Re: Pharmaceutical Benefits Advisory Committee (PBAC) Guidelines version 5.0

Novo Nordisk Pharmaceuticals welcomes the Review of the PBAC guidelines and the opportunity to comment. The Review is an opportunity to ensure the PBAC Guidelines are aligned with world best practice, incorporate new, updated and proven health technology assessment (HTA) methodologies and allow for a discussion to address the overall challenge the pharmaceutical industry is facing in Australia with respect to increased lag time when listing new medicine access (Media release June 2015, The Hon Sussan Ley).

Summary

Novo Nordisk overwhelmingly supports views expressed by Medicines Australia in its Guidelines submission, namely:

2a) Revised guidance on the selection of the Main Comparator;
2b) Guidance not adequately covered in draft Version 5.0; and
2c) Procedural elements not adequately covered in draft Version 5.0

In respect of (2a), Novo Nordisk is extremely concerned at the proposal to include the wording 'least expensive alternative medicine' in relation to selection of the main comparator in Version 5.0, which on the face of it is designed to replace the wording 'therapy that prescriber would most replace' in Version 4.5.

We concur with Medicines Australia's view that the requirement for a sponsor to select the main comparator on a price-only basis as distinct from actual clinical practice has undesirable consequences for patients as a result of companies being unable to viably address historic comparator erosion and linkages between the F1 and F2 formularies.

This would have the added effect of raising reference pricing implications for listed PBS medications linked in therapeutic groups, if a new medicine were to be allocated a comparator within a reference group.

This measure appears to have been calculated to deny patient access to new medications at a time when the Turnbull government is reaching out to the pharmaceutical industry, amongst other things, to become part of its innovation package. This measure will inevitably destroy the industry's ability to innovate in this country due to cost-driven measures on the PBS.

A key issue in Australia is that some medications have been remained unavailable for up to 8 years after becoming available overseas (example Myozyme®). Novo Nordisk has experienced lengthy delays with Victoza® (liraglutide, rys), due to seven PBAC rejections on the grounds of cost since 2009. In contrast, Victoza® has been reimbursed in 43 other leading countries since 2009 and has become the most used GLP1 analogue globally to treat people with Type 2 Diabetes (IMS data).

Novo Nordisk would like to make recommendations specifically on key aspects of the new guideline, which if implemented could enable faster access to new innovative and

potentially life-saving medicines. Novo Nordisk has identified four key issues with the new guidelines:

1) Reconsideration of the wording of the lowest price comparator in section 1.1
2) A broader assessment of value in section 3A including societal & patient benefits and recognition of incremental benefit
3) More transparency in section 3.6 around the assessment and definitions of resources that can be used for a HE technology assessment
4) Acceptability of well validated, referenced HE models used by other payers, without the need to additionally validate a model through an external validator as part of the submission as stated in section 3.2 & 3.7

1) Reconsideration of the wording of the lowest price comparator in section 1.1

Since the cessation of the Pharmaceutical Benefit Pricing Authority (PBPA) in early 2014, there is a broad and growing perception that the PBAC is acting as price negotiator and that the post PBAC outcome process is unclear. This results in the overall assessment becoming more of a price discussion than a clinical comparison. It is of particular concern and alarming for patients to see that the new guideline in section 1, when choosing the main comparator and "where multiple comparators with large disparities in cost are available",…,"the sponsor should be prepared to provide both a comparison against the comparator with the greatest market share and a comparison against the most cost-effective comparator".

It is of additional concern that "if there is a reasonable expectation that a medicine will enter the Australian market in the near future for the proposed indication, this may be regarded as a supplementary comparator".

The reference to 101(3a) to justify a lowest cost comparator is unreasonable and leaves room for interpretation and does not guide the sponsor appropriately. Requiring a sponsor to compare a new innovative product to bioequivalent, biosimilar or generic, which are generally lower priced is a grave risk, which has the potential to negatively impact future investment in bringing new innovative medicines to Australia. New medicine prices in Australia are already at the lower end of the global pricing range (data on file).

Novo Nordisk submits that there is a lack of clarity within the new guidance in relation to comparator selection and what the selection criteria are – proposing that the most appropriate comparator remains the ***current*** **product** most likely to be displaced.

2) A broader assessment of value in section 3A including societal & patient benefits and recognition of incremental benefit

The new PBAC guideline does not acknowledge cost-benefit analyses (CBA) as part of their HTA assessment in section 3A, but prefers to cost utility analysis (CUA) and cost effectiveness analysis (CEA). Novo Nordisk agrees that CUA allows for a deeper comparison across different health programs and policies by using quality adjusted life years (QALYs) and that CUA provides a more complete analysis of total benefits than

simple cost–benefit analysis. Nevertheless, discounting CBA and its measure on the effect on the patient, their opinion on value or other social benefits may discount the incremental benefit a drug may bring to the individual patient.

Novo Nordisk can point to many studies that demonstrate willingness to pay (WTP) on the part of patients, showing the significant societal effects a drug may have on patients. These are not captured in CUA and Novo Nordisk submits WTP should be recognised by the PBAC as a measure of value. Studies show approximately 50% of patients globally do not take medications as prescribed, and that there are many factors involved, (including age, social and psychological factors, education etc). Studies demonstrate it may also include negative treatment effect (i.e. tolerability) or complexity of medication (i.e. once vs twice daily dosing), which have a strong and favourable influence on outcomes.

Novo Nordisk believes the draft PBAC guidelines do not permit optimum assessment and acknowledgement of incremental benefits to society and the patient. Incremental benefits such as improved convenience, improved tolerability and improved mode of administration are of significant and measurable societal and patient benefits. For example in one of the Novo Nordisk submissions patient incremental benefits regarding once vs twice daily injections of a drug and proven reduced duration of nausea were not considered to hold additional value by PBAC, although once vs twice daily injection and lower rates of nausea are deemed in studies to be of significant benefit. Real world evidence shows increasingly that incremental benefits such as those referred to do increase adherence and thus reduces risk of complications and therefore reduce overall costs. It is these tangible costs/benefits, which are of value to patient, which can only be elicited through willingness-to-pay type studies. Therefore the new PBAC guideline, should adopt a broader definition of value and product benefit beyond the cost of a drug to the health system, and should consider patient preferences, quality of life, product acceptability, treatment compliance and adherence as well as willingness to pay studies.

Novo Nordisk supports Medicines Australia's expressed view that there remains an unaddressed need for the 'patient voice' in relation to PBAC decision-making processes as in fact was noted during the Senate Community Services Inquiry into availability of cancer medicines. The PBAC process (as such) remains ad hoc and without clear directions as to how the value of patient input is reasonably assessed.

3) **More transparency in section 3.6 around the assessment and definitions of resource that can be used for a HE technology assessment**

Section 3.6 of the proposed new guideline should include clearer resources and references stating, for example, defined unit costs and (dis)utility values for CUA that should be used as benchmarks when submitting a health economic analysis. PBAC could implement similar process and resources that are used by NICE, which clearly define costs to be used in the health technology assessment. Novo Nordisk acknowledges the PBAC manual of resource mentioned in Section 3.6, but would welcome the guideline being modified to clarify cost indications per health state. A Similar approach should be considered for (dis)utility values, where it would be useful to have preferred or accepted (dis)utility value ranges for HE modelling, as for example shown by a literature search found in Figure 2 in Amélie Beaudet et al (2014)[i]. Novo Nordisk has accumulated evidence internationally which would refute the basis of PBAC challenges regarding

associated (dis)utilities used in HE modelling in a number of Novo Nordisk submissions, commenting on the uncertainty of the chosen (dis)utility, as a direct result of which, a rejection becomes inevitable, consequently and unnecessarily delaying access to innovative medicines.

We submit that to the best of our knowledge the PBAC has never formally acknowledged the use of an ICER threshold[ii]. However, some threshold is required to make a yes-or-no funding decision, even if the threshold is implicit and vague[iii]. For example NICE acknowledges that an ICER of ~ < 20'000 pounds is cost effective. Clearer guidance from the PBAC in the guideline as to what is considered cost effective would be a step towards a process becoming more transparent for all stakeholders.

Novo Nordisk believes transparent and consistent use of (dis)utilities and costs as well as well defined, published statistical models would improve the comparability of utility-related research and will definitively improve patient access by improving listing time for new medicines on the PBS.

4) Acceptability of well validated, referenced HE models used by other payers, without the need to additionally validate a model through an external validator as part of the submission as stated in section 3.2 & 3.7

Section 3.2 the new guideline seeks a literature review and representation of a conceptual model structure for comparison to the implemented model structure. The guideline also requires the inclusion of a simple model in addition to any complex individual-based model, to demonstrate the effect of the different approaches (and insufficiencies of simple vs complex model approaches). Section 3.7 contains expanded guidance on the chosen model validation, data inputs, operational validation, including the requirement to validate the model by an external reviewer, as well as including cross-validation to other similar published conceptual models. These new additions to validation involve a significant extra burden and costly new workload for the sponsor.

Novo Nordisk understands PBAC's desire for increased transparency in the modelling and validation step in the submission procedures. Novo Nordisk has been challenged previously by PBAC on the use of well validated HE models, such as the globally recognized and internationally validated diabetes CORE model developed by IMS. This model has been acknowledged as appropriate by other countries heath technology assessors, payers and international HTAs & diabetes experts around the globe and we are at a loss to explain why PBAC does not see fit to accept international precedence on this issue. Instead, PBAC has commented in response to a Novo Nordisk submission that without the possibility of appropriate independent verification, there has been – in Novo Nordisk submission - an "overall uncertainty" in the modelled prediction of the treatment benefit (pre-Subcommittee response, Victoza® July 2011). However, the CORE model has been examined and published by Palmer et al (2004)[iv], where the authors validated a total of 66 second- (internal) and third- (external) order analyses across a range of complications and outcomes simulated by the CORE model. Within this study the CORE model provided an accurate simulation of outcomes observed in real-life settings.

Novo Nordisk would therefore respectfully request that the PBAC reconsiders in the new guidelines the requirement for resource heavy validation process and suggest that instead, it should be sufficient to rely on already-published validations of models such as

for the diabetes CORE model submitted by Palmer et al, even if it is a complex model and cannot be validated by the PBAC without external help. If published validated models are utilised, the PBAC should not need to request additional validation of the model, nor the need to include a conceptual or simpler model comparison.

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[i] A. Beaudet, J. Clegg, P. Thuresson, A. Lloyd, P. McEwan. Review of Utility Values for Economic Modeling in Type 2 Diabetes. Value in health 17(2014)462 – 470

[ii] Bulfone L, Younie S, Carter R. Health technology assessment: reflections from the Antipodes. Value Health. 2009;12(Suppl 2):S28–38. doi:10.1111/j.1524-4733.2009.00556.x.

[iii] Giacomini M. How good is good enough? Standards in policy decisions to cover new health technologies. Healthc Policy. 2007;3(2):91–101.

[iv] Palmer, A. J., et al. (2004). "Validation of the CORE Diabetes Model Against Epidemiological and Clinical Studies." Current Medical Research and Opinion **20**: S27–S40.