

# Medical Services Advisory Committee (MSAC)

## STAKEHOLDER MEETING OUTCOME STATEMENT

### **Imlifidase as a desensitisation treatment to enable kidney transplant in highly sensitised adult transplant candidates**

**Tuesday, 4 February 2025**

## **1. Introduction**

### **Attendees**

Meeting attendees included the Chair and members of the Medical Services Advisory Committee (MSAC); representatives of Australian Redcross Lifeblood, the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), the Australian and New Zealand Paired Kidney Exchange Clinical Oversight Subcommittee, the Renal Transplant Advisory Committee (RTAC) of the Transplantation Society of Australia and New Zealand (TSANZ), Hansa Biopharma (Applicant); a consumer representative from the Consumer Consultative Forum (CCF) also on behalf of the TSANZ; representatives from the Northern Territory (NT), New South Wales (NSW), Victoria, Queensland, Western Australia (WA), South Australia (SA), Tasmania, and Australian Capital Territory (ACT) (including clinician representatives and representatives from the health departments of these jurisdictions); and representatives from the Australian Government Department of Health and Aged Care. OrganMatch provided a written response ahead of the meeting.

The Chair opened the meeting at 10am. The Chair advised that the stakeholder meeting was not an MSAC decision making forum but would inform MSAC's future deliberations and advice to the Minister for Health and Aged Care by providing a better understanding of issues raised during its August 2024 consideration of *Application 1732.1 - Imlifidase as a desensitisation treatment to enable kidney transplant in highly sensitised adult transplant candidates* with the expectation that the outcomes of this meeting would inform a resubmission by the applicant. The MSAC Chair advised that the committee intend to reconsider an updated proposal expeditiously, preferably at the April 2025 meeting.

The Chair reminded participants that this was a confidential discussion, and an Outcome Statement would be published on the MSAC website.

The Chair provided an overview of MSAC's role and membership.

### **Purpose**

The key objectives of the meeting were to allow MSAC to seek input from stakeholders on:

- Eligibility criteria for imlifidase
- Availability of crossmatch conversion testing
- Transplant Centres
- Funding arrangements
- Data Collection
- Guidelines (clinical and ethical)

## Conflicts of interest

The Chair noted that conflicts of interest had been declared and recorded, but in the context of this meeting conflicts did not need to be managed by exclusion from discussions.

## 2. Background

At its August 2024 meeting MSAC considered a resubmission requesting public funding for imlifidase (Idefix®) as a Highly Specialised Therapy under the National Health Reform Agreement (NHRA). Funding is sought for use of imlifidase in the desensitisation treatment of highly sensitised (HS) adult kidney transplant patients with a positive crossmatch against an available deceased donor (DD) or living donor (LD), who are unlikely to be transplanted under current kidney allocation systems. After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC deferred its decision on public funding ([Public Summary Document \(PSD\) for MSAC Application 1732.1](#)).

MSAC considered there is a high unmet clinical need for imlifidase. MSAC considered that while imlifidase was likely to have superior effectiveness and safety compared with dialysis and most of the clinical issues identified by MSAC in the previous application have been resolved, some concerns remained, in particular the long-term effectiveness and safety outcomes of imlifidase for delayed graft function, antibody mediated rejection, and chronic kidney disease.

MSAC recommended engagement with relevant stakeholders to work through the remaining implementation issues including:

- refining the proposed eligibility criteria including the current proposed criteria for LD transplant recipients which refers to logistical incompatibility with other desensitisation regimes, and with reference to the established ethical principles that guide allocation of transplants in Australia
- development of national guidelines for imlifidase use
- addressing accessibility to single antigen bead testing for kidney transplantation centres where imlifidase would be used
- designing an appropriate pay for performance (PfP) scheme with a two tiered patient financial cap to manage the remaining clinical, economic and financial uncertainties identified.
- collection of data for post-implementation review for MSAC consideration (and potential sharing of data between the Therapeutic Goods Administration (TGA) and MSAC and the timing of the TGA re-consideration of the provisional registration for imlifidase with respect to MSAC review and potential implications for PfP payment scheduling.

## 3. Summary of discussion and outcomes

### Eligibility Criteria

#### *Waiting period for DD transplant recipients*

The Chair summarized the eligibility criteria for LD and DD transplant recipients and noted that there was a proposed wait time restriction of 2 years for the eligibility criteria for DD transplant recipients which did not apply to LD transplant recipients (as expected given the nature of the donation process in these two scenarios). The Chair clarified that restrictions were based on data, provided by ANZDATA and therefore the 2 year waiting time applied from the time of first listing on the active kidney transplant list. It was noted that some

patients may face extended time (often years) on dialysis before being activated on the kidney transplant list and therefore these patients may effectively face a wait time of more than 2 years (including the time they were inactive on the wait list but on dialysis) before they qualify to use imlifidase and receive a transplant. Stakeholders noted that other clinical guidance in the renal transplant area was based on time from dialysis rather than time on the waitlist. However, there was broad consensus that time from being first active on the deceased donor waitlist was an appropriate measure for eligibility criteria.

Stakeholders also discussed whether a uniform 2 years wait restriction for all patients with a calculated Panel Reactive Antibody (cPRA) of greater than or equal to 99% including those with a cPRA of close to 100% was appropriate given that patients with a cPRA close to 100% have consistently less opportunities to access a kidney transplant regardless of wait time. Stakeholders discussed whether it was necessary to require such patients to wait 2 years for a transplant. It was concluded that while there may be merit in having no or a shorter waiting time for people with a cPRA of close to 100% there were also counter-arguments to this, particularly that this might introduce additional complexity to the waiting time criteria for DD transplant recipients and that the same waiting time should be applicable to all patients with  $cPRA \geq 99\%$ .

#### *Desensitisation treatments unlikely to be successful*

There was consensus that while the first two clauses of the eligibility criteria for LD transplant recipients were appropriate, the final three clauses of the eligibility criteria should be amended to 'For whom alternate desensitisation regimens for organ transplantation have failed or are contraindicated **or are unlikely to be successful.**' This was because stakeholders considered that desensitisation is an evolving practice across Australia so that it was unnecessary to specify the types of desensitisation treatments that were unlikely to be successful.

#### *Eligible patients*

The Chair noted that the projected number of eligible patients would have implications for the financial costs of funding imlifidase and cost effectiveness and therefore it was important to obtain a robust understanding of likely patient numbers. The Chair clarified that imlifidase will not increase the number of kidney transplantations, but instead was aimed at improving equity in transplantation outcomes by increasing kidney transplantation opportunities for the highly sensitised patients meeting the eligibility criteria for imlifidase.

States and Territories provided an estimate of the number of patients within their jurisdiction who may be eligible for imlifidase treatment based on the number of patients on their waiting lists who met the cPRA requirements and an ANZDATA registry representative reminded the stakeholder that in 2022, there were 135 patients nationally on the active waitlist with a  $cPRA \geq 99\%$ . It was noted that the number of patients who ultimately qualified for imlifidase-facilitated transplantation would be smaller than the number of patients who might be considered eligible based on cPRA and waiting time. Stakeholders advised that some patients would not be suitable for an imlifidase-enabled transplant because of comorbidities.

Stakeholders distinguished between the prevalent pool of existing patients on the waiting list versus the incident number of new patients every year. It was considered that within the prevalent pool, up to 50% of patients may be unsuitable for an imlifidase-enabled transplantation, thus approximately 50% of 135 patients may make up a prevalent 'bolus' of imlifidase eligible waitlisted patients

Within the incident population, which the applicant advised to be on average 29 patients per year according to OrganMatch data, stakeholders noted that a higher percentage of this

population may be suitable for imlifidase-facilitated transplantation over time as the time on waiting lists decreased, meaning that the uptake rate of imlifidase may increase in future years once the prevalent population had been 'cleared'. This difference was because the prevalent population had a higher share of patients who had already been on waiting lists for longer (including years when they were inactive on the waiting list) and had developed dialysis-related and other comorbidities which make them unsuitable for an imlifidase-enabled transplantation. There was broad consensus that after taking account of the servicing of this prevalent population, a reasonable estimate of uptake could be based on a consistent incidence or 'steady state' of about 10-15 patients per year across the LRD and DD groups eligible for an imlifidase facilitated transplantation.

### **Cross Match testing**

Stakeholders agreed that testing a sample taken 2 hours after imlifidase administration for donor specific antibodies generally sufficiently confirms crossmatch conversion from positive to negative. The applicant noted that there were data indicating with the administration of imlifidase a crossmatch test is likely to become negative in 96% of the patients after 2 hours, and after 6 hours at least 99.5% of the patients are likely to become crossmatch test negative.

The States and Territories discussed the resources required to complete timely testing. Stakeholders noted that the resources required to perform imlifidase transplants included staff to complete patient work ups and screenings prior to administration of imlifidase, as well as scientists to test and process results following administration of imlifidase. It was noted that there may be additional logistical issues associated with patients located outside major metropolitan centres which may present extensive resourcing challenges such as rural patient transport. Stakeholders noted that although Australian Redcross Lifeblood immunogenetics labs are currently only located in Sydney, Melbourne and Adelaide, however Single Antigen Bead HLA testing is available across all jurisdictions, although kidney transplantation did not occur in the NT or Tasmania. It was therefore agreed that testing could occur at all tissue typing laboratories and should not just be restricted to Australian Redcross LifeBlood laboratories.

### **Transplant Centres**

Stakeholders noted that imlifidase is a highly specialised therapy which requires significant coordination and expertise to perform. As such, it may be appropriate to designate specific centres which can perform kidney transplants with imlifidase. Broad consensus among State and Territories was that the jurisdictions should decide which center may be best placed to provide this treatment and the number of centres in each jurisdiction. It was noted that MSAC considered equity was important and that ideally all eligible patients should be able to receive imlifidase irrespective of location.

### **Funding Arrangements**

Imlifidase is a highly specialised, high cost therapy. The MSAC Chair discussed the need to mitigate key risks associated with imlifidase including imlifidase use not leading to a transplant and poorer long-term outcomes associated with patients than was evident in the trials, hence a pay for performance (PFP) arrangement was discussed involving payments for specific measurable outcomes to assess imlifidase effectiveness.

There was a consensus that proceeding to transplantation should be considered a key outcome for first payment.

While it was important to have a second payment conditional on longer term outcomes, such as a metric based on longer term post-transplant graft outcomes, it was noted that post-

transplant graft failure could be due to factors unrelated to imlifidase effectiveness. Stakeholders discussed whether the post-transplant graft outcome measure should be one year after transplant or a shorter period such as 3 months. However, the consensus was that a metric based on post-transplant graft outcome was appropriate as this aligned with the clinical evidence relied on in the TGA provisional approval for imlifidase. It was also noted that patient reported outcome measures (PROMs) may also be a metric of successful treatment. Stakeholders agreed that the PFP should be based on a single price, potentially paid over multiple time points noted. Stakeholders agreed that time points for payment in a PFP arrangement should be related to the key outcomes.

### **Data Collection**

The Chair noted that a review of matters related to the public funding of successful MSAC applications is often undertaken to ensure that the uncertainties identified when MSAC supported public funding had been adequately resolved. It was noted that robust and accurate data is essential in such reviews and collection of pre and post-transplant data would need to be undertaken to perform a review on imlifidase, if the application is recommended. The Chair also noted that PFP arrangements rely on the reporting of outcomes, and as such relevant data would need to be recorded for use in the payment process.

It was noted by stakeholders that ANZDATA currently collects a majority of the transplant data that would be required. ANZDATA advised that to collect any additional data relating to antibody reduction following administration of imlifidase (as per the discussion of funding arrangements) it would need to undertake further work with OrganMatch and the working group that had been convened by RTAC on desensitisation protocols for imlifidase use. ANZDATA further noted that although patient numbers would be low, there would still be resource considerations associated with capturing this additional data. ANZDATA also advised that they were working on implementing PROM data capture in the coming year. The applicant noted they collect their own data, in a non-Australian context, on imlifidase usage, related to the patients' quality of life outcomes. It was noted by stakeholders that it was also important for patients to be involved in collection of their outcomes data.

Stakeholders agreed ANZDATA would be the most appropriate registry for data collection for imlifidase patients. The Chair noted that data collection is vital to the PFP and any reviews of imlifidase in Australian practice.

### **Guidelines**

There was broad consensus on the need to ensure that the transplant community is encouraged to use imlifidase in a careful manner. The stakeholders noted that currently there is a lack of Australian guidelines and protocols, and treatment is heavily guided by clinician judgement. RTAC advised that a committee has been established to create clinical guidelines to guide desensitisation protocols for imlifidase use in Australia. It was noted that the UK and French Guidelines provide a comprehensive approach to imlifidase use and could be adapted to develop Australian guidelines. Stakeholders considered that the use of imlifidase could be accommodated within the current kidney allocation algorithm and therefore ethical guidelines for imlifidase use would not be necessary.

## **4. Meeting close**

The Chair thanked the participants for their valuable insights and closed the meeting at 12.00pm.