23 February 2024

[redacted]
HTA Review Secretariat
Health Technology Assessment Policy and Methods Review Reference Committee
htareviewconsult@health.gov.au

Dear Committee Members,

**Re. Submission from Ipsen Pty Ltd in response to the Consultation options paper developed through the Health Technology Assessment (HTA) Policy and Methods Review.**

Ipsen welcomes this opportunity to provide a submission to the Reference Committee.

Ipsen Australia is a mid-sized pharmaceutical company that specialises in the development of treatments for cancer, rare diseases and neurological disorders.

This submission aims to highlight options that Ipsen believe have the potential to create a welfare gain and are mutually beneficial to stakeholders and conversely some options that if implemented, we believe may lead to a welfare loss to the Australian community.

[redacted]

Yours sincerely,

Julien Dagher

General Manager, Ipsen Australia & New Zealand

# HTA Policy and Methods Review – Options paper consultation

## Introduction

The *New Frontier Report* found that Australian Health Technology Assessment (HTA) processes for the funding of medications on the Pharmaceutical Benefits Scheme (PBS) are designed primarily for more common diseases.[1] These processes make the evaluation of treatments for rare diseases and rare and less common cancers difficult given the requirements for comparative evidence, suitable for demonstrating cost-effectiveness of those treatments, in small patient populations.

At present, the average time from regulatory approval to reimbursement of innovative medicines across all diseases in Australia is 466 days, compared to 102 days in Japan, 136 days in Germany and 156 days in the UK.[2] In some cases, Australian patients miss out entirely on treatments where other countries have established HTA processes tailored to evaluate treatments for rare diseases and cancers.[3] Analysis undertaken by Ipsen investigating the time from TGA registration to PBS reimbursement for drugs designated as Orphan revealed that the median time to listing was 739 days.[4]

This *Health Technology Assessment Policy and Methods Review* is timely as it coincides with the Senate inquiry into *Equitable access to diagnosis and treatment for individuals with rare and less common cancers, including neuroendocrine cancer,* and hopefully when viewed together (and with other previous inquiries and reviews) will lead to meaningful reductions in the time between TGA approval of a treatment and PBS funding.

The Options Paper makes numerous references to the economic principal of 'welfare gain'. This is largely under the section on 'overall value of health technologies'. Ipsen interprets welfare gain as "the impact of a government policy, or a decision by firms, on total economic welfare, taking into account the gains, less any losses". The Options Paper considers that the adjustment of economic inputs to 'increase the recognised value' would increase costs and reduce the net welfare gain to society. Absent in this consideration is the reality that there is potential for welfare loss where health technologies are not brought to market, or where their access is delayed. [5]

The notion of welfare gain is important in the context of the HTA Review, as it reflects a logical maximand that bridges key issues identified in the Options Paper – timely access for patients and value recognition of health technology.

---

[1] House of Representatives Standing Committee on Health, Aged Care and Sport. The New Frontier – Delivering better health for all Australians 2021. https://parlinfo.aph.gov.au/parlInfo/download/committees/reportrep/024755/toc_pdf/TheNewFrontier-DeliveringbetterhealthforallAustralians.pdf;fileType=application%2Fpdf Viewed 23 February 2024

[2] Medicines Australia. Medicines Matter 2022. https://www.medicinesaustralia.com.au/wp-content/uploads/sites/65/2023/04/Medicines-Matter-2022-FINAL.pdf Viewed 23 February 2024

[3] The McKell Institute. Funding Rare Disease Therapies in Australia 2021. https://mckellinstitute.org.au/wp-content/uploads/2022/02/McKell-Funding-Rare-Disease-Therapies-in-Aus-2021.pdf Viewed 23 February 2024

[4] Data on File. Orphan Drugs: Analysis of time to PBS listing. 23 January 2024

[5] https://www.economicsonline.co.uk/definitions/net_welfare_gain.html/#:~:text=A%20net%20welfare%20gain%20refers,the%20idea%20of%20well%2Dbeing.

This submission does not consider all options presented, but focusses on those options that Ipsen believes have the potential to create a welfare gain and are therefore mutually beneficial to stakeholders, and conversely, some options that if implemented, may lead to a welfare loss to the Australian community.

These are summarised in the table below:

**Table 1 Consideration of Options with respect to welfare gain**

| Options that may lead to a net welfare gain | Options that may lead to a net welfare loss |
|---|---|
| • 2.2 Early resolution mechanisms in areas of HUCN<br>• 4.1 Bridging funding in areas of HUCN<br>• 1.2 Consumer, clinician and other stakeholder engagement and consideration in HTA | • 4.1 Requirement for lower price offer for cost-minimised submissions<br>• 2.2 Setting a maximum allowable number of submission (e.g. only 1 resubmission allowed<br>• 2.1 PBAC to become the sole HTA committee for drugs for ultra-rare diseases to eliminate double handling.<br>• 3.3 Economic evaluation – comparator selection and valuing long term outcomes. |

As a small to mid-sized company with a small portfolio, Ipsen has only 5 products on the PBS in Australia. Pricing and policy changes such as those introduced in the 2022-27 Strategic Agreement with the medicines industry, as well as those considered in the Options paper create considerable uncertainty, and can have a differentially large impact compared to companies with broad portfolios.

Ipsen welcome the opportunity to comment and will continue to ensure that the perspective of smaller companies is reflected to ensure that policy change does not disproportionately impact our ability to operate in Australia, bringing life-changing medicines to Australian patients.

## Assessment of key options that may lead to a net welfare gain.

**Section 2.2. Proportionate appraisal pathways: Development of pathways to calibrate the level of appraisal required for HTA submissions to the level of risk (levels of uncertainty and potential fiscal impact) and clinical need that the submission represents.**

- **Option - Early resolution mechanisms for submissions of major new therapeutic advances in areas of high unmet clinical need (HUCN).**

In principle, Ipsen supports development of early resolution or fast-track mechanisms to evaluate medicines that represent high added therapeutic value (HATV) in areas of high unmet clinical need (HUCN), but where there is uncertainty related to its cost-effectiveness. We will be interested in the criteria that defines HUCN and HATV and would advocate for stakeholder consultation on this specific issue.

There are four alternative options discussed. Ipsen supports *Alternative option 4: Introducing an optional resolution step after HTA committee consideration but before advice is finalised*, as this will include the considerations of the PBAC and lead to greater certainty of outcome.

Ipsen do have concerns about inclusion criteria for early resolution, in particular the requirement that the "submission lodged within 6 months of receiving first regulatory approval from a comparable overseas regulator (e.g. Food and Drug Administration (FDA)/European Medicines Agency (EMA))"

In some cases, the licensing of products for commercialisation in Australia occurs later than in other markets. Strict adherence to a requirement to lodge submissions within 6 months of a comparable overseas regulator may make it impossible for in-licenced products already approved overseas to be considered through this pathway. Therefore, this specific criterion is unlikely to act as an incentive for sponsor prioritisation and may have the unintended consequence of creating a barrier to early access. We recommend that it be removed.

**Section 4.1. Approaches to funding or purchasing new health technologies.**

- **Option - Bridging funding coverage for earlier access to therapies of likely HATV and HUCN**

In principle, Ipsen support an option for bridging funding coverage for earlier access to therapies of likely HATV and HUCN.

Practically, such mechanisms exist in other markets and have been implemented with success. Ipsen note the potential uncertainties impacting the potential for progress which include (but are not limited to) how products are selected for eligibility, methods for initial and final price determination as well as conditions relating to reassessment and potential continuation or termination.

Therefore, in principle such a mechanism has the potential to accelerate access to critical therapies in some areas. However, unless conditions of such mechanisms appropriately balance risk between sponsors and Government then the viability of bridging funding may be compromised.

Engagement with impacted parties to develop a clear and viable implementation plan for such a mechanism will be critical to its success in positively impacting patient outcomes.

**Section 1.2. Consumer, clinician and other stakeholder engagement and consideration in HTA**

Ipsen welcomes any opportunity for deeper consumer engagement in the HTA process.

The value of consumer and clinician input into defining the target patient population can be illustrated by a contemporaneous example. Currently, treatments reimbursed on the PBS for renal cell carcinoma are restricted to patients with the clear cell variant i.e. clear-cell renal cell carcinoma (ccRCC). Non-clear cell renal cell carcinoma (nccRCC) accounts for approximately 20-25% of all renal cell carcinoma (RCC), [6] but unlike ccRCC, nccRCC is a diverse group of tumours with distinct histological and molecular features.[7] For this reason, registrational clinical trials for all RCC treatments have focussed on the more common and homogenous, clear cell population. Whilst there are TGA approved treatments for patients with nccRCC

[6] Geynisman DM, Plimack ER. Systemic Therapy for Advanced Non-clear-Cell Renal Cell Carcinoma: Slow but Definite Progress. Eur Urol. 2021 Aug;80(2):171-173. doi: 10.1016/j.eururo.2021.04.031. Epub 2021 May 7. PMID: 33972094

[7] John A et al. Navigating the Current Landscape of Non-Clear Cell Renal Cell Carcinoma: A Review of the Literature. Curr Oncol 2023;30:923-37 https://doi.org/10.3390/curroncol30010070

histologies, patients are currently excluded from funded access to treatment in Australia. This distinction that has not been made in other major HTA countries making funding decisions on cabozantinib for RCC. [8] [9] [10]

Without PBS funded treatment for nccRCC, treatment options include clinical trials or self-funded or compassionate access to systemic therapies.

Community consultation in relation to PICO would highlight such potential inequities in our healthcare system before they arise, but mere identification of the issues may not be sufficient for sponsors to include patient sub-types in their submissions if doing so increases the risk of rejection or adverse valuations of the technology.

Ipsen would welcome community consultation and input into patient population definition in the following circumstances:

1. Similar incentives attached to the submission as per HUCN medicines/ identified in horizon scanning. See *section 5.1 Proactive submission invitation and incentivisation.*
2. Where the number of patients that might be treated for any new indication is also uncertain and where PBS listing is dependent upon Risk Sharing Arrangements, it is imperative that any risk is indeed appropriately shared.

Ipsen also support *"including a feedback loop for consumer inputs to show how and where consumers have been consulted and how HTA committees considered this input"* ***AND*** *"Including consumers in the HTA committee meetings".* We see these as helpful ways to ensure that the PBAC have an opportunity to better understand the patient perspective and over time to improve quality of patient input to the process.

Finally, reference is made in various places to Plain Language Summaries (PLS). Ipsen support development of these in principle and can see their value in them being developed in relation to guidelines, submissions and outcomes, however, PLS documents come with their own set of challenges and to be done well are resource intensive. If PLS of submissions were to be considered, Ipsen propose that they be tailored to best support consumer input in relation to the areas most relevant to the PBAC evaluation of a particular submission. This would necessitate collaboration between the sponsor and the secretariat to ensure what was distributed to consumers was useful, accessible, focussed and unbiased. Resource allocation by stakeholders and cost-recovery implications would need to be considered.

[8] Pan-Canadian Oncology Drug Review Expert Review Committee (pERC) final recommendation 2019. https://www.cadth.ca/sites/default/files/pcodr/Reviews2019/10163CabozantinibRCCResub_FnRec_2019-02-20_ApprovedByChair_Post_20Feb2019_final.pdf. Viewed 23 February 2024

[9] Italian Republic. Gazzetta Ufficiale (Italian) 2019. https://www.gazzettaufficiale.it/eli/gu/2019/09/05/208/sg/pdf. Viewed 23 February 2024

[10] Benefit assessment dossier. Cabometyx. 206 (German). https://www.g-ba.de/downloads/92-975-1727/2016-10-28_Modul1_Cabozantinib.pdf Viewed 23 February 2024

## Assessment of key options that may lead to a net welfare loss.

**Section 4.1. Approaches to funding or purchasing new health technologies.**

- **Option – Recognising competition between new health technologies that deliver similar outcomes.**

Streamlining cost-minimisation submissions is a win-win for all stakeholders. The recommendations in section 2.2 are sensible and can lead to efficient resource utilisation.

However, Ipsen disagree with *Section 4.1 Approaches to funding or purchasing new health technologies* options. These either 'require' or 'incentivise' offers of a lower price in conjunction with options for proportionate assessment of cost-minimisation submissions. This approach doesn't recognise incremental value or innovation associated with the technology, nor price interventions that already apply to current comparators funded on the PBS.

A foreseeable adverse consequence of this approach would be sponsors electing not to seek reimbursement for alternative treatment regimens that it believes are highly beneficial e.g. IO/TKi combination vs IO/IO combination in oncology. The current process is already quite complex and adding greater uncertainty will be a barrier to sponsors submitting and patient access.

Even so called '*me-too'* drugs have been proven to demonstrate meaningful innovation. Consider the fifth statin to market rosuvastatin in comparison to simvastatin or the angiotensin II receptor blocker, irbesartan in comparison to the ACE Inhibitors it replaced.

Another example of cost-minimised interventions that deliver similar clinical outcomes but are meaningful advances for patients relate to changes in dose schedule or route of administration. Our current system doesn't value the benefits to patient such as oral vs IV treatment or monthly vs weekly injections.

Even cost-minimised products usually bring some welfare gain even if not able to be measured with certainty via CEA. Market data, however, may provide some evidence that patients and clinicians value these incremental improvements in health technologies, ones which may not have come to market with the adverse pricing option proposed.

**Section 2.2. Proportionate appraisal pathways: Development of pathways to calibrate the level of appraisal required for HTA submissions to the level of risk (levels of uncertainty and potential fiscal impact) and clinical need that the submission represents.**

- **Option - Setting a maximum allowable number of submission (e.g only 1 resubmission allowed).**

The reference committee acknowledge that the HTA process effectively defines a price negotiation to establish value for health technologies.

It is also noted within the Options papers that "s*uppliers often present prices in economic evaluations for their first submission that are higher than what they will later accept in resubmissions. The cost-effectiveness of these early higher prices is often calculated using assumptions in economic models that are more optimistic than will be accepted by advisory committees*" and that "*advisory committee acceptance of assumptions can also shift through resubmissions*."

Therefore, it is acknowledged that there is movement through the process from both parties. Constraining a process that is effectively a negotiation, increases the risk that a mutually acceptable outcome is unable to be reached and increases the risk of a welfare loss where this prevents or delays a health technology from reaching the market.

**Section 2.1. Streamlining and aligning HTA pathways and advisory committees - Overarching goal: a staged approach (including short, medium and longer-term steps) to achieving a simplified (single entry) HTA gateway reflecting nationally consistent HTA approach.**

- **Option - Pathway for drugs for ultra-rare diseases (Life Saving Drugs Program (LSDP)). PBAC to become the sole HTA committee for drugs for ultra-rare diseases to eliminate double handling**

Whilst Ipsen support in principle a single HTA Committee approach and the potential efficiencies this creates, the application of this to ultra-rare diseases in the context of the Life Saving Drugs Program is not without risk.

It is acknowledged that there are significant challenges within HTA systems for ultra-rare diseases given the availability of evidence and the uncertainty this creates. Currently LSDP consideration is relevant where the PBAC determines that a health technology is effective but not cost-effective. This approach implicitly acknowledges the challenges for ultra-rare diseases in HTA. However, the Options Paper suggests that the "P*BAC advises the Minister on key requirements to enable listing on the LSDP based on a comparative assessment of effectiveness and cost*". The inclusion of a formal cost consideration by the PBAC increases the risk of a welfare loss where these submissions are unable to meet the PBAC requirements for cost-effectiveness.

**Section 3.3. Economic evaluation: Comparator selection and valuing long term outcomes.**

Ipsen supports the position within the Medicines Australia submission to the Options Paper relating to the need to strengthen options for comparator selection and valuing long term outcomes.