

**GUIDELINES FOR  
APPLICATIONS TO PHARMAC AND PTAC ON  
NEW CHEMICAL ENTITIES,  
NEW INDICATIONS AND FORMULATIONS,  
COMBINATION PRODUCTS AND GENERIC  
PHARMACEUTICALS**

**Version 1.2**

**2005**

Minor amendments made December 2006 and May 2008

Please note that these Guidelines are currently under review. PHARMAC plan to consult on a revised version in early 2009.

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# **Section A: Applications for New Chemical Entity Pharmaceuticals, New Indication, Formulation, or Combination Product**

## **1 Introduction**

This document sets out the information to be submitted in any application for an addition or amendment to the Pharmaceutical Schedule.

Applications and supporting information should be sent to:

Chief Executive  
PHARMAC  
Level 14  
Cigna House  
40 Mercer Street  
PO Box 10-254  
WELLINGTON 6011

**Attention: Funding and Procurement Assistant**

These guidelines are subject to the policies and procedures set out in PHARMAC's Operating Policies and Procedures ("OPPs") (which are available on line at <http://www.pharmac.govt.nz/download/OPPs.pdf>), including those in section 4 of the OPPs.

## **2 General Matters**

### **2.1 Balanced Information**

The application must include all relevant information known to the applicants, including data that is contrary to or does not necessarily support their case.

### **2.2 Estimates and Assumptions**

In all cases where estimates and assumptions are made, these should be clearly and explicitly stated and include the underlying reasons for making them and their source. Estimates and assumptions may be indicated in ranges.

### **2.3 Recommended Methods to Derive Clinical Inputs**

Details of desirable clinical information to supplement the information asked for in section 3.2 (B) 'Therapeutic Information' below, can be found in PHARMAC's Version 2 of the Prescription for Pharmacoeconomic Analysis (PFPA) (on-line at <http://www.pharmac.govt.nz/pdf/PFPAFinal.pdf>) and in the 'Recommended Methods to Derive Clinical Inputs for Proposals to PHARMAC' (which supplements chapter 4 'Clinical Inputs' of Version 2 of the PFPA, and is on-line at <http://www.pharmac.govt.nz/pdf/62465.pdf>).

Please note that some of the information requested is an ideal, and may not be relevant or necessary for every application. As a general guide, greater clinical and

epidemiological detail is needed for pharmaceuticals with major potential impacts on total costs and/or population health gains compared with those having a smaller impact.

## **2.4 Confidentiality**

The confidentiality of applicants' submissions is addressed in clause 4.3 of the OPPs.

## **2.5 Incomplete Applications**

If an application is incomplete in any way, or if clarification is required, PHARMAC may contact the applicant and may defer consideration by PTAC until the applicant has resolved any outstanding issues.

# **3 Format and Content**

The synopsis, application and supporting information should be provided in spiral bound volumes with the date of the application on the front cover. Applicants should also supply one electronic copy of the application on Compact Disk with three documents – synopsis, application and references/literature.

## **3.1 Synopsis**

Applicants must provide **fifteen** copies of a brief synopsis (we recommend ten pages or less) of all material issues referred to in the application and supporting information. The synopsis will be used as a general information guide for PHARMAC staff and will be included in the PTAC meeting agenda papers.

Copies of the synopsis must be provided separately from the rest of the application.

## **3.2 Full Application**

Applicants must provide **fifteen** copies, containing the following information (in the order set out below). Where any information is not available or is otherwise not supplied, please state this explicitly under the relevant heading(s).

### **3.2 (A) Pharmacological Information**

Please provide the following pharmacological information:

- (i) official or approved names of the pharmaceutical;
- (ii) forms, strengths and arranged pack sizes:  
*In the case of a preparation such as an aerosol, state the number of doses available from the container;*
- (iii) principal pharmacological action of the pharmaceutical;
- (iv) indications registered in New Zealand, and other common uses;
- (v) recommended dosages for each of the indications provided in connection with (iv) above:  
*In the case of a pharmaceutical that is not used for chronic therapy, provide information on the average length of a treatment course and anticipated frequency of repeat courses of treatment; and*
- (vi) any contra-indications, interactions and adverse effects:

*Include information on any necessary dosage adjustments and cautions required when using the pharmaceutical in conjunction with other pharmaceuticals.*

### **3.2 (B) Therapeutic Information**

Please provide the following therapeutic information:

- (i) the therapeutic group and/or sub-group into which the applicant considers the pharmaceutical should be listed on the Pharmaceutical Schedule;
- (ii) a summary statement of the main therapeutic claims for the pharmaceutical and its proposed use;
- (iii) how the pharmaceutical compares clinically with pharmaceuticals already listed on the Pharmaceutical Schedule, including:
  - what (if any) advantages the pharmaceutical offers over existing pharmaceuticals in terms of efficacy and/or side effects:
    - whether the pharmaceutical is equivalent to existing pharmaceuticals;
    - whether the pharmaceutical is more effective than existing pharmaceuticals;
    - whether the pharmaceutical has a similar efficacy to existing pharmaceuticals but has fewer side effects;
  - whether the pharmaceutical is associated with similar, greater or fewer side effects and/or toxicity than existing pharmaceuticals;
  - whether the pharmaceutical offers greater convenience (e.g., once daily dosing) than existing pharmaceuticals;
- (iv) whether the pharmaceutical has a longer shelf life than existing pharmaceuticals; and
- (v) other pharmaceuticals, medical devices, related products or things, if any, likely to be prescribed for use in conjunction with the pharmaceutical as part of a course of treatment.

*Include pharmaceuticals that may be used to manage any side effects.*

For further details of desirable supplementary clinical information, and in what order to place any such information, refer to section 2.3 above, Version 2 of the PFPA (<http://www.pharmac.govt.nz/pdf/PFPAFinal.pdf>), and its supplementary 'Recommended Methods to Derive Clinical Inputs for Proposals to PHARMAC' (<http://pharmac/pdf/62465.pdf>)

### **3.2 (C) Price Information**

Please provide the following price information:

- (i) the supplier's selling price in \$NZ (ex-manufacturer, GST exclusive);
- (ii) the supplier's selling prices to wholesalers in other countries where the pharmaceutical is marketed (in local currencies (excluding local taxes) and New Zealand dollar equivalents – please note the exchange rates used); and
- (iii) alternative pricing proposals (e.g., possible price/volume trade-offs).

### **3.2 (D) Epidemiological Information**

For each recommended indication, please provide estimates for the first five years of listing (shown on a year-by-year basis) of:

- (i) the number of people in New Zealand with the particular condition(s);
- (ii) where available, the number of Maori people in New Zealand with the particular condition(s);
- (iii) where available, the number of Pacific peoples in New Zealand with the particular condition(s);
- (iv) the number of people in New Zealand likely to seek treatment for the condition(s); and/or the number of people in New Zealand likely to be prescribed the pharmaceutical; and
- (v) a breakdown of the number of people in New Zealand treated for the condition by:
  - those who can be successfully treated by the pharmaceutical only;
  - those who can be treated by both the pharmaceutical and other pharmaceuticals that treat the same condition;
  - those who can be treated by only other pharmaceuticals; and
  - those who can be treated, completely or partially, by other therapies.

Further details of desirable epidemiological information can be found in the two sections 'Epidemiology, Public Health Significance and Estimated Utilisation' and 'Need by Maori and Pacific peoples' of the supplementary 'Recommended Methods to Derive Clinical Inputs for Proposals to PHARMAC' (<http://pharmac/pdf/62465.pdf>).

In all cases where estimates and assumptions are made or used, please clearly and explicitly state the bases underlying those estimates and assumptions, including sources. Estimates and assumptions may be indicated in ranges.

### **3.2 (E) Market Information**

Please provide the following market information:

- (i) estimated average daily dose (ADD) information for New Zealand (and other markets where possible) and estimated average daily cost (ADC) of treatment for New Zealand;
- (ii) expected sales (dollars and volume) for the first five years of listing, to be shown on a year-by-year basis with anticipated market segments and projected market shares; and
- (iii) what marketing will be used for the pharmaceutical and how this will relate to market penetration.

The ADD, ADC and expected sales information referred to in (i) and (ii) above should be supported by data from major OECD markets and other markets where the pharmaceutical is available (i.e. therapeutic indication(s) and use, ADD information, ADC of treatment, and sales). These data should cover the time period from product launch within each market to the date of the application, on a year-by-year basis.

### 3.2 (F) Costs and Benefits

Where available, please provide a cost-utility analysis (CUA) on the proposal to list or widen access to the pharmaceutical. Please refer to Version 2 of the Prescription for Pharmacoeconomic Analysis (PFPA) for details on CUA methodology that should be used for consideration by PHARMAC (<http://www.pharmac.govt.nz/pdf/PFPAFinal.pdf>)

Economic principles used by PHARMAC include:

- using costs to the Pharmaceutical Schedule, other health sector (Vote: Health) costs and direct patient costs when measuring effects on overall costs;
- measuring gains in quality-adjusted life expectancy (QALY gains);
- discounting both costs and QALY gains according to PHARMAC's current rate (3.5%); and
- uni/multivariate sensitivity analyses.

Please include these aspects in any economic analyses submitted to PHARMAC, along with the detail of their clinical assumptions as described by the supplementary 'Recommended Methods to Derive Clinical Inputs for Proposals to PHARMAC' (<http://pharmac/pdf/62465.pdf>).

### 3.2 (G) Decision Criteria Assessment

Please provide evaluation of the proposal against as many as possible of PHARMAC's nine decision criteria, described below.

#### ***Some important contextual notes about the decision criteria and questions listed beneath them***

When making decisions on proposals, PHARMAC uses the decision criteria set out below and gives such weight to each criterion as it considers appropriate. These decision criteria are set out in section 2.2 of PHARMAC's OPPs. The criteria are also used by PTAC when it assesses applications.

Below, under each of the listed criteria, is a series of questions. The questions have been included to help applicants to address each criterion. PHARMAC has also identified some potentially relevant supporting information, which it would, where available, be helpful for applicants to provide in relation to each criterion.

The questions and supporting information identified below do not limit either the application of each criterion or the factors PHARMAC may consider under each criterion.

The decision criteria are:

- The health needs of all eligible people within New Zealand;**  
What health need(s) does this proposal meet?
- The particular health needs of Maori and of Pacific peoples;**

What particular health need(s) of Maori and of Pacific peoples does this proposal meet?

- (iii) **The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;**

What other interventions are currently available to meet these health needs – if there are none, what other health sector resources are used managing the need(s)?

- (iv) **The clinical benefits and risks of pharmaceuticals;**

What health benefits and risks does the proposal provide, including in comparison with the other interventions outlined above?

Where available, include estimates of

1. absolute risk reductions (ARR) in events (specify) or improvement in health states (specify) caused by the proposal; and
2. discounted QALY gains per patient treated over one year.

- (v) **The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services;**

What is the incremental cost (or saving) and incremental benefit (or risk) compared with the other interventions?

Where available, include an estimate of incremental cost-utility ratio (ICUR) in cost per QALY.

- (vi) **The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule;**

What impact does this proposal have on the pharmaceutical budget and the overall health budget, both for the current financial year and the net present value (NPV) of the effects over future years?

- (vii) **The direct cost to health service users;**

How are patients' out-of-pocket expenses changed by the proposal?

- (viii) **The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere; and**

- (ix) **Such other criteria as PHARMAC thinks fit. PHARMAC will carry out appropriate consultation when it intends to take any such "other criteria" into account.**

Note that PHARMAC is not bound to accept the applicant's evaluation of the application against the decision criteria, and may attribute different weightings to the criteria.

### **3.2 (H) Supporting Literature**

Please provide a copy of your search strategy.

Where possible, please provide copies of articles published in the peer-reviewed international medical literature.

All articles submitted should be written in English or accompanied by a certified English translation.

Information provided should relate only to the pharmaceutical and disease(s)/indications under consideration. Unrelated or irrelevant articles will not be reviewed.

Copies of unpublished articles or studies that have been submitted for peer review will also be accepted for consideration. If the published article becomes available after the application has been submitted, applicants may substitute the draft with the final version.

Please do not submit copies of any case histories or clinical correspondence relating to individual patients.

Where possible, critically appraise and grade the articles using the methods described in PHARMAC's 'Recommended Methods to Derive Clinical Inputs for Proposals to PHARMAC' (on-line at <http://pharmac/pdf/62465.pdf>).

Subdivide the copies of the articles, with their accompanying appraisals and gradings (where applicable), into each of the following three categories:

- (i) **published Grade 1 evidence of effectiveness**, i.e. randomised controlled trials (RCTs) of efficacy (individual RCTs and meta-analyses of RCTs);
- (ii) **published Grade 2-3 evidence of effectiveness**, i.e. controlled but non-randomised experimental studies and non-analytic uncontrolled descriptive data for efficacy (prospective cohort studies, case control studies, before-and-after studies longitudinal studies, uncontrolled observational studies, case reports); and
- (iii) **published Grade 4 evidence of effectiveness PLUS all other published material**, i.e. non-systematic reviews, expert opinion, economic modelling/analyses in absence of direct empirical data, background epidemiology and natural history of the disease/indication, and other published material relevant to the proposal.

Within each group, please order articles by date of publication.

### **3.2 (I) Gazette Notice**

Please include a copy of the gazette notice or the notice to distribute a changed medicine.

### **3.2 (J) Data Sheet**

Please include a copy of the approved data sheet.

**3.2 (K) Sample**

Please provide one labelled sample of the pharmaceutical, as appropriate. More samples may be required.

**3.2 (L) MAAC Response**

Please include a copy of New Zealand Medicines Assessment Advisory Committee (MAAC) response to registration application.

## **Section B: Guidelines for Applications to PHARMAC/ PTAC on Generic Pharmaceuticals**

### **1 Introduction**

This document sets out the information to be submitted in any application made by suppliers for an addition or amendment to the Pharmaceutical Schedule with respect to generic pharmaceuticals. Please note that if the chemical entity has not previously been considered by PTAC, please refer to Section A of the application guidelines.

Applications and supporting information should be sent to:

Chief Executive  
PHARMAC  
Level 14  
Cigna House  
40 Mercer Street  
PO Box 10-254  
Wellington 6023

**Attention: Funding and Procurement Assistant**

### **2 General Matters**

#### **2.1 Balanced Information**

The application must include all relevant information known to applicants, including data that is contrary to or does not necessarily support their case.

#### **2.2 Estimates and Assumptions**

In all cases where estimates and assumptions are made, these should be clearly and explicitly stated and include the underlying reasons for making them and their source. Estimates and assumptions may be indicated in ranges.

#### **2.3 Confidentiality**

The confidentiality of applicants' applications is addressed in Clause 4 of PHARMAC's Operating Policies and Procedures (OPPs) (on line at <http://www.pharmac.govt.nz/download/OPPs.pdf>).

#### **2.4 Incomplete Applications**

If an application is incomplete in any way, or if clarification is required, PHARMAC may contact the applicant and may have to defer consideration by PTAC until the applicant has resolved any outstanding issues.

## **3 Format and Content of Applications**

### **3.1 Synopsis**

Applicants must provide one copies of a brief synopsis of all material issues referred to in the application and supporting information. The synopsis and supporting information should be provided in a soft cover folder, with two holes punched, and the date of application on the front cover. Please also provide an electronic copy of the application.

Copies of the synopsis must be provided separately from the supporting information.

If it is decided that the application needs to be discussed at PTAC, then a further fourteen copies of the synopsis, and supporting information will be required.

### **3.2 Other Required Information**

#### **Registration Status**

Supporting the application should be one copy of the following information (in the order set out below):

#### **3.2 (A) Pharmacological Information**

Pharmacological information about:

- (i) official or approved names of the pharmaceutical;
- (ii) forms, strengths and arranged pack sizes:  
*In the case of a preparation such as an aerosol, the number of doses available from the container should be stated;*
- (iii) expected date of Medsafe registration and indication if being fast-tracked; and
- (iv) approved indications.

#### **3.2 (B) Therapeutic Information**

Therapeutic information about:

- (i) the efficacy of the generic compared with existing pharmaceuticals and the side effect and toxicity profile of the generic;
- (ii) its bioequivalence study;
- (iii) whether the pharmaceutical has a longer shelf-life than brands currently listed; and
- (iv) any differences between generic and other brands currently listed.

#### **3.2 (C) Price Information**

Price information about:

- (i) the supplier's selling price (GST exclusive); and
- (ii) alternative pricing proposals (e.g., possible price/volume trade-offs).

#### **3.2 (D) Market Information**

Estimated size of market and expected uptake.

**3.2 (E) Patents**

Any patent investigation carried out by the supplier

**3.2 (F) Gazette Notice**

A copy of the gazette notice or the notice to distribute a changed medicine.

**3.2 (G) Data Sheet**

A copy of the approved data sheet.

**3.2 (H) Sample**

One labelled sample of the pharmaceutical, as appropriate. More samples may be required.