

Guidelines

for Funding Applications to PHARMAC

Amended in 2017



PHARMAC
Pharmaceutical Management Agency

newzealand.govt.nz

Foreword

PHARMAC, the Pharmaceutical Management Agency, is primarily responsible for managing the funding of pharmaceuticals for New Zealanders, on behalf of the district health boards. PHARMAC's objective is to secure, for eligible people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the amount of funding provided.

Each year, PHARMAC receives a large number of Applications containing proposals for the funding of a pharmaceutical or changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule, for example a proposal to widen or restrict access. As PHARMAC must work within a fixed budget, difficult choices need to be made about which of the proposals should be progressed to a funding decision. This involves assessing a large amount of often complex information to identify proposals that would provide the best health outcomes.

In deciding which proposals to fund, PHARMAC assesses each proposal against its Factors for Consideration (Factors), which include consideration of health benefits, need, costs and savings, and suitability. All proposals are ranked against all other funding options according to the Factors.

In this context of what we call 'relative assessment' (comparing one option against another), it is important that applicants provide good-quality, complete and balanced Applications that follow these *Guidelines*.

Good-quality Applications will focus on information relating to the Factors, which include:

- critical appraisal of key clinical evidence, particularly health benefits to the person, wider society and the health system
- complete market and epidemiological information and, when relevant, the impact on Māori health and/or other populations with health disparities
- information on cost-effectiveness (based on PHARMAC's methodology for cost-utility analysis), including direct and indirect health care costs
- evidence indicating health need/impact on and cost/savings to the person, others (family, whānau, and wider society), and the health workforce
- disclosure of information on all known ongoing trials and patents.

Good-quality Applications will be clear, cite all sources, explain all assumptions, and include all information of material importance. A **thorough yet succinct** Application is likely to expedite PHARMAC's review, potentially enabling the proposal in the Application to be ranked earlier.

Please note that the information requested in these *Guidelines* is not mandatory. The information we have requested is information that PHARMAC requires when assessing a proposal. The purpose of these *Guidelines* is to provide you with some guidance on how to compile an Application that is useful to us. We do not want to impose any unnecessary burden or create any barriers to submitting an Application. For this reason we strongly recommend that you contact PHARMAC before submitting an Application, as in certain circumstances less information may be required.

If the information requested in these *Guidelines* is not provided, it is likely that PHARMAC will either contact you for the information at some stage or undertake its own searches or analysis (which may result in time delays). Therefore, even though the information requested is not mandatory, there are significant advantages in providing thorough Applications following these *Guidelines*.

If the application is for the funding of a generic or biosimilar pharmaceutical, and the pharmaceutical (including the indication applied for) has previously been assessed by PHARMAC, less information may be required. Please refer to section 7 and 8 of these *Guidelines* for further details.

Anyone can submit a funding Application to PHARMAC; however, these *Guidelines* may be of most use to suppliers of pharmaceuticals. We strongly encourage all applicants to contact PHARMAC (+64 4 460 4990 or 0800 660 050) before submitting an Application. You will be transferred to the relevant Therapeutic Group Manager, who can answer any questions you may have and confirm what the appropriate procedure is and what information needs to be provided.

First step

Please call PHARMAC (+64 4 460 4990 or 0800 660 050) for all inquiries about Applications for the funding of a pharmaceutical or changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule, for example a proposal to widen or restrict access. We will direct you to the relevant Therapeutic Group Manager.

Send all Funding Applications and supporting information to:

Manager Pharmaceutical Funding
PHARMAC
Level 9
40 Mercer Street
PO Box 10254
WELLINGTON 6143

Checklist for funding Applications

The checklist below outlines the information required when submitting an Application to PHARMAC for an amendment to the Pharmaceutical Schedule. If anything is unclear, please check the glossary in Appendix 1 and contact PHARMAC if you need further clarification.

CHECKLIST FOR FUNDING APPLICATIONS TO PHARMAC		
	Page	
CRITERIA		
Application is for an amendment to the Pharmaceutical Schedule	11	Y/N
STRUCTURE OF APPLICATION		
Separate synopsis provided	21	Y/N
Spiral bound copies clearly labelled and each section indexed	19	Y/N
Front cover states pharmaceutical name, brand name, date of Application, name of pharmaceutical supplier and name of applicant (including name, phone number and email address of contact person)	19	Y/N
Table of contents included	19	Y/N
Three hard copies provided and one electronic copy	19	Y/N
MAIN CONTENT		
Pharmacological information	22	Y/N
Proposed changes to the Pharmaceutical Schedule	23	Y/N
Epidemiological information	24	Y/N
Price information	26	Y/N
Market information	23	Y/N
Patent information	27	Y/N
Impact on health sector	28	Y/N
Search strategy used for identifying clinical trials	28	Y/N
Clinical evidence to include in application	29	Y/N
Order of attachments	30	Y/N
Presentation of randomised controlled trials	30	Y/N
Critical appraisal and grading of clinical evidence	31	Y/N
Safety	32	Y/N
Impacts on health outcomes	32	Y/N
Applicability of the evidence to the New Zealand health sector	32	Y/N
Suitability	33	Y/N
Summary of Application evaluated against PHARMAC's Factors for Consideration	33	Y/N
MAIN ATTACHMENTS		
Medsafe-approved datasheet	22	Y/N
New Zealand Medicines Assessment Advisory Committee (MAAC) response to the registration application	22	Y/N
Copies of all identified randomised controlled trials published in peer-reviewed journals, subdivided by grade of evidence and ordered by date of publication	29	Y/N
One complete hard copy of the clinical study report summaries from the pivotal trials	29	Y/N

CHECKLIST FOR FUNDING APPLICATIONS TO PHARMAC		
Copies of all errata, editorials and journal correspondence relating to published trials	29	Y/N
Register of all ongoing trials on the pharmaceutical	29	Y/N
Declaration that all known unpublished clinical trials have been disclosed	29	Y/N
One labelled sample of the pharmaceutical inside its packaging (unless Application is for widening of access)	34	Y/N
ADDITIONAL CONTENT		
Cost-utility analysis based on the methods outlined in the Prescription for Pharmacoeconomic Analysis (including all costs estimated in \$NZ)	36	Y/N
Additional information on health need and public health significance	25	Y/N
Additional information on health need by Māori	38	Y/N
Additional information on population groups experiencing a health disparity	38	Y/N
ADDITIONAL ATTACHMENTS		
Copies of relevant EMEA European Public Assessment Reports (EPARs) and FDA medical reviews	35	Y/N
Review articles and published critiques	35	Y/N
International guidance and recommendations	35	Y/N
Published cost-utility analyses	35	Y/N
Expert opinion and consensus reports from expert panels	35	Y/N
Where a cost-utility analysis is included, an electronic copy of the TreeAge™ model or Excel™ spreadsheet	36	Y/N
REAPPLICATIONS		
The Reapplication addresses all of the issues/concerns raised when the original Application was assessed	41	Y/N
List of all new information provided, along with copies of the new information	41	Y/N
APPLICATIONS FOR THE FUNDING OF GENERIC OR BIOSIMILAR PHARMACEUTICALS		
Registration and indication details	42	Y/N
Pharmaceutical information (including one labelled sample)	42	Y/N
Price information	43	Y/N
Market information	43	Y/N
Patent information	43	Y/N
Lead times	43	Y/N
APPLICATIONS FOR THE FUNDING OF BLOOD GLUCOSE METER SYSTEMS		
International information	44	Y/N
Product information	44	Y/N
Price information	45	Y/N
Lead times	45	Y/N

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1. Background

1.1 What Is PHARMAC?

PHARMAC, the Pharmaceutical Management Agency, is a Crown entity that is directly accountable to the Minister of Health. Our functions are set out in section 48 of the New Zealand Public Health and Disability Act 2000 (NZPHD Act).

One of PHARMAC's functions is to maintain and manage a pharmaceutical schedule that applies consistently throughout New Zealand, including determining eligibility and criteria for the provision of subsidies, which is the list of pharmaceuticals that are publicly funded. Thus, we may refer to a funded pharmaceutical as being 'listed', or to Applications as containing proposals to 'list' a pharmaceutical or to 'make amendments to the Pharmaceutical Schedule'.

We also negotiate national contracts for pharmaceuticals used by district health board (DHB) hospitals and these are also listed in the Pharmaceutical Schedule (Part II of Section H, also known as the Hospital Medicines List or HML).

PHARMAC's principal objective is:

to secure for eligible people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the amount of funding provided. Section 47(a) of the NZPHD Act

Further information can be found at: <https://www.pharmac.govt.nz/>

1.2 What Is a 'Pharmaceutical'?

The term 'pharmaceutical' is defined in the NZPHD Act as "a medicine, therapeutic medical device, or related product or related thing".

The term pharmaceutical should be interpreted for the purposes of these *Guidelines* to mean a medicine, including for example vaccines, generics and biosimilars or medical devices.

It will generally be evident which type of pharmaceutical is being referred to by its description within the *Guidelines*.

1.3 Purpose of the Funding Application Guidelines

The purpose of these *Guidelines* is to provide guidance on how to prepare Applications to PHARMAC for proposed amendments to the Pharmaceutical Schedule.

The *Guidelines* are subject to PHARMAC's Operating Policies and Procedures: <https://www.pharmac.govt.nz/about/operating-policies-and-procedures/>

This document is intended to assist anyone wanting to make an Application to PHARMAC for a proposed amendment to the Pharmaceutical Schedule. See section 2.2 of this document for further information on using these *Guidelines*.

2. The application process

PHARMAC has an established process for deciding which pharmaceuticals, and which of their possible uses (indications), to fund. The decision-making process described in this document is the process that PHARMAC generally follows with an Application for a proposed amendment to the Pharmaceutical Schedule.

2.1 Who can initiate an application?

There are no restrictions on who can make an Application to PHARMAC. Applications can be made by anyone, including a health professional, a supplier or an individual.

Before making an Application for a proposed amendment to the Pharmaceutical Schedule, please call PHARMAC on +64 4 460 4990 or 0800 660 050. We will direct you to the relevant Therapeutic Group Manager, who will discuss the nature of the proposed amendment with you. They will confirm what the appropriate procedure is and what information needs to be provided to PHARMAC.

2.2 When do these Guidelines apply?

Proposed amendments to the Pharmaceutical Schedule where these *Guidelines* apply include Applications for:

- (i) funding new pharmaceuticals for use in the community, including community medical devices*
- (ii) funding new hospital pharmaceuticals, excluding hospital medical devices*
- (iii) changing funded access to an already listed pharmaceutical (eg for new uses or patient groups)
- (iv) funding generic or biosimilar pharmaceuticals where PHARMAC has not previously considered an application to fund the pharmaceutical
- (v) funding new formulations or strengths of already funded pharmaceuticals
- (vi) funding combination products (products that consist of two or more pharmaceuticals).

*PHARMAC currently funds a small number of medical devices that are used in the community. Applications for Pharmaceutical Schedule listings for these kinds of medical devices need to be made in accordance with these *Guidelines*. As PHARMAC is in the relatively early stages of its hospital medical devices work, it is generally not asking suppliers to submit Applications as described in this document. There may be pharmaceuticals that have characteristics of both medicines and medical devices that fall into a grey area. Suppliers seeking to sell these kinds of pharmaceuticals to DHBs are advised to check with PHARMAC whether their pharmaceutical falls within the scope of PHARMAC's activity.

Medical device suppliers that are seeking to list products on the Pharmaceutical Schedule, and are unsure of what information PHARMAC requires, should contact PHARMAC for advice.

Applications relating to a generic or biosimilar pharmaceutical where funding of the pharmaceutical has previously been considered by PHARMAC should follow section 8 of these *Guidelines* only.

Clinicians, consumers and clinical groups can apply for an amendment to the Pharmaceutical Schedule using the application form available at: <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/new-funding-applications/>.

These *Guidelines* **do not** apply to funding of pharmaceuticals for individual patients. More information for the funding of individuals through the Named Patient Pharmaceutical Assessment process can be found at: <https://www.pharmac.govt.nz/tools-resources/forms/exceptional-circumstances/>.

If you have concerns about the safety of a pharmaceutical funded by PHARMAC, or consider that a pharmaceutical should be removed from the Pharmaceutical Schedule, please write to PHARMAC outlining your concerns. PHARMAC staff will let you know what course of action will be taken. Please note that it is Medsafe (the New Zealand Medicines and Medical Devices Safety Authority, a business unit of the Ministry of Health) that is responsible for pharmaceutical regulation and safety matters), so Medsafe should be approached in the first instance on all issues related to the safety of a pharmaceutical.

Applications to PHARMAC should be for Medsafe-registered products and indications. If the pharmaceutical is not registered, or if the Application is for a registered pharmaceutical for use in an unregistered indication, please contact PHARMAC to discuss the Application with the relevant Therapeutic Group Manager before submitting an Application to PHARMAC.

2.3 What is the process for submitting an Application?

Please ensure Applications adhere to the content, format and organisation stipulated in this document. Section 3 of these *Guidelines* gives details on the format required for Applications to PHARMAC.

2.3.1 Confidentiality and application of the Official Information Act

Any information we receive as part of an Application is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing information should be aware the content of the information and identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your information as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential, proprietary or personal information included in your Application, please clearly state this in your Application and identify the relevant sections of your Application that you would like withheld. PHARMAC will give due consideration to any such request.

2.4 How does PHARMAC process and assess Applications?

When an Application is received, PHARMAC reviews the Application to ensure it contains the information PHARMAC requires to assess the proposal. If an Application is incomplete in any way, or if clarification is required, PHARMAC may contact the applicant and may defer consideration of the Application until the applicant has resolved any outstanding issues.

Application details will be published on PHARMAC's website, including the name of the pharmaceutical and the proposed indication for funding:
<http://www.pharmac.govt.nz/patients/ApplicationTracker>.

If PHARMAC considers that clinical advice on the Application is required, the first step in the assessment process will be a review of the Application by the Pharmacology and Therapeutics Advisory Committee (PTAC) or, in some cases, one of the specialist PTAC subcommittees.

PHARMAC, in consultation with the PTAC Chair, may consider:

- (i) whether a particular Application should be referred directly to PTAC for advice
- (ii) whether a particular Application should be referred directly to the relevant subcommittee (i.e. before PTAC considers it)
- (iii) whether it wishes to invite relevant medical groups and other interested parties to comment on the pharmaceutical that is the subject of the Application before the Application is considered by PTAC or a Subcommittee. Where we seek comments, the main objective will be to enable interested parties to outline specific issues relating to the pharmaceutical (in relation to PHARMAC's Factors) early in the PHARMAC decision making process. These comments will then be considered by PTAC or a Subcommittee when it considers the Application.

The decision to submit an Application to PTAC (including the decision about which PTAC meeting to send it to) after the Application is received is at the discretion of PHARMAC in consultation with the PTAC Chair. If PHARMAC decides not to submit the Application to PTAC, PHARMAC will inform the applicant of the reasons for this.

If an Application is submitted for consideration at a particular PTAC or Subcommittee meeting, PHARMAC staff will usually draft a cover paper for the Application, which will generally include (but will not be limited to):

- a summary of the proposal (the pharmaceutical, indications, pharmaceutical supplier, proposed subsidy, etc)
- questions to PTAC and/or the Subcommittee
- previous PTAC and/or Subcommittee minutes (if relevant)
- a brief description of the disease and current treatment in New Zealand
- a brief description of the pharmaceutical under consideration (including clinical evidence and any proposed restrictions or changes to access)
- international prices of the pharmaceutical
- an estimated cost of funding
- cost-effectiveness (if available and relevant)
- PHARMAC's Factors.

2.4.1 PTAC review of Applications

PTAC is PHARMAC's primary clinical advisory committee. Its role is to provide objective advice to PHARMAC on pharmaceuticals and their benefits. PTAC's members are appointed by the Director-General of Health in consultation with the PHARMAC Board. PTAC comprises senior health practitioners with expertise in critical appraisal and broad experience and knowledge of pharmaceuticals and their therapeutic uses. There are also several PTAC Subcommittees, made up of experts in specialist clinical fields such as cardiology and oncology. PHARMAC and/or PTAC often seek advice from a specialist PTAC Subcommittees.

When considering an Application, PTAC will review and critically appraise the clinical evidence. It uses the same Factors as PHARMAC when evaluating Applications. PTAC makes recommendations to PHARMAC regarding amendments to the Pharmaceutical Schedule and assigns priority ratings to these recommendations (typically high, medium or low). PTAC may also recommend that an Application be cost-neutral, declined or deferred, giving reasons for the deferral, such as supply of further information. When making recommendations to PHARMAC, PTAC indicates which Factors it has given particular weight to. These recommendations are taken into account when PHARMAC sets its funding priorities. Generally, if a proposal in an Application is given a high PTAC priority and the proposed amendment to the Pharmaceutical Schedule is relatively cost-effective or has other value under PHARMAC's Factors, it may be progressed sooner than a proposal that has been given a low PTAC priority or one that is not as cost-effective. A positive recommendation by PTAC and/or its Subcommittees, however, is no guarantee of funding as the role of PTAC and PTAC Subcommittees is to advise PHARMAC on matters referred to them. PHARMAC is not bound to follow the recommendations made.

If PTAC considers that further specialist advice is needed before making a recommendation to PHARMAC, the Application may be referred to a PTAC Subcommittee. Applications may also be referred to PTAC Subcommittees for advice on developing or refining access criteria. If PTAC considers that further information is required from the applicant, this will be referred back to the applicant.

A copy of the relevant part of the PTAC/subcommittee minute is sent to the applicant. The applicant then has 10 working days to review the minute and to make a request for the withholding of all or part of the minute from public release. When we consider requests for withholding part or all of the PTAC/Subcommittee minutes, PHARMAC is guided by the grounds for withholding information specified in the OIA. In some instances where the Application has not been made by the pharmaceutical supplier, the minute may be sent to the relevant pharmaceutical supplier as well as the applicant for review and feedback. This usually occurs if we consider that there is a possibility that the supplier may object to the release of part or all of the minute. Following this review, the minutes may be published on the PHARMAC website.

Further details about PTAC and PTAC Subcommittees can be found in the PTAC Terms of Reference, which are available on the PHARMAC website <https://www.pharmac.govt.nz/about/committees/ptac/> or by contacting PHARMAC on +64 4 460 4990.

2.4.2 Economic assessment

PHARMAC will generally undertake or review two forms of economic analysis on a proposal:

- (i) a cost-utility analysis (CUA)
- (ii) a budget-impact analysis (BIA).

PHARMAC estimates the budgetary impact of the proposed change to the Pharmaceutical Schedule, usually over a period of five years (discounted at 8%)¹. In some cases a longer time horizon is required.

If a treatment is more effective and more costly than a currently funded alternative, a CUA will be undertaken. CUA is a form of economic analysis that quantitatively assesses the health outcomes and costs of a proposed treatment compared with an alternative treatment (often current clinical practice). The methods PHARMAC uses when undertaking CUA are outlined in PHARMAC's *Prescription for Pharmacoeconomic Analysis* (PFPA) – <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/>

We encourage applicants to provide a CUA when submitting an Application. Providing robust quality analysis, following the methods outlined in the PFPA, may help expedite PHARMAC's assessment of the Application.

When PHARMAC receives a CUA from an applicant, our health economists review it, and amend it as required or build another model if needed. In order to be able to review CUAs more efficiently, applicants should provide a copy of the TreeAge™ model and/or Microsoft Excel spreadsheet. If PHARMAC's analysis differs from that of the applicant, PTAC will usually be supplied with a copy of both the applicant's CUA and PHARMAC's amended analysis, with the differences between them clearly explained.

¹ Note that the discount rate used by BIA differs from the rate used for CUA (the (nominal) discount rate for BIA is 8%, and the (real) discount rate for CUA is 3.5% for both costs and benefits). The rationale for using these rates is outlined in the *Prescription for Pharmacoeconomic Analysis* (PFPA) – <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/>

If an economic analysis has not been provided in the Application to illustrate the cost-effectiveness of the proposed amendment to the Pharmaceutical Schedule, PHARMAC will generally undertake this after receiving clinical advice.

Supplier CUAs should be supported with a summary document explaining the sources of assumptions and methods. PHARMAC CUAs are documented in Technology Assessment Reports. All CUAs are reviewed by PHARMAC staff. Analyses may also be reviewed by PTAC or the relevant specialist PTAC Subcommittee, or by other relevant external experts.

PHARMAC has no threshold below which a proposed amendment to the Pharmaceutical Schedule is considered 'cost-effective'. The main reason for this is that cost-effectiveness is only one of our considerations. One Application may be more cost-effective than another but rate poorly in terms of other Factors for Consideration and, therefore, may not be progressed since, on 'successfulness grounds', it will not be considered of value.

Another reason for not having a threshold value is that spending on community pharmaceuticals is required to be kept within a fixed budget. Given this constraint, and all other things being equal, what is and is not considered 'cost-effective' will vary with the amount of funding available (not just in terms of the total budget each year, but the available budget at any point in time). An Application to fund a pharmaceutical can, therefore, only be considered 'cost-effective' in comparison with other Applications under consideration by PHARMAC at any particular time.

2.4.3 Prioritisation

Once our assessment of an Application is completed (including PTAC recommendation and cost-effectiveness where necessary), the information is compiled and considered by PHARMAC. We use the Factors (more detail below) to compare the Application with all other funding options available to PHARMAC, and rank it to set our funding priorities – we refer to this process as ‘Prioritisation’.

The Factors are grouped into four different dimensions/quadrants (need, health benefits, costs and savings, and suitability), and the three levels of impact (to the person; to the person’s family, whānau and wider society; and to the broader health system), seen in the following diagram:

Figure1: PHARMAC’s Factors for Consideration²



² Note that the Health Needs of others (the health needs of the family or whānau of the person receiving the treatment, and for wider society) is an element of the Health need quadrant. This is described in the Supporting information on the PHARMAC website at <https://www.pharmac.govt.nz/assets/factors-for-consideration-supporting-information-v2.pdf>

All Applications are ranked against other funding options (for either the funding of a pharmaceutical or changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule, for example a proposal to widen or restrict access), whether received via Application or via PHARMAC-initiated proposals. The overall aim is to identify potential amendments to the Pharmaceutical Schedule that would provide the best health outcomes and thus help us to meet our statutory objective. PHARMAC conducts regular reviews of the ranking of all outstanding Applications.

2.4.4 Negotiations

Therapeutic Group Managers are responsible for negotiating listing and supply agreements with pharmaceutical supplier(s) where these are relevant to a proposed change to the Pharmaceutical Schedule. This commercial activity may include: price negotiations; Special Authority or other targeting criteria; expenditure caps; rebates on the pharmaceutical price; and/or multi-product agreements. Negotiation outcomes may lead to re-ranking of an Application.

2.4.5 Decision

Section 49(a) of the NZPHD Act requires that PHARMAC must, when it considers it appropriate to do so, consult on matters that relate to the management of pharmaceutical expenditure with any sections of the public, groups or individuals that, in the view of PHARMAC, may be affected by decisions on those matters.

Before PHARMAC makes a decision on a proposed change to the Pharmaceutical Schedule, we will, when we consider it appropriate, consult with people that may be affected by the proposed change (which may, according to the circumstances, include suppliers, PTAC and PTAC Subcommittees, health professionals, patients groups, Māori, Pacific peoples and other groups). Consultation responses are considered by PHARMAC with an open mind and, if appropriate, the proposal may be amended.

Decisions on any amendments to the Pharmaceutical Schedule are made by PHARMAC's Board (or its delegate acting under delegated authority).

3. Structure of Applications

Applications to PHARMAC for the funding of a pharmaceutical or changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule, for example a proposal to widen or restrict access, should be separated into the following three sections:

- (i) Synopsis.
- (ii) The main body of the Application.
- (iii) Supporting information.

Hard copies of the Application should be provided in separate spiral bound volumes. It is particularly important that copies of the synopsis are provided separately from the rest of the Application.

Each binder should be clearly labelled and the Application indexed so that information can be easily located. Please provide a table of contents in each binder. It is also useful if the Application has labelled tabs for each of the sections it contains (ie pharmacology, epidemiology, etc).

The front cover of the Application should include the:

- (i) pharmaceutical, brand name and indication
- (ii) date of the Application
- (iii) name of the pharmaceutical supplier and (if different) the name of the applicant (including name, phone number and email address of contact person).

The Application must include all relevant information known to the applicant, including data that is contrary to, or does not necessarily support, the case presented in the Application. Any information required for the Application (as outlined below) that is not available or is otherwise not supplied, should be stated explicitly under the relevant heading(s). Explain all sources and assumptions. If PHARMAC is not provided with information it considers necessary to assess the Application, this is likely to result in delays. Please be clear and succinct, yet thorough.

Applications must also include one labelled sample of the pharmaceutical inside its New Zealand packaging, as appropriate. Sometimes more samples may be required. A sample is not required with Applications for changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule, for example a proposal to widen or restrict access. Please refer to section 5.11 for further details on the provision of samples.

3.1 Submitting an Application

Applicants must initially provide three hard copies and one electronic copy of the Application to PHARMAC. PHARMAC will undertake an initial screening of the Application (as outlined in section 2.4), usually within 10 working days of receiving it, to ensure that it is complete and includes the key information that PHARMAC requires in order to assess the proposal. If the Application is incomplete or further

clarification is required, PHARMAC may contact the applicant and may defer consideration of the Application until any outstanding issues are resolved.

If an Application is approved for consideration by PTAC, PHARMAC will notify the applicant. Following notification, the applicant must provide a further three (3) additional spiral bound copies of the application (including synopsis and all supporting references). A sample of the pharmaceutical is also required if the application is for funding a new pharmaceutical.

Applicants must also supply one additional electronic copy of the entire Application. If an economic analysis is included in the Application, please also provide a copy of the analysis along with the TreeAge™ model and/or Excel spreadsheet as outlined in section 2.4.2 and 6.2.

If you have any questions, please contact the relevant Therapeutic Group Manager at PHARMAC.

4. Information Required in the Synopsis to an Application

Sections 4 and 5 outline the information required for Applications to PHARMAC for the funding of new pharmaceuticals, including new formulations or strengths as set out in section 2.2.

Applications for generic or biosimilar pharmaceuticals (where the pharmaceutical has previously been considered by PHARMAC) should refer to section 8.

Please refer to section 7 of these *Guidelines* for details on the format and content required for reapplications.

4.1 Synopsis

The synopsis should include a high-level summary of key aspects and issues presented in the Application. This should generally not be more than 10 pages long and should include:

- (i) official or approved names of the pharmaceutical
- (ii) form(s), strength(s), pack size(s)
- (iii) registered indication(s)
- (iv) proposed restriction(s) for listing
- (v) recommended course of treatment
- (vi) an overview of general health benefits and impact for the patient
- (vii) main comparator(s) and the main expected changes in the clinical management algorithm
- (viii) numbers of patients treated (restricted and unrestricted listing)
- (ix) proposed price
- (x) net cost of the proposed drug each year over five years
- (xi) the number and date of expiry for all relevant New Zealand patents (both granted and pending)
- (xii) cost per patient per course (for acute therapy) or the cost per patient per year (for chronic therapy)
- (xiii) general suitability of the pharmaceutical in the New Zealand context
- (xiv) any wider health sector resources/costs incurred or avoided by the listing of the proposed drug
- (xv) wider health benefits and impact for family and whānau, and wider society
- (xvi) main results of the clinical evaluation in terms of comparative effectiveness and comparative toxicity, including key data sources
- (xvii) if available, a summary of the cost-utility analysis, including the main sources of uncertainty in the structure and variables in the economic evaluation and the results of associated sensitivity analyses.

The synopsis will be used as a general information guide for PHARMAC and will be provided to PTAC members.

5. Information Required in the Application

5.1 Pharmacological Information

Please provide:

- (i) official or approved names of the pharmaceutical
- (ii) pharmaceutical form (e.g. ampoule, vial, sustained-release tablet)
- (iii) pharmaceutical strength
- (iv) arranged pack sizes (in the case of a preparation such as an aerosol, state the number of doses available from the container)
- (v) principal pharmacological action of the pharmaceutical
- (vi) indications registered for use in New Zealand – attach the Medsafe-approved data sheet and the New Zealand Medicines Assessment Advisory Committee (MAAC) response to the registration application
- (vii) where known, names of OECD countries where registration has been approved or declined
- (viii) where known, names of OECD countries where an application for funding has been approved or declined
- (ix) other presentations or formulations of the pharmaceutical that have been submitted for approval, or are already approved, in other OECD countries
- (x) recommended dosages for each of the indications provided in connection with (vi) 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
- (xi) any contra-indications and drug interactions. Include information on any necessary dosage adjustments and cautions required when using the pharmaceutical in conjunction with other pharmaceuticals
- (xii) common adverse effects (including frequency)
- (xiii) serious adverse effects
- (xiv) a summary statement of the main therapeutic claims for the pharmaceutical and its proposed use.

5.2 Proposed Amendments to the Pharmaceutical Schedule

Please provide:

- (i) the therapeutic group and/or subgroup where the applicant considers the pharmaceutical should be listed on the Pharmaceutical Schedule
- (ii) details of any proposed restrictions to access (eg Special Authority criteria, endorsement criteria or hospital restrictions)
- (iii) details of the comparator treatments available in New Zealand (funded and unfunded)
- (iv) the current clinical treatment algorithm (or pathway), also outlining the main expected changes in the treatment algorithm and describing:
 - how the pharmaceutical compares clinically with pharmaceuticals already listed on the Pharmaceutical Schedule (this is specific to the 'suitability and need' factor), and include the advantages (if any) the pharmaceutical offers over existing listed pharmaceuticals in terms of efficacy and/or side effects:
 - whether the pharmaceutical is equivalent to existing listed pharmaceuticals
 - whether the pharmaceutical is more effective than existing listed pharmaceuticals
 - whether the pharmaceutical has a similar efficacy to existing listed pharmaceuticals but has fewer side effects
 - whether the pharmaceutical is associated with similar, greater or fewer side effects and/or toxicity than existing listed pharmaceuticals
 - whether the pharmaceutical offers greater compliance (eg once daily dosing) than existing listed pharmaceuticals (include evidence supporting this claim)
- (v) if available, include dose equivalencies with comparator pharmaceuticals (whether listed or not) and justify these. State whether dose equivalencies were derived from direct or indirect comparisons
- (vi) whether the pharmaceutical has a longer shelf life than existing listed pharmaceuticals, or other points of difference
- (vii) other pharmaceuticals, if any, likely to be prescribed for use with the pharmaceutical as part of a course of treatment (whether listed or not). Include pharmaceuticals that may be used to manage any side effects
- (viii) where available, information and data to support health benefits to family, whānau and wider society. In some cases a pharmaceutical may have health benefits that impact directly on the health of the family and whānau (including caregivers).

5.3 Health need and public health significance

PHARMAC encourages applicants to provide information on health need and public health significance. Health need is described in the 'Health needs' section in the Factors for Consideration Supporting Information at

<https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/#need> .

Information necessary for PHARMAC's consideration of health need includes:

5.3.1 Epidemiological information

For each requested indication(s), please provide estimates for the first five years of the proposal (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 Māori people in New Zealand with the particular condition(s), along with their age-standardised prevalence rate per 1000 population
- (iii) where available, the number of Pacific people in New Zealand with the particular condition(s), along with their age-standardised prevalence rate per 1000 population
- (iv) where available, the number of non-Māori, non-Pacific people in New Zealand with the particular condition(s), along with their age-standardised prevalence rate per 1000 population
- (v) the number of additional people in New Zealand likely to be prescribed the pharmaceutical under the proposal
- (vi) a breakdown of the number of people in New Zealand treated for the condition, including those who can be:
 - successfully treated by the pharmaceutical only
 - treated by both the pharmaceutical and other pharmaceuticals (whether listed or not) that treat the same condition
 - treated by only other pharmaceuticals (whether listed or not)
 - treated, completely or partially, by other therapies.

In all cases where estimates and assumptions are made or used, please clearly and explicitly state what underlies them, including sources. These may be indicated in ranges (ie the minimum and maximum plausible range of values).

Further information on deriving numbers of Māori and other population groups facing a health disparity with the particular condition(s) can be found in section 6.3.

When estimating the likely number of patients eligible under access scenarios, please use an epidemiological approach. This means the prevalence and/or incidence of the condition to be treated; current patterns of how the pharmaceutical is used across different disease/indications; patterns over time in usage across diseases/indications; and patterns seen in other pharmaceutical markets internationally with the introduction of the new pharmaceuticals.

Please cite data sources, and clearly and explicitly state the bases of the assumptions made for the estimated numbers, including the quality of the data and relevance to the New Zealand setting. Estimates and assumptions can be indicated in ranges or similar.

The table below provides a suggested format for presenting this information.

Assumption/ parameter	Central estimate	Type of estimator used (mean, median, mode, etc)	Variation (as a range, percentile, standard deviations, 95% confidence interval, etc)	Source (eg publication, reference from the literature – give citation; expert estimate – give name and credentials)	Rationale for using this/these particular source/s

As with evidence of effectiveness (section 5.8), all prevalence estimates and assumptions should be obtained systematically. Please supply details of the search strategies used to identify these (the medium used; databases searched; time period when undertaken; search strategy and keywords/MeSH headings used). Also specify the pre-defined inclusion and exclusion criteria for selecting the relevant epidemiological data used for estimates and assumptions.

Prevalence and outcomes data may be located using relevant online Medline searches (<http://www.ncbi.nlm.nih.gov/pubmed>) using search terms that incorporate [the disease/indication], (epidemiology OR prevalence OR risk factors OR natural history OR prognosis OR outcomes OR survival), and specific outcomes relevant to the disease/indication. Local epidemiology/outcomes data can be located more specifically by including the terms (Austral* OR Zealand OR NZ OR Aotearoa) in the search. If you are unsure about how to do such searches (including search strategy and keywords/MeSH headings), you may wish to discuss this with a medical librarian or PHARMAC.

You may find useful sources of New Zealand mortality and morbidity data in cancer registry data, hospitalisation episode data, mental health episode data, and mortality data. These are available from the Ministry of Health and can be found at <http://www.health.govt.nz/blue-health-statistics>.

5.3.2 Burden of disease

Where possible, describe the burden of the disease or condition (impact of the disease or condition on the individual and the community), including:

- (i) the annual incidence of the disease/condition in New Zealand (number of new cases each year)
- (ii) the morbidity associated with the condition (eg annual number of hospitalisations)
- (iii) the premature mortality associated with condition in New Zealand (eg annual number of deaths; number of potential years of life lost before age 80 (PYLL(80))³)
- (iv) the average quality-adjusted life years (QALYs) lost and/or disability-adjusted life years (DALYs) lost by an individual patient due to the disease(s)⁴

³ PYLL(80) = sum across all individuals of (80 years minus age at death for an individual).

⁴ Where an individual's normal life expectancy minus their loss of disability-adjusted life years (DALY loss) from their disease/condition equals their disability-adjusted life expectancy (DALE).

- (v) the population loss of disability-adjusted life years (DALY loss) for the disease(s)⁵
- (vi) the population DALY loss attributable to the disease as a percent of all diseases (where in 2006 there were 955,000 total DALYs lost from all disease and injury⁵).

Detailed burden of disease estimates for New Zealand, including by limited ethnicity (Māori versus non Māori), are available from the NZ Burden of Disease, Injuries and Risk Factors Study, 2006-2016 (with its statistical annexe) at <http://www.health.govt.nz/nz-health-statistics/health-statistics-and-data-sets/new-zealand-burden-diseases-injuries-and-risk-factors-study-2006-2016>.

5.3.3 Uptake

Describe the estimated uptake rate of the pharmaceutical (ie the number of people likely to be prescribed the pharmaceutical, divided by the number of people with the particular disease or condition who should benefit from the pharmaceutical). This should use both the above epidemiological data and the above estimates of likely usage from section 5.3.1 and 5.3.2.

5.3.4 Impact on Government health priorities

Where relevant, please provide information where the disease, condition or illness is a government priority

More information on current Government priorities for health funding can be found in:

- [Ministry of Health Statement of Intent](http://www.health.govt.nz/publication/statement-intent-2014-2018)
<http://www.health.govt.nz/publication/statement-intent-2014-2018>
- [PHARMAC's Statement of Intent](https://www.pharmac.govt.nz/about/accountability-documents/#StatementOfIntent)
<https://www.pharmac.govt.nz/about/accountability-documents/#StatementOfIntent>
- [Output Agreement](https://www.pharmac.govt.nz/about/accountability-documents/#OutputAgreement)
<https://www.pharmac.govt.nz/about/accountability-documents/#OutputAgreement>
- [Letter of Expectations](https://www.pharmac.govt.nz/about/accountability-documents/#LetterOfExpectations)
<https://www.pharmac.govt.nz/about/accountability-documents/#LetterOfExpectations>

5.4 Price information

Please provide:

- (i) the supplier's selling price in \$NZ (ex-manufacturer, GST exclusive)

⁵ Ministry of Health. Health Loss in New Zealand: A report from the New Zealand Burden of Diseases, Injuries and Risk Factors Study, 2006-2016. Wellington: Ministry of Health, 2013. <http://www.health.govt.nz/publication/health-loss-new-zealand-report-new-zealand-burden-diseases-injuries-and-risk-factors-study-2006-2016> New Zealand Burden of Diseases Statistical Annexe <http://www.health.govt.nz/publication/new-zealand-burden-diseases-statistical-annexe>.

- (ii) the supplier's selling prices to wholesalers in other OECD countries where the pharmaceutical is marketed (in local currencies (excluding local taxes) and New Zealand dollar equivalents – please specify the exchange rates used)
- (iii) alternative pricing proposals (e.g. possible price/volume trade-offs).

5.5 Market information

Please provide:

- (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
- (iii) estimated change in the extent of use of other pharmaceuticals.

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 (ie 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.

5.6 Patent Information

Please provide the information set out below on each patent (granted and pending) that has claims relating to the pharmaceutical that is the subject of the Application, and with respect to which a claim of patent infringement could reasonably be asserted if a person, not licensed by the owner of the patent, distributed or sold the pharmaceutical in New Zealand.

For each pharmaceutical substance (ingredient) patent and finished pharmaceutical product (formulation and composition) patent and method of use and 'Swiss-type' claim patents, please provide:

- (i) patent number and the date on which the patent will (or would, if granted) expire
- (ii) type of patent (ie drug substance, finished drug product, method of use or 'Swiss-type' claim)
- (iii) name of the patent owner
- (iv) if you are not the patent owner, details of your right to sell or distribute the pharmaceutical in New Zealand
- (v) if you or the patent owner do not reside or have a place of business within New Zealand, the name of your representative or the representative of the patent owner who resides or maintains a place of business in New Zealand and who is authorised to receive notices related to the patent.

PHARMAC does not require information on manufacturing process patents.

If a patent is issued after the Application is made to PHARMAC but before funding is approved, please submit the required patent information in an amendment to the Application within 30 days of the date of issuance of the patent.

If you believe there are no relevant patents with respect to which a claim of patent infringement could reasonably be asserted if a person, not licensed by the owner of the patent, distributed or sold the pharmaceutical in New Zealand, please specify this in your Application.

PHARMAC recognises that some applicants, particularly those that are not pharmaceutical suppliers, may not have access to this information. If this is the case, please specify it in your Application. PHARMAC may subsequently seek this information from the relevant pharmaceutical supplier.

5.7 Impact on health sector

Please provide information that details what the consequences for the health system would be if the pharmaceutical was funded. These consequences may include the benefits and the costs to the health system, as well as any suitability considerations that may be relevant. This information may include:

- (i) hospital outpatient or community-based services required for administration of the pharmaceutical (e.g. nurse and specialist time required for infusions)
- (ii) laboratory and diagnostic tests
- (iii) inpatient hospitalisation
- (iv) emergency department visits
- (v) specialist visits and primary care services
- (vi) community-based services (eg nurse home visits, residential care (specify), home help, hospice care)
- (vii) features of the pharmaceutical that may impact on its use by health professionals. For example, please detail if extra training would be required to administer the pharmaceutical effectively.

If possible, please quantify this impact (refer to section 7 of the PFFA for details on how to estimate these costs).

5.8 Evidence of effectiveness and safety

Please use key clinical data sources when estimating relative treatment effects, including published randomised controlled trials (RCTs) and meta-analyses. Other possible sources include observational studies, unpublished trial data, expert opinion, and case reports.

5.8.1 Search strategy

All evidence should be obtained systematically. Describe the search strategy used to identify clinical studies, including:

- (i) who carried out the search? Using which medium? What databases were searched?
- (ii) over what time period was the search undertaken?
- (iii) what search strategy and keywords/MeSH headings were used?

Please specify the pre-defined inclusion and exclusion criteria used for selecting relevant studies.

5.8.2 Clinical evidence to include in application

Treatment effects may include both the effect on the person receiving the pharmaceutical and the effect of the treatment on those around the person receiving the pharmaceutical. When presenting clinical data to PHARMAC on relative treatment effects, please include:

- (i) all identified RCTs published as full articles in peer-reviewed journals in the English language that report (or give sufficient data to calculate) outcomes by intention-to-treat (ITT)
- (ii) one complete hard copy of the clinical study report summaries from the pivotal RCTs
- (iii) a register of all ongoing trials on the pharmaceutical for the relevant indication(s) known to the applicant, including trials not directly funded by the pharmaceutical supplier (this can be in the form of a print-out from clinicaltrials.gov)
- (iv) copies of all published errata (or corrections), retractions, editorials, and journal correspondence directly relating to the published trials included in the Application
- (v) if including data from unpublished trials, specify why each trial has not been published and expected dates of publication (if applicable)
- (vi) a declaration that all unpublished clinical trials known to the applicant have been disclosed, including those known to the applicant to have been undertaken by other companies that may distribute, market or license the pharmaceutical in New Zealand.

In evaluating therapeutic effectiveness and safety, we place greater weight on well-designed RCTs than other data sources. Of particular interest are head-to-head comparison RCTs between the proposed product and principal comparators.

Please include unpublished articles or studies that have been submitted for publication in peer-reviewed journals. In cases where the study is published after the Application has been submitted, applicants may substitute the draft submitted version with the final published version. Note, however, that PHARMAC may place greater weight on trials registered on public trial registers. PHARMAC is committed to international efforts to mitigate publication bias through the provision of central trial registries.

Details on supplementary information that may be provided in a separate section of the Application are included in section 6 of these *Guidelines*.

Please do not include the following information in the Application as such information will not be reviewed:

- Information unrelated to the pharmaceutical and disease(s)/indications under consideration.
- Phase I clinical trials relating to the pharmaceutical.

Abstracts and posters are not usually appropriate sources for descriptions of the study methodology or primary outcomes of studies. However, if they are adequately detailed, they may be used as references to update information after the primary analyses or any analyses of secondary outcomes not detailed in the published report.

5.8.3 Order of attachments

To make it easier for us to deal with attachments, please subdivide copies of articles, with their accompanying appraisals (see 5.8.5 below), into the three categories outlined in Table 2.

Within each group, please order articles by date of publication, starting with the most recent.

Table 1: Categories for Order of Attachments

Category	Examples
Grade 1 evidence	Randomised controlled trials (RCTs) of efficacy (individual RCTs and meta-analyses of RCTs)
Grade 2-3 evidence	Controlled but non-randomised experimental studies and non-analytic uncontrolled descriptive data for efficacy or prognosis/natural history
	Adverse effects (prospective cohort studies, case control studies, before-and-after studies, longitudinal studies, uncontrolled observational studies, case reports)
Grade 4 evidence	Non-systematic reviews
	Expert opinion
	Economic modelling/analyses and intervention logic in absence of direct empirical data
	Other background epidemiology and natural history of the disease/indication
	Other published material relevant to the proposal

5.8.4 Presentation of randomised controlled trials (RCT's)

For each direct RCT, provide the:

- (i) objective of trial
- (ii) study design including eligibility criteria, sample size, interventions (including dose and treatment duration), methods for randomisation and blinding, duration of follow-up, and outcomes measures and methods

- (iii) results including number of withdrawals and dropouts; and results for prospectively-defined primary outcomes, secondary outcomes and adverse effects for ITT population.

Clinical trials should be analysed using data from the ITT population in order to take into account outcomes of all patients irrespective of whether they received treatment. Where ITT analysis has not been reported, ideally recalculate effectiveness rates by adding to the 'on treatment' participant population for the group (i.e. the denominator) all of the patients who withdrew, dropped out, or were otherwise lost to follow-up. This is the group's true ITT starting participant population. In addition, information should be provided on Numbers Needed to Treat (NNT) and Numbers Needed to Harm (NNH).

The prospectively-defined primary and secondary outcome measures (as determined in the study protocol) should include both published and unpublished outcomes. Published outcomes data should be obtained from the complete published reports of the trials. If these are not available, use clinical study reports. These should be clearly highlighted and will be treated as commercial- or academic-in-confidence.

Where clinical trial data have been taken from more than one source, this should be made clear. Examples include:

- a clinical trial report and a published paper
- an open-label extension to a trial
- additional analyses (e.g. interim or post-hoc).

5.8.5 Critical Appraisal and Grading of Clinical Evidence

Where possible, critically appraise and grade the evidence using the methods described in PHARMAC's *Prescription for Pharmacoeconomic Analysis* (PFPA).

PHARMAC recommends the use of the Graphic Appraisal Tool for Epidemiology (GATE) for the critical appraisal of clinical trials, and the use of the Scottish Intercollegiate Guidelines Network (SIGN) to grade clinical evidence. Details on the GATE framework, including critical appraisal spreadsheets, are available at <https://www.fmhs.auckland.ac.nz/en/soph/about/our-departments/epidemiology-and-biostatistics/research/epiq/evidence-based-practice-and-cats.html>. It is described further in Evidence Based Medicine at <http://ebm.bmj.com/cgi/content/full/11/2/35>. Further details on these tools are also included in the PFPA: <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/>

The following table outlines a number of issues to consider when critically appraising a clinical trial.

Table 2: Factors to Consider in Critical Appraisal of Trials

Validity	Factors for Appraisal	Questions to Consider
Internal validity	Availability of data	Was the trial published in a peer-reviewed journal?

Validity	Factors for Appraisal	Questions to Consider
	Number of patients	Was the sample size large enough to indicate efficacy (ie that the results did not occur due to chance)? Or was the effect large enough to be statistically significant even in a small sample size?
	Method of randomisation, including adequate concealment	Was there likely to be any selection bias or confounding? Were patients, clinicians and assessors blinded?
	Length and completeness of follow-up	Were patients followed for an adequate time period? How often were patients assessed? Was analysis undertaken on the ITT population?
	Selection of endpoints	Was the selection of endpoints relevant?
External validity	Patient population	Was the patient population in the trial similar to those considered for funding?
	Comparator	Was the comparator consistent with current clinical practice in New Zealand?
	Dose, formulation and administration regimen	Were these consistent with recommended treatment regimes in New Zealand?

5.8.6 Safety

Information on the incidence and descriptions of adverse drug reactions should include data collected from:

- observational longitudinal clinical studies
- RCTs
- case reports on adverse drug reactions and expected/unexpected side effects
- post-marketing surveillance data.

5.8.7 Impacts on health outcomes

For further information about impacts on health outcomes, please see both the PFPA and 'The health benefit dimension' section in the Factors for Consideration Supporting Information at <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/#health>.

5.9 Applicability of evidence to the New Zealand health sector

For each clinical study provided in the Application, please assess how applicable the study is to the New Zealand health sector and pharmaceutical funding environment.

Please try to answer the following questions:

- (i) Are there any known biological factors that may alter the effect of the pharmaceutical?

- (ii) What effects does the time of taking the pharmaceutical have?
- (iii) What effects do variations in the nature and severity of the disease have?
- (iv) Does the effectiveness of the pharmaceutical depend on the way it is administered and/or by whom (eg by a nurse rather than by the patient)?
- (v) Is the giving or taking of the pharmaceutical part of a complex procedure with many components?
- (vi) Is any infrastructure required/available, such as monitoring with regular blood tests?
- (vii) Are there any other factors that may affect transferability of study results to the New Zealand clinical setting?

5.9A Evidence for suitability

For each Application, please provide data relevant to the non-clinical features of the pharmaceutical that may have an impact on health outcomes. Where relevant, these may include:

- (i) features of the pharmaceutical that impact on use by the person, such as the method of delivery. These features are particularly relevant if they may affect adherence
- (ii) features of the pharmaceutical that may affect use by family, whānau and wider society, for example features that affect a caregiver's ability to administer the pharmaceutical and consequently affect patient outcomes
- (iii) features of the pharmaceutical that affect use by the health workforce.

For further information about suitability, please see 'The suitability dimension' section in the Factors for Consideration Supporting Information at <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/#suitability>.

5.10 Factors for Consideration

When making decisions on proposals, PHARMAC considers the Factors set out below and in section 2.4.3 above. From 1 July 2016, these Factors will be set out in PHARMAC's Operating Policies and Procedures (OPPs), which are available on the PHARMAC website. The Factors are also considered by PTAC when it gives advice to PHARMAC on Applications.

Please provide a summary of the Application, evaluated against the Factors for Consideration described below. The questions included for each Factor have been included to help applicants consider what information may be relevant. PHARMAC does not have a prescriptive method of use of the Factors. PHARMAC uses the Factors for Consideration where applicable and giving such weight to each Factor as PHARMAC considers appropriate. For further information please see <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/> and <https://www.pharmac.govt.nz/about/operating-policies-and-procedures/>.

5.11 Sample

Please provide one labelled sample of the pharmaceutical inside its New Zealand packaging, as appropriate (more samples may be required). If the pharmaceutical is cytotoxic or a controlled pharmaceutical, please send a sample separately directly to the PHARMAC Medical Director with clearly labelled packaging.

Nothing in this requirement to send samples acts as an exemption for the applicant from relevant legislation relating to the importation or distribution of pharmaceuticals, including but not limited to the Medicines Act 1981 (and its Regulations), the Misuse of Drugs Act 1975 or relevant patents legislation.

You do not need to provide a sample with Applications for changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule, for example a proposal to widen or restrict access.

6. Additional information in Applications

This section outlines the information that would be useful to provide in addition to the core information detailed in section 5 of these *Guidelines*. Some of this information may not be relevant or necessary for every Application. While not compulsory, providing this information may reduce delays in the assessment and prioritisation of the Application.

Please provide this information in a separate section from the main body of the Application.

6.1 Additional Clinical Information

The following supplementary clinical information may be provided in a separate section:

- (i) Review articles and published critiques.
- (ii) Publications produced by international regulatory authorities, including European Public Assessment Reports (EPARs) produced by the European Medicines Agency (EMA) and medical reviews produced by the American Food and Drug Administration (FDA).
- (iii) International guidance and assessments by regulatory authorities or health technology assessment agencies (eg reports produced by the National Institute of Health and Clinical Excellence, the Canadian Agency for Drugs and Technologies in Health, the Scottish Medicines Consortium, and the Pharmaceutical Benefits Advisory Committee).
- (iv) Published CUAs.
- (v) Reviews by expert bodies such as specialist colleges/professional bodies.
- (vi) Consensus reports from expert panels.
- (vii) Expert opinion.

'Expert opinion' is provided by groups with any relevant expertise in the area of concern, for example, specialist professional societies or consumer support groups. Expert opinion cannot substitute for sound scientific evidence, but will help interpret

data, particularly the relevance and potential impact of clinical trial results and economic aspects.

Where expert opinion is provided, applicants should justify the need for any such expert opinion, and describe the methods used to obtain and collate those opinions, which must be systematic and robust. Applications with expert opinion should include:

- (i) criteria for selecting the experts
- (ii) number of experts approached
- (iii) number of experts who participated
- (iv) whether a declaration of potential conflict(s) of interest was sought from all experts
- (v) medical specialty groups whose opinions were sought
- (vi) background information provided and its consistency with the totality of the evidence provided in the submission
- (vii) method and medium used to collect the opinions
- (viii) questions asked
- (ix) whether iteration was used in the collation of opinions and, if so, how it was used
- (x) number of responses received for each question
- (xi) whether all experts agreed with each response, and, if not, then the approaches used to both finalise the estimates and present the variability of the opinions
- (xii) whether the experts received benefits (monetary or non-monetary) for the advice provided
- (xiii) relevant conflicts of interest.

Applicants should indicate how the opinions have been used in the Application, and state the extent to which opinions may have varied. Any clinicians providing expert advice must declare all potential conflicts of interest, including (but not limited to) financial interests in the development of the technology, likely financial gains arising from the proposed technology, and research funding. Experts must not supply any data that could identify individual patients.

6.2 Economic analysis

PHARMAC encourages applicants to provide a cost-utility analysis (CUA) when submitting a funding Application. Providing a robust and quality analysis, based on the methods outlined in the PFPA, may assist the Application to be assessed and ranked more quickly. Details on PHARMAC's CUA methodology are outlined in the PFPA <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/>

For PHARMAC to be able to review CUAs more efficiently, please provide an electronic copy of the model in TreeAge™ and/or Microsoft Excel. If an economic analysis has been submitted to the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, PHARMAC will accept the same analysis in the Application to PHARMAC, providing an electronic copy of the TreeAge™ model and/or Excel

spreadsheet is included. This ensures that PHARMAC can amend the costs (and any other relevant inputs) so the model is applicable to the New Zealand clinical and funding environment. PHARMAC also asks suppliers to update the model's inputs to New Zealand values. If available, please also provide a copy of any reports from PBAC-contracted reviewers.

PHARMAC has no threshold below which a proposed amendment to the Pharmaceutical Schedule is considered 'cost-effective'. Cost-effectiveness is reflected in the Costs and Saving dimensions and the Health Benefit dimensions of the Factors for Consideration. However, there are other Factors for Consideration. An Application may be more cost-effective than another but rate poorly on other Factors. Hence PHARMAC has no threshold.

When PHARMAC receives a CUA from an applicant it is reviewed, and often amended. The guidelines PHARMAC uses to review analyses are included in Appendix 3 of the PFPA (<https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/>).

6.2.1 Recommended methods for economic analysis

Economic analyses should be in the form of a CUA, with benefits measured in terms of quality-adjusted life years (QALYs). In cases where the clinical outcomes of the drug and the comparator have been shown to be equivalent, a cost-minimisation analysis may be appropriate. Other forms of cost-effectiveness or cost-benefit analyses (CBA) should not be provided to PHARMAC.

Please avoid unnecessary complexity in the economic models, and ensure they are transparent, well described and reproducible. The structure, data and process of building the model should be detailed enough to enable competent analysts who are not familiar with the model to reproduce it.

The key recommendations to consider when undertaking CUAs for funding Applications (as outlined in the PFPA) are summarised in Table 5 below.

Table 3: CUA Inputs/Outputs

Input/Output	Recommendation
Perspective	PHARMAC's Factors for Consideration.
Target population	Population most likely to receive treatment.
Comparator	Treatment that most prescribers would replace in New Zealand clinical practice, and the treatment prescribed to the largest number of patients (if this differs from the treatment most prescribers would replace).
Clinical outcomes	Statistically and clinically significant outcomes obtained, preferably from high-quality RCTs, systematic reviews or meta-analyses (grade of evidence of 1+ or 1++). Include impact of non-compliance if significant.
HR-QoL	Base on NZ EQ-5D Tariff 2. Use Global Burden of Disease weights to check for consistency.

Input/Output	Recommendation
Pharmaceutical costs	Pharmaceutical costs should take into account any proposed rebate, and should be based on the dose used in the key clinical trials (unless there is evidence of efficacy for different doses in clinical practice). Dispensing fees and pharmacy mark-up should be included if these are likely to differ between treatment arms. The analysis should also include the lower cost of a future generic pharmaceutical.
Other costs	Hospital, outpatient and direct patient costs should be included. Direct patients should be restricted to health care costs that the government partially subsidises, and should be based on the cost to government plus the additional cost to the patient. These costs include general practitioner visits, pharmaceutical co-payments and continuing care. Costs to non-health care government departments and indirect patient costs should not be included in CUAs for PHARMAC.
Discount rate	Discount all costs and benefits in CUAs at a 3.5% discount rate. Include rates of 0% and 5% in sensitivity analyses.
Results	The overall incremental QALYs per \$1 million invested result should be reported as a point estimate as well as the range over which result is likely to vary. In addition, information on discounted real and nominal costs, savings, life expectancy and quality of life gains/losses resulting from treatment should be reported separately.
Sensitivity analysis	Sensitivity analysis should include univariate (simple) analysis, multivariate analysis and extremes (scenario) analysis.

6.3 The Need of Māori and other population groups facing a health disparity

The particular health needs of Māori, and the particular health needs of other population groups that may already be facing a health disparity, are reflected in the Need dimension of the Factors.

Information on both the impact on the Māori health areas of focus and Māori health outcomes and the impact on the health outcomes of population groups experiencing health disparities can be found in the 'Health needs' section in the Factors for Consideration Supporting Information at:

<https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/#need>.

6.3.1 Māori Health areas of focus

As a Crown entity, PHARMAC has a commitment to Te Tiriti o Waitangi/the Treaty of Waitangi. This is reflected in the Factors through PHARMAC taking into consideration the health areas of focus that Māori have identified are priorities for Māori. These areas of focus are detailed in Te Whaioranga (PHARMAC's Māori Responsiveness Strategy), available at <https://www.pharmac.govt.nz/maori> and are subject to change following engagement with Māori.

PHARMAC encourages applicants, where relevant, to note where a funding application may have relevance to the following Māori health areas of focus:

- Diabetes and renal disease.
- Respiratory disease including asthma, chronic obstructive pulmonary disease (COPD), lung disease.

- Heart/cardiovascular disease including management of cardiovascular risk: smoking cessation, raised blood pressure, thrombosis, dyslipidaemia, metabolic syndrome.
- Mental health.
- Arthritis and gout.
- Obesity.
- Rheumatic fever.

6.3.2 Population groups experiencing a health disparity

PHARMAC acknowledges that there are population groups within New Zealand that face an underlying health disparity, irrespective of the disease/indication. PHARMAC defines a health disparity as an avoidable, unnecessary and unjust difference in the health of groups of people.

Identified population groups with health disparities include (but are not necessarily limited to):

- Māori
- Pacific peoples
- People living in areas of New Zealand that have the most deprived levels (9-10) of the New Zealand deprivation index scores (NZDep levels 9-10, (<http://www.health.govt.nz/publication/nzdep2013-index-deprivation>))
- Refugee populations
- Sub-regionally deprived populations (geographical areas in New Zealand where residents face significantly greater health disparities than other geographical areas).

PHARMAC encourages applicants, where possible, to provide any information on the health needs and public health significance specific to population groups experiencing health disparities when submitting a funding Application. This information should include the extent of disparity that may exist within the disease/indication for identified population groups.

PHARMAC acknowledges that it may not be possible to include data on all potential groups with a health disparity, but the following information should be sought and included in the funding application:

- (i) A description of the availability and quality of data indicating the extent of disparity between Māori, Pacific peoples and any other identified population groups with a health disparity and the New Zealand population not facing a health disparity (the remaining/residual general population). This may include further data on disease prevalence, incidence, notifications of new cases, public hospital hospitalisations, and/or deaths.
- (ii) Where available, the degree of impact of the disease on Māori, Pacific peoples and any other identified population groups with a health disparity and relative to the residual general population. Please use age-adjusted relative risks for annual incidence rates for notifications, hospitalisations and mortality. In each instance this could include:
 - the annual number of events occurring among identified population groups with health disparities, along with the age-

standardised annual incidence rate per 1000 (further details below)

- the annual number of events among the residual general population, along with the age-standardised annual incidence rate per 1000
 - both risk differences for age-standardised annual incidence rates and age-adjusted rate ratios with 95% confidence limits for identified population groups with health disparities versus the residual general population.
- (iii) Where available, the key age-specific differences in annual incidence between Māori, Pacific peoples and any other identified population groups with a health disparity and the residual general population. This may include data on particular age-sex specific groups for Māori, Pacific peoples and any other identified population groups with a health disparity that have the greatest age-specific risk differences when compared with the residual general population.
- (iv) The extent to which annual incidence rates (notification, hospitalisation and mortality rates) correlate with the need for pharmaceuticals.

Please use standard sources for this information (eg Ministry of Health mortality, hospitalisation and mental health data), supplemented where required by discussion with relevant experts and/or Medline searches. Sources could include prevalence data, incidence/notifications data, hospitalisation data, mental health episode data, and mortality data for relevant indicator(s). This could be combined with New Zealand age-ethnic-specific populations (available from <http://www.stats.govt.nz/>).

Where possible, please calculate age-standardised prevalence and annual incidence rates using the direct method against Segi's Standard World population. You can calculate age-standardised rate ratios (relative risks) and 95% confidence limits using standard binomial techniques. (Age-standardised rate ratios summarise disparity for Māori, Pacific peoples and any other identified population groups with a health disparity over all ages when compared with the residual general population, mitigating bias due to differences between ethnic groups' age structures. Further information is available in Robson B, Purdie G, Cram F, Simmonds S. Age standardisation – an indigenous standard? Emerg Themes Epidemiol. 2007;4:3. <http://www.ete-online.com/content/4/1/3.>)

Applicants providing such information need to be aware that the use of annual incidence (notification) rates to proxy need for pharmaceuticals is valid only if survival times are similar between ethnic groups. This is often not the case with Māori, Pacific peoples and any other identified population groups with a health disparity, who have worse mortality and case fatality rates. In addition, hospitalisation rates do not necessarily correlate well with prevalence (here, the need for pharmaceuticals), although they might indicate the total burden of disease.

6.3.3 Background information

Historically, there have been major problems with the accuracy and validity of the data available within the New Zealand health sector, especially with ethnicity data. In general there is little relevant information available about the types of patients, disease/disability rates and pharmaceuticals used to treat primary care conditions, particularly when subdividing ethnicity by disease/indications. Mortality data are less timely than hospitalisations data and give less precise estimates of risk (because of

smaller numbers of deaths). Māori death rates have in past decades been substantially under-represented because their ethnicity was often miscoded. Causes of death described on death certificates can be inaccurate. Routinely collected hospitalisations data are less accurate than mortality data – historically over one-quarter of discharge diagnoses were incorrectly coded. Because hospitals had systematically under-counted Māori admissions, there were numerator-denominator mismatches. Hospital admissions only indirectly measure need, being also affected by supply factors (such as regional variations in admitting practices relating to bed/service availability and clinical protocols). This in turn affects ethnic rates. Double counting of readmissions and of inter-hospital transfers as ‘new’ admissions further biases the data.

Describing the representation of population groups that may be facing a health disparity (ie what proportion of patients in the community are made up of these groups) has only partial relevance to PHARMAC’s decision making. Disease prevalence does not necessarily correlate with need for pharmaceuticals. In addition, deviations from expected need for disparate groups have little relevance if these groups are not accessing appropriate treatment. This is where accessing appropriate treatment means being able to visit a GP or similar primary care professional, the disease being identified and treatment prescribed – all equally available to the general population. There is evidence with many aspects of health care that particularly Māori (but likely other identified population groups with health disparities) have lower levels of access than for the general population.

For further information about the health need of Māori, please see the ‘Health Needs’ section in the Factors for Consideration Supporting Information at <https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/#need>.

7. Reapplications

Key reasons for Reapplications include:

- new information has become available (e.g. clinical trials, cost-utility analyses)
- the applicant wishes to respond to issues or questions raised by PTAC or specialist PTAC subcommittees (as recorded in the minutes of the meeting).

7.1 Information Requirements

It is important that Reapplications address all of the concerns raised by PTAC or the PTAC Subcommittee when the original Application was considered. Please provide a list of all new information (not included in the original Application or previous Reapplications), along with copies of all new information and supporting documentation.

Applicants are not required to provide copies of their original Application; however, PHARMAC may contact you if this information is required.

8. Applications for the funding of generic or biosimilar pharmaceuticals

This section of the *Guidelines* should be used only for Applications to fund a generic or biosimilar pharmaceutical where the pharmaceutical, including the indication applied for, has previously been assessed by PHARMAC. If PHARMAC has not assessed other brands of the pharmaceutical, a full application is required. You can confirm this by contacting the relevant Therapeutic Group Manager at PHARMAC (+64 4 460 4990).

Please provide as much of the following information as possible in your Application.

8.1 Registration and indication

Please provide a copy of the Medsafe gazette notice and approved New Zealand data sheet. If the pharmaceutical is not registered for use in New Zealand, please outline the date, or likely date, of submission of the dossier, and whether or not this would be subject to any of Medsafe's abbreviated registration processes. If known, please indicate the expected date of registration.

Please state whether there are any differences, or likely to be any differences, in the approved indications for the pharmaceutical compared with the other brand(s) of the pharmaceutical previously considered by PHARMAC.

Please also state the indication for which funding is being sought.

8.2 Pharmaceutical information

Please provide:

- (i) the official or approved names of the pharmaceutical
- (ii) available forms, strengths, pack sizes and packaging for which funding is sought (in the case of a preparation such as an aerosol, state the number of doses available from the container)
- (iii) whether there are any other available forms, strengths and pack sizes
- (iv) if available, one labelled sample of the pharmaceutical inside its New Zealand packaging. If the pharmaceutical is cytotoxic or a controlled pharmaceutical, please send the sample separately directly to the PHARMAC Medical Director (note that more samples may be required later)⁶
- (v) details of any differences between the pharmaceutical and any other brand(s) of the pharmaceutical previously considered by PHARMAC, including (but not limited to):
 - differences in the efficacy, side effect and toxicity profiles

⁶ Nothing in this requirement to send samples acts as an exemption for the applicant from relevant legislation relating to the importation or distribution of pharmaceuticals, including but not limited to the Medicines Act 1981 (and its Regulations), the Misuse of Drugs Act 1975 or relevant patents legislation.

- differences in the pharmacokinetic profile with respect to age, concomitant pathological status, or polymorphic metabolism
- differences in the shelf-life
- differences in appearance/taste (eg colour, shape, size, coating, ability to be split)
- difference in excipients (ie the inactive substances used to carry the active ingredients)
- any other differences that the applicant is aware of that could be relevant.

8.3 Price information

Please provide:

- (i) the selling price (GST exclusive)
- (ii) any alternative pricing proposals (e.g. possible price/volume trade-offs).

8.4 Market information

Please provide:

- (i) which (if any) international markets the generic or biosimilar pharmaceutical is registered for use
- (ii) which (if any) international markets where registration of the generic or biosimilar pharmaceutical has been declined
- (iii) the market share of the generic or biosimilar pharmaceutical in international markets
- (iv) a description of uptake and acceptance of the generic or biosimilar pharmaceutical in international markets.

8.5 Patent information

Please provide the information set out in section 5.6 on each patent (granted and pending) that has claims relating to the generic or biosimilar pharmaceutical that is the subject of the Application, and with respect to which a claim of patent infringement could reasonably be asserted if a person, not licensed by the owner of the patent, distributed or sold the pharmaceutical in New Zealand.

If you believe there are no relevant patents with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent distributed or sold the pharmaceutical in New Zealand, please specify this in your Application.

8.6 Lead times

Please provide information about the length of time following a funding decision required to obtain sufficient stock to supply the market in New Zealand.

9. Applications for the funding of blood glucose meter systems

This section of the *Guidelines* should be used only for Applications to fund a blood glucose diagnostic test meter and/or blood glucose diagnostics test strip where the brand has not previously been assessed by PHARMAC. We recommend you discuss your blood glucose meter system by contacting the relevant Therapeutic Group Manager at PHARMAC (+64 4 460 4990) before submitting your Application.

Please provide as much of the following information as possible in your Application.

9.1 International information

Please provide information advising where your brand is marketed and supplied overseas and include any relevant international regulatory evaluation reports (e.g. CE Certification or FDA approval).

Please state whether there are any differences in your brand of blood glucose diagnostic test meter and/or blood glucose diagnostic test strip from the currently funded brands in the Pharmaceutical Schedule.

9.2 Product information

Please provide:

- (i) the official or approved names of the blood glucose diagnostic test meter and/or blood glucose diagnostic test strip
- (ii) date of notification to WAND database
- (iii) available pack sizes and packaging for which funding is sought
- (iv) whether there are any other available forms, strengths and pack sizes
- (v) operating information about your brand of blood glucose diagnostic test meter and/or blood glucose diagnostic test strip, including:
 - a. coding
 - b. volume of blood required
 - c. time taken for test
 - d. temperature range of operation
 - e. open and unopened strip vial stability
 - f. strip expiry detection
- (vi) computer software information (including the ability to download information, compatibility of software and availability of software to health care providers and patients)
- (vii) other relevant information:
 - a. availability of an 0800 number (including hours of operation)
 - b. repair/replacement policy
 - c. other customer services

- (viii) if available, two samples of the blood glucose diagnostic test meter and/or blood glucose diagnostic test strip inside its New Zealand packaging.

9.3 Price information

Please provide:

- (i) the selling price (GST exclusive)
- (ii) any alternative pricing proposals (e.g. possible price/volume trade-offs).

9.4 Lead times

Please provide information about the length of time following a funding decision required to obtain sufficient stock to supply the market in New Zealand.

Appendix 1 – Glossary

Term	Definition
Absolute Risk Reduction (ARR) or Absolute Risk Increase (ARI)	The absolute difference in event rates between an intervention and its comparator.
Adherence	Continuation of and consistency with recommended treatment regimen.
Applicant	Any person or organisation making an application to PHARMAC.
Application	An application or proposal made by a third party to PHARMAC for (a) the funding of a pharmaceutical; or (b) changes to the funding of a pharmaceutical that is already on the Pharmaceutical Schedule (eg a proposal to widen or restrict access).
Average cost	Total cost divided by total number of units.
Budget impact analysis (BIA)	Estimate of planned resource use and impact on budget over a period of time.
Community pharmaceutical	A pharmaceutical that is funded from the Pharmaceutical Budget and used in the community (ie outside of the hospital).
Combination product	Products that consist of two or more pharmaceuticals.
Combined Pharmaceutical Budget	<p>The combined pharmaceutical budget, set by the Minister of Health, includes funding for pharmaceuticals used in the community (including vaccines and medical devices), cancer medicines (whether used in hospital or in the community) and some haemophilia treatments.</p> <p>The CPB does not include funding for other hospital medicines or hospital medical devices (both of which are currently funded by district health boards); funding for PHARMAC's operations; or payments for distribution such as the fees a community pharmacist receives.</p>
Comparator	Treatment most prescribers would replace in New Zealand clinical practice, and the treatment prescribed to the largest number of patients (if this differs from the treatment most prescribers would replace).
Confidence interval	Numerical measure of the range within which the true treatment effect is likely to lie.
Cost/QALY gained	Result of cost-utility analysis. Monetary cost per quality-adjusted life year (QALY).

Term	Definition
Cost-benefit analysis (CBA)	Cost-benefit analysis (CBA) measures costs and benefits in monetary terms, and expresses the results as one figure representing the difference between benefits and costs ($B-C > 0$), or as a ratio (B/C).
Cost-effectiveness analysis (CEA)	Cost-effectiveness analysis (CEA) compares the relative costs of interventions with some clearly definable outcome; such an outcome may be, for example, hospitalisation days avoided, strokes prevented or hip fractures averted. The final result is a value called the incremental cost-effectiveness ratio (ICER).
Cost-minimisation analysis (CMA)	Cost-minimisation analysis (CMA) assumes that there is no net health change between different treatment options (ie there is no significant difference in the effectiveness of the treatments). In this case the analysis is essentially a search for the least costly alternative.
Cost-utility analysis (CUA)	Cost-utility analysis (CUA) is similar to CEA, but health outcomes are measured using a common denominator – quality-adjusted life years (QALYs) gained. The incremental cost-utility ratio (ICUR) is defined as the change in the costs and benefits (where benefits are measured in terms of quality-adjusted life years) resulting from substituting one treatment for another.
Decision tree	Graphical representation of alternative treatments for use under conditions of uncertainty.
Diagnosis Related Group (DRG)	Patient classification scheme which provides a clinically meaningful way of relating the number and types of patients treated in a hospital to the resources required by the hospital.
Direct age standardisation	<p>Age standardisation (age adjustment) is a technique to better compare populations when their age profiles differ. It uses a weighting approach to match the age distribution of a common reference population, thereby obtaining a weighted average of age-specific rates to derive a summary event rate.</p> <p>Methods of age standardisation can be direct or indirect. Direct age standardisation gives a summary rate of events that would have been observed had the study population had the same age structure as the reference group (eg the number of cases of disease that would be expected if the disease rates in the study population were applied to the reference population). Further details are available in standard epidemiology texts.</p>
Direct cost	Fixed and variable costs (medical and non-medical) directly related to the treatment.
Discount rate	Rate used to convert future costs and benefits into present values (current dollars and benefits have greater value than future dollars and benefits).

Term	Definition
Disinvestment	May involve reduction in eligibility for a treatment (i.e. tightening of access), or cessation of treatment.
Disability-adjusted life year (DALY)	Burden of disease measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health.
District health board (DHB)	The Crown entities responsible for ensuring the provision of publicly funded health and disability support services for the population of a specific geographic area in New Zealand. There are currently 20 DHBs.
Health-related quality of life	Physical, social and emotional aspects of patient's wellbeing.
Hospital medicine	Pharmaceutical that is predominantly administered within the hospital and is funded by DHBs.
Effectiveness	Benefit of treatment in 'real world' setting.
Efficacy	Benefit of treatment in defined population in controlled or ideal circumstances (e.g. randomised controlled trials).
Factors	Factors for Consideration
Gazette notice	Announcement of Medsafe approval for the marketing of a pharmaceutical in New Zealand.
Generic pharmaceutical	A pharmaceutical that contains the same active ingredients as the original branded (and usually patented) formulation. Generic pharmaceuticals are bioequivalent to the branded pharmaceutical with respect to pharmacokinetic and pharmacodynamic properties.
Graphic Appraisal Tool for Epidemiology (GATE)	Tool developed for the critical appraisal of clinical literature.
Incidence	The count of new cases of disease in a defined population during a specified period of time.
Incidence rate	The count of new cases of disease in a defined population within a specified period of time, divided by the number of persons (ie population) at risk (or person-time) of developing the disease during that time period.
Incremental cost	The difference between the cost of an intervention and the cost of the comparator.
Indication	A valid, or generally accepted, use of a medicine.

Term	Definition
Marginal cost	The additional cost of one extra unit of product or treating one additional patient.
Markov model	A statistical representation of discrete, recurrent events over time in which the probability of transition from one to another depends on the current state.
Medicines	Medicines as defined in s.3 Medicines Act 1981.
Medsafe	New Zealand Medicines and Medical Devices Safety Authority.
Medsafe datasheet	Prescribing information provided by the pharmaceutical supplier (and approved by Medsafe) on a specific medicine registered by Medsafe.
Meta-analysis	A systematic process for finding, evaluating and combining the results of data from independent sources.
Monte Carlo simulation	Simulation modelling that uses random numbers to capture effects of uncertainty.
Named Patient Pharmaceutical Assessment (NPPA)	Operating alongside the Schedule, NPPA refers to PHARMAC's consideration of applications for individual patients seeking funding approval for treatments not listed on the Schedule, either at all or for that individual patient's clinical circumstances.
Number needed to harm (NNH)	The number of patients who are treated that would lead to one additional person being harmed compared with patients who receive the control treatment. $NNH=1/ARI$
Number needed to treat (NNT)	The number of patients who need to be treated in order to prevent or create one additional event occurring over a predefined period of time. $NNT=1/ARR$
OIA	Official Information Act 1982.
Opportunity cost	Value of the alternative options that could be undertaken with the same resources.
Patent	The official document (also known as letters patent) setting out the government's grant of an exclusive right to an inventor to manufacture, use or sell an invention for a certain number of years.
Perspective	Viewpoint of analysis (e.g. funder, society, government, individual).

Term	Definition
Pharmaceutical	Pharmaceuticals as defined in s.6 New Zealand Public Health and Disability Act 2000.
Pharmaceutical Benefits Advisory Committee (PBAC)	Independent statutory body in Australia that makes recommendations and gives advice to the Australian Minister of Health about which drugs and medicinal preparations should be made available as pharmaceutical benefits.
Pharmaceutical Budget	See <i>Combined Pharmaceutical Budget</i> .
PHARMAC	The Pharmaceutical Management Agency (PHARMAC).
Pharmaceutical Schedule	<p>The Pharmaceutical Schedule is the list of all the medicines and therapeutic products that District Health Boards (DHBs) fund. The Schedule lists medicines by chemical name (e.g. aspirin) and brand name (e.g. Ethics Aspirin). It lists the formulations, doses and subsidy price of the medicine, as well as any prescribing guidelines or access criteria.</p> <p>The Schedule is divided into nine sections (A-I). It lists medicines that are funded via the Pharmaceutical Budget (community medicines, cancer treatments, vaccines and haemophilia treatments) and those that must be funded by DHB hospitals for use in the hospital (some of which are contracted to be given in public hospitals at specified prices). It also lists more than 6000 hospital medical devices that DHBs may order at a nationally contracted price.</p>
Pharmacology and Therapeutic Advisory Committee (PTAC)	An expert committee of senior health practitioners which provides objective advice to PHARMAC on pharmaceuticals and their benefits.
Prescription for Pharmacoeconomic Analysis (PFPA)	The document that provides an overview of PHARMAC's cost-utility analysis methodology.
Prevalence	The number of existing cases of disease in a defined population at a notional point in time.
Prevalence rate	The number of existing cases of disease in a defined population at a notional point in time, divided by the number of persons in the population at that time.

Term	Definition
PYLL(80)	<p>Potential years of life lost before the age of 80. PYLL measures the time (in years) lost by a population due to premature death. This involves choosing an arbitrary limit to life, so that the duration of life lost due to each death is that potential limit minus the age at death. In the case of PYLL(80), the arbitrary age limit chosen is 80 years. Note that the subtraction is truncated, so that any deaths occurring after people attain that arbitrary age limit have a potential loss of life of zero years.</p>
Quality-adjusted life years (QALY)	<p>A QALY ('quality adjusted life year') is a standard economic measure, which combines the effects of changes in the length and quality of life that result from treatment. Quality-adjusted life years help compare gains in the quality of life with gains in the quantity (length) of life, in a simple and direct manner.</p> <p>Quality of life weightings (or utilities) are typically measured on a scale of 0 to 1, where 0 is equivalent to death and 1 to perfect health. These weights can then be summed over life expectancy in order to calculate the total number of QALYs.</p> <p>The difference in QALYs and overall costs gained between two treatments informs the relative cost-effectiveness of an intervention.</p>
Relative risk	<p>Ratio of incidence of disease in exposed group divided by incidence of disease in non-exposed (control) group.</p>
Relative Risk Increase (RRI)	<p>Proportional increase in rates of events between the experimental group and control group.</p>
Relative Risk Reduction (RRR)	<p>The relative (not absolute) difference in events between two treatment groups, expressed as a proportion of the event rate in the untreated group. Similar to RRI, an RRR is therefore a proportional <u>decrease</u> in rates of events between the control and experimental group.</p>
Sensitivity analysis	<p>Process through which the robustness of an economic model is assessed by examining the changes in the result of the analysis when key variables are varied over a specified range.</p>
Special Authority criteria	<p>A subsidy or additional subsidy may only be claimed for certain pharmaceuticals if an application, relating to the specific patient, meeting the Special Authority criteria specified in the Schedule has been approved, and the valid Special Authority number is present on the prescription.</p>

Term	Definition
Subsidy	The maximum amount paid to a person, entitled to receive payment from the Crown (usually a pharmacy), for the supply of a pharmaceutical to a patient (this may not be the same as the final cost paid by the Crown, depending on the nature of PHARMAC's contractual arrangements with the pharmaceutical supplier).
Technology Assessment Report (TAR)	Documentation of the economic analysis (including cost-utility analysis).
Therapeutic Group Manager (TGM)	PHARMAC staff member responsible for managing PHARMAC's processes for pharmaceutical funding, within an assigned therapeutic group.
TreeAge™	Decision analysis software used for modelling cost-effectiveness.
Utility	Values of the strength of preferences for, or desirability of, a specific level of health status or a specific health outcome.
Value for money	Refers to whether the benefits of a pharmaceutical are considered significant enough to compensate for the cost.