MEDICINES Australia

Better Health through Research and Innovation

Submission

Post-Market Review of Products Used in the Management of Diabetes, Stage 3

2 July 2013

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Executive Summary

Medicines Australia is the peak organisation representing the research-based pharmaceutical industry in Australia. Our members comprise over 80% of the prescription medicines market and play an integral role in delivering better health outcomes for Australians. Medicines Australia's members include sponsors who manufacture and supply the medicines under review in the *Post-Market Review of Products Used in the Management of Diabetes, Stage 3* (herein, the 'Diabetes Review').

Medicines Australia is alarmed that the Department of Health and Ageing continues to implement its post-market reviews program without resolution of the significant process and policy issues that we have raised on numerous occasions. In this submission, Medicines Australia again highlights these issues in relation to the Diabetes Review and reiterates industry's call for improvements to the post-market reviews program.

Medicines Australia has serious concerns that the Diabetes Review in the current form is not fully examining clinical management of diabetes and thus will be unlikely to improve health outcomes for diabetes patients. Despite statements from the Department that the Review is *"aimed to improve morbidity, mortality, safety and quality of life for patients with diabetes"*[1] we believe that in not doing this thoroughly or appropriately the reviewers will overlook the value that clinicians and patients place on treatment benefits and choice to deal with the practical challenges of living with diabetes.

As detailed in this submission, there is limited public information on the triggers and/or possible outcomes that the review might deliver. It is not known what questions will be most relevant to the decision-making or if they represent the full extent of questions to be addressed by the review. It is not known what evidence or analysis will be used to answer these questions.

This lack of transparency extends to the medicines that the review is supposed to consider, creating inconsistencies and confusion. Insulin, an indisputably key treatment in type 2 diabetes, was initially relevant under the original terms for the overall diabetes review. Insulin was then excluded under later, stage 3 terms. Most recently the Department communicated that *"the information or data on the efficacy and safety of insulin compared to other medicines will be considered"*, although insulin is not a *"specific focus"*[2] of the review.

The absence of a transparent and meaningful consultation process prevents stakeholders from contributing meaningfully and effectively to this review's stated purpose of improving health outcomes for diabetes patients. It is generally accepted that Australia's treatment guidelines for type 2 diabetes have fallen behind global best practice. The Diabetes Review presents an opportunity to ensure the availability of Australian treatments meet best practice standards, however, as currently being administered, the Review is unlikely to deliver these outcomes.

Key outcomes from previous Government reviews have resulted in price cuts from industry, while loosening restrictions to accommodate utilisation that was previously deemed inappropriate or not cost effective. If the key outcome from the Diabetes Review is a price reduction or a price reduction with a changed restriction, without assessing appropriateness or value for money, the Review will have failed.

Furthermore, the objective to improve the management of diabetes, including QUM, patient safety and appropriate guidelines for the products used in the management of the disorder will not be addressed with a price penalty. It would be disappointing if the

[1] Grant McArthur. (2013, June 4) Review risk to diabetes, *Herald Sun*, p10.
[2] Department of Health an Ageing. Post-Market Review of Products Used in the Management of Diabetes, http://www.pbs.gov.au/info/reviews/diabetes Accessed 3 June 2013

review was reduced to a cost-cutting exercise without consideration of these broader opportunities.

The narrow, cost-focused approach evident in past reviews poses substantial risks, not only to the clinical areas where reviews are implemented, but also to Australia's ongoing access to innovative medicines in general. These reviews have undermined the policies that allow Australia to gain access to innovative medicines which represent value for money, while ensuring savings on older therapies.

Medicines Australia has lodged a number of submissions to post-market reviews, most recently to Stage 1 of the Diabetes Review (November 2012) and to the *Post-Market Review of PBS Medicines to Treat Asthma in Children* (Children's Asthma Review) (March 2013).

We have emphasised in our submissions and in our engagements with the Department of Health and Ageing (the Department) that Medicines Australia is seriously concerned about the policy implications and deficient processes of the post-market reviews program. Transparent, predictable processes are critical for the business planning and commercial viability of Medicines Australia's members and important for rigorous, evidence-based outcomes that benefit Australian patients.

Recommendations:

Medicines Australia recommends that:

1. The Australian Government works with stakeholders to address the policy implications and procedural concerns highlighted in this and other submissions.
2. The outcome of the Diabetes Review clearly reports on the most appropriate policy options available for addressing the findings of the review, including education, quality use of medicines (QUM) options, price changes
3. The outcome of the Diabetes Review clearly identifies the implications of the review findings for stakeholders, such as;
    i. Immediate and short term access to medicines for patients and treating clinicians; and
    ii. Likely long term consequences for access to new therapies
4. The Diabetes Review centres on health outcomes for people living with type 2 diabetes and demonstrates attention to:
    a. full examination of the clinical management of diabetes including the value clinicians and patients place on treatment selection;
    b. examination of prescribing patterns in relation to clinical evidence and Australian and international clinical guidelines
    c. establishing whether PBS restrictions are out-dated and therefore do not reflect best clinical practice;
    d. improvement of evidence-based individualised treatment options to ensure alignment with world's best practice;
    e. consideration of appropriate policy, QUM and other solutions to ensure appropriate use of medicines; these options must take into account the scope of responsibility for each stakeholder; and
    f. fully addressing the stated Terms of Reference, including the clinical evidence covering multiple medicines.

    These recommendations highlight that more time is required before any outcomes arise from the Review.

Clinical concerns with the Diabetes Review

The Diabetes Review in its current form is not fully examining the clinical management of diabetes, despite statements from the Department that the Review is *"aimed to improve morbidity, mortality, safety and quality of life for patients with diabetes"*[3]. The clinical importance of individualised treatment selection to address the numerous challenges of living with diabetes, are unlikely to receive adequate consideration under the current review.

Diabetes is a progressive disorder characterised by failing pancreatic insulin secretion over time. Diabetes patients need regular assessments of their medications and response. Patients face an almost inevitable addition of oral hypoglycaemic agents to their treatment regime and often insulin. The best possible way to achieve optimal health outcomes is to provide individualised treatment.

The current PBS restrictions for diabetes medicines do not reflect clinician insights on issues that are of significant practical importance to patients when selecting a treatment approach. These include management of treatment side-effects such as weight gain, and hypoglycaemia; consideration of patient-centric benefits such as convenience; and other features which can facilitate compliance and quality of life. These are important considerations for people living with type 2 diabetes and must be central to any post-market review.

Notably, when evaluating new listings, the PBAC guidelines do not permit adequate consideration of these wider issues when adding treatments under the existing PBS restrictions. Experience to date suggests that the PBAC is narrowly focused on blood sugar levels (HbA1c) and does not give adequate consideration to other health outcomes including the patient benefits of different treatment options. It is acknowledged that these may be more difficult to measure, in part because clinical trials are designed to collect data and treat toward a specific target. However, the PBAC should be equipped to address the broader needs of Australian patients.

From a clinical perspective it is generally accepted that Australia's treatment guidelines have fallen behind; Australian patients are currently missing out on worlds' best practice for the treatment of type 2 diabetes. The Diabetes Review presents a timely opportunity to address this. The National Health and Medical Research Council (NHMRC) type 2 diabetes clinical guidelines are narrow and are acknowledged to have been designed to ensure consistency with PBS restrictions. It is a concern that clinical guidelines are constrained by the PBS restrictions. Public policy should adjust to swiftly moving evidence on best practice. Best practice in diabetes has evolved in response to rapid changes in clinical experience and opinion. PBS restrictions need to evolve in equal measure if they are to support best practice.

Diabetes Australia has recently released "A National Diabetes Strategy and Action Plan", and identifies goals pertinent to the Diabetes Review. They note that diabetes will become the number one disease burden in Australia in the next 5 years[4]. To address this, Diabetes Australia identifies "access to treatment and technologies to support prevention of complications and burden" as an essential part of optimal management and early diagnosis.

The National Diabetes Strategy and Action Plan reiterates that the "Regulatory and approval processes must ensure that all Australians with all types of Diabetes have affordable access to a range of medicines to enable clinicians to tailor management and

[3] Grant McArthur. (2013, June 4) Review risk to diabetes, *Herald Sun*, p10.
[4] Diabetes Australia. 2013. A National Diabetes Strategy and Action Plan. P1

best prevent complications and burden" and further assert that "Diabetes management guidelines should reflect best clinical practice"[5].

Ultimately, if the Diabetes Review serves only to cut expenditure on diabetes treatment it will have failed to deliver on its potential to advance the clinical management of diabetes.

[5] Ibid P7

Process and transparency deficiencies relevant to the review

The Diabetes Review and other post-market reviews to date have been conducted with inadequate and inconsistently applied guidelines, limited stakeholder engagement, insufficient timeframes and an overall lack of transparency.

Stakeholders expect the Department to administer all programs with transparent, predictable and accepted processes. This is especially critical for post-market reviews, which have significant implications for stakeholders. These implications include clinical outcomes for patients alongside commercial effects for industry. They may add delays or limitations to accessing medicines including new innovations for patients, as well as affecting quality use of medicines.

Primarily the Department's guidelines for reviews are inadequate. The post-market reviews guidelines provided on the Department's general reviews webpage fail to address adequately several important aspects, including:

- the process undertaken to identify stakeholders
- the methods of notification of stakeholders, including for those less likely to regularly interact with the Department on PBS issues
- the health technology assessment (HTA) standards and guidelines which are applied for evaluation of evidence and data
- detailed information on the opportunities for sponsors and other stakeholders to provide evidence and other information at multiple points throughout the review (For example: In the ordinary PBAC submission process, sponsors have opportunities for pre-submission consultations; pre-subcommittee responses; pre-PBAC responses; and the opportunity to seek an independent review).
- the implementation of recommendations for the post-review process under the existing framework. The most egregious examples of procedural deficiencies in previous reviews have been in the post-review process. A specific example is that sponsors were afforded less than ten business days to respond to a fundamental change in reimbursement conditions requested following the *Review of PBS anti-dementia drugs to treat Alzheimer's disease* (Anti-Dementia Review).

As indicated above, engagement with stakeholders in post-market reviews is inadequate. In the first instance, Diabetes Review stakeholders were not given the opportunity to provide feedback on the most appropriate review work plan; terms of reference; scope; timeframes or evidence likely to be valuable in the review. This is inappropriate. Consumer groups, health care professionals, the pharmacy sector and the medical research sector are best placed to provide advice to the Government on the questions that should be asked and answered in a review to improve clinical practice and patient outcomes, which should be the key objectives of any post-market review.

It would also be appropriate to consult pharmaceutical industry sponsors as soon as a review is triggered, to gain their input as experts on their own products and providers/owners of much of the data relevant to post-market reviews. For example, a sponsor may be able to provide advice on a realistic timeframe for providing (or generating) necessary data. The limited engagement that has been allowed for in previous reviews has been insufficient.

The quality and rigor of post-market reviews must be of a standard that is at least comparable to the PBAC and listing processes, for which sponsors invest over a year developing submissions with adequate evidence and modelling. Earlier engagement with sponsors in the Diabetes Review would have indicated that six-weeks is an inadequate timeframe to develop and lodge a comprehensive submission in line with the

scope, quality and detail expected from the PBAC. *See section below responding to Terms of reference 3 and 4.*

The broad terms of reference and constrained timeframes for lodging submissions to the review may give stakeholders the impression that either: their input is not valid; or the review will not be held to the same high standards of HTA as is expected of the listing of new medicines.

Medicines Australia is disappointed that post-market reviews roles and responsibilities remain unclear. No information is provided on the general reviews webpage or on the Diabetes Review webpage as to who will receive and review submissions lodged by stakeholders. This is inappropriate.

Meaningful engagement in the review process can only occur if stakeholders understand what is at stake, who is the reviewer and how their submissions will be assessed. Some stakeholders have noted that the report on stage 1 of the Diabetes Review did not consider their submissions.

It is also noted on the Diabetes Review webpage that an advisory group will be convened yet no information has been provided on the membership of this group or how this action has been progressed. No information has been provided on the selection of members or what expertise the members have or are expected to have. This lack of transparency gives the appearance that the process is ad hoc and unpredictable or that the Department intends for this information to be hidden from public view. As a further example, there is still no information available regarding the advisory group engaged to provide advice on the Children's Asthma Review.

Medicines Australia also observes that there is a misalignment of the stated overall purpose of the review and stage 3 terms of reference. The purpose of the overall, three-stage Diabetes Review announced last year is;

> *"to systematically evaluate the body of clinical evidence regarding diabetes interventions to ensure the most appropriate management of diabetes in clinical practice"*, and
>
> *"to ensure that patients are using the most appropriate medicines and products, effectively, and safely, to achieve optimal health outcomes and support quality use of medicines"*[6].

However, incongruously the terms of reference for stage 3 focus on whether PBS medicines being prescribed are meeting current PBS restrictions and their overall cost effectiveness. This narrow cost focus overlooks the health outcomes objective framed in the overall review purpose and appears designed to leverage price reductions from sponsors, rather than addressing any real or perceived concerns in the clinical management of patients, and certainly without addressing the key question of what value for money these medicines represent to the Australian population.

There is justifiable concern under the review program that sponsors will therefore be penalised for medicines being used outside PBS restrictions in the form of a price reduction. This mechanism appears intended to legitimise ongoing use of the medicine in a broader population, and is the least difficult solution for Government to implement. This solution does not address any perceived or actual concerns with quality use of medicines or provide relevant evolution in the clinical management of diabetes. Nevertheless this will compound the challenges of accessing new and innovative therapies in the future, which will likely be required to demonstrate cost-effectiveness against lower priced medicines.

[6] Department of Health an Ageing. Post-Market Review of Products Used in the Management of Diabetes, http://www.pbs.gov.au/info/reviews/diabetes Accessed 3 June 2013

This emphasises Medicines Australia's broader concerns that the post-market reviews are merely cost-saving exercises and are not intended to improve quality use of medicines and patient outcomes. For example, the Government identified $55.7 million in savings in the 2012-13 Federal Budget from the Anti-Dementia Review. These savings must have been estimated weeks before there was even a call for submissions for the Anti-Dementia Review and several months before the PBAC considered and provided recommendations for its final report (December 2012). This demonstrates the Government's intention to use the review as a cost cutting mechanism, rather than a policy tool to genuinely prioritise quality use of medicine outcomes.

The *Review of Anticoagulation Therapies in Atrial Fibrillation* (Anticoagulation Review) is another example contributing to Medicines Australia's concerns that post-market reviews are focused on cost-savings, budget control and delays to availability of new medicines rather than improved patient outcomes. Medicines Australia would like to further highlight that in the six months since the release of the final report of that review, the Government has not implemented any of the review recommendations related to quality use of medicines, education or guidelines. Neither has it listed any of the new oral anticoagulants included in the review, one of which was recommended for listing in March 2011. In fact in a May 2013 response to a Question in Writing in Parliament, the Minister for Health, the Hon Tanya Plibersek noted that the Anticoagulation Review recommendations were still "being investigated" and that the only other progress was an information booklet distributed by the warfarin manufacturer Aspen Australia regarding patients' diet while on warfarin.[7]

Perhaps the most worrying procedural issue is the inference that the Government, the Department and/or the PBAC have pre-determined the outcome of the Diabetes Review. Relevant to these concerns, the PBAC recently recommended two new diabetes medications for listing on the PBS with a significant price reduction and a changed restriction based on the Drug Utilisation Sub Committee (DUSC) report completed as an input to the Diabetes Review. The PBAC made statements in the publication of its outcomes from the special April 2013 meeting referring explicitly to the use of the DUSC utilisation report in consideration of the recommendations[8].

Medicines Australia contends that the DUSC analysis used in the evaluation of the gliptin fixed-dose combination submissions has yet to be considered alongside other relevant inputs to the Government's Review, and should not be applied in isolation to those inputs. While the Government's Diabetes Review continues, it appears that the PBAC has pre-empted the Review's conclusions.

The impact of these recommendations is unknown at the time of writing, however could either a) lead to a delay in access for Australian patients to two new diabetes medicines options or b) render the Diabetes Review redundant through the establishment of a broader PBS restriction for type 2 diabetes medicines at a lower benchmark price. In

[7] Commonwealth of Australia. House of Representatives, *Questions in Writing responses* (Official Hansards), 14 May 2013, Question No. 1478 - page 92-93. http://parlinfo.aph.gov.au/parlInfo/search/display/display.w3p;db=CHAMBER;id=chamber%2Fhansardr%2F9876e2b9-5961-455f-aa38-455af1c59cb8%2F0195;query=Id%3A%22chamber%2Fhansardr%2F9876e2b9-5961-455f-aa38-455af1c59cb8%2F0000%22

[8] Department of Health and Ageing. April 2013 PBAC Outcomes – Positive Recommendations. *"From the findings of the DUSC utilisation analysis....the PBAC noted that a significant proportion of patients initiated on a regimen containing a gliptin + metformin FDC had been supplied only metformin as pre-initiation...[and] ...recommended listing of the [linagliptin or saxagliptin] + metformin FDC on a cost-minimisation basis with the individual components for the proportion of use previously determined to be cost effective, and on a cost minimisation basis with metformin plus the average daily dose of a sulfonylurea for the proportion of use where cost effectiveness has not been established"*

doing so, industry is concerned that the PBAC is attempting to short-circuit the Diabetes Review process to the potential detriment of Australian patients.

Stakeholders should be concerned and disappointed that the post-market reviews program appears to be narrowly focused on cost-savings. The clinical areas reviewed to date, especially type-2 diabetes, require serious improvement in terms of unmet need, quality use of medicines and improvement of patient outcomes. Stakeholders commit significant resources to responding to reviews and their input must be thoroughly reviewed and considered in review reports and outcomes, with clear demonstrated evidence that this has been done.

Policy issues relevant to the review

Under the current framework for post-market reviews, Medicines Australia is unaware of any safeguards in place to ensure the program does not undermine existing PBS policy settings and the National Medicines Policy.

In the short term post-market reviews could re-establish pricing relativity between PBS formularies and put at risk the PBS reforms intended to drive savings from the off-patent market.

The PBS is divided into two formularies. The F1 formulary is for single-brand medicines (medicines for which there are no equivalent alternatives and no competition) which are typically patented originator medicines. The price paid by Government for these medicines is based on evidence of 'value-for-money' as determined by health technology assessment and recommendation by the PBAC (*see response to TOR 2, below)*. F1 medicines take a statutory price cut and move into the F2 formulary at the expiry of their patent and the entry of competition in the market.

The F2 formulary is for multiple brand medicines or medicines that are deemed interchangeable at the patient level. Competition between brands establishes the price paid by the Government, and the Government benefits from the discounted prices sponsors offer in order to compete in the market.

This system of pricing—'value for money' pricing for new medicines and market-based competition pricing for older, off-patent medicines—is supported by the pharmaceutical industry and other stakeholders because it allows for the listing of new, innovative medicines while ensuring savings from older, generic medicines.

However, if the prices of medicines in the F1 formulary are eroded down to the prices of medicines which have moved into the F2 formulary through the post-market reviews program, this system will be undermined. Innovative pharmaceutical companies which manufacture F1 medicines rely on a period of exclusivity to recoup the costs of research and development. Manufacturers may be unable to supply to the Australian market if on-patent medicines are priced down to the levels of F2 medicines.

The premature downgrade of F1 medicine prices to F2 prices due to a post-market review undermines the pricing policy framework that justifies the very distinction between the formularies. Government has an obligation to ensure that PBS listings are not compromised by a race to the bottom through activities such as post-market reviews, designed to drag down prices of medicines in the F1 formulary.

Post-market reviews and the resultant cost-savings being sought by the Government through this program may jeopardise access to existing medicines and, more importantly, new medicines, which will be compared to the low cost medicines already on the market when considered by the PBAC.

When assessing a new medicine, the PBAC considers the cost effectiveness of the proposed medicine compared to existing treatments. Despite the high investment in time and money to research, develop and trial new treatment options, new medicines are only valued for the health outcomes provided to patients and to the health system above and beyond the standard, existing treatment. Benefits such as easier adherence to treatment, improvements in tolerability and providing an alternative for patients who are intolerant to an existing medication are difficult to capture in the current system and therefore the benefits to patients and their clinicians, and ultimately the Australian healthcare and economy, are not adequately valued.

This means, for example, that if the existing comparable diabetes treatment is available at a very low cost to Government (either through F2 market-based pricing or price erosion through programs such as post-market reviews), the sponsor of a new diabetes medicine must demonstrate 'value for money' against this low cost alternative.

Some new medicines are significantly more effective than existing treatments, and evidence to support this helps sponsors to justify a higher price than existing treatments. However, in some cases, new medicines are incrementally superior to the existing treatment or provide patient benefits that are not easily quantified for the purposes of a health technology assessment. In those cases, sponsors may face difficulties bringing new medicines to market in Australia.

These serious policy implications underscore the need for rigorous processes for the Diabetes Review. Safeguards against these policy issues are critical for long term progress in treating Australians with type 2 diabetes. Industry is concerned that post market reviews like the Diabetes Review are short-term fixes to whole-of-government budget issues that threaten to jeopardise access to medicines in the longer term. Additional information is included in the appendices.[9]

[9] Appendix A responds to concerns specifically related to the individual terms of reference
Appendix B details an example of the literature review required to respond to Term of Reference 3
Appendix C highlights the concerns regarding ambiguity in the scope of the review

Conclusion

Medicines Australia has highlighted a number of clinical, procedural and policy concerns related to the Diabetes Review and post market reviews in general. The concerns raised in this submission should not be ignored if the Government is genuinely seeking "*to improve morbidity, mortality, safety and quality of life for patients with diabetes*". The Diabetes Review, as other reviews before it, presents serious risks for patients' access to medicines and could represent a lost opportunity to improve the management of diabetes. Recommendations other than costs, such as quality use of medicines, education or guidelines need to have transparent implementation processes and appropriate stakeholder consultation.

Sponsors are concerned that they will be penalised for medicines being used outside PBS restrictions in the form of a price reduction. This mechanism will be presented as legitimising ongoing use of the medicines in the broader population. However, this response will not address any perceived or actual concerns with quality use of medicines nor improve the clinical management of diabetes. Disturbingly, this will compound the challenges of bringing new and innovative therapies to Australia, which will likely have to demonstrate cost-effectiveness against lower priced medicines.

Recommendations:

Medicines Australia recommends that:

1. The Australian Government works with stakeholders to address the policy implications and procedural concerns highlighted in this and other submissions.
2. The outcome of the Diabetes Review clearly reports on the most appropriate policy options available for addressing the findings of the review, including education, quality use of medicines (QUM) options, price changes
3. The outcome of the Diabetes Review clearly identifies the implications of the review findings for stakeholders, such as;
    i. Immediate and short term access to medicines for patients and treating clinicians; and
    ii. Likely long term consequences for access to new therapies
4. The Diabetes Review centres on health outcomes for people living with type 2 diabetes and demonstrates attention to:

    g. full examination of the clinical management of diabetes including the value clinicians and patients place on treatment selection;
    h. examination of prescribing patterns in relation to clinical evidence and Australian and international clinical guidelines
    i. establishing whether PBS restrictions are out-dated and therefore do not reflect best clinical practice;
    j. improvement of evidence-based individualised treatment options to ensure alignment with world's best practice;
    k. consideration of appropriate policy, QUM and other solutions to ensure appropriate use of medicines; these options must take into account the scope of responsibility for each stakeholder; and
    l. fully addressing the stated Terms of Reference, including the clinical evidence covering multiple medicines.

    These recommendations further highlight that more time is required before any outcomes arise from the Review.

APPENDIX A: Responses to the Terms of Reference

In Response to Term of Reference 1 (TOR1)

"Describe the utilisation and patterns of treatment of PBS listed drugs for T2DM, and compare these with PBS restrictions"

The Diabetes Review needs to fully examine the current clinical management of diabetes in Australia. While there are PBS restrictions that guide the use of medicines for type 2 diabetes, the Diabetes Review has to also examine the registered indications for these medicines; it has to seek advice from clinicians how these medicines are used in practice and where clinicians deem use as necessary and appropriate despite the PBS restrictions. It is not appropriate to simply impose the cost of any perceived use beyond the PBS restrictions on sponsors. To only rely on the analyses of the Drug Utilisation Sub-Committee that are based on a sample, that is limited in time and representativeness, without wider consideration is not informative.

Under TOR 1, stakeholders are asked to describe utilisation and treatment patterns for PBS drugs for type 2 diabetes.

The Diabetes Review should fully examine the clinical management of diabetes and the value clinicians and patients place on treatment selection, and any consideration of utilisation should include careful assessment of outcomes. Considering utilisation and treatment patterns in the context of cost alone, in isolation of barriers to access and adherence, education, health benefits and outcomes, is a one-sided assessment of a complex problem that prioritises the Government's cost savings objectives over patient outcomes.

Term of reference 1 for the Diabetes Review is another example of deficient process and a flawed review which may not deliver comprehensive advice on the medicines used to treat diabetes.

As outlined below in response to terms of reference 3 and 4, there is a considerable commitment required to adequately address the TOR in any review including the Diabetes Review. The impact on resources is not only in providing input to the review but also the displacement of resources already assigned to ongoing projects, projects which are predominantly PBAC submissions to secure PBS listing for new, innovative medicines. However, the ability to plan resourcing to ensure all projects are addressed requires substantial lead time.

These issues are compounded not only by the uncertainties around the timelines of reviews but also the inconsistency in the advice being provided on the medicines under consideration in the Diabetes Review. Sponsors of insulins, which are PBS-listed for the management of type 2 diabetes, are unclear on where this key therapy class fits within the Review.

Despite the stated objective that the Diabetes Review *"examine and characterise the complexity and heterogeneity of PBS listings for drugs used in type 2 diabetes mellitus"*[10], insulin, an indisputably key treatment in type 2 diabetes, could have been interpreted as part of the original (August 2012) terms of the overall diabetes review, it

[10] Ibid

was then excluded under later phase 3 terms and most recently the Department communicated in May 2013 that "*the information or data on the efficacy and safety of insulin compared to other medicines will be considered*", although insulin is not a "*specific focus* of the review. This creates ambiguity in the scope of the review and is another example of an overall deficient process.

It may be argued that manufacturers have had sufficient time to review, document and analyse the evidence base for the use of insulin in the management of patients with type 2 diabetes. However, without certainty that the scope of the review will not fundamentally change over time, there is little that a sponsor can do pre-emptively without expending considerable time and resources which might be directed to other PBAC submissions for the listing of new medicines (*see Appendix C*).

To build a review of the clinical evidence requires clarity on the questions being asked in order to identify which trials are relevant to the consideration. Building on this the determination of the cost effectiveness ('value for money') again is determined by the scope of review and choice of comparator; if for example the proposed treatment population or the range of treatment options changes, the major cost effectiveness analyses model developed will need to be restarted from the beginning.

The inconsistency of whether insulin products are included or excluded from the review is just one example of the deficient process of the Diabetes Review raised as a concern by Medicines Australia. The unpredictability of new requests and the release of each additional or changed piece of information create confusion as to the scope and purpose of the review. This further leads to inefficient use of company resources and insufficient time to prepare an appropriate and relevant response for the Committee to make a fully informed recommendation. As an industry, our opportunity to input into reviews is highly valued and an essential part of any PBS listing process, however clarity and consistency on the scope of the review is necessary.

In Response to Term of Reference 2 (TOR2)

"*Consider if the utilisation of PBS listed drugs in current clinical practice represents expected cost effective use"*

The focus of the second term of reference is on cost-effectiveness. Based on past government reviews, price reductions have been deemed necessary based on any proportion of utilisation that was identified as beyond the PBS restrictions. Medicines Australia would like to highlight that in order to fully consider cost-effectiveness for medicines used in the treatment of type 2 diabetes, all relevant clinical evidence, all the relevant costs have to be considered versus the agreed "comparator" and the health outcomes modelled in the longer term as diabetes is a chronic condition. Cost-effectiveness should not mean price reduction as it is currently being applied by government.

Under TOR 2, stakeholders are asked to consider utilisation of the drugs under review in current clinical practice and whether this represents expected cost-effective use.

The cornerstone for pricing new medicines in the Australian reimbursement system is the use of economic evaluation with due regard to clinical evidence. In assessing the value for money of a particular product, the PBAC considers the 'clinical place, overall effectiveness, cost and cost-effectiveness of a proposed drug against a comparator, which may be another drug already listed'[11] or the standard medical treatment, where there is no PBS-listed alternative.

The PBAC Guidelines set out what evidence should be presented; how clinical and economic evidence should be interpreted, and how uncertainty in the evidence could be addressed. Industry sponsors of proposed new medicines have the onus to gather and present evidence which meets the standards and format required by the PBAC. Much of the evidence comes from clinical trials conducted to demonstrate that the medicine is safe and effective for marketing approval by the Therapeutic Goods Administration.

Clinical trials are typically designed to demonstrate the clinical effectiveness of a medicine and are likely to meet this requirement of the PBAC guidelines; however, clinical trials often do not produce the necessary array of evidence, and its application to the Australian system, as required for the economic evaluation undertaken by the PBAC. Typically, the sponsor must present data from an acceptably designed and scientifically rigorous trial and analyse the data for the purposes of the economic assessment. For example, where the duration of the clinical trial was shorter than the expected duration of treatment in practice, the sponsor must extrapolate the trial data.

Major applications for new listings to the PBS largely fall into two categories: those products shown to be therapeutically superior to the main comparator, and those products shown to be non-inferior or equivalent to the main comparator. There are several types of economic evaluations that may be presented depending on the type of application. Where a drug has been shown to be therapeutically superior to the main comparator, the 'base case' involves a cost-utility analysis. In a cost-utility analysis, health outcomes are presented in the Quality-Adjusted Life-Years (QALY) gained with use of the proposed listing compared with the main comparator. The QALY

[11] Department of Health an Ageing. December 2008. Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee, (Version 4.3) P5. http://www.pbs.gov.au/industry/listing/elements/pbac-guidelines/PBAC4.3.2.pdf

measurement attempts to identify the value patients place on different health states, usually through the use of questionnaires to participants in clinical trials. The QALY is a common measurement tool, allowing the PBAC to compare the value added by different medicines regardless of the disease area and population size.

Other less common economic evaluations used in cases where the proposed product has been shown to be therapeutically superior include cost-effectiveness analysis (health outcomes reported in units of health) and cost-benefit analysis (health outcomes reported in monetary terms).

Sponsors of new, superior medicines are tasked with demonstrating the incremental benefit the new medicine provides over the existing treatment, which is sometimes an older, off-patented and inexpensive medicine. Sponsors must show that the high cost of the new medicine and the incremental benefits it provides are as cost-effective as the low cost existing medicine which provides standard, accepted benefits to patients and the health system. Incremental advancements in medicine are important for patients and for ongoing innovation, but marginal achievements can be difficult to demonstrate to the PBAC given the limitations and uncertainties in trial data.

Some major applications to the PBAC propose the listing of medicines which have been demonstrated to be non-inferior or equivalent to the main comparator in terms of effectiveness and safety. These medicines cannot justify a higher price based on health outcomes and therefore cost-minimisation analysis is appropriate. It should be noted that if the PBAC recommends a medicine based on cost-minimisation analysis, the Government will pay no more than what it pays for the comparator medicine for the same benefits. Because patients respond differently to medicines, the treatments recommended for listing under cost-minimisation analysis may be superior at the individual patient level. This method of analysis is important because it enables the listing of multiple medicines to treat a condition, even where the medicines listed later are not proven to be superior, due for example to limitations in the trial data. Expanding potential treatment options adds another layer of value to the PBS.

What the various economic evaluations undertaken by the PBAC have in common is an assessment of cost and health outcomes against a comparator. An equation called the incremental cost-effectiveness ratio (or 'ICER') is used to compare the costs and effects (typically measured in Quality-Adjusted Life-Years, as discussed above) of a new medicine with the costs and effects of the comparator.

$$\textbf{Incremental cost-effectiveness ratio (ICER)} = \frac{\textbf{Cost of medicine 1 – Cost of medicine 2 (comparator)}}{\textbf{Effect of medicine 1 – Effect of medicine 2 (comparator)}}$$

In order to conduct an HTA assessment, the costs and effects of the medicines under review must be considered and a significant amount of work is required to build an appropriate model. The applicant must build a complex model which measures the impacts of the new (proposed) medicine versus the existing medicine/s on health benefits and patient quality of life; costs to the healthcare system such as the pattern of use of clinical and pathology services; treatment of adverse events and pre-medication over the lifetime of the patient, which can range from 1 year to 30 years. Each of the model inputs must be sourced, assessed for quality and then applied. This level of rigor ensures that the equation on how to determine cost-effectiveness can be appropriately addressed and provided a common measure for determining the value for money a medicine provides.

Together with the consistent guidance of the PBAC Guidelines and the use of the QALY measure in the ICER equation, the PBAC is able to compare the value added by

different medicines regardless of the disease area and population size. This enables the PBAC to assess medicines consistently over time; and in theory, this also ensures that HTA is applied appropriately and consistently over time.

The economic methods are well understood and clearly outlined in the PBAC Guidelines. The economic framework used in price setting of new medicines has served industry and the Government well by ensuring taxpayers achieve value for money.

Relying on post-market utilisation data, without incorporating clinical information, fundamentally undermines the present system that allows pricing predictability within a well-understood economic framework. This was a fundamental flaw observed in the Anti-Dementia Review, where the PBAC made a series of recommendations; that products were being used outside of restrictions; restrictions should be loosened; and price reductions should be applied.

If we consider the recommendation made in the review of anti-dementia drugs in the context of the simple cost-effectiveness equation presented above we can see that not all information was considered in order to make a decision regarding cost-effectiveness. The recommendation linking over-utilisation to a price reduction was completely, and inappropriately, correlated with the DUSC review asserting that the number of prescriptions dispensed was 40 per cent higher than projected. However, there was no assessment as to whether the additional 40 per cent of prescriptions were used in the appropriate patient population or delivered the PBAC prescribed health outcomes. Essentially, the review of anti-dementia medicines assumed, without evidence to the contrary, that these 40 per cent of prescriptions were not being used cost effectively and the consequence was that prices should be adjusted downwards by 40 per cent.

This basic mathematical derivation by the PBAC is that, *ceteris paribus,* every script not deemed to be used in cost effective setting provides absolutely no health gain. As such, the only logical conclusion if this were true would be to enhance the restrictions to prevent usage in the population experiencing no health gain. Instead, the PBAC, using implausible rationale, recommended loosening restrictions to enable usage consistent with observations. Therefore, the PBAC recommendation is either materially flawed or is fundamentally biased to drive down expenditure and not in keeping with their remit under the National Health Act. In either case, the Government chose to ignore these concerns despite Medicines Australia raising them with both the bureaucracy and the Minister.

The solution to address excess utilisation of new medicines not deemed to be cost effective is to re-weigh the clinical and economic data in the post-marketing environment, rather than affecting a price reduction of a magnitude similar to the excess utilisation. The latter approach assumes that all excess utilisation has zero economic value, when this is not the case. These examples are concerning and give industry the impression that the standards of HTA required for new listings are not being applied to post-market reviews.

In Response to Terms of Reference 3 and 4 (TOR 3&4)

"Consolidate the clinical trial evidence used to support PBS listings of diabetes medicines listed since 2002" and

"Collate and evaluate any additional clinical studies or meta-analyses for drugs currently PBS listed for T2DM that the Pharmaceutical Benefits Advisory Committee (PBAC) has not seen and that would inform their consideration"

Australia's reimbursement system and processes have been recognised by other countries for its rigor and due process. Medicines Australia believes that the current reviews undermine the health technology assessment processes in Australia. These terms of reference highlight the inadequate time provided to sponsors to fully inform the Diabetes Review on the clinical evidence for medicines used in the treatment of type 2 diabetes. To systematically identify and review over 16,000 citations since 2002 for bias, relevant efficacy and safety outcomes, and to present meta-analyses of the most relevant trials in a matter of weeks is clearly not possible and again highlights the inadequacy of the processes for this and other reviews.

Under TORs 3 and 4, stakeholders are asked to consolidate clinical trial evidence used to support listings since 2002 (TOR 3); and, evaluate any additional clinical studies and meta-analyses (TOR 4). The six-week submission timeframe is not sufficient given the volume, complexity and level of analysis required to address these terms of reference to the appropriate standard.

As discussed above, the industry firmly believes that the standard for post-market reviews must be the same high standard as is applied for new listings on the PBS, which is outlined in the PBAC Guidelines[12].

In order to uphold the high standard of HTA in Australia, it is crucial that any consideration of the clinical evidence in a post-market review takes the same systematic approach as is requested by the PBAC for any proposed new medicine or new indication. Figure 1 below is taken from the PBAC Guidelines and demonstrates the complexity and interrelated steps which are essential to address the questions of whether a medicine presents 'value for money' in terms of clinical and cost effectiveness[13]. Medicines Australia does not accept that the Diabetes Review can systematically evaluate the available clinical evidence in the time proposed for this review.

[12] Department of Health an Ageing. December 2008. Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee, (Version 4.3). http://www.pbs.gov.au/industry/listing/elements/pbac-guidelines/PBAC4.3.2.pdf

[13] Ibid (Figure 5.1, p.29)

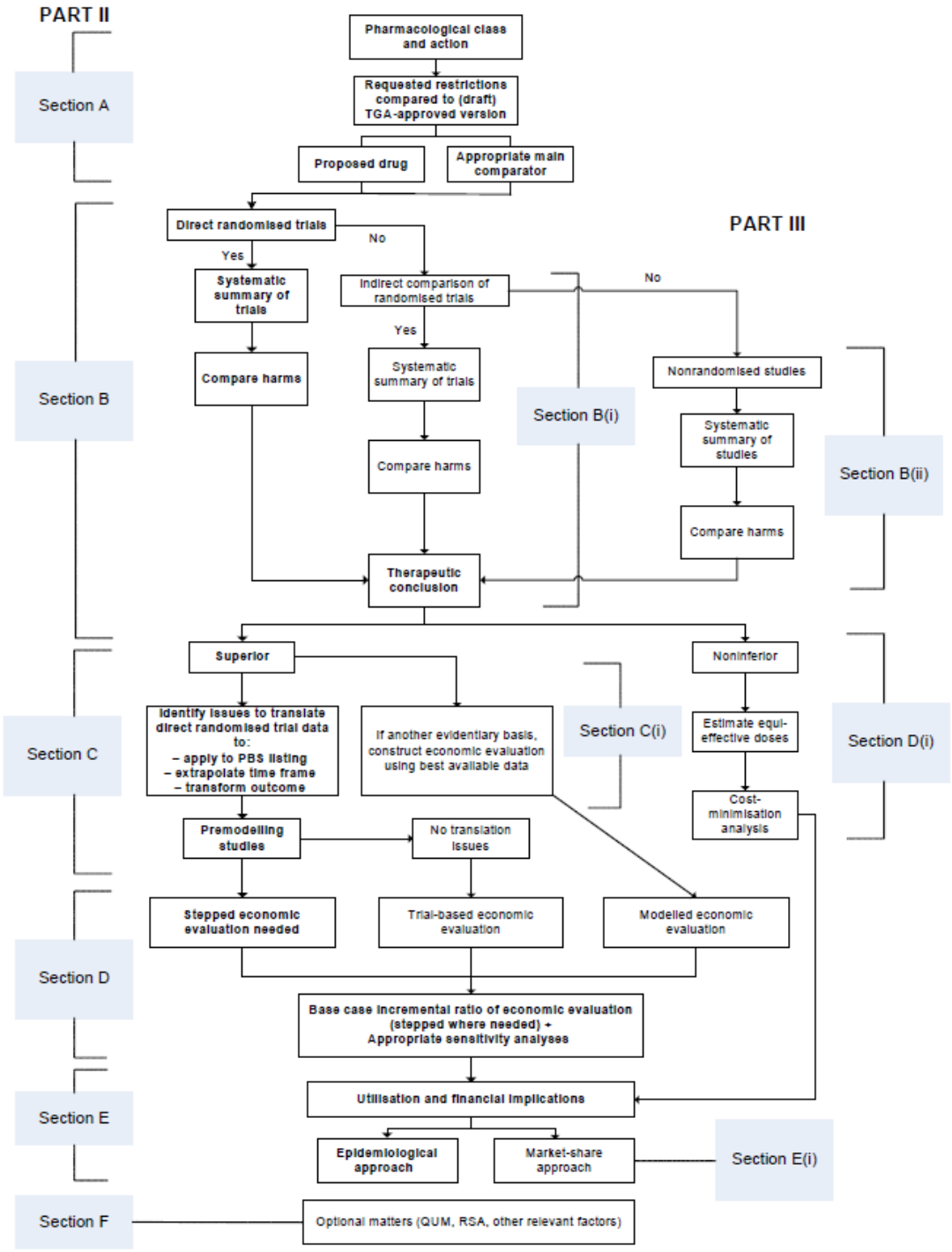

Figure 1, Key decisions and stages in preparing a major submission to the PBAC. (PBAC Guidelines Figure 5.1, p.29)

To respond to TOR 3 (consolidate clinical trial evidence used to support listings since 2002), a sponsor would expect to follow the process detailed in Section B of the PBAC Guidelines for clinical evaluation for the main indication, as is the case for the listing of new medicines on the PBS.

The PBAC Guidelines to inform the identification, synthesis and analysis of the efficacy and safety data are extensive and reflect the burden of proof this section of the guidelines provides in determining overall 'value for money'. To evaluate the clinical evidence, the sponsor would follow Section B (pages 61-87) or Section B(i) (pages 173-183) if an indirect comparison of the evidence is required. However, the scope of this section for a post-market review of diabetes medicines would likely be more complex

than an application to initially list a medicine on the PBS. For example, the consideration of the body of evidence of non-randomised trials (Section B(ii), pages 184-192) may be applicable if consideration of use of these medicines outside of the clinical trial setting (i.e. in a registry or real-world setting) is considered relevant.

For sponsors, the first step in addressing Section B of the PBAC Guidelines is a systematic review of the literature meeting the requirements of the PBAC as follows:

> *"the specific databases and registers of clinical trials searched, including at least MEDLINE13, EMBASE14, The Cochrane Library (including the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials), the National Institutes of Health16 and the Australian Clinical Trials Registry (ACTR). The search should also include databases internal to the company and any other known registers of randomised trials relevant to the therapeutic area."*[14]

This is resource-intensive task for sponsors, especially for terms of reference as broad as those outlined for Stage 3 of the Diabetes Review. As an example, a search of the EMBASE database for all relevant publications reporting on trials of the diabetes medicines relevant to this review was conducted (*see Appendix B*):

- This search identified over 22,000 individual publications which would need to be assessed for relevance to the review.
- Even if the search was confined to after 2002, over 16,000 references would need to be assessed.
- Almost certainly a search of the additional databases specified by the PBAC would identify a significantly higher total number of publications relating to diabetes medicines.
- Some of the above would have been already assessed by the PBAC and/or provided by other sponsors; however, operating in isolation and without full knowledge of what information is expected or useful in a post-market review submission, each sponsor could anticipate that they should conduct a full review, potentially duplicating the work of the PBAC or other sponsors unnecessarily.

These results do not reflect solely those publications released after 2002 and will include a number of studies previously considered by the PBAC. However, as each sponsor's medicine will be considered in comparison to other medicines in the same therapeutic class and across the classes, it would be unfair to assume that a sponsor would only need to consider the clinical evidence for their own medicine. The volume of work to simply assess and decide which of these publications is relevant is only the first step but a crucial one given the different types of studies published for type 2 diabetes.

The next steps in the consideration of the body of clinical evidence following a systematic review of the literature are summarised in Figure 2, taken from the PBAC Guidelines.[15]

[14] Ibid, p63
[15] Ibid. Figure B.1 (p.62).

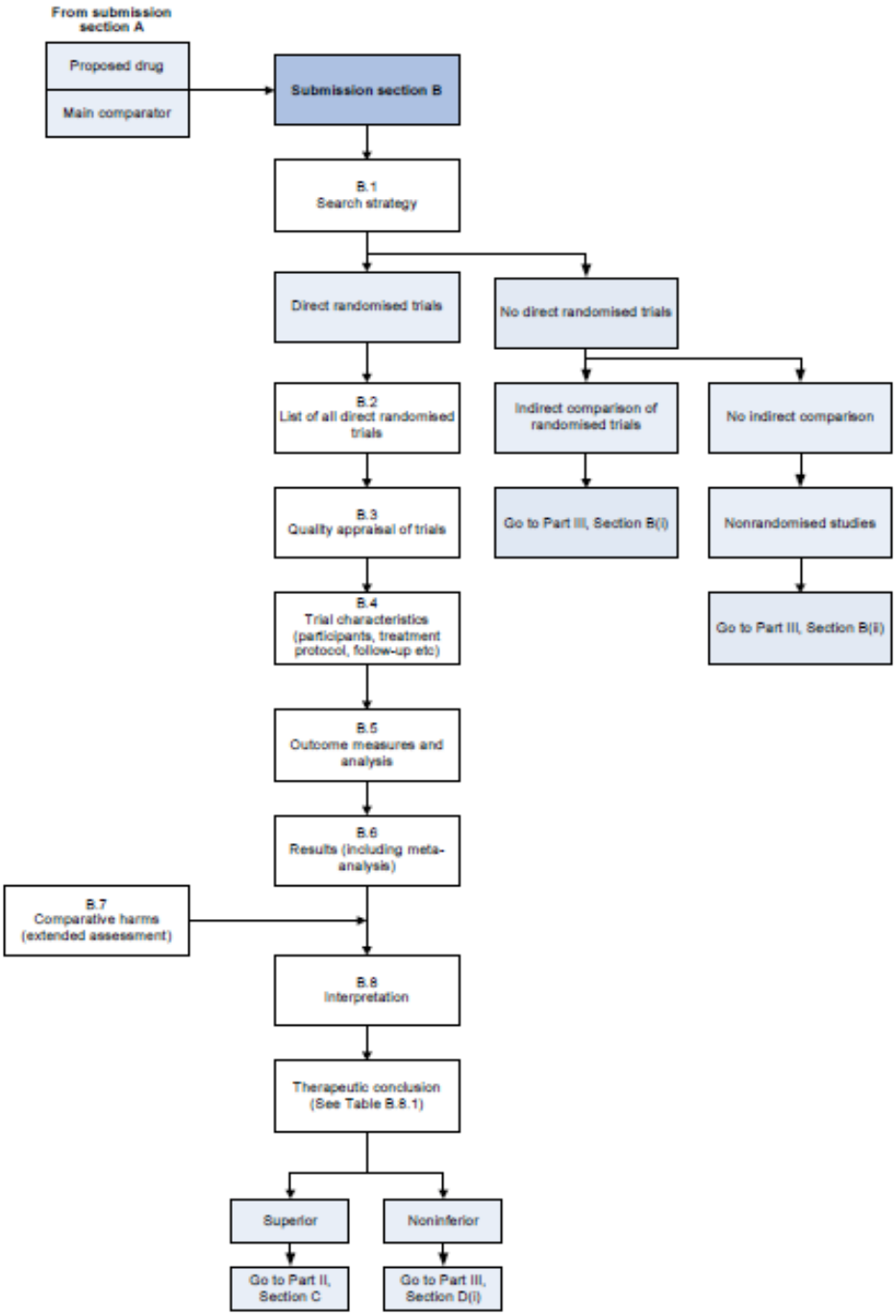

Figure B.1 Key information requests for submission section B of a major submission to PBAC

Figure 2, (PBAC Guidelines, Figure B.1, p.62)

Following the systematic literature review, each study that is identified must be evaluated for relevance to the application to the PBAC:

- If relevant all trial characteristics[16], design and statistical robustness of the health benefits must be tabulated and assessed;

[16] Department of Health an Ageing. December 2008. Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee, (Version 4.3). http://www.pbs.gov.au/industry/listing/elements/pbac-guidelines/PBAC4.3.2.pdf

    - All trials deemed not relevant for inclusion must still be documented with the rationale for non-inclusion

- Where there are multiple trials the results must then be statistically analysed to provide a single estimate of the benefit to patients;
    - These analyses range from relativity straightforward meta-analysis to complex mixed treatment comparisons which require dedicated experience and expertise from statisticians.
- All safety data, including data from clinical trials and also the pharmacovigilance data, Periodic Safety Update reports (PSURs) the sponsor must collect, is collated and presented. The background data which must be reviewed for safety can run to hundreds of pages.

Whilst every submission to a post-market review will take a substantial amount of time to prepare once the specific terms of reference are known, it is clear that a comprehensive submission would be a significant piece of work for a sponsor to complete. The timeframe of 6 weeks is clearly insufficient and again highlights a lack of process for consideration of the evidence and a haste to seek lower prices for medicines under review. This is clearly evident in the PBAC's April 2013 consideration of the gliptin fixed-dose combination products referred to previously.

Under TOR 4, stakeholders are asked to submit studies and meta-analyses *"that the PBAC has not seen and that would inform their consideration"*[17]. This is unreasonable, as sponsors and other stakeholders could not be expected to know what the PBAC has seen and assessed before nor what would be useful for their considerations. This is especially true given the lack of information provided to stakeholders about the triggers and potential outcomes of the Diabetes Review.

If the PBAC has considered a medicine recently, the sponsor may have fewer new evidence sources to incorporate. However, for any medicine which was considered a number of years ago, the evidence to be incorporated represents a greater burden. The breadth of the terms of reference compounds this issue.

Even the National Health and Medical Research Council (NHMRC), Australia's peak body for supporting health and medical research, noted in their handbook for reviewing scientific literature that the average hours a specialist company spent conducting a systematic review was 1,139 (approximately 30 person-weeks of full-time work), ranging from 216 hours to 2,518 hours (6 person-weeks to 67 person-weeks)[18].

While there are variables affecting the length of time it will take to complete a systematic review, estimates confirm how resource-intensive the work is. By way of comparison, it is reported that a Cochrane review[19] on average takes 18 months to complete, although it is recognised this may be shorter or longer depending on the area of investigation.[20]

Furthermore, a systematic review underpins a cost effectiveness analysis, which is a separate complex piece of work on top of the systematic review required to address the question of whether an intervention provides 'value for money'.

[17] Department of Health an Ageing. Post-Market Review of Products Used in the Management of Diabetes, http://www.pbs.gov.au/info/reviews/diabetes Accessed 3 June 2013

[18] NHMRC. 2000. *How to review the evidence: systematic identification and review of the scientific literature, Handbook series on preparing clinical practice guidelines.* Commonwealth of Australia. http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cp65.pdf Access on 3 June 2013.

[19] Cochrane Reviews are systematic reviews and meta-analyses which summarise the results of primary medical research on a specific question. See http://www.cochrane.org/cochrane-reviews (accessed on 12 June 2013)

[20] South African Medical Research Council. 2012. South African Cochrane Centre. http://www.mrc.ac.za/cochrane/systematic.htm Accessed 12 June 2013

We acknowledge that the scope of every sponsor response to a review will vary depending on the evidence available. However, based on the Diabetes Review's terms of reference and the availability of numerous published studies covering many different medicines and classes, it is clear much more time is required for full consideration of the evidence for this review. Medicine Australia maintains that the process for this and other reviews is not clear, there is insufficient time for sponsors to consider the terms of reference, and there is a rush to get to the ultimate outcome.

APPENDIX B: Example EMBASE literature search results

EMBASE search 22 May 2013 for all references for medicines used for the treatment of type 2 diabetes

1	*metformin/	7461	Advanced
2	*glipizide/	702	Advanced
3	*gliclazide/	854	Advanced
4	*glibenclamide/	3345	Advanced
5	*glimepiride/	724	Advanced
6	*acarbose/	1234	Advanced
7	*rosiglitazone/	3185	Advanced
8	*pioglitazone/	2977	Advanced
9	*linagliptin/	202	Advanced
10	*saxagliptin/	245	Advanced
11	*sitagliptin/	854	Advanced
12	*vildagliptin/	423	Advanced
13	*glucagon like peptide 1/	2957	Advanced
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	21817	Advanced
15	limit 14 to yr="2002 -Current"	16363	Advanced

APPENDIX C: Examples of ambiguity in the scope of the review

Information provided on scope of Diabetes Review

In August 2012 the PBAC endorsed the Terms of Reference (TOR) to guide the review of diabetes management for Australian patients. On this basis the overarching objective of the Diabetes Review is:

> "to examine and characterise the complexity and heterogeneity of PBS listings for drugs used in type 2 diabetes mellitus (type 2 diabetes); and to review self-monitored blood glucose testing for people with type 2 diabetes and insulin pumps for people with type 1 diabetes mellitus (T1DM) to inform an assessment of their effectiveness in terms of clinical outcomes and cost."[21]

In Table 1 below, each TOR relevant to Stage 3 of the Diabetes Review is presented alongside the interpretation of whether insulin products would be a key component.

Table 1

#	TOR	Anticipated relevance to insulin in Stage 3 Review
1	Describe the utilisation and patterns of treatment of PBS listed drugs for TYPE 2 DIABETES, and compare these with PBS restrictions	Yes PBS: 11 different insulin products with at least 11 manufacturers
2	Consider if the utilisation of PBS listed drugs in current clinical practice represents expected cost effective use	Yes See above
3	Consolidate the clinical trial evidence used to support PBS listings of diabetes medicines listed since 2002	Yes The majority of insulins were PBS listed after 2002; there is no guarantee that there hasn't been new clinical evidence published since the time of listing. One insulin (insulin glargine (Lantus) was PBS listed in 2006. A number of the newer oral agents have included insulin as a comparator in a number of key trials.
4	Collate and evaluate any additional clinical studies or meta-analyses for drugs currently PBS listed for TYPE 2 DIABETES that the Pharmaceutical Benefits Advisory Committee (PBAC) has not seen and that would inform their consideration	Yes See answer to TOR 1 & 3

Manufacturers of insulin products interpreting this information would be preparing to put forward a major cost effectiveness review of the use of insulin. Of the twelve different forms of insulin with a PBS listing the majority (11 of the 12) are for use in the management of type 2 diabetes. The section on products and medicines included in this review clearly states, "the Diabetes Review will focus on the management of the condition overall and how all medicines and products are being used to benefit patients, alongside other aspects of diabetes management."[22] As detailed in response to Terms of

[21] Department of Health an Ageing. Post-Market Review of Products Used in the Management of Diabetes, http://www.pbs.gov.au/info/reviews/diabetes Accessed 3 June 2013
[22] Ibid

Reference 3 and 4 above, the volume of evidence available for this particular treatment option is extensive and would require significant and dedicated resources to adequately analyse not only the clinical effectiveness but also the cost effectiveness and the current financial impact to the Commonwealth (i.e. an assessment of the 'value for money' insulin providers in the Australian setting).

However, in the notification received by manufacturers of diabetes medications, including insulins, dated 3 May 2013 the list of medicines under review clearly states that insulin is not under consideration. (Please note that in a further example of inefficiency, some but not all insulin manufacturers received this notification) (*See Table 2*).

Post-market Review of Diabetes – Stage 3 – *Medicines used in the Management of Type 2 Diabetes*[23]

Table 2	
Class	**Drugs**
Biguanides	Metformin
Sulfonamides	Glipizide Gliclazide Glibenclamide Glimepiride
Alpha glucosidase inhibitors	Acarbose
Thiazolidinediones	Rosiglitazone Pioglitazone
Dipeptidyl peptidase 4 (DPP-4) inhibitors	Linagliptin Saxagliptin Simvastatin and sitagliptin Sitagliptin Vildagliptin
Other blood glucose lowering agents	Exenatide
Combinations of oral blood glucose lowering agents	Sitagliptin and metformin Rosiglitazone and metformin Vildagliptin and metformin Metformin and glibenclamide

[23] Pharmaceutical Policy Branch, Attachment B: Notice of upcoming public call for submissions: stage three of the post-market review of products used for the treatment of diabetes; Department of Health and Ageing, 3 May 2013.

On 20 May 2013 the PBS website was updated to announce publically that Stage 3 of the Diabetes Review was open to stakeholders. In comparison to the information circulated to stakeholders on 3 May 2013:

1. The TOR and the focus on items 1 to 4 are consistent; however,
2. The medicines considered relevant to Stage 3 are unclear and inconsistent with previous advice (*see Table 2*), the information provided is:
    a. "Stakeholders and other interested parties may wish to consider the range of treatment options available to manage type 2 diabetes, and how these are being used. ….We acknowledge that insulin is widely used in the management of type 2 diabetes although it is not the specific focus of this review. However, the utilisation of insulin will provide context for medicines used in type 2 diabetes given the place of insulin in the clinical treatment algorithm for prescribers. Therefore, the information or data on the efficacy and safety of insulin compared to other medicines will be considered."[24]

In general it is not clear how the totality of interventions for the management of diabetes will be evaluated Evidence from the February 2013 DUSC review indicates that:

> "*DUSC further examined the utilisation of medicines for type 2 diabetes in a prevalent population of patients. ….a large proportion of prescriptions supplied through the PBS for the dipeptidyl peptidase-4 inhibitors ('gliptins') do not meet the criteria for PBS subsidy. …some prescribing of exenatide, rosiglitazone and pioglitazone is outside of the PBS restrictions. DUSC considered that the PBS restrictions do not align with recent clinical guidelines and the perceived place of newer medicines for type 2 diabetes in practice….The utilisation findings will contribute to the Post-market Review of Products Used in the Management of Diabetes."*[25]

As stated earlier, the inconsistency of whether insulin products are included or excluded from the review is just one example of the deficient process of the Diabetes Review raised as a concern by Medicines Australia. The unpredictability of new requests and the release of each additional or changed piece of information create confusion as to the scope and purpose of the review.

[24] Department of Health an Ageing. Post-Market Review of Products Used in the Management of Diabetes, http://www.pbs.gov.au/info/reviews/diabetes Accessed 3 June 2013

[25] Department of Health an Ageing.Drug Utilisation Sub-Committee Outcome Statement 7-8 Febraury 2013. http://www.pbs.gov.au/industry/listing/elements/dusc-meetings/dos/dusc-dos-feb-2013.pdf Accessed 13 June 2013.