Dear PAH Review Secretariat

RE: Thoracic Society of Australia and New Zealand Response to Final Terms of Reference for the Post-market Review of PAH Medicines

Introduction

The Thoracic Society of Australia and New Zealand (TSANZ) is the only health peak body representing a range of professions (medical specialists, scientists, researchers, academics, nurses, physiotherapists, students and others) across various disciplines within the respiratory/sleep medicine field in Australia and New Zealand.

The TSANZ is committed to improving knowledge and understanding of lung disease, with the ultimate goals being to prevent respiratory illness through research and health promotion and to improve health care for people with respiratory illness.

The TSANZ comprises of approximately 1500 members and 16 special interest groups (SIGs). The sub-specialist area of pulmonary hypertension lies within the scope of the Orphan lung disease, Lung transplant, Interstitial lung disease and pulmonary Vascular disease (OLIV) SIG.

Terms of Reference

With regards to the final terms of reference for the Post-market Review of PAH medicines, we would like to contribute the following:

1. **Review recent clinical guidelines for the management of PAH and compare this to the PBS restrictions and Therapeutic Goods Administration (TGA) indications for the use of PAH medicines.**

This review of clinical guidelines should also extend to a review of recent clinical evidence in order to stay current. If PBS decisions are based only upon guidelines, the application of evidence based medicine in this country will always be lagging.

2. **Review the utilisation of PAH medicines in Australia, including sources of data that can provide additional information on clinical use that is not available from PBS data.**

Utilisation of PAH medicines in Australia is not accurately reflected by PBS prescriptions alone. PAH medicines are obtained through a variety of alternate sources including private prescriptions, hospital funding, compassionate access schemes and through clinical trials. We support this TOR but recommend that the Department also seeks to explore methods to ensure efficient and effective data capture of PAH medicine utilisation and outcomes moving forward to continue with informed decision making.

Furthermore, we recommend that this TOR be extended to explore the equity of utilisation of PAH medicines, including what constitutes a designated centre for prescribing and how designated centres engage and support each other.

3. **Review the clinical outcomes that are most important or clinically relevant to patients with PAH, and the extent to which these outcomes are included in the evidence previously considered by PBAC.**

We acknowledge that the evidence supporting PAH medicines has evolved over the past decade from short term trials with surrogate endpoints to longer term clinical trials with more meaningful composite clinical outcomes. There is concern of using modern standards of clinically relevant endpoints to re-evaluate evidence previously considered by the PBAC as we anticipate there to be a lack of sufficient outcome data. Furthermore, we would not support the removal of current medicines from the PBS when such clinical endpoints are lacking from older studies.

Nevertheless, we support the review of appropriate clinical outcomes for patients. In addition, recommend that clinical outcomes be prospectively captured in conjunction with utilisation of PAH medicines (TOR 2) so as to inform decision making.

4. **Collate and evaluate evidence on the comparative effectiveness of PAH medicines, including combination use and use in the WHO functional class II patient populations.**

We support this TOR.

5. **Following ToR 1-4 consider reviewing the cost-effectiveness of existing PBS listings for PAH medicines, and in treatment of WHO functional class II and combination treatment in class III and class IV patients.**

We support this TOR however would like the decision regarding combination therapy for WHO functional class II patients to be assessed based on the evidence from TOR 4. The AMBITION trial (Galie et al, NEJM 2015) demonstrated that combination therapy was most effective in reducing the hazard ratio for clinical events in WHO functional class II patients compared with WHO functional class III patients (Figure S5).

Conclusion

As pulmonary arterial hypertension is a rare and complex disease with a range of aetiologies, we support this review. In addition, we see this as an opportunity to review the application of PAH prescribing in this country so as to facilitate expert, timely access to treatment in an equitable manner. Finally, we recommend ongoing post-market surveillance / registry analysis to support ongoing evidence-based decision making.

Yours Sincerely

A/Professor Tamera Corte (OLIV convener) and Dr Jeremy Wrobel (OLIV deputy convener), on behalf of Thoracic Society of Australia and New Zealand