comparison.

- The marketed paracetamol plus phenylephrine products carry labelling warnings as per the TGA Medicines Advisory Statements Specification (MASS) 2014, advising people with heart conditions and hypertension to consult their doctor or pharmacist before use.

  In addition to compliance with the Australian labelling regulation, all [redacted] products containing phenylephrine must include the safety warning statement *"Ask your doctor before use if you are presently taking or have recently taken blood pressure medicine or sympathomimetics"* in compliance with corporate requirement.

- Review of the safety data reported to Medsafe between January 2000 to 01 July 2014 showed no increase in cardiovascular system reported and concerns over CNS adverse events. As stated by Dr. Stewart Jessamine, Medsafe do not see any signs that this product is causing a significant number side effects or patient harm, adding *"that there was no need for regulators such as Medsafe or the FDA or anyone else to take any action around phenylephrine."*

- Concerns regarding the biased interest of AFT Pharmaceuticals since new applications have been submitted for their new paracetamol 500mg and phenylephrine 2.5mg combination products to Medsafe and possibly to TGA.

References

All references cited in this letter are listed on a separate page as Appendix 1.

Request for Confidentiality

I would be grateful if you would have my name and contact details as well as sponsor's name removed from any public version of the submission. I also would like my name to be removed from all documents prior to publication and not be included within the list of submissions on the Medsafe website.

Yours sincerely,

[redacted]

Appendix 1

References:

1. Atkinson H C, Stanescu I. Increased phenylephrine plasma levels with administration of acetaminophen. N Eng J Med 2014; 370 (12): 1171-2
2. The PRESS: Flu remedies pose dosage risk: http://www.stuff.co.nz/the-press/news/9848950/Flu-remedies-pose-dosage-risk
3. NZDoctor.co.nz: http: http://www.nzdoctor.co.nz/un-doctored/2014/march-2014/21/nzsmi-says-new-information-on-phenylephrine-interesting-but-of-limited-value.aspx
4. NDPSC Record of Reasons, 50th meeting, June 2007: http://www.tga.gov.au/pdf/archive/ndpsc-record-50.pdf
5. Medsafe Medicines Classification Committee Agenda for 52nd meeting: http://www.medsafe.govt.nz/profs/class/agen52_Paracetamol-and-Phenylephrine.pdf

THE PAEDIATRIC SOCIETY OF NEW ZEALAND

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Medicines Classification Committee
Medsafe
New Zealand Medicines and Medical Devices Safety Authority
PO Box 5013
Wellington 6145

18 September 2014

Dear Sir/Madam,

Submission to Medicines Classification Committee: 6.2 Omeprazole – proposed reclassification from pharmacy-only medicine to general sale medicine (Losec®, Bayer New Zealand Limited)

On behalf of the Pharmacists and Therapeutics Special Interest Group of the Paediatric Society of New Zealand, I would like to comment on the above submission.

This application seeks to make omeprazole more available with less input from a health professional. Some consumers of omeprazole are young children, who are therefore reliant on their caregivers to make diagnostic and treatment decisions.

The application is to have oral solid dosage forms of 10mg available as general sale and assumes that defining a list of indications and providing written usage instructions will result in safe use of omeprazole in all age groups. The risk is that making omeprazole 10mg capsules more easily available will increase exposure in a vulnerable population, which may increase the risk of misdiagnosis and incidence of adverse events. Monitoring of electrolytes should be part of any long term therapy with omeprazole and deranged electrolytes can have serious consequences in young children. We find omeprazole use can cause hyponatraemia and is often overused.

Omeprazole also can affect bone growth and development. Insoluble calcium requires an acidic environment for optimal absorption and PPI's remove that acidic environment. At CDHB we are limiting its use in our Children's Haematology and Oncology Centre and are asking prescribers to stop it when treatment with steroids have finished. We also have a problem with interactions with methotrexate and have one incident where a parent was going to give his own omeprazole to his child to settle his stomach whilst undergoing chemotherapy. We are concerned that if omeprazole was more easily available, interactions with other medicines would be missed.

We have outlined our concerns further by commenting on specific aspects of the application, and these comments are below.

'The proposed indication for Losec as a General Sales Medicine is:-
Short-term relief of gastric reflux-like symptoms that occur more than once a week, but not every day, in sufferers aged 18 years and over.' '.. This modified indication specifically restricts usage of the product to the appropriate patient population for over-the-counter omeprazole.'

Despite this comment on the packaging, there will be no restrictions on who checks this or how many packets are being purchased.

'Improved consumer choice of effective treatments *- the availability of omeprazole 10 mg as a General Sales Medicine will improve the choice of effective treatments available to consumers for self-selection at any outlet, particular for those that suffer symptoms more than one a week (but not every day).'*

The justification of increasing convenience for consumers is overstated, and should be seen in the context that it is being put forward by retailers whose true motivation is likely to be increased sales.

'Encourage Self-care *– reclassification of omeprazole 10 mg to General Sales Medicine would empower patients to independently address their health care needs for reflux/heartburn treatments.'*

Being able to purchase omeprazole in the supermarket will change the ease of access to omeprazole significantly for the paediatric population who are most vulnerable to inappropriate use.

'Consumer Convenience/Accessibility *– omeprazole at the lowest strength is suitable to be added to the range of products that can be self-selected at non-pharmacy type outlets, where more than 50% of remedies for reflux-like symptoms are currently purchased, offering consumers the opportunity to consider and compare at all points of purchase.'*

We are concerned that omeprazole 10mg capsules, if available via supermarkets, will be seen as a 'safe' option to purchase for children. Omeprazole has become a common choice for prescribers when choosing medicines for children with reflux. It is used in infants less than 1 year (the recommended age the medicine is registered for) on the advice of many clinical guidelines and paediatric texts. Community pharmacists are aware of the appropriate usage of omeprazole for this age group and are able to direct parents to seek further medical advice from their doctors if enquiring about purchasing omeprazole. Our concern is that parents may choose to self-medicate their children without seeking appropriate advice.

Comparison to H2 antagonists - *"…….the safety and effectiveness of omeprazole is well documented, and that short term use of omeprazole has no additional risk compared to H2 antagonists currently available as general sale medicines.'*

Parents are unlikely to purchase H_2 antagonists for children given the dose form. Children are prescribed ranitidine 150mg/10ml liquid which is not available via general sale. However, children are sometimes prescribed omeprazole 10mg capsules (the contents can be sprinkled onto soft food) once doses are at this level, so are more likely to purchase these if available via general sale.

Prolonged use

With up to 14 day's supply of omeprazole 10mg capsules in each packet, there is no guarantee that parents will seek medical advice before this. They may well purchase multiple boxes.

We have also attached links to two sources of information regarding the use of omeprazole in children. Please take note of the safety concerns with use of omeprazole as well as information regarding length of therapy. These are all things that will not be available when consumers purchase omeprazole via non-pharmacy outlets.

http://www.cryingoverspiltmilk.co.nz/wp-content/uploads/2013/02/OmeprazoleSuspensionLetter.pdf

http://www.saferx.co.nz/full/Omeprazole.pdf.

We are concerned that the information in the crying over spilt milk has some misinformation regarding splitting capsules for doses (inaccurate) and the risk of aspiration of the beads in very young children. Recently the Waitemata Neonatal Clinical Governance group has discussed this leaflet and contacted the author in regard to their concerns.

We oppose the classification of omeprazole to general sales due to safety concerns for the paediatric population.

We look forward to hearing from you soon with a response to our concerns.

Yours faithfully,

Louise McDermott
Chairperson,
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This letter is supported by members of the Pharmacist and Therapeutics Special Interest Group
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[redacted]

19 September 2014

The Secretary
Andrea Kerridge
Medicines Classification Committee
PO Box 5013
Wellington

Dear Sir,

Re: Agenda Item 6.3 for the 52nd Medicines Classification Committee Meeting 21st October 2014

[redacted] refers to the pre-October 2014 Medicines Classification Committee (MCC) Meeting. [redacted] would like comment on the proposed amendment to the re-classification of paracetamol in combination with Phenylephrine (PE).

The submission for reclassification is a company submission made by AFT Pharmaceuticals, and a similar proposal was also made to the *Advisory Committee of Medicines Scheduling* (ACMS) in Australia. [redacted] is taking the position that the information provided to the ACMS in Australia is consistent with the information provided to the MCC.

[redacted] strongly opposes this reclassification application, as we believe that the proposal is **not** in the best interest of public health and question the robustness of the pharmacological and medical rationale.

The proposed combination has already been demonstrated to appropriately meet the MCC requirements in previous decisions which have deemed the current classification of Pharmacy Only Medicines as well as General sale medicines as appropriate.

History of availability and scheduling of Phenylephrine in New Zealand

PE is a well-established active ingredient, and has been available as Pharmacy Only Medicine as well as General sale medicine for cough, cold/ flu and sinus relief preparations both as a single ingredient, as well as in combination products for many years.

The safety and efficacy of the proposed combination has already been assessed and approved by the Over-the-counter section at Medsafe and deemed appropriate at the current levels. The

[redacted]

indications associated with this combination include, but not limited to 'Cold and Flu relief,' that are common illnesses and easily recognised by consumers. They are self-limiting, with symptoms generally present for three to four days for colds and six to eight days for flu. They are illnesses which are suitable for self-diagnosis and self-treatment by the consumer, and they are not associated with protracted use. Therefore given the short-term usage of these products, we further question the need to lower the dose of phenylephrine.

The Proposed Changes

The application request consideration for the following proposal:

Proposal to include the following to a Restricted Medicine classification:

- Any number of solid dose units containing paracetamol 500 mg in combination with more than 2.5 mg phenylephrine per dose unit from general sale or pharmacy only medicine to restricted medicine
- Any number of sachets of powder containing 1000 mg paracetamol in combination with more than 5 mg phenylephrine per sachet from general sale or pharmacy only to restricted medicine.

Proposal to include in the following to a Pharmacy only Medicine classification:

- More than 20 solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit to remain a pharmacy only medicine
- More than 10 sachets of powder containing 1000 mg paracetamol in combination with 5 mg phenylephrine or less per sachet to remain pharmacy only

Proposal to include the following to a General sale classification:

- 20 or less solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit to remain a general sale
- 10 or fewer sachets of powder containing 1000 mg paracetamol in combination with 5 mg of phenylephrine or less per sachet to remain in general sale.

Risk & Benefits - Proposed Changes

In March 2014, a letter to the editor of the New England Journal of Medicine was published (1). The author, Hartley Atkinson, Founder and Managing Director of AFT Pharmaceuticals reported that administration of phenylephrine hydrochloride 10mg in combination with paracetamol 1000mg (two tablets) effectively doubles the bioavailability of PE and quadruples the maximum plasma concentration, allegedly giving a dose equivalent to 20mg of PE.

Unfortunately details of the studies (including the number of individuals involved in the study) conducted by AFT are not provided in the letter to the editor, making a critical analysis impossible, but it is our understanding, based on the information available in the Australian and New Zealand Clinical trials registry (www.anzctr.org.au) that the sample sizes are small ranging from n = 6 to n = 30 in a limited number of trials conducted at a single centre in Jordan.

In the public submission by AFT, there is a suggestion that the alleged doubling of bioavailability of PE could potentially increase the risk of cardiovascular side effects in susceptible individuals, such as those who are overweight/obese and/or the elderly and also those individuals who have undiagnosed or asymptomatic cardiovascular disease(s) that may be exacerbated by an increase of blood pressure.

The applicant speculates that there is a potential increased risk to consumers with cardiovascular conditions when taking a combination of paracetamol and PE at the current levels. However on [redacted] labelling consumers are clearly advises that if the consumer has heart conditions or hypertension to consult their doctor or pharmacist before using the medication.

The applicant contends that moving these products to Restricted Medicines classification will potentially reduce the risk to consumers who may have undiagnosed hypertension or underlying, asymptomatic cardiovascular disease.

Pharmacists are not in a position to diagnose individuals that have underlying asymptomatic cardiovascular conditions. The pharmacists questioning of consumers will be based on the warning statements that are present on the label and in the pharmacy texts such as the New Zealand Formulary or MIMS. Pre-diagnosis of cardiovascular disease or hypertension are not typically conducted by pharmacists prior to recommending particular products.

The following questions must be asked:

- **Does the co-administration of phenylephrine hydrochloride (HCL) and paracetamol at 10mg per dose result in clinically significant AEs suggestive of excess or unsafe phenylephrine dosing? and**
- **Does the co-administration of phenylephrine hydrochloride (HCL) and paracetamol actually result in a clinically more superior symptomatic relief of nasal congestion compared to phenylephrine hydrochloride taken on its own?**

Martindale thirty-fifth edition, recognises 20mg of PE as a safe oral dose, - *'Phenylephrine hydrochloride may be given by mouth in doses up to 20mg every four hours'.* In the submission to the MCC, the applicant's rationale for restricting supply of the paracetamol 500mg plus phenylephrine 5 mg (2 tablets) to Restricted medicine is based on **theoretical** safety concerns

regarding the use of the currently registered Pharmacy only and general sale products by consumers.

It is incorrectly stated that Paracetamol & PE combinations have only been available in New Zealand and the rest of the world since 2006 when PE was substituted for Pseudoephedrine. This combination has had extensive use within the community and in the United Kingdom since as early as 1997. In the 17 years of market experience globally, there has been no evidence or any safety issues relating to cardiovascular disease or hypertension that could justify the reclassification of these medicines to "Restricted Medicine".

There is also no evidence to our knowledge to suggest that consumers taking this combination at the currently approved levels are getting superior symptomatic relief from the PE than if they took a dose of single ingredient PE at the same level. Further, there is no evidence to suggest that the *"potentiation effects of paracetamol"* negatively impacts the safety profile of PE due to a dose response. [redacted] markets a very wide range of products indicated for cough/cold and flu containing this combination (approximately [redacted] units per annum across Australia and New Zealand) and company Adverse Events data over the last 5 years, does not indicate there are any Adverse Events relating to cardiovascular disease or hypertension in both markets.

In the absence of signals that suggest that the combination of paracetamol and PE represents a safety concern in the community, any theoretical or predicted issues should be addressed in an appropriately designed and powered clinical study with the appropriate endpoints.

The patients at risk, as highlighted in the Atkinson letter to the editor (1), already have warnings statements included on [redacted] labelling. What is not clear in the letter is whether the apparent increase in bioavailability of PE when combined with paracetamol results in an increased therapeutic benefit of the PE, which is a fundamental consideration before any reclassification decisions are made. If the therapeutic benefit of a lower dose of phenylephrine (5mg per dose) as proposed is less than what consumers are currently accustomed to, or not truly equivalent to 10mg of phenylephrine per dose as claimed, there may be a temptation for a consumer to ignore the dosage instructions and consume more than the recommended dose. The consequence of this scenario will be paracetamol overdose, which can have significant clinical outcomes.

Considering the product usage is for short term symptomatic relief, any effect on blood pressure will be short lived and of limited clinical significance for the vast majority of people who use this product. Therefore the risk of consumers not getting the relief they expect from their combination product at the lower level of PE outweighs the theoretical risk to those individuals that are overweight/obese and/or the elderly, and also those individuals who have undiagnosed

or asymptomatic cardiovascular disease(s) that may be exacerbated by an increase of blood pressure, for all the points highlighted above.

In fact the submission to the MCC states that the doubling of PE plasma levels is expected to have minimal safety implications to young healthy consumers. It is important to note that there are many OTC medicines that cannot be taken by consumers with certain health issues, and for these groups of individuals, mandatory warning labels are required as included in the Label Statements Database.

Dosage, formulation, labelling, packaging and presentation of the substances

All [redacted] products that contain the combination of paracetamol and phenylephrine have the following mandatory statements which address the theoretical concern raised in the reclassification application:

Ask your doctor before use if you:

- Have high blood pressure
- Are taking anti-depressants
- Have heart problems
- Are pregnant

Burden on the Public Health System

Burden on the pharmacist

The current classification of products containing paracetamol and PE means that cold and flu preparations containing these actives are available without the need for consultation from a pharmacist. Restricted medicines are substances for which mandatory professional advice is required. Self-limiting cold and flu symptoms treated with short term OTC substances with a history of safe use does not fit within this framework and would result in an unnecessary burden on pharmacists, if counselling or a transaction with a pharmacist must occur with every request for products used to relieve the symptoms associated with cold and flu.

In conclusion, [redacted] strongly opposes the proposal to amend the classification of paracetamol plus PE combinations for the following reasons:

1. The combination of paracetamol and phenylephrine has had extensive use as Pharmacy only medicine as well as a general sale medicines, with over [redacted] units sold annually (equates to over [redacted] units) across Australia and New Zealand with **no** significant adverse events relating to cardiovascular disease or hypertension. The

rationale for restricting supply to Restricted Medicines is based on a theoretical safety concern which has not been reflected in company or public adverse events databases.

2. The absence of safety signals indicates that the combination of paracetamol and PE represents no safety concern. Any theoretical or predicted issues should be addressed in appropriately designed and powered clinical studies
3. The risk of paracetamol overdose outweighs the risk to those consumers with hypertension or cardiac conditions, especially given warning statements are already included on packaging for the "at risk" populations.
4. Paracetamol and PE combination products are used for short-term, symptomatic cold and flu symptoms relief, therefore effects on blood pressure will be short lived and of limited clinical significance for the vast majority of people who use the product.
5. Reclassification of this combination to Restricted medicine will not be in the best interest of public health and will increase the workload burden on pharmacists given the sound safety profile of this combination and the years of extensive use of these medicines with no significant Adverse Events data reported to date.

Yours faithfully,

[redacted]

1. **Atkinson, H. C., I. Stanescu, and B. J. Anderson.** 2014. Increased phenylephrine plasma levels with administration of acetaminophen. N Engl J Med **370:**1171-2.
2. **Horak, F., P. Zieglmayer, R. Zieglmayer, P. Lemell, R. Yao, H. Staudinger, and M. Danzig.** 2009. A placebo-controlled study of the nasal decongestant effect of phenylephrine and pseudoephedrine in the Vienna Challenge Chamber. Ann Allergy Asthma Immunol **102:**116-20.

Reference 1
Atkinson, H. C., I. Stanescu, and B. J. Anderson. 2014. Increased phenylephrine plasma levels with administration of acetaminophen. N Engl J Med **370:**1171-2.

ularly in settings where liver transplantation is not available. As stated in our review, since the evidence base for care is very limited, the use of most therapies is based on opinion. Although the use of lactulose may be beneficial in some patients with cirrhosis and low-grade encephalopathy, its role in critically ill patients with acute liver failure is not established. Its use may be deleterious because patients with acute liver failure frequently have ileus that may be worsened, particularly if oral fluid intake is inadequate. There are no clinical data to suggest a prolongation of survival, and we and others do not recommend the use of lactulose for the great majority of patients.[1]

Dhaliwal and Singh bring up autoimmune hepatitis and specific infections as causes of acute liver failure; space considerations prevented us from an exhaustive discussion of all of these in our review. Severe liver involvement may be seen in some systemic infections, and in such cases the early administration of targeted antimicrobial medication is central to effective management. Autoimmune processes may be important in the pathogenesis of liver injury in acute liver failure due to a number of causes, including new presentations of autoimmune hepatitis[2]; however, this cause of acute liver failure is very uncommon, and clinical management may be challenging.[3] Although some patients may have a response to immunosuppressive therapy, a key issue is that inappropriately prolonged therapy in an attempt to achieve medical control of disease may preclude successful and definitive transplantation, owing to the development of treatment-related sepsis and other complications.[4]

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Since publication of their article, the authors report no further potential conflict of interest.

1. Stravitz RT, Kramer AH, Davern T, et al. Intensive care of patients with acute liver failure: recommendations of the U.S. Acute Liver Failure Study Group. Crit Care Med 2007;35:2498-508.
2. Stravitz RT, Lefkowitch JH, Fontana RJ, et al. Autoimmune acute liver failure: proposed clinical and histological criteria. Hepatology 2011;53:517-26.
3. Czaja AJ. Review article: the management of autoimmune hepatitis beyond consensus guidelines. Aliment Pharmacol Ther 2013;38:343-64.
4. Ichai P, Duclos-Vallée J-C, Guettier C, et al. Usefulness of corticosteroids for the treatment of severe and fulminant forms of autoimmune hepatitis. Liver Transpl 2007;13:996-1003.

DOI: 10.1056/NEJMc1400974

Increased Phenylephrine Plasma Levels with Administration of Acetaminophen

TO THE EDITOR: Over-the-counter combinations containing acetaminophen and phenylephrine for the treatment of the common cold and influenza are widespread after the substitution of phenylephrine for pseudoephedrine. This substitution has been allowed in the United States and elsewhere without any additional safety or efficacy studies, since phenylephrine has been called "generally recognized as safe and effective" at oral doses of 10 mg on the assumption that the pharmacokinetic behavior of one drug is not altered by another, despite a lack of supporting data.[1-3]

Three randomized, open-label, crossover studies in healthy volunteers were undertaken as part of the development of a new-fixed dose combination containing acetaminophen, ibuprofen, and phenylephrine. The results showed an unexpected pharmacokinetic interaction among the three drugs: the administration of phenylephrine (at a dose of 10 mg) in combination with acetaminophen (1000 mg) and ibuprofen (300 mg), as compared with the administration of 10 mg of phenylephrine alone, resulted in nearly a quadrupling in the maximal plasma concentration (3220 pg per milliliter vs. 874 pg per milliliter) and a doubling in the area under the curve (2220 pg per milliliter per hour vs. 1020 pg per milliliter per hour) (Fig. 1). Ibuprofen was subsequently shown not to contribute to this increase. Halving the dose of phenylephrine that was combined with acetaminophen to 5 mg produced a plasma concentration–time curve similar to that for 10 mg of phenylephrine administered alone.

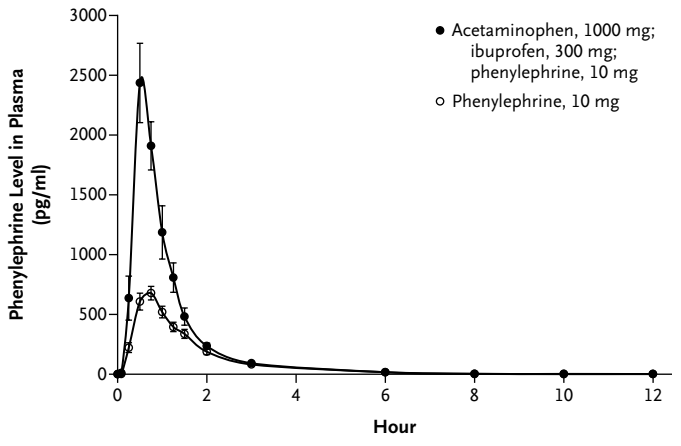

Figure 1. Pharmacokinetic Interaction for Phenylephrine, Acetaminophen, and Ibuprofen.

Shown are the mean plasma levels of phenylephrine after the single administration to healthy human volunteers of a combination of 1000 mg of acetaminophen, 300 mg of ibuprofen, and 10 mg of phenylephrine (black circles), as compared with 10 mg of phenylephrine alone (white circles). The I bars indicate standard errors.

These findings have implications from both regulatory and safety perspectives. First, it is clear that many approvals for the addition of phenylephrine to any number of analgesic agents were based on assumptions that were incorrect for acetaminophen. Second, the plasma exposure of phenylephrine combined with acetaminophen (measured as the area under the curve) is doubled, increasing exposure beyond levels that were previously deemed to be safe and effective and increasing the potential risk of adverse events.

Since phenylephrine is metabolized by sulfation in the intestinal wall, it seems likely that acetaminophen interferes with this process and increases the level of phenylephrine with respect to bioavailability.[4] If so, other drugs may also interact with phenylephrine, including ascorbic acid. Multiple variants of acetaminophen combined with phenylephrine are now available on worldwide markets. Is further investigation required?

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Cold, cough, allergy, bronchodilator, and antiasthmatic drug products for over-the-counter human use: 21 CFR Parts 310, 341 and 369. Fed Regist 1994;59(162):43386-412.
2. Australian Department of Health. Registration of products containing phenylephrine in place of pseudoephedrine. February 10, 2006 (http://www.tga.gov.au/industry/otc-phenylephrine-pseudoephedrine.htm).
3. A justification for changing the current wording of the GSL classification of phenylephrine to include a cut-off point for solid dose products containing 10 mg or less of phenylephrine. Wellington, New Zealand: Medsafe (http://www.medsafe.govt.nz/downloads/MCC32Phenylephrine.pdf).
4. Ibrahim KE, Midgley JM, Crowley JR, Williams CM. The mammalian metabolism of R-(-)-m-synephrine. J Pharm Pharmacol 1983;35:144-7.

DOI: 10.1056/NEJMc1313942

Speech in an Orally Intubated Patient

TO THE EDITOR: We report the successful use of an electrolarynx in an orally intubated 59-year-old man who was receiving mechanical ventilation. The device enabled him to produce intelligible speech (Fig. 1). A video-assisted bilobectomy of the right lung for adenocarcinoma had been performed at another hospital, and the procedure was complicated by the development of a bronchopleural fistula. Because of this complication, there was a need for continued mechanical ventilation. His family informed us that the patient was frustrated by his inability to talk. He consented to the plan to use the electrolarynx, and to his surprise — and ours — the device immediately returned the gift of speech to him, without the passage of air through the vocal cords. In response to the question "Were you able to sleep this evening?" he replied, "I slept reasonably well." (See video, in Dutch, with English translation, available with the full text of this article at NEJM.org.) Nurses were able to place the device after just 2 minutes of instruction, and the usefulness of the device in other intubated patients has been confirmed.

A video showing the patient speaking with use of an electrolarynx is available at NEJM.org

The electrolarynx, which is known for its use after laryngectomy, is an oscillating device that

Reference 2

Horak, F., P. Zieglmayer, R. Zieglmayer, P. Lemell, R. Yao, H. Staudinger, and M. Danzig. 2009. A placebo-controlled study of the nasal decongestant effect of phenylephrine and pseudoephedrine in the Vienna Challenge Chamber. Ann Allergy Asthma Immunol **102:**116-20.

A placebo-controlled study of the nasal decongestant effect of phenylephrine and pseudoephedrine in the Vienna Challenge Chamber

Friedrich Horak, MD*†; Petra Zieglmayer, MD*; René Zieglmayer, DI†; and Patrick Lemell, PhD†; Ruji Yao, PhD‡; Heribert Staudinger, MD‡; and Melvyn Danzig, PhD‡

Background: Studies on the efficacy of phenylephrine in the treatment of nasal congestion have yielded inconsistent results, notwithstanding its approval for this indication.

Objective: To evaluate and compare the decongestant effect of a single dose of phenylephrine to placebo and pseudoephedrine in patients with seasonal allergic rhinitis.

Methods: This randomized, placebo-controlled, 3-way crossover study evaluated patient-scored nasal congestion, peak nasal inspiratory flow, and rhinomanometry at more than 6 hours in 39 grass-sensitive patients exposed to grass pollen in the Vienna Challenge Chamber. Patients were dosed with immediate-release formulations of phenylephrine, 12 mg, pseudoephedrine, 60 mg, as a control, or placebo.

Results: Phenylephrine was not significantly different from placebo in the primary end point, mean change in nasal congestion score at more than 6 hours ($P = .56$), whereas pseudoephedrine was significantly more effective than both placebo ($P < .01$) and phenylephrine ($P = .01$). Phase 1 results showed a difference between phenylephrine and placebo that was 64% of the difference between pseudoephedrine and placebo, substantially greater than the 17% difference observed for all phases. Carryover bias due to patient recall of the pseudoephedrine effect may have influenced these results. Rhinomanometry and peak nasal inspiratory flow results were consistent with these data. Neither phenylephrine nor pseudoephedrine had an effect on the nonnasal symptoms. No adverse events were reported in this study.

Conclusions: During a 6-hour observation period, a single dose of pseudoephedrine but not phenylephrine resulted in significant improvement in measures of nasal congestion. Neither phenylephrine nor pseudoephedrine had an effect on nonnasal symptoms.

Ann Allergy Asthma Immunol. 2009;102:116–120.

INTRODUCTION

In several recent surveys of impact and burden of allergic rhinitis, nasal congestion was consistently ranked the most bothersome symptom in both adult respondents and guardians of children with allergies.[1–3] In addition, nasal congestion was the symptom that most respondents (50% of adults and 63% of guardians of children with allergies) wanted to prevent from occurring.[3] Therapeutic options for the prevention and treatment of nasal congestion include oral decongestants (sympathomimetic agents), such as pseudoephedrine and phenylephrine, which can be administered alone or in combination with antihistamines.[4]

Many manufacturers have changed the formulation of decongestant products to include phenylephrine because of safety and tolerability concerns associated with the use of pseudoephedrine in certain patient populations and recent legislation, including the Combat Methamphetamine Epidemic Act, which requires that all products containing pseudoephedrine be kept "behind the counter."[4,5] The efficacy of phenylephrine as a substitute for pseudoephedrine has been questioned because several reports have indicated that phenylephrine does not provide consistent relief of nasal congestion or nasal resistance above that provided by placebo[5,6]; therefore, the purpose of the current study was to compare the decongestant effect of a single dose of phenylephrine to placebo and pseudoephedrine in patients with allergic rhinitis.

Allergen challenge chambers are useful in determining drug effects in allergic patients exposed to pollen in a homogeneous environment.[7] The Vienna Challenge Chamber is the longest standing allergen challenge system and has been used to determine proof-of-concept, time course, and magnitude of effect and onset of action of antihistamines, nasal corticosteroids, and similar agents.

Affiliations: * ENT University Clinic, University of Vienna, Vienna, Austria; † Allergy Center, Vienna West, Vienna, Austria; ‡ Schering-Plough Research Institute, Kenilworth, New Jersey.

Funding Sources: This study was supported by a grant from Schering-Plough Research Institute.

Disclosures: Drs Danzig, Yao, and Staudinger are employees of Schering-Plough Research Institute.

Trial Registration: clinicaltrials.gov Identifier: NCT00276016

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METHODS

This was a single-center, randomized, placebo-controlled, 3-way crossover study of the decongestant effect of phenylephrine compared with placebo and pseudoephedrine in patients with at least a 2-year history of symptomatic and skin test positive seasonal allergic rhinitis to grass pollen after exposure to grass pollen in the Vienna Challenge Chamber. Patients were to be treated with 1 dose of phenylephrine, 12 mg, pseudoephedrine, 60 mg, or placebo at each treatment visit with a minimum washout period of 5 days between visits. Pseudoephedrine (Sudafed Decongestant Tablets; Pfizer Consumer Healthcare, Eastleigh, Hampshire, England) and phenylephrine (Sudafed Congestion Relief Capsules; Pfizer Consumer Healthcare) were purchased locally. Placebo (blue capsules containing inactive ingredients) was supplied by Schering-Plough Research Institute. All 3 medications came packaged in individual blisters. A third party was provided a master randomization code and prepared the medication for each patient for each period by placing 1 of the appropriate blisters into a prelabeled vial. The investigator and staff did not know the identities of the medications taken; the patients knew that they took either a tablet or a capsule.

The methods for the Vienna Challenge Chamber have been previously described.[8] In brief, patients met the following minimum symptoms severity criteria during a 120-minute predose challenge in the Vienna Challenge Chamber: score of at least 2 (moderate) for nasal congestion; score of at least 6 for combined nasal symptoms (symptoms are rhinorrhea, nasal congestion, sneezing, and nasal itch); and score of at least 2 for combined nonnasal symptoms (symptoms are eye itching or burning, eye tearing, and itching of ears or palate).

The study drug was dispensed when the patient met these scores; patients remained in the Vienna Challenge Chamber for 7.5 hours. Patients were required to complete symptoms evaluations on a scale of 0, indicating none, to 3, indicating severe, at 15-minute intervals. Rhinomanometry, peak nasal inspiratory flow (PNIF), and collection of tissues used for determination of nasal secretion weights were performed at 30-minute intervals.

The primary efficacy variable was the subjective evaluation of nasal congestion expressed as an average change from baseline during the first 6.0 hours of the evaluation period. Additional efficacy end points included 2 objective measures of nasal congestion, rhinomanometry, and PNIF, which were evaluated as the average change at more than 6 hours for each of these measures. The average change at more than 6 hours also was evaluated for each of the individual nasal symptoms of rhinorrhea, sneezing, and nasal itching and nonnasal symptoms of eye itching or burning, eye tearing, and itching of the ears or palate. Safety was evaluated by recording of adverse events and measurement of vital signs.

The study was performed in accordance with applicable statutes and regulations regarding the protection of patients' rights and welfare and was approved by institutional review boards at each study site. All patients provided written informed consent before any study procedure was performed.

The primary comparison for the primary efficacy variable, subjective evaluation of nasal congestion, was phenylephrine, 12 mg, vs placebo tested at 2-sided $\alpha = .05$. Pseudoephedrine, 60 mg, was included as a positive control and was also compared with placebo. The comparison of pseudoephedrine vs placebo was performed at unadjusted $\alpha = .05$, primarily to validate the trial results. In addition, phenylephrine was compared with pseudoephedrine to evaluate relative efficacy. Pairwise comparisons were made using linear contrasts of the treatment means obtained from an analysis of variance model that extracts sources of variation due to treatment, patient, and phase. The primary comparison for all of the secondary end points was phenylephrine vs placebo tested at 2-sided $\alpha = .05$; pseudoephedrine was also compared with placebo.

RESULTS

Thirty-nine patients were randomized; 38 patients completed treatment, and 1 patient discontinued participation in the study for reasons unrelated to treatment with study drug after the first dose (pseudoephedrine). Patients were predominantly white (97%) and female (59%); age ranged from 19 to 46 years (mean, 27 years). Baseline (at the time the patients qualified) nasal congestion scores were 2.20 for phenylephrine and placebo and 2.26 for pseudoephedrine.

Phenylephrine was not significantly different from placebo in decreasing nasal congestion scores at any evaluation time. The average first 6-hour postbaseline decrease nasal congestion score was 7.1% for phenylephrine treatment compared with 2.2% for placebo treatment ($P = .56$). Comparatively, pseudoephedrine, with an average 6-hour mean percentage decrease from baseline in nasal congestion score of 21.7%, was significantly more effective than either placebo ($P < .01$) or phenylephrine ($P = .01$). The difference between phenylephrine and placebo in the average change from baseline during the first 4 hours after dosing (0.19 to 0.16 point) was similar to the difference in the average change from baseline during the first 6 hours after dosing (0.18 to 0.12 point). The time course for nasal congestion is shown in Figure 1. The first time point where pseudoephedrine was statistically different from placebo in nasal congestion was at 30 minutes; because phenylephrine did not differentiate from placebo, we could not determine its onset of action.

No significant phase effect ($P = .72$) was found in the analysis of the primary end point. In addition, no significant sequence effect ($P = .89$) was found. When data from the first phase of a crossover are evaluated, however, the results can be similar to what could be expected in a parallel-group design. For phase 1 data in this study, the difference between phenylephrine and placebo (0.31 to 0.10 point) was 64% of the difference between pseudoephedrine and placebo (0.43 to 0.10 point), which is greater than the 17% phenylephrine to pseudoephedrine ratio noted when all phases were considered.

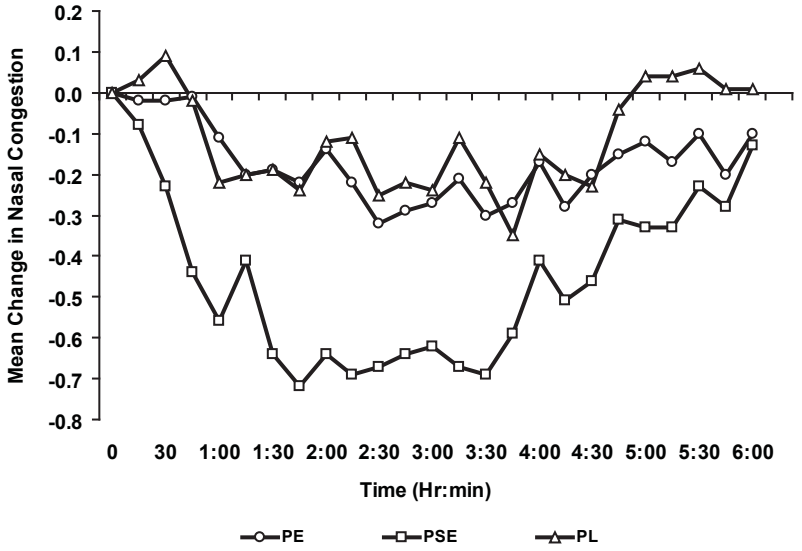

Figure 1. Mean change in subjective nasal congestion scores at each 15-minute interval after drug administration. Baseline values were 2.20 (phenylephrine [PE]), 2.26 (pseudoephedrine [PSE]), and 2.20 (placebo [PL]).

The results of rhinomanometry (Fig 2) and PNIF (Fig 3), 2 objective measures of nasal decongestant effects, were consistent with the results of the primary measurement. Phenylephrine had no significant effect on nasal airflow compared with placebo as evidenced from the rhinomanometry results ($P = .12$), whereas pseudoephedrine was significantly more effective than placebo ($P = .03$, sum of right and left nostrils, average 6 hours after dosing). When averaged for the first 6 hours of the evaluation period, PNIF showed no significant effect on nasal airflow for phenylephrine ($P = .94$) vs placebo and a borderline significant improvement for pseudoephedrine ($P = .07$) vs placebo. However, the pseudoephedrine group showed significant improvement during the first 4 hours after dosing, in line with the expected duration of action of a 60-mg dose of pseudoephedrine. At the hour 4 measurement, the pseudoephedrine group had improved significantly ($P = .01$) vs placebo, whereas the phenylephrine group had not separated from placebo ($P = .87$).

For the other individual nasal symptom scores averaged during the first 6 hours, pseudoephedrine was significantly better than placebo for rhinorrhea ($P = .04$) and sneezing ($P = .01$), whereas phenylephrine was similar to or worse

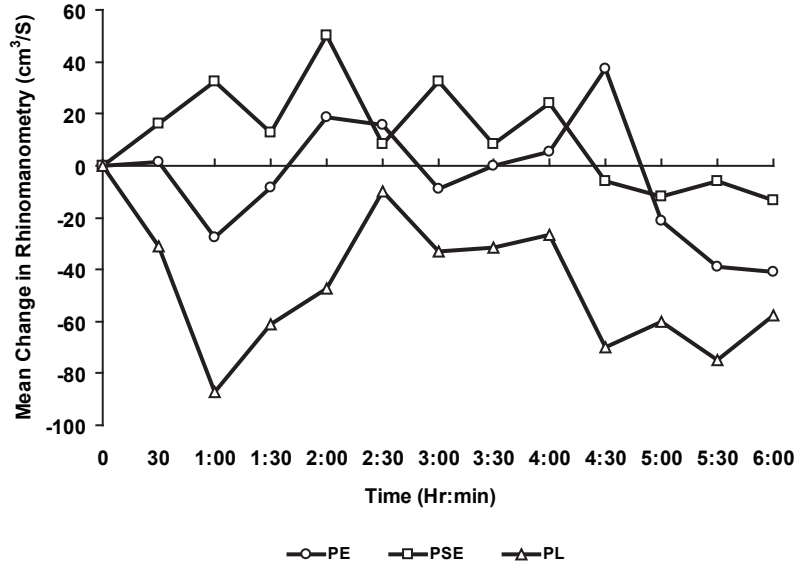

Figure 2. Mean change in rhinomanometry measurements (sum of right and left nostrils) at each 30-minute interval after drug administration. Baseline values were 366.1 (phenylephrine [PE]), 406.2 (pseudoephedrine [PSE]), and 400.9 (placebo [PL]) at 150 Pa (cm^3/s).

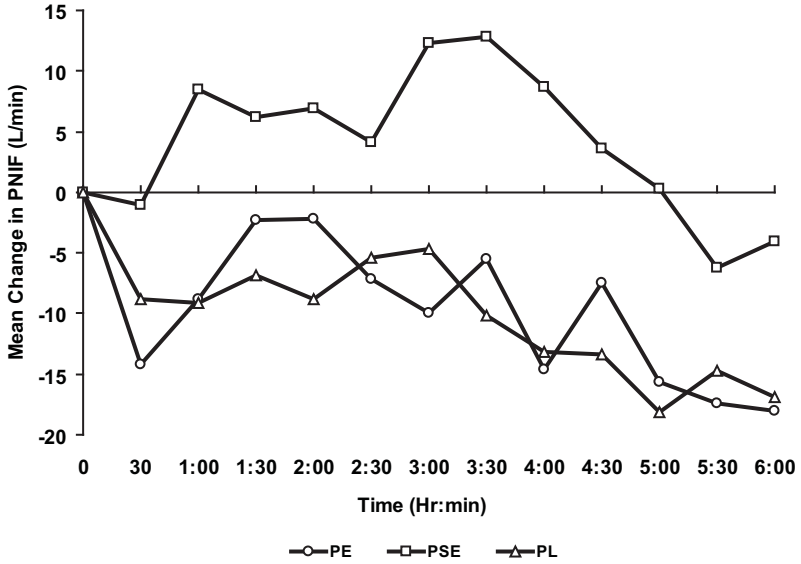

Figure 3. Mean change in peak nasal inspiratory flow (PNIF) scores at each 30-minute interval after drug administration. Baseline values were 104.6 (phenylephrine [PE]), 108.7 (pseudoephedrine [PSE]), and 107.0 (placebo [PL]) L/min.

than placebo for each (data not shown). Neither phenylephrine nor pseudoephedrine had a significant improvement compared with placebo on nasal itching or the nonnasal symptoms (eye itching or burning, eye tearing, itching of ears or palate) (data not shown). A greater decongestant effect was found compared with placebo in female patients than in male patients taking pseudoephedrine; this differential treatment response was not seen for phenylephrine.

No adverse events were reported in this single-dose study, and no treatment differences were observed in vital signs. These results indicated that the single doses of phenylephrine, 12 mg, and pseudoephedrine, 60 mg, were safe and well tolerated, although the study was not powered to find statistically significant differences in safety.

DISCUSSION

In this study, statistical significance ($P = .56$) was not observed for the primary efficacy variable, the average change from baseline during a 6-hour evaluation period in nasal congestion, in patients with seasonal allergic rhinitis treated with a single dose of phenylephrine, 12 mg, vs patients treated with placebo. Comparatively, treatment with a single dose of pseudoephedrine, 60 mg, showed significant improvement in nasal congestion compared with placebo ($P < .01$) and phenylephrine ($P = .01$). Phenylephrine showed 17% of the decongestant activity demonstrated by pseudoephedrine over placebo.

When results were evaluated by phase of the crossover, the phase 1 difference between phenylephrine and placebo was 64% of the difference between pseudoephedrine and placebo. This result is similar to what would be expected in a parallel-group design. In this crossover-design study, patients may have recalled the effect of pseudoephedrine when pseudoephedrine was taken before other treatments and influenced their symptom evaluation. The 3 sequences that had phenylephrine taken before pseudoephedrine in any phase had greater changes in the mean decongestant effects compared with placebo of phenylephrine, whereas the other 2 sequences that had phenylephrine taken after pseudoephedrine in any phase had raw mean decongestant effects that were considerably lower when compared with placebo of phenylephrine. This finding suggests that bias may have been introduced because of patient recall of the pseudoephedrine effect in a previous phase.

Changes in patients' symptom scores for nasal congestion and objective measures of nasal airflow as a result of the administration of a therapeutic agent do not always occur in parallel[9] because, unlike other symptoms of allergic rhinitis, the discomfort felt by patients with nasal congestion does not always correlate with the aspects of the symptom that a physician can evaluate, such as nasal patency.[10,11] To reduce the possibility that the current study would underestimate the efficacy of phenylephrine in the relief of nasal congestion, 2 objective measures were also used. Both PNIF and rhinomanometry were consistent with the subjective measure of efficacy in this study with no demonstrated improvement in either measure after the administration of phenylephrine, whereas a significant improvement in rhinomanometry and an increase in PNIF were seen with pseudoephedrine treatment.

As noted, pseudoephedrine provided a significant improvement over placebo for rhinorrhea and sneezing but not nasal itching or the nonnasal symptoms. Similar reductions in other rhinitis symptoms after treatment with pseudoephedrine have been noted,[12] although it is generally thought that the oral decongestants have no effect on other symptoms because

there is no direct effect of decongestants on allergic mediators.[4] It has been suggested that the relief of symptoms other than nasal congestion by decongestant agents may reflect a "halo effect" because a reduction in nasal congestion may lead to an overall improvement in the patient's sense of well-being and reduced perception of the severity of other rhinitis symptoms.[12]

Although patients were exposed for 7.5 hours after dosing, the primary end point was the average for the first 6 hours. This approach was in keeping with the dosing regimens of the short-acting form of phenylephrine (every 6 hours) and pseudoephedrine (every 4 to 6 hours) that were used in this study. Although the dosing regimen for these decongestants is similar, the half-life of phenylephrine is shorter than that of pseudoephedrine,[10,13] so it may be possible that a significant effect of phenylephrine occurred during the initial response to the treatment. To determine if phenylephrine treatment resulted in significant improvements in either the subjective or objective measures of nasal congestion, the 4-hour time point was also examined, showing similar results. This finding suggests that it is unlikely that the lack of efficacy with phenylephrine was a result of using the short-acting formulation.

Both pseudoephedrine and phenylephrine have been described as safe and effective drugs.[14] A recent letter questioned the effectiveness of phenylephrine as a nasal decongestant when given orally.[6] Our study was clinically complete when this letter appeared online in May 2006. Within the limitations of the first phase data from this small chamber study, it appears that phenylephrine may have activity, although the magnitude and the duration of effect may not be optimized by the current existing doses and formulations. However, because no difference between phenylephrine and placebo for any of the primary subjective or objective measures of nasal congestion was found at any time point, this would suggest that there is little, if any, appreciable effect of phenylephrine compared with placebo in the relief of nasal congestion. The results of the current study are similar to the results of a recent meta-analysis that examined the efficacy and safety of phenylephrine in relieving nasal congestion that occurred because of a variety of causes (eg, "head cold," chronic sinusitis, allergies).[5] In that study, the decongestive effects of phenylephrine also were not consistently any better than placebo.[5]

The following conclusions can be drawn from this study. First, in this crossover design, patients with seasonal allergic rhinitis treated with a single dose of 12 mg of phenylephrine were not significantly different from placebo-treated patients in reduction of their nasal congestion scores from baseline; pseudoephedrine at a dose of 60 mg was superior to placebo. It is possible that recall bias in the crossover design may have influenced this result. Second, treatment with a single dose of phenylephrine, 12 mg, and pseudoephedrine, 60 mg, in male and female patients with seasonal allergic rhinitis, ages 19 to 46 years, was safe and well tolerated.

ACKNOWLEDGMENTS

We thank Sandria De Sapio and Karin Gansch for study monitoring; Lucy Shneyer, MS, for statistical oversight; and Craig Ostroff, PharmD, for logistical and regulatory support.

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pharmacycouncil
OF NEW ZEALAND
Te Pou Whakamana Kaimatu o Aotearoa

File ref: T10

19 September 2014

Andrea Kerridge
Secretary, Medicines Classification Committee
Medsafe
PO Box 5013
Wellington 6145

Dear Andrea

Pharmacy Council comment on MCC 52nd meeting agenda items

The Council is the statutory body instituted with the primary purpose of protecting the health and safety of the public. It has the following key functions:

- Determining the scopes of practice for pharmacists
- Prescribing the qualifications required for copes of practice within the profession
- Registering pharmacists
- Setting standards and guidelines
- Reviewing practising pharmacists when concerns are raised about competence, professional conduct or health
- Promotion of education and training in the profession.

Although Council's mandate under the HPCA Act 2003 is public safety, Council is very cognisant of its role in setting an accountability regime for pharmacists in terms of the care and information provided to the public about the medicines they provide. Pharmacists are obliged to supply a medicine, complementary therapy, herbal remedy or other healthcare product to a patient only when satisfied the patient understands how to use it safely and appropriately. All healthcare practitioners are aware that medicines are not ordinary articles of commerce; a concept that is undermined by their availability through outlets where no appropriate advice is available and therefore where public safety may be compromised.

Agenda item 6.1 **Reclassification of Beclomethasone from pharmacy-only medicine to general sale medicine**

Although Council accepts that intranasal steroid sprays are generally safe for long-term use, and there is little evidence to indicate they cause significant systemic side effects, there are still risks associated with their use. Patients with chronic rhinitis who might use them for long periods should be advised to use them only intermittently and at the lowest dose that controls their symptoms. Patients who regularly use steroid sprays should also undergo examination of the nasal cavity at least annually to check for damage to the septum. Lacking advice from a health professional about the onset of effect for nasal corticosteroids, the potential for concurrent overuse of nasal decongestant sprays cannot be overstated. Council does not support reclassification of intranasal steroids from a public safety perspective.

Agenda item 6.2 **Reclassification of Omeprazole tablets 10mg from pharmacy-only medicine to general sale medicine**

The Council has previously submitted that it does not support the reclassification of omeprazole to General Sales and retains that position with this submission.

There are a number of serious medical conditions ranging from peptic ulcers to gastric cancer that present as reflux and dyspepsia, and it is important that an appropriately trained healthcare professional is involved in assessing the purchaser for any alarm signs/symptoms.

In a short period of time, omeprazole classification has changed from Pharmacist Only to Pharmacy Only. This current classification still provides an opportunity for pharmacist oversight of the sale and to assess the patient for appropriate use. Pharmacists are naturally cautious about treating patients where there are possible alarm symptoms or the patient is on concomitant medicines that interact with omeprazole, and will continue to refer patients to their medical practitioner where necessary.

The Council firmly believes reclassification of any medicine, whether from Prescription Medicine to Pharmacist-Only, or from Pharmacy Only to General Sales can only be made when there is certainty that public safety is not compromised.

We trust these comments will be helpful for the Committee's decision-making.

Yours sincerely

Claire Paget-Hay
Chief Executive and Registrar

NEW ZEALAND FOOD & GROCERY COUNCIL

Medicines Classification Committee 52nd Meeting
21 October 2014

Comment on Agenda Item 6.3 regarding AFT Pharmaceuticals Ltd Application for Reclassification of Paracetamol in combination with Pheylephrine in New Zealand

By: New Zealand Food & Grocery Council

To: Medicines Classification Committee

September 2014

25 September 2013

Andrea Kerridge (Secretary)
Medicines Classification Committee
PO Box 5013
WELLINGTON

COMMENT ON AGENDA ITEM 6.3 FOR THE 52nd MEDICINES CLASSIFICATION COMMITTEE MEETING

The New Zealand Food & Grocery Council (FGC) makes this submission on Agenda Item 6.3 for consideration at the 52nd meeting of the Medicines Classification Committee:

> 6.3 Paracetamol in combination with phenylephrine (Maxiclear Sinus and Pain Relief and Maxiclear Cold and Flu Relief, AFT Pharmaceuticals)

The FGC wishes to ***oppose*** the application for reclassification proposed by AFT Pharmaceuticals Ltd.

Introduction

The applicant is seeking reclassification of paracetamol in combination with phenylephrine in packs containing:

- any number of solid dose units containing paracetamol 500 mg in combination with more than 2.5 mg phenylephrine per dose unit
    - from general sale or pharmacy-only medicine to restricted medicine
- any number of sachets of powder containing 1000 mg paracetamol in combination with more than 5 mg phenylephrine per sachet
    - from general sale or pharmacy-only medicine to restricted medicine.

The applicant is proposing no change to the classification of paracetamol in combination with phenylephrine in packs containing:

- more than 20 solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit; and
- more than 10 sachets of powder containing 1000 mg paracetamol in combination with 5 mg phenylephrine or less per sachet
    - both to remain a pharmacy-only medicine
- 20 or less solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit; and
- 10 or fewer sachets of powder containing 1000 mg paracetamol in combination with 5 mg phenylephrine or less per sachet
    - both to remain a general sale medicine

In summary, NZFGC is concerned at the limited evidence on which this application appears to be based. The weight of evidence reflected in the number of units sold since 2006 and the absence of adverse effects reported in relevant databases or company records suggests that a single study is insufficient grounds on which to reclassify paracetamol in combination with phenylephrine.

Background

The AFT Pharmaceuticals Ltd application for reclassification is for:

- restricted medicine status (pharmacist supervising the sale) for all solid dose units containing paracetamol 500 mg in combination with more than 2.5 mg phenylephrine per dose unit and all sachets of powder containing 1000 mg paracetamol in combination with more than 5 mg phenylephrine per sachet.

These products would move from either general sale or pharmacy-only medicine.

It appears that the application for reclassification is based primarily on a single study: a letter to the editor of the New England Journal of Medicine (NEJM)[1] which describes a pharmacokinetic study that was undertaken on a combination paracetamol /ibuprofen/ phenylephrine product in development. This showed an incidental finding of mean plasma levels of phenylephrine being higher when phenylephrine is co-administered with paracetamol.

The authors describe a purported pharmacological interaction between paracetamol and phenylephrine, stating that paracetamol increases the bioavailability of phenylephrine, resulting in increased plasma levels of phenylephrine.

Reclassification based on such limited evidence, results in the basis being theoretical safety concerns regarding the use of currently registered pharmacy-only and general sale products by consumers. In terms of satisfying the criteria for a restricted medicine classification, the evidence should comprise clinical studies to confirm suggested effects.

Comment

History of use

NZFGC understands that the medicines proposed for reclassification have been approved for use in New Zealand for eight years (since 2006) and prior to that for almost a further decade in the UK (since 1997). The safety record of these medicines has been very satisfactory. The products are for short-term use according to the labelled directions and cover medical conditions that are easy to self-diagnose. They contain appropriate warning statements as required by Medsafe and in the case of pharmacy-only sales can be accompanied by advice and assistance from pharmacy staff.

Consumers clearly benefit from the current classification arrangements both in location and hours of purchase as well as in the flexibility available by the purchase arrangements. Consumers who are aware that they have heart conditions or hypertension are clearly advised to consult their doctor or pharmacist before taking the medicine.

Basis for application for reclassification

The application from AFT Pharmaceuticals Ltd points to safety concerns for the use of the medicines by consumers with undiagnosed hypertension and suggests that a reclassification would reduce the risk to such consumers. In response the FGC points out that an undiagnosed condition would remain undiagnosed irrespective of classification and the purported need to reduce risk is from restricting supply. One of the two formulation proposed for reclassification is already a pharmacy-only product and supply is therefore already limited. The issue is whether the evidence is strong enough to support a reclassification to 'restricted medicine' and pharmacist-only dispensing.

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[1] Atkinson HC, Stanescu I. Increased phenylephrine plasma levels with administration of Acetaminophen. N. Eng J Med 2014; 370(12):1171-2

Absence of evidence for reclassification

Although a relationship between sympathomimetic drugs (such as phenylephrine) and vasopressor effects has been documented and have a pharmacological basis, a base literature search (Pub Med) did not identify any studies documenting any specific dose response relationship between phenylephrine combined with paracetamol and blood pressure. Considering the product usage is for short term symptomatic relief, any effect on blood pressure would be short lived and of a limited clinical significance for the vast majority of people who use the product.

It has already been noted that the safety record of these medicines has been very satisfactory. At its 50th meeting the Medicines Classification Committee "agreed that when used appropriately, paracetamol is one of the safest medicines on the market." We note that at its 43rd meeting a reclassification of phenylephrine for the treatment of the symptoms of cough and cold in adults and children over 12 years of age did not proceed due to insufficient evidence of harm. The Committee had reviewed the safety of phenylephrine at its 30th, 31st and 32nd meetings and determined classification at that time. NZFGC contends that remains insufficient evidence of harm that would sustain reclassification.

Impact of possible reclassification

Over one hundred products in various pack sizes that contain paracetamol combined with phenylephrine are available in New Zealand. NZFGC understands that all these are either oral tablets/caplets/capsules containing paracetamol 500mg and phenylephrine 5mg or granules/powders containing paracetamol 1,000mg plus phenylephrine 10mg. All of these products would be affected by a reclassificaiton.

There would be a significant business impact for existing sponsors. Consumers familiar with the current availability of products in pharmacies as pharmacy-only medicines and as general sale products in the grocery sector will be confused with the restricted availability. Pharmacists may be affected by the volume of queries and requests from consumers for these commonly used products.

Recommendation

NZFGC does not support the application to change the classification of paracetamol plus phenylephrine combination products and recommends no change be made to the current classification. This is on the basis that there continues to be insufficient evidence of harm that would justify reclassification to restricted medicine status.

There is no documented safety issue with the existing products and their current classifications. The research to date does not justify the significant impact on consumer access, the business of sponsors and pharmacists. The new information is of interest and suggests areas for future study but is insufficient to justify reclassification of products that have been delivered millions of doses millions of people over the last decade. The clinical risk to patients taking these products for short term durations to alleviate the symptoms of sinus and the common cold and flu, should not give rise to any serious safety concerns.

Yours sincerely

Katherine Rich

Katherine Rich
Chief Executive Officer

12 September 2014

Andrea Kerridge (Secretary)
Medicines Classification Committee
PO Box 5013
WELLINGTON

Application for Reclassification- RESPONSE

Agenda Item 6.3 for the 52nd Medicines Classification Committee Meeting
21st October 2014

SUBJECT: Paracetamol in combination with Phenylephrine

Dear Secretary

The New Zealand Self Medication Industry (NZSMI) is the representative trade organisation for the major *"over the counter"* (OTC) medicine sponsor companies within New Zealand.

We appreciate the opportunity to make comment on the agenda item and hope our comments are taken in a constructive manner to assist in the committee's decision.

Yours faithfully

New Zealand Self-Medication Industry

EXECUTIVE SUMMARY

- Paracetamol and phenylephrine has had extensive use as pharmacy only and general sales medicine with millions of units sold annually with no significant adverse events relating to cardiovascular disease or hypertension. The proposal for restricting supply to restricted medicine is based on a theoretical safety concern which has not been reflected in company or public adverse event databases.

- The absence of safety signals indicates that the combination of paracetamol and phenylephrine represents no safety concern. Any theoretical or predicted issue should be addressed in extensive, appropriately designed and robust wide ranging clinical studies. Paracetamol and phenylephrine combination products are used for short term symptomatic cold and flu symptoms relief, therefore the effects on blood pressure will be short-lived and of limited clinical significance for the vast majority of people who use the product.

- Up-scheduling this combination to restricted medicine will not be in the best interest of public health and will increase the workload burden on pharmacists given the sound safety profile of this combination and the years of extensive use of these medicines with no significant adverse events data reported to date.

- The proposed changes would have a significant impact on sponsors and their products and would cause confusion to consumers in terms of the way in which the medicines can be purchased without any sound safety concerns to justify the move.

APPLICATION FOR RECLASSIFICATION FOR PARACETAMOL AND PHENYLEPHRINE COMBINATION

- Any number of solid dose units containing paracetamol 500 mg in combination with more than 2.5 mg phenylephrine per dose unit from general sale or pharmacy only medicine to restricted medicine

- More than 20 solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit to remain a pharmacy only medicine

- 20 or less solid dose units containing paracetamol 500 mg in combination with 2.5 mg phenylephrine or less per dose unit to remain a general sale.

- Any number of sachets of powder containing 1000 mg paracetamol in combination with more than 5 mg phenylephrine per sachet from general sale or pharmacy only to restricted medicine.

- More than 10 sachets of powder containing 1000 mg paracetamol in combination with 5 mg phenylephrine or less per sachet to remain pharmacy only

- 10 or fewer sachets of powder containing 1000 mg paracetamol in combination with 5 mg of phenylephrine or less per sachet to remain in general sale

BACKGROUND

The proposed rescheduling application requests an upward scheduling for existing, currently marketed paracetamol and phenylephrine combination products, which would result in products that are currently either in pharmacy only or GSL being up-scheduled to restricted medicine (pharmacist supervising the sale).

NZSMI understands that an application has also been submitted by AFT to the ACMS for their forthcoming meeting in Australia. NZSMI contends that there are hundreds of combination paracetamol plus phenylephrine products in a number of pack sizes currently registered in New Zealand that would be affected by such a rescheduling. NZSMI does not agree that the existing pharmacy only and GSL paracetamol and phenylephrine combination products meet the criteria for a restricted medicine classification and strongly opposes the above rescheduling proposal.

NZSMI is of the view that this application for rescheduling is based primarily on one piece of evidence.

- A letter to the editor of the New England Journal of Medicine (NEJM)[1] which describes a pharmacokinetic study that was undertaken on a combination paracetamol /ibuprofen/ phenylephrine product in development, which showed an incidental finding of mean plasma levels of phenylephrine being higher when phenylephrine is co-administered with paracetamol.

[1] Atkinson HC, Stanescu I. Increased phenylephrine plasma levels with administration of Acetaminophen. N. Eng J Med 2014; 370(12):1171-2

The authors proceed to describe a purported pharmacological interaction between paracetamol and phenylephrine, stating that paracetamol increases the bioavailability of phenylephrine, resulting in increased plasma levels of phenylephrine.

Assuming that the basis of the rescheduling application relates to the single item of evidence described above, the author's stated rationale for restricting supply of the paracetamol 500mg plus phenylephrine 5mg to pharmacist only is based on theoretical safety concerns regarding the use of currently registered pharmacy only and GSL products by consumers.

NZSMI comment on the basis for the rescheduling application

The applicant states that "*Paracetamol and phenylephrine combinations have been available in New Zealand and* ***the rest of the world since 2006*****…..**" The fact is this combination has been extensively used within the community and in the UK since as early as 1997. Therefore there has been extensive global market experience within the OTC environment.

Despite this extensive use within the community there is no evidence of any documented safety issues that could justify the up-scheduling of these medicines to restricted medicine. These products have had many years of use and have a favourable safety profile.

These products are used for symptomatic relief of cold and flu, for short treatment duration. Products are labelled with appropriate safety warning statements as dictated by Medsafe, the Regulator, which advise the patient whether or not to seek the advice of a doctor or other health professional before taking the medicine; specifically if the patient has high blood pressure or heart problems or is taking other medication that could interact with the product.

Consumers who are aware that they have heart conditions or hypertension are clearly advised to consult their doctor or pharmacist. We note in the application from AFT that the authors raise safety concerns relating to the possible scenario of use of the existing combination paracetamol and phenylephrine combination products by people with undiagnosed hypertension.

In this submission the applicant contends that moving these products to restricted medicine will reduce the risk to consumers who may have undiagnosed hypertension. NZSMI contends this is purely an assumption based on no firm evidence. Pharmacists will not be in a position to diagnose individuals who have cardiovascular conditions or hypertension in any case, and their questioning of consumers will be informed by warning statements that are present on the label and in the pharmacy texts, such as the New Zealand formulary or MIMS. Pre-diagnosis of cardiovascular disease or hypertension is not something carried out by pharmacists prior to recommending particular products.

Although a relationship between sympathomimetic drugs (such as phenylephrine) and vasopressor effects has been documented and has a pharmacological basis, a base literature search (Pub Med) has not revealed any studies documenting any specific dose response relationship between phenylephrine/phenylephrine combined with paracetamol and blood pressure. Considering the product usage is for short term symptomatic relief, any effect on blood pressure will be short lived and of a limited **clinical significance** for the vast majority of people who use the product.

Impact of possible rescheduling

There are well in excess of 100 products in various pack sizes that contain paracetamol combined with phenylephrine. To NZSMI's knowledge all of the products currently on the New Zealand market are either oral tablets/caplets/capsules containing paracetamol 500mg and phenylephrine 5mg or granules/powders containing paracetamol 1,000mg plus phenylephrine 10mg. All of these products would be affected by this rescheduling if it were to be implemented.

There would be a significant business impact for existing sponsors should such a change take place, as well as consumer confusion for the many consumers who are familiar with the products existing availability in pharmacy as a pharmacy only medicine and as GSL within the grocery sector.

Pharmacists will also be significantly affected by the volume of queries and requests from consumers for these commonly used products; it is likely that this will have an unwanted effect on the day to day practice of busy pharmacists due to the high volume of these products supplied under well-known brand names that would switch to pharmacist only.

NZSMI recommendations

NZSMI does not support the proposal to amend the scheduling of paracetamol plus phenylephrine combination products and believes that the current scheduling remains appropriate.

There is no documented safety issue with the existing products and the way that they are scheduled. NZSMI believes that up-scheduling should only take place when a public health risk is demonstrated and the scheduling proposal does not appear to meet this criterion.

The banning of pseudoephedrine containing products in New Zealand occurred as a consequence of a public campaign that indicated that methamphetamine production from pseudoephedrine was causing a rise in crime within the country. It could be argued that the public benefit gain was achieved by removing these products from sale. Similarly codeine containing analgesics have been up-scheduled where there has been firm evidence to suggest that the public would benefit from such a move. The rationale for this rescheduling application appears to fall far short in comparison.

The NEJM letter showing an observed increase in plasma levels of phenylephrine when co-administered with paracetamol is interesting but does not justify the significant impact on the business of sponsors and pharmacists. NZSMI made a media statement on 21 March 2014 similarly commenting on the fact that the new information was of interest but limited in the sense that more work was required before changes to reclassification would be merited. Indeed Medsafe at that time commented that it had seen the data but had no concerns for patient harm given the 40 year history of the drug where millions of doses had been administered.

In the application for reclassification AFT suggest that there have been 28 adverse events to phenylephrine in 11 separate reports to Medsafe from 1 January 2000 to 1 July 2014. No deaths have been reported. This represents 2 adverse events per year. It is difficult to put a number on how many patients have been treated with products containing paracetamol and phenylephrine in combination in a similar period, but it would run into millions of patients and millions of doses. When that is put into context it is clear that the clinical risk to patients taking these products for short term durations to alleviate the symptoms of sinus and the common cold and flu, should not give rise to any serious safety concerns.

Submission to Medicines Classification Committee

My name is Don Sache
I am a pharmacist who has owned and worked in community pharmacy for 40+years.
My practice is based in eastern Christchurch, basically a suburban pharmacy with an even balance of OTC sales and prescriptions

My real concerns relate to the proposed reclassifications of Beclomethasone
and Omeprazole.
I strongly oppose any move to restrict access to the above two products. This concern is based on my many years of experience counselling customers and patients who request OTC products to treat ailments similar to what these two products are indicated for.

I do not believe this reclassification is in anybody's interest, except the manufacturers
who see this as a business opportunity and nothing more.

BECLOMETHASONE FOR NASAL USE (BECONASE)

My pharmacy sells Flixonase and Butacort, both corticosteroid nasal sprays.
These cannot be sold without a pharmacist intervention to ensure the product is appropriate for the condition and that is also being used correctly.
Technique and duration of use is discussed prior to sale.
I have on occasions declined sales as being inappropriate and then referred the patient to a doctor for further diagnosis and treatment.
e.g. infected sinusitis, non-allergic rhinitis, non-responsive allergic rhinitis

Randomly selecting a Beconase from the shelf and then self medicating or administering to children is not good practice from any point of view.

OMEPRAZOLE SOLID DOSE (LOSEC)

Once again a pharmacist is involved in any Omeprazole sales in my pharmacy.
Diagnosis and differentiation of varying indigestion-like symptoms is critical. Many patients present themselves with a variety of complaints and call it indigestion or heartburn.
By asking a series of questions trained staff are able to assess whether the condition is indeed indigestion/reflux related or a more serious potentially life threatening heart condition.

Recently in my pharmacy a man in his 50's came in looking for "something for indigestion". It was quickly evident that he was in the early stage of a hear attack and I directed him immediately to the medical practice next door. He was admitted to hospital having suffered a severe cardiac event.

Self medicating with Omeprazole is in no-one's interest and with increasing evidence coming to light regarding adverse effects from ongoing regular doses
of Omeprazole it is important to discuss the need to see a doctor if symptoms persist.

I only sell Omeprazole as the short course it is intended to be and discourage resales.

Explaining correct dosing procedures to
patients and what to do if symptoms do not improve is very important.

This control will be lost if Omeprazole can be randomly selected and added to
the grocery pile.

Supermarkets/grocery currently sell adequate indigestion remedies
e.g. Mylanta, Quickeze
There is no need to add Omeprazole to this list.
It is not an antacid as many public perceive it to be.

I am also concerned that one of the reasons to "free-up" the availability of these two medicines is to increase access.
I disagree. This is not a valid reason and will only lead to misdiagnosis by consumer and inappropriate treatment.

There are plenty of pharmacies in NZ and access is not a valid reason.
Where there is a supermarket there is nearly always a pharmacy nearby offering professional patient focused advice that is not commercially
driven.

I request that the Committee decline the reclassification applications.

Don Sache
Pharmacist
QEII Pharmacy
North New Brighton
Christchurch

TO: **Medicines Classification Committee**

FROM: **Iain Buchanan at Buchanans Pharmacy Limited**

RE: **Reclassification of Beclomethasone and Omeprazole from Pharmacy to General Sale**

DATE: **19th September 2014**

General Statement

We do not support the reclassification of these two products from Pharmacy to General Sale. In addition to the reasons detailed, the grocery chain is not the appropriate place for the health conversation to take place as there is no advice available and patients choose the wrong product. We see this continually in the category of "Cough Cold" where patients have purchased goods at the supermarket next door to us and then come in for our advice – the end result is that often they have purchased a product that may be harmful to them given their existing medication regime and health conditions.

Furthermore, grocery cannot be considered proactive in supporting a healthy lifestyle as the products they sell include cigarettes and alcohol.

We further advise in relation to the individual products:

Beclomethasone

Pharmacist counselling of patients is essential to ensure that they chose 'the right product for the right job'. Our ENT specialists would prefer that we steer patients away from the 'quick fix' steroid nasal

Better to encourage patients into a daily routine of using a sinus rinse to maintain a healthy nasal membrane. Many times we end up counselling patients about 'overuse / inappropriate use' of steroid nasal sprays – causing nose bleeds.

Another thing that springs to mind is that if steroid nasal sprays are indicated, they need to be introduced well in advance of the hay-fever season – or via a doctor's prescription when treating other allergies.

Concern over inappropriate use in underage children without a doctor's referral.

Omeprazole

Concerns:

- Inappropriate use to support poor lifestyle choices, particularly in younger men – we are what we eat
- Patients presenting > 50 years of age mask important signals of heart attack / angina / gastric cancer. Omeprazole may 'mask the symptoms' and delay diagnosis

- Caution interactions with omeprazole – how many patients read the PIL inside the box? Omeprazole is a CYP2C19 inhibitor and interacts with many medications.
- Hypomagnesaemia – of concern in patients with heart problems
- As a knock on effect of lowering the amount of gastric acid produced in the stomach – can affect the absorption of other medications from the stomach
- Serious side effect occurring in a few people but with huge significance – Interstitial nephritis – we have seen it in a couple of patients.

Please feel free to contact me should you have any questions or require clarification on any matter. Thank you

Iain Buchanan BPharm(Otago)

PO Box 7100

Tikipunga

Whangarei

021 511 534

PHARMACEUTICAL SOCIETY
of New Zealand Incorporated

19 September 2014 O1 02 01 03

Medicines Classification Committee Secretary
Medsafe, Wellington
via email: committees@moh.govt.nz

Dear Sir/Madam

MEDICINES CLASSIFICATION COMMITTEE
SUBMISSIONS TO THE 52nd MEETING AGENDA October 2014

Thank you for the opportunity to submit comments on the Agenda for the 52nd meeting of the Medicines Classification Committee.

The Pharmaceutical Society of New Zealand Inc (the Society) is the professional association representing over 3,000 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:

5.2 Reclassification of rizatriptan from prescription medicine to restricted medicine following a recommendation at the 43rd meeting on 13 April 2010. Committee to discuss potential options.

The Pharmaceutical Society **supports** keeping the classification of rizatriptan as a restricted medicine. We do not see the current unavailability of a specific product as affecting the classification status, or safety of supply from a pharmacist. Should a product become licensed and enter the market, readdressing a previous classification decision seems both unnecessary and a waste of the committee's time as well as those making submissions.

6.1 Beclomethasone – proposed reclassification from pharmacy-only medicine to general sale medicine

> Reclassification of beclomethasone, in aqueous nasal sprays delivering up to 50 micrograms per actuation when the maximum recommended daily dose is no greater than 400 micrograms (200 micrograms per nostril) in a pack containing 200 actuations or less, from pharmacy-only medicine to general sale medicine for the treatment or prophylaxis of allergic rhinitis in adults and children over 12 years of age.

The Pharmaceutical Society **opposes** the reclassification of beclomethasone nasal spray from pharmacy-only to general sale medicine.

The argument for reclassification by Pharmaceutical Solutions seems to be based predominantly on an argument that supermarkets are open longer hours than pharmacies,

however their evidence is based on a survey of opening hours published in 2003 and based on data collected in 2002. Opening hours information from 12 years ago bears no resemblance to current pharmacy practice where significantly greater numbers of pharmacies are now open longer hours, including 7 day trading; and not just by pharmacies situated in shopping malls.

We struggle to accept the proposal statements that reclassification would provide greater access "especially for after-hours emergencies", when allergic rhinitis is not a life-threatening emergency, and symptoms generally improve in the evening or "after hours". Furthermore, the claim that it will "potentially reduce the number of physician visits" is difficult to understand when this product is currently supplied as a pharmacy-only medicine, with pharmacy staff and pharmacists identifying those patients who are not achieving adequate symptom control and discussing further treatment options or *then* referring to a doctor for a medical assessment and consideration of alternative diagnoses.

We acknowledge that studies continue to add to the reassurance of the safety of intranasal corticosteroids in the treatment of allergic rhinitis. However, as one article in the 'Allergy And Asthma Proceedings' recently noted:

> "these still do not answer the question if these agents are appropriate for long-term use without oversight by a health care professional"(1)

In addition, a further study looking at the role of intranasal corticosteroids in the management of allergic rhinitis in the elderly stated that

> "the diagnosis and management of AR in the elderly require approaches tailored to specific age-related factors" (2)

While another looking at the characteristics and formulation of the various intranasal corticosteroids noted that

> "physicians need to be aware of the different intranasal steroid attributes to try to match patients' preferences in order to achieve better adherence and improve outcomes in sufferers of allergic rhinitis" (3)

We have not been presented with any evidence of an unmet clinical need in the community where consumers are not accessing treatment in reasonable timeframes through the current classification of beclomethasone as a pharmacy-only medicine. Secondly, current evidence and specialist opinion is that the supply of intranasal corticosteroids requires the oversight of a health professional. Furthermore, as is discussed below, we cannot rely on product labelling to appropriately inform consumers of the contraindications, precautions and risks of general sale medicines which are sold without any supervision or regard for the appropriateness or otherwise.(4)

6.2 Omeprazole - proposed reclassification from pharmacy-only medicine to general sale medicine

> Reclassification of omeprazole, in solid dose form containing 10 mg or less, from pharmacy-only medicine to general sale medicine for the short-term symptomatic relief of gastric reflux-like symptoms in sufferers aged 18 years and older.

The Society **strongly opposes** this proposed reclassification, and refers the committee to our previous submission to the 50th Meeting of MCC:

> Omeprazole is not completely free of the potential for adverse effects, even recently Medsafe has advised health professionals to be alert to the possibility of

hypomagnesaemia in patients taking omeprazole and displaying symptoms such as muscle cramps, weakness, irritability or confusion. [1]

Omeprazole is selective inhibitor of CYP2C19[2] and is therefore capable of interacting with medications that are substrates of this enzyme. An example includes clopidogrel, which was highlighted by Medsafe in their warning in Prescriber Update from 2010 noting a 30% reduction in the mean inhibition of platelet aggregation observed when omeprazole was given at the same time as clopidogrel compared to clopidogrel alone.[3] An earlier Prescriber Update article noted reports that suggested the addition of omeprazole to therapy with clozapine may cause elevated clozapine plasma levels and dose-related adverse effects between clozapine and omeprazole.[4]

While interactions can occur with a number of medications and warnings placed on product packaging etc, the CYP2C19 inhibition and potential to cause clinically significant interactions does place omeprazole in a different level of risk to the public compared to H2-receptor antagonists and antacids or alginates currently classified as general sale.

The submission from Bayer considerably plays down the potential for omeprazole to interact with other medications through it's inhibition of CYP2C19. The submission states a warning will be placed on the product to "seek extra advice if you are taking any other medicines", we would argue that this needs to be qualified advice such as that available when omeprazole is purchased as a pharmacy-only medicine. We doubt many people standing in a supermarket aisle with dyspepsia would refrain from purchasing it just so they could go seek this advice first.

In response to this proposal, pharmacists have sent us comments of the numerous occasions when they have they have determined the patient was experiencing angina symptoms with some also referring the patient to the doctor only to find a gastric cancer and myocardial infarctions.

The Society is extremely concerned that having omeprazole available general sale completely disrupts the generally accepted step-wise approach to dyspepsia management and consumers would see this product as being at the same level as antacids and alginates, when PPIs are our strongest treatment option. The submission from Bayer claims that omeprazole is first line treatment and should be available to consumers, when it is not.

Recent BPAC[5] guidance, which also reflects currently accepted international opinion, explains that lifestyle advice is the usual first-line management. If this does not adequately control symptoms, antacids or alginates can be tried if symptoms are relatively mild. If symptoms are more severe, or persist despite treatment with an antacid or alginate, then ranitidine or omeprazole should be considered. A step-down treatment regimen is appropriate for most patients, where they are gradually weaned

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[1] 'Omeprazole and risk of hypomagnesaemia'. Prescriber Update 2010;31(2):13 http://www.medsafe.govt.nz/profs/PUArticles/OmeprazoleJune2010.htm

[2] Ko JW, Sukhova N, Thacker D, Chen P, Flockhart DA.Evaluation of omeprazole and lansoprazole as inhibitors of cytochrome P450 isoforms. Drug Metab Dispos. 1997 Jul;25(7):853-62.

[3] 'Clopidogrel and omeprazole - interaction now confirmed'. Prescriber Update 2010;31(1):2 http://www.medsafe.govt.nz/profs/puarticles/clopidogrelandomeprazole.htm

[4] 'Omeprazole May Elevate Clozapine Levels'. Prescriber Update 2002;23(3):39 http://www.medsafe.govt.nz/profs/puarticles/clozomep.htm

[5] 'Managing dyspepsia and heartburn in general practice - an update'. Best Practice Journal 34 February 2011. http://www.bpac.org.nz/BPJ/2011/february/dyspepsia.aspx

off the PPI over a period of several weeks. PPIs are not indicated for long-term use and if available for self-selection as a general sale medicine, they will be perceived and used as antacids currently are for those who can afford them.

Antacids, alginates and even H2-receptor antagonists are currently available through supermarkets as a general sale medicine. If these do not adequately manage a consumer's symptoms, then they should be seeking the advice of a health professional who can discuss the symptom history, what treatments have been tried, how they have been taken and what result was obtained. Then an appropriate management plan can be determined, including medical assessment.

Section 2.1 of the submission states "in the event that there is incorrect self-diagnosis, the patient would not unduly aggravate the condition as the label instructs the patient to seek medical advice if symptoms persist for more than 14 days". We believe in the event that this medication was purchased without prior assessment of it's appropriateness by a health professional, that having unresolved symptoms for 14 days is grossly inappropriate advice. The statement that the patient "would not unduly aggravate the condition" after 14 days is incredulous in the context of potential angina or other cardiac symptoms. Furthermore, in saying that "this balance has already been accepted by MCC" fails to recognise that as a Pharmacy Only Medicine, a professional has had input at the point of sale to ask about previous use and presentation of symptoms. This is not available from a supermarket and must not be seen as comparable circumstances. We also believe a 14 day period of supply to be inappropriately long in itself; and in comparison ranitidine is restricted to a 7 day supply as a general sale medicine.

The Bayer submission proposes to reclassify omeprazole as general sale for consumers aged 18 years and over, however no explanation of how such an age limit would be enforced. Would supermarket staff be required to ask for identification? Surely if an age limit is warranted for a medication then it should not be available through general sale. The Society strongly believes that an age limit is appropriate for omeprazole supply without prescription, and this can only be enforced through Pharmacy-Only sales. A number of infants are currently prescribed omeprazole for reflux or "spills", whether appropriate or not, any conversation with a group of mothers or a read of online forums for mothers will highlight the significant use of this treatment in infants. There is every chance a mother at her wits end trying to manage an infant with reflux or colic will try to crush some omeprazole bought through the supermarket in an attempt to manage this.

We cannot rely on product labelling to appropriately inform consumers of the contraindications, precautions and risks of general sale medicines. A study examining 'Societal perspectives on over-the-counter (OTC) medicines' of 1000 patients found that while detailed information may be found in a package insert of an over the counter product, one in every ten people would be at risk of misusing OTC medicines due to rarely or never reading, or only 'sometimes' reading this information on the packaging.(4). This also means that any attempt at restricting supply based on age are left largely redundant, particularly when sales are completely unmonitored and made without any regard for appropriateness or in consideration of the obligations under the Code of Health and Disability Services Consumer Rights.

The Society supports having proton pump inhibitors available over the counter through pharmacies, where symptoms can be discussed with the consumer. The Pharmaceutical Society has previously prepared a treatment algorithm to ensure that supply of omeprazole was safe and appropriate for consumers. This was approved by MCC when it was reclassified from a prescription to pharmacist-only medicines, and continues to be used for supply as a pharmacy-only medicine. The pharmacist or pharmacy staff can ask about treatment history,

how these have worked (including previous PPI use), but also screen for occasions where the presenting symptoms suggest something other than dyspepsia and promptly refer to the GP for a full medical assessment.

We therefore **strongly oppose** this proposed reclassification.

6.3 Paracetamol in combination with phenylephrine

The Society **supports** the reclassification of paracetamol in combination with phenylephrine as proposed. The data presented in the submission, in addition to the NEJM study referenced (5) raises some important considerations.

The NEJM study appears to demonstrate a significant pharmacokinetic interaction, with a markedly increased maximum concentration (Cmax) and Area Under the Curve (AUC) of phenylephrine when combined with paracetamol. The mechanism is proposed to occur through a competitive inhibition of intestinal wall sulfation of phenylephrine by paracetamol. Intestinal wall and 'first-pass metabolism' type interactions generally have greater significance when the affect agent has a low oral bioavailability, which appears to be occurring with this combination.

The interaction also appears to have been reported independently of the evidence presented in the submission by AFT Pharmaceuticals, although these authors hypothesised the difference in bioavailability of phenylephrine was caused by differences in the excipients between the two products (6).

The question of clinical significance of this finding, especially when the efficacy of phenylephrine as a nasal decongestant has been questioned over the years(7),(8) must then be raised. A report by Eccles published in the British Journal of Clinical Pharmacology focused predominantly on the available evidence of efficacy, particularly in comparison to pseudoephedrine, however he makes the important point that:

> *"it is difficult to be confident about the true incidence of side effects and adverse events [of phenylephrine]"* (8).

He goes on to comment on the limited safety data available on phenylephrine:

> *"some concern has been expressed that any switch from pseudoephedrine to phenylephrine may expose patients with cardiovascular disease to a medicine whose safety profile is not so well documented"*

Eccles notes in his report there are a number of patient groups in whom taking phenylephrine would be a concern, including: patients with hypertension, hyperthyroidism, Raynaud's syndrome or heart disease because of the vasoconstrictor effects of the medicines. Similarly those who are taking monoamine oxidase inhibitors should not take phenylephrine due to the interaction increasing oral bioavailability(8). Further evidence is warranted to ensure the combination with paracetamol does not require similar concerns.

It seems we don't have a clear picture of the true risk of adverse effects of phenylephrine. Spontaneous adverse reaction reporting data available online in NZ and the UK do not show a significant prevalence of clinically significant adverse effect reports. However we would expect that spontaneous reporting would grossly underestimate the actual risk of adverse effects presented by phenylephrine use due to difficulties in distinguishing adverse effects such as changes in heart rate, raised blood pressure, headache, from the signs and symptoms of a cold or flu.

In otherwise healthy, young consumers, it would seem that the combination of paracetamol with phenylephrine poses limited clinical risks. However, the Society is concerned at the

potential for previously unappreciated adverse effects in certain patient groups, particularly when:

- General sale classification of the paracetamol + phenylephrine combination means supply is unmonitored
- There appears to be limited epidemiological evidence for the safety of phenylephrine
- Much of the safety data that is available, is clouded by the low and variable bioavailability of phenylephrine, and predominantly taken from studies where phenylephrine was taken alone and by healthy volunteers.

The submission by AFT Pharmaceuticals presents new doubts about the risk:benefit ratio of the paracetamol and phenylephrine combination as a general sale classification.

Thank you for consideration of this submission.

Yours sincerely,

1. Blaiss MS. Safety update regarding intranasal corticosteroids for the treatment of allergic rhinitis. Allergy Asthma Proc Off J Reg State Allergy Soc. 2011 Dec 11;32(6):413–8.

2. Slavin RG. Special considerations in treatment of allergic rhinitis in the elderly: role of intranasal corticosteroids. Allergy Asthma Proc Off J Reg State Allergy Soc. 2010 Jun 5;31(3):179–84.

3. Petty DA, Blaiss MS. Intranasal corticosteroids topical characteristics: side effects, formulation, and volume. Am J Rhinol Allergy. 2013 Dec 11;27(6):510–3.

4. Wazaify M, Shields E, Hughes CM, McElnay JC. Societal perspectives on over-the-counter (OTC) medicines. Fam Pract. 2005 Apr 1;22(2):170–6.

5. Atkinson HC, Stanescu I, Anderson BJ. Increased Phenylephrine Plasma Levels with Administration of Acetaminophen. N Engl J Med. 2014 Mar 19;370(12):1171–2.

6. Janin A, Monnet J. Bioavailability of paracetamol, phenylephrine hydrochloride and guaifenesin in a fixed-combination syrup versus an oral reference product. J Int Med Res. 2014 Apr 1;42(2):347–59.

7. Hatton RC, Winterstein AG, McKelvey RP, Shuster J, Hendeles L. Efficacy and Safety of Oral Phenylephrine: Systematic Review and Meta-Analysis. Ann Pharmacother. 2007 Mar 1;41(3):381–90.

8. Eccles R. Substitution of phenylephrine for pseudoephedrine as a nasal decongeststant. An illogical way to control methamphetamine abuse. Br J Clin Pharmacol. 2007 Jan 1;63(1):10–4.