THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Funding community medicines by exception: a descriptive epidemiological study from New Zealand

Dilky Rasiah, Richard Edwards, Peter Crampton

Abstract

Aims To assess rates of approval and identify factors associated with successful applications for funding to the New Zealand Community Exceptional Circumstances (CEC) scheme.

Method Descriptive quantitative analysis of data in CEC applications database. The main outcome was initial application approval rate. Analysis included calculation of unadjusted and adjusted associations between potential determinants (for example patient age, gender) and outcomes using logistic regression analysis. All CEC applications with a decision about approval or decline 1 October 2001 to 30 September 2008 were included.

Results Application numbers were high, but had reduced since 2001. A small number of medicines (11) and indications comprised about a third of the applications to the scheme. While some common applications were clearly outside the remit of the scheme, many applications were for patients who fitted the scheme's eligibility criteria. The overall initial application approval rate was 16% and the renewal application approval rate was 88%. Approval rates varied widely by type of medicine, therapeutic group and indication.

After adjusting for other potential determinants there were no statistically significant differences in initial approval rates by gender, ethnicity or socioeconomic status of the patient. There were however, significant differences in initial application approval by age of the patient, type of applicant doctor and by geographical location of the applicant doctor.

Conclusions There was no evidence that gender, ethnicity and socioeconomic status of patients were factors associated with successful applications. However, applications for younger patients, those made by specialists, and those made by applying clinicians from the Auckland District Health Board area were more likely to be successful. It is possible that this may to some degree be appropriate, but requires further research.

Many countries face considerable challenges in allocating resources to non-mainstream use of medicines and there is growing interest in the funding of medicines for non-mainstream uses through exceptional circumstances-type schemes.[1–3] A literature review carried out as a preliminary investigation for this study indicated very little had been published internationally evaluating the operation of exceptions-type schemes.

The New Zealand scheme at the time this research was undertaken was similar to some in the United Kingdom (UK).[2] Mainstream pharmaceutical subsidies are

provided for patients in the community at a national population level through the New Zealand Pharmaceutical Management Agency (PHARMAC), via a national community formulary (called the Pharmaceutical Schedule).[4] There has been recent interest in the performance of the mainstream New Zealand scheme in relation to containing pharmaceutical costs.[5]

The Community Exceptional Circumstances (CEC) scheme until early 2012 is New Zealand's community medicines named-patients exceptions funding scheme. It provides access to non-mainstream community pharmaceutical funding for individual patients, and is one of PHARMAC's tools for fulfilling a legislated requirement: "...in exceptional circumstances providing for subsidies for the supply of pharmaceuticals not on the pharmaceutical schedule" (New Zealand Public Health & Disability Act 2000). A risk-pool, currently of up to NZ$3 million is available from within the community pharmaceutical budget to cover the funding of such treatments.

In June 2011 PHARMAC announced changes to the Exceptional Circumstances schemes following a two-stage consultation process that began in 2010. Under the new scheme, to be introduced early 2012, called Named Patient Pharmaceutical Assessment (NPPA), patients no longer need to have rare conditions to be considered for funding and there are a number of other changes. As a result the data presented in this study represents a useful historical analysis and stock-take of aspects of a scheme that has been in existence for approximately a decade. This study used national level data from the New Zealand CEC scheme. The study aimed to describe the extent and scope of the applications for funding to the CEC scheme; to analyse the PHARMAC database to assess the rates of approval/decline for CEC applications and to identify factors which are associated with successful applications.

Methods

All applications for CEC funding made from 1 October 2001 (when PHARMAC became responsible for administration of the scheme) to 30 September 2008 in which a decision about approval or decline available on the PHARMAC database were eligible for inclusion in the study. All other CEC application types, such as those awaiting further information or transferred to another scheme were excluded. Eighty-eight paper CEC applications not held on the database were added. The main outcome considered in the analysis was the initial application approval rate. The outcome of CEC renewal applications were not considered in detail because these applications had a very high approval rate.

There were three main components to the analysis:

- A descriptive analysis of distributions of key variables, of overall approval rates and approval rates in relation to potential determinants;
- Calculation of unadjusted estimates of association (odds ratios) between potential determinants and initial approval; and
- Calculation of adjusted estimates of association (using multivariate logistic regression) between potential determinants and initial approval.

The potential determinants of initial application outcome which were identified and included in the analysis were:

- Type of medicine applied for (medicine and therapeutic group);
- Clinical indication;
- Patient demographic factors including age, gender, ethnicity and socioeconomic status (SES);
- Type of applicant doctor classified by training and geographical location; and
- Application year.

We used multivariate logistic regression analysis to calculate odds ratios adjusted for the following: patient gender, age, SES (deprivation index of census area unit where patient lived), and ethnicity of patient; geographical location (in Auckland or outside Auckland District Health Board (DHB) area) of applicant doctor; nature of applicant doctor (specialist, GP, general registrant (including specialist trainees and those not vocationally registered or training)) and application year.

Due to the large number of indications and therapeutic groups, and the strong correlation between them it was not possible to enter these both into the logistic regression model as it would have created statistical instability. We therefore created a specialty group variable. This was a derived variable which was a combination of indication and therapeutic group grouped into categories according to the initial application approval rate. This variable was used to adjust for indication and therapeutic group within the multivariate model.

Results

Currently, to qualify for Community Exceptional Circumstances approval, one of the following criteria must be met: the condition must be rare; or the patient must have an unusual reaction to alternative funded treatments; or an unusual combination of circumstances applies. 'Rare' conditions and 'unusual' reactions are those which affect as a guide around 10 or fewer people nationally (New Zealand population approximately 4 million).

Supplementary eligibility criteria include suitability of the pharmaceutical, clinical benefit, the cost effectiveness of the treatment, and, although not considered in practice now, the patient's ability to pay for the treatment. In practice, applications are made for a wide range of medications and conditions; no pharmaceutical application is not considered.

Any medical practitioner can apply for CEC funding on behalf of their patients using a CEC application form or by writing to the CEC scheme. Applications are considered by a panel of six doctors which may: approve funding; decline funding; seek further information from the applicant before making a decision; or where the cost of treatment is more than $15,000 make a positive recommendation but refer the decision to PHARMAC . Applicants have the right of appeal following the CEC funding decision.

Number of applications and approval rates by year—Over the 7 years from October 2001 to September 2008 there were 3234 CEC applications that were either approved or declined (Table 1). Most (2564, 79.3%) were initial applications. Overall the initial application approval rate was 16% and the renewal application approval rate was 88%. This suggested that once an approval had been given it was likely to continue to be given via renewals.

The number of applications per year reduced by around two-thirds between 2001/2 and 2006/7, then increased slightly in 2007/8 (Table 1). The initial and renewal approval rates were lowest in 2001/2002 and then increased and fluctuated around the higher level. Initial approval rates were highest in 2007/8 at 34% and renewal approval rates approached 100% in 2006/7 and 2007/8.

Table 1. Outcome of initial and renewal applications by application year

Year	Initial			Renewal			Grand Total
	Approved	Declined	Proportion Approved (95%CI)	Approved	Declined	Proportion Approved (95%CI)	
2001/2002	72	756	0.09 (0.07-0.11)	53	36	0.60 (0.49-0.70)	917
2002/2003	90	323	0.22 (0.18-0.26)	86	12	0.88 (0.80-0.94)	511
2003/2004	57	346	0.14 (0.11-0.18)	62	14	0.82 (0.71-0.90)	479
2004/2005	49	242	0.17 (0.13-0.22)	80	7	0.92 (0.84-0.97)	378
2005/2006	39	198	0.16 (0.12-0.22	78	6	0.93 (0.85-0.97)	321
2006/2007	47	148	0.24 (0.18-0.31)	88	1	0.99 (0.94-1.00)	284
2007/2008	66	131	0.34 (0.27-0.41)	145	2	0.99 (0.95-1.00)	344
Grand Total	**420**	**2144**	**0.16 (0.15-0.18)**	**592**	**78**	**0.88 (0.86-0.91)**	**3234**

Common indications and medicines—The top 20 indications accounted for over 30% of the applications (initial and renewal) over the 7-year period (Table 2). The most common three indications were osteoarthritis, depression then hypertension. Other than four transplant-related indications (approval rate 58–71%), schizophrenia (7.4%) and epilepsy (21.9%), the initial approval rate for all these common indications was less than 3%.

There were 11 medicines with over 40 applications, which accounted for 32% of the initial & renewal applications over the 7 years. They were applied for under multiple indications. For six of these medicines—celecoxib, rofecoxib (both COX-2 inhibitors), venlafaxine, tramadol, clopidogrel and gabapentin—all initial applications were declined. Initial approval percents for the other five medicines most commonly applied for were cyclosporin (60%), sirolimus (48%), tacrolimus (84%) and mycophenolate (40%) (mostly for transplant indications) and fluoxetine (0.02%) (not including dispersible formulation).

Approval rates by therapeutic group—Initial approval rates varied widely by type of medicine and therapeutic groups. The highest initial approval rates were for agents to treat infections and oncology agents and immunosuppressants, at 0.41 (Table 3). The lowest initial approval rate was for musculoskeletal applications at 0.01. The largest number of applications (around a quarter of the total) was for nervous system medicines, which had one of the lowest approval rates.

Analysis of potential determinants of approval rates—Table 4 shows that there were significantly increased odds of initial approval among Asian, Pacific Island and Māori patients compared with European patients in the unadjusted analysis, but after adjustment for other potential confounders, all associations were non-significant except that unknown ethnicity patients had reduced odds of initial approval.

The unadjusted odds ratio for females suggested there was a lower odds of initial approval among females but once adjusted for potential confounders there was no statistically significant association between initial approval and gender. There was no significant association between deprivation and initial approval rate in the unadjusted or adjusted analyses.

Table 2. Twenty most common or applied for indications (initial & renewal applications) October 2001 to September 2008

Indication	Total (initial & renewal) applications	Percent of all (initial & renewal) applications	Percent of each indication's initial applications approved
Osteoarthritis	162	5.0	0.6
Depression	129	4.0	2.4
Hypertension	107	3.3	0.0
Pain	74	2.3	2.9
Transplantation of heart including failure/rejection	61	1.9	58.1
Transplantation of kidney including failure/rejection	58	1.8	61.3
Arthritis	57	1.8	0.0
Rheumatoid arthritis	52	1.6	0.0
Neuropathic pain	50	1.5	2.0
Back pain	49	1.5	2.0
Transplantation of lung including failure/rejection	45	1.4	71.4
Bipolar disorder	43	1.3	0.00
Epilepsy	40	1.2	21.9
Obesity	38	1.2	0.0
Unknown	36	1.1	2.8
Asthma	34	1.1	0.00
Dementia	33	1.0	0.00
Transplantation of liver including failure/rejection	31	1.0	61.1
Musculoskeletal pain including knee, neck, joints	30	0.9	0.0
Schizophrenia including psychosis	30	0.9	7.4
Total	**1159**	**35.8%**	**8.1**

There were however, strong associations between age group and initial application approval, with odds of approval much higher for patients aged 0–4 years (Table 5).

Table 6 shows that the odds of initial approval were over seven times higher among specialist applicants compared with GPs, even after adjusting for other potential determinants. Odds of approval were also increased to a lesser degree among applicants with unknown status or in the general registrant category.

Finally, rates of initial approval were much higher among applicant doctors from the Auckland area than elsewhere in New Zealand. The adjusted odds ratio of initial approval for applicant doctors from non-Auckland DHBs compared with Auckland DHB was 0.52 (95% CI 0.39 to 0.69).

Table 3. Approved and declined initial and renewal applications and proportion approved by Therapeutic Group

Therapeutic Group	Approved	Declined	Proportion Approved (95%CI)	Grand Total
Infections—agents for systemic use	59	86	0.41 (0.33-0.49)	167
Oncology agents and immunosuppressants	144	208	0.41 (0.36-0.46	549
Alimentary tract and metabolism	85	179	0.32 (0.27-0.38)	391
Sensory organs	13	30	0.30 (0.17-0.46)	72
Various	1	4	0.20 (0.01-0.72)	6
Hormone preparations-systemic excluding contraceptive hormones	29	131	0.18 (0.12-0.25)	198
Special foods	9	43	0.17 (0.08-0.30)	73
Blood and blood forming organs	19	125	0.13 (0.08-0.20)	180
Dermatologicals	4	34	0.11 (0.03-0.25)	73
Cardiovascular system	14	155	0.08 (0.05-0.14)	222
Genito-urinary system	4	50	0.07 (0.02-0.18)	64
Nervous system	33	677	0.05 (0.03-0.06)	777
Respiratory system and allergies	3	72	0.04 (0.01-0.11)	84
Musculoskeletal system	3	347	0.01 (0.00-0.02)	375
Grand Total	**420**	**2144**	**0.16 (0.15-0.18)**	**3234***

* Grand total is slightly higher than the sum of the individual therapeutic groups as three applications for which therapeutic group could not be determined have been excluded from the Table.

Table 4. Unadjusted and adjusted odds ratios for initial application approval by ethnicity, gender and deprivation

Variables	Unadjusted odds ratio (95%CI)	*Adjusted odds ratio (95%CI)
Ethnicity (number of initial applications)		
European (1400)	1.00	1.00
Asian (73)	2.48 (1.52-4.04)	1.40 (0.77-2.52)
Pacific Island people (40)	2.44 (1.27-4.70)	1.46 (0.68-3.12)
Māori (189)	1.74 (1.24-2.45)	1.04 (0.66-1.62)
Other including African, Hispanic, Middle Eastern (67)	1.08 (0.59-1.97)	1.30 (0.62-2.73)
Unknown (795)	0.21 (0.14-0.29)	0.26 (0.16-0.42)
Gender (number of initial applications)		
Male (1070)	1.00	1.00
Unknown (11)	2.67 (0.75-9.53)	1.65 (0.35-7.77)
Female (1483)	0.66 (0.53-0.81)	1.08 (0.83-1.41)
Deprivation (number of initial applications)		
Deprivation quintile 1 (365)	1.00	1.00
Deprivation quintile 2 (409)	0.85 (0.59-1.23)	0.99 (0.63-1.56)
Deprivation quintile 3 (484)	0.83 (0.58-1.19)	0.79 (0.51-1.23)
Deprivation quintile 4 (542)	0.97 (0.69-1.37)	1.11 (0.73-1.69)
Most deprived (466)	1.14 (0.81-1.61)	0.95 (0.61-1.48)
Unknown (298)	0.28 (0.16-0.48)	1.50 (0.71-3.15)

*Adjusted for gender, SES and ethnicity of patient (as applicable). All analyses adjusted for age of patient, Auckland/non-Auckland DHBs of applicant; specialty groups (a derived variable which was a combination of indication and therapeutic group, grouped by initial application approval rate); type of applicant; and application year.

Table 5. Unadjusted and adjusted odds ratios for initial application approval by age

Age (number of initial applications)	Unadjusted odds ratio (95%CI)	*Adjusted odds ratio (95%CI)
0 to 4 (143)	1.00	1.00
5 to 16 (210)	0.37 (0.24-0.58)	0.51 (0.30-0.87)
17 to 25 (139))	0.30 (0.18-0.50)	0.41 (0.23-0.75)
26 to 44 (568)	0.17 (0.12-0.26)	0.32 (0.20-0.51)
45 to 64 (735)	0.12 ().08-0.17)	0.25 (0.16-0.41)
65 to 80 (527)	0.06 (0.04-0.10)	0.23 (0.13-0.41)
over 80 (122)	0.09 (0.05-0.19)	0.31 (0.14-0.68)
Unknown (120)	0.04 (0.02-0.10)	0.29 (0.11-0.77)

*Adjusted for gender, SES and ethnicity of patient; Auckland/non-Auckland DHBs of applicant; specialty groups (a derived variable which was a combination of indication and therapeutic group, grouped by initial application approval rate); type of applicant; and application year.

Table 6. Unadjusted and adjusted odds ratios for initial application approval by nature of applicant doctor

Vocational Scope (number of initial applications	Unadjusted odds ratio (95%CI)	*Adjusted odds ratio (95%CI)
GPs (798)	1.00	1.00
Specialist (1353)	19.62 (11.61-33.15)	7.38 (4.24-12.83)
Unknown (214)	6.27 (3.21-12.25)	4.37 (2.13-8.99)
General registrant (199)	5.30 (2.62-10.71)	3.41 (1.59-7.28)

*Adjusted for age, gender, ethnicity and SES of patient; Auckland/non-Auckland DHBs of applicant; specialty groups (a derived variable which was a combination of indication and therapeutic group, grouped by initial application approval rate); and application year.

Discussion

Principal findings—We found that the New Zealand CEC scheme is well used, but the annual numbers of initial applications had declined since 2001. There was a low overall rate (16%) of initial approval, though this may have increased recently at 24% in 2006/7 and 34% in 2007/8.

The reason for the low rate would have been that the applications did not meet any of the entry criteria of the condition being rare or the patient having an unusual reaction to alternative funded treatments or an unusual combination of circumstances applying.

There was a very high rate of renewal approval. There was great variation in approval rates by indication, medicine and therapeutic group. Applications for a small number of medicines and indications comprised a large proportion of the applications to the scheme. Applications for some medicines and indications had very low initial approval rates and appeared to be routinely declined.

The analysis to investigate potential determinants of approval for initial CEC applications found no significant variation in initial approval rate by gender, SES or ethnicity after adjusting for other factors. The three main factors associated which were independently associated with greater approval were younger age of patient,

specialist applicants (as compared to other applicant doctors) and Auckland DHB applicant doctors (as compared to non-Auckland DHB applicants).

Strengths and limitations—The main strength of the study was the availability of a large and comprehensive dataset for a CEC type scheme. The dataset included information on a wide range of potential determinants. When Austin[8] outlined how to formulate a good CEC-type Individual Funding Request scheme, she included having a logging and tracking system as good practice. Because the New Zealand CEC scheme has a used and well-maintained logging and tracking system, we had access to good quality data. Most data was entered by a single person and the data was used to inform a decision so it was more likely to be of a high quality. The limited data to date available on exceptions funding suggests that having such a database is rare.[1]

A limitation of this study was that it only investigated factors associated with successful applications and did not assess whether the volume of applications in relation to need (prevalence of disease) was appropriate. Hence no conclusions can be reached about this aspect of performance of the CEC scheme. A weakness was the frequency of missing data. Of all the determinants considered in the analysis, this was greatest for ethnicity, with over 800 of the 3234 applications (25%) lacking ethnicity data. Furthermore the patients with unknown ethnicity had far lower initial approval rates (Table 4). Therefore, the analysis of initial approval in relation to ethnicity needs to be interpreted with caution. While there is no indication that the unknown group is more likely to come from particular ethnic groups, if they were, the low initial approval rate may mean that this would introduce a bias within the estimates of ethnicity-specific approval rates.

Implications for research and practice—The results show that there is a clear group of commoner indications (and medicines) that rarely meet CEC funding criteria. The PHARMAC information sheet and website provided some information about which indications and medicines are rarely funded. The results of this study suggest that more comprehensive information and communication to prescribers and patients about medicines and indications which are most and least likely to be approved would be helpful; this is likely to be the case for both the current (old) and any new scheme. This could facilitate setting realistic expectations about the likely outcomes of applications, and maximise appropriate applications, ensuring that patients who might meet the CEC eligibility criteria do not miss out because their doctor fails to apply for funding. A more in-depth case-based analysis of the complete process might also be informative in further research.

There are several possible explanations for the differences in initial application outcome by age group, type of doctor and geographical location of doctor. These could include variability in eligibility of applications (which may result in appropriate variations in approval), patient mix (Auckland having some supra-regional and national services especially for rarer diseases and more complex cases) and differences in the quality and completeness of applications. The great degree of variability suggests that further work should be carried out to assess the reasons for the differences in approval rate.

Conclusions—There was no evidence that gender, ethnicity and socioeconomic status of patients were factors associated with successful applications; further research is

required to explore the reasons for the association of applicant doctor type, DHB of applicant doctor and patient age with likelihood of initial approval.

Competing interests: None declared.

Sources of funding: The study was carried out as a dissertation for the Master of Public Health. University fees for the first author were paid by her employer, PHARMAC. The co-authors were involved via their role as university supervisors. The first author (but not the second and third author) and all additional contributors (acknowledged below) are PHARMAC staff members. Study and consultation with additional contributors was carried out during a mixture of personal and work time. There were no other sources of funding and no study sponsor. To the extent that there is a funder, researchers are independent of the funder. PHARMAC management were aware of the contents of the article and the proposal that it be submitted for publication.

Author information: Dilky Rasiah, Deputy Medical Director, PHARMAC, Wellington; Richard Edwards, Head of Department, Department of Public Health, University of Otago, Wellington; Peter Crampton, Pro-Vice-Chancellor, Division of Health Sciences, University of Otago, Dunedin

Acknowledgements: We thank Geoff Lawn and Jayne Watkins for assisting with data extraction; Jason Arnold for running the SAS statistical software analysis package; and Peter Moodie and Scott Metcalfe for reviewing manuscript drafts.

Correspondence: R D Rasiah. PHARMAC, PO Box 10-254, Wellington 6011, New Zealand. Email: dilky.rasiah@pharmac.govt.nz

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