6 June 2017

Medicines Australia's submission on the Final Report of the Ezetimibe Post Market Review

Executive Summary

Medicines Australia (MA) acknowledges that the Ezetimibe Post Market Review has followed the procedural guidelines set out in the Post Market Review Framework. This has resulted in greater consultation and predictability than in previous reviews.

With specific regard to ezetimibe, the final report finds that ezetimibe is generally used within restriction and use is well aligned to clinical guidelines. Further, the report acknowledges that the IMPROVE-IT trial confirms the relationship between LDL-C reduction and cardiovascular events that the PBAC has previously assumed.

Nevertheless, MA considers there are some issues in the final report relating to:
- evidentiary requirements for estimating utilisation and cost-effectiveness
- unintended impacts on PBS policy and the architecture of PBS reform, and
- concerns regarding the procedural deficiencies for the implementation of outcomes.

Medicines Australia thanks the Post Market review team for its efforts, and is committed to working with the Government to address the issues highlighted above through the Access to Medicines Working Group (AMWG).

Medicines Australia (MA) welcomes the opportunity to make a submission on the Final Report of the Post-Market Review of Ezetimibe. Ezetimibe is listed on the PBS for the treatment of high cholesterol associated with cardiovascular disease.

MA is the peak organisation representing the research-based pharmaceutical industry in Australia. Our members comprise over 80% of the prescription medicines market by value and play an integral role in delivering better health outcomes for Australians. Medicines Australia's members include sponsors who supply medicines affected directly and indirectly by the ezetimibe review.

This is the first review under the agreed post-market reviews framework. Therefore, in this submission, MA will consider process as well as the specific review's outcomes. Our submission notes the potential consequences of post market reviews for patients, clinicians and the industry, and for the two formulary system that underpins the PBS.

MA members affected by this review support the following advice (I and II) provided in the report and would support initiatives to address them:

I. Education is needed to improve the quality use of lipid lowering medicines
II. PBS restrictions on statins should be eased based on the available evidence

Taken together, points I and II illustrate the benefits of PMR, and are among the reasons MA and its members support the PMR framework. PMRs reflect changes in practice and clinical experience, and advance the necessary evidence base of the PBS.

In relation to this review, and post market reviews more broadly, MA would also like to raise the following issues (III, IV and V) for PBAC consideration:

III. Evidentiary requirements for post market reviews
IV. Consequences on PBS policy and the architecture of PBS reforms
V. Procedural considerations for the implementation of outcomes

I. Education is needed to improve the quality use of lipid lowering medicines

Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in Australia. Important recent advances in hyperlipidaemia treatment could further reduce the significant public health burden that CVD imposes.

MA would support Quality Use of Medicines measures that improve patient adherence to medicines, as they in turn improve broader health outcomes. MA would welcome the opportunity to work across all stakeholders at models to improve patient compliance and education. For example, further development of NPS MedicineWise or similar broad programs would be welcome. This would improve understanding of, and adherence to, PBS restrictions, and continuous LDL-C treatment.

II. PBS restrictions on statins should be eased

The reference group's conclusion that statin therapy clinical practice is well-established. For this reason, MA members affected by this review would support removal of the General Statement on Lipid Lowering Drugs from the PBS and easing in the restrictions on statins based on the clinical and real world experience considered in this review.

III. Evidentiary requirements of post market reviews

MA considers that reviews should be assessed using the same evidentiary standards that apply to all PBAC evaluations. It is essential that Australia assesses both existing and future treatments with clear, consistent standards. This will ensure that Australian patients have the best opportunity to access necessary medicines.

MA has previously expressed concerns that prior reviews have made recommendations based on data and analysis that do not represent the full body of evidence. Further, there is not sufficient information to provide an understanding of the data's impact. For example, it is difficult to determine conclusively appropriateness of use when there is only limited utilisation data. Based on this, there is a clear need for greater data collection and sharing. Medicines Australia would welcome the opportunity to work with Government on proposals in this area.

Notwithstanding this, the data is perhaps not as robust or comprehensive as might be expected by the PBAC in a new product listing submission. It is critical that the appropriate evidence base is used when making of value for money recommendations. This should include consideration of

the generalizability and applicability to the Australian population. A proper cost-effectiveness consideration should include not only utilisation, but also the impact on patient outcomes.

The review reference group has previously concluded that the use of ezetimibe on the PBS is largely consistent with both PBS restrictions and clinical guidelines. Specifically, ezetimibe should be used as a second line agent following the maximally tolerated dose of a statin.

Nonetheless, the final report advises the PBAC to consider a pricing recommendation informed by very wide utilisation range. The report only finds evidence to suggest 18% of utilisation out of restriction. Further, this finding relies on restricting the observed prior statin use period to two years. This interpretation is relevant to utilisation, but should not determine a price variation based on cost-effectiveness. The PBAC should ensure that any report recommendations it adopts are supported by cost-effectiveness evidence.

A further concern arises in the report's conclusions on cost effectiveness, which again seem to rely on assumptions and analysis that would be difficult to sustain, without further data, in a submission for a new PBAC listing. The first draft report, which was released in January 2017, suggested that both the comparator and time horizon used in the original ezetimibe submissions should be altered. Medicines Australia' submission at that time noted that these suggestions were at variance to the new version of the PBAC guidelines (v5).

The final report introduces new data that would not meet the usual PBAC submission standards. For example, the review has already accepted that the IMPROVE-IT study is not representative of the PBS population. It is therefore difficult to support broad ranging risk stratification conclusions drawn from this analysis.

More generally, there has been a very limited time to review the new data in detail, and it is not clear why these issues were not raised in the initial round of review. It would be helpful to understand what has changed to make these issues weigh so heavily in the analysis.

IV. Consequences on PBS policy and the architecture of PBS reform

The issues raised above risk eroding formulary separation for clinical and cost effectiveness comparisons. This would inadvertently undermine the PBS reform that created the F1 formulary for single brand medicines undergoing value-based assessment of cost effectiveness. These were deliberately de-linked from the F2 formulary, created to drive savings in the multi-brand, post-patent market through competition. Linking a single brand product to price reductions seen through competition over the lifecycle would undermine the distinct functions achieved through the formulary architecture.

This would risk re-linking the formularies for clinical and cost comparisons, and would create policy and investment environment uncertainty, evidentiary barriers and ultimately access risks in Australia.

V. Procedural considerations for the implementation of outcomes of a review

MA considers that outcomes from this review should be implemented collaboratively over appropriate timeframes. MA has raised previously through the AMWG that PBAC outcomes implementation processes could be improved. For example, recommendations that have a

material impact on a sponsor or other stakeholders should enable time for a full range responses to be explored.

Industry and Government jointly developed the Post Market Review framework to provide a reliable framework within which to conduct reviews. The ezetimibe review demonstrates that the framework is a useful guide on how to manage the process.

However, the AMWG noted that further work was required to resolve the process for the review outcomes implementation process to ensure a robust, fair and effective process. MA reaffirms our interest in progressing this matter, and looks forward to working with Government on this important work.