



## Application or referral for other medical service or health technology

**Application ID:**

HPP200111

**Application title:**

1732.1 – Imlifidase as a desensitisation treatment to enable kidney transplant in highly sensitised adult transplant candidates.

**Submitting organisation:**

HANSA BIOPHARMA (AUSTRALIA) PTY LTD

**Submitting organisation ABN:**

74650167221

## Application description

**Succinct description of the medical condition/s:**

End-stage kidney disease (ESKD) is defined by partial or completely failed kidney function. Patients require regular dialysis or a kidney transplant for survival. Haemodialysis has a substantial time commitment, requiring 2-3 five hour sessions per week. Long-term dialysis has a negative impact on patient morbidity, mortality and quality of life. Kidney transplantation is the optimal treatment for ESKD patients. Some highly sensitised (HS) patients are cross match incompatible with living or deceased donor kidneys due to elevated levels of Donor Specific Antibodies against Human Leukocyte Antigens. Despite the immunologic risk, HS patients who are transplanted with less compatible donors have better outcomes than remaining on dialysis. Previous pregnancy, Aboriginal/Torres Strait and other ethnic minority ESKD patients are at higher risk of being HS. Despite HS patients being prioritised by the organ allocation system, some HS patients remain waiting indefinitely for a suitable organ.

**Succinct description of the service or health technology:**

Imlifidase helps enable equity of access to kidney transplantation for a small number of highly sensitised patients who are unable to be transplanted despite being prioritised in available kidney allocation systems. Imlifidase is given intravenously to highly sensitised patients just prior to kidney transplant to convert a cross match positive test to a donor kidney to cross match negative making the kidney acceptable for transplantation. It is an immunoglobulin G (IgG)-degrading enzyme which cleaves the heavy chains of all human IgG subclasses but no other immunoglobulins. By cleaving all IgG, imlifidase reduces the levels of donor specific antibodies to avoid hyper acute rejection thus enabling transplantation. Imlifidase is TGA approved. Imlifidase provides a rapid, reliable, and convenient means for crossmatch conversion for an End Stage Kidney Disease population who would otherwise remain on chronic dialysis.

## Application contact details

**Are you applying on behalf of an organisation, or as an individual?**

Organisation

**Is the applicant organisation the organisation you are representing in the HPP today?**



Yes

**Applicant organisation name:**

HANSA BIOPHARMA (AUSTRALIA) PTY LTD



## Application details

**Please select the program through which the health technology would be funded:**

National Health Reform Agreement Addendum (Highly specialised therapies)

**Please provide justification for selecting the above program:**

The application 1732- Imlifidase as a desensitisation treatment to enable kidney transplant in highly sensitised adult transplant candidates was previously determined to meet the criteria for a Highly Specialised Therapy under the National Health Reform Agreement (NHRA) Addendum 2020-25 per email correspondence received by the applicant on 8th September 2022 from the MSAC secretariate. Refer reference documentation 'MSAC Application 1732 outcome of suitability assessment.

**Is the application for a new listing or a change to an existing listing?**

New listing

**Provide a rationale for the change to an existing listing:**

**What is the type of service or health technology?**

Therapeutic



## PICO set

### PICO sets:

PICO set number	PICO set name
1	1732.1 PICO sets v2



## Application PICO set 1: 1732.1 PICO sets v2

### Supporting documentation

Document type	Document file name
Application PICO set documents	1732.1 PICO sets v2
Reference list	Baker 2017.pdf; Cass 2006.pdf; Jordan 2017 Am J Trans.pdf; Jordan 21.pdf; Kjellman 2021.pdf; Lonze 2018.pdf; Lorant-2018.pdf; Meier-Kriesche 2004.pdf; Montgomery 2011 NEJM.pdf; Orandi 2016 Am J Trans.pdf; Sinnakirouchenan 2011.pdf; Sypek 2021.pdf; Wyld 2021.pdf

### Population

**Describe the population in which the proposed health technology is intended to be used:**

The reader is referred to the Ratified PICO confirmation and the MSAC Public Summary Document, both posted on the MSAC website under application 1732, for a more detailed description of the population.

The Australian Therapeutic Goods Administration (TGA) has approved (10/7/23) imlifidase for the following indication: Idefirix has provisional approval for the desensitisation treatment of highly sensitised adult kidney transplant candidates prior to kidney transplantation from a donor against whom there is a positive cross-match. The use of Idefirix should be reserved for patients who are otherwise unlikely to receive a kidney transplant.

The population is a subset of the most highly sensitised patients with end-stage kidney disease (ESKD) who have little to no access to life-saving kidney transplantation, because of a lack of immunologically suitable donors. Finding a match for these patients can be particularly difficult within a reasonable time or ever, meaning they spend a longer average time on transplant waiting lists, and therefore have an increased risk of dying on dialysis while waiting for a suitable donor.

MSAC in the PSD noted "The current population restriction [ initial application] was not restricted to those with a clinical need. Patients with cPRA from 95% to less than 99%, who have the highest rate of transplantation given recent changes in allocation algorithms, should not be included in the eligible population. Eligibility should be restricted to patients with cPRA of 99% or more. MSAC noted that while PASC had previously endorsed a cPRA ≥ 95% this had been before the impacts of the recent amendment to the allocation algorithm could be assessed. MSAC suggested that the applicant consider revising the population restriction to that as framed in the recommendation from the National Institute for Health and Care Excellence (NICE), UK to restrict use to "those who have a positive crossmatch with the donor and are unlikely to have a transplant under the available kidney allocation system (including prioritisation programmes for highly sensitised people)." MSAC suggested that such a definition, after accounting for the new algorithm, might limit the eligible population on the DD waiting list to those with cPRA of 99% or more and who have been on the waitlist for more than two years (that is, HS patients who have not received a kidney despite prioritisation) and limit the eligible population who are potential recipients of LD kidneys to those with cPRA of 99% or more who have failed plasma exchange desensitisation treatment so that it is a



second line treatment for those who are potential recipients of LD kidneys. The applicant has taken heed of the MSAC advice and modified the eligible patient population accordingly and will apply alternate scenarios for MSAC consideration in the Applicant Development Assessment Report.

NB MSAC SECRETARIAT:

The applicant kindly requests confirmation of an exemption from returning to the PICO Advisory Sub Committee, (PASC) noting that the applicant was only advised to return to the Evaluation Sub Committee ESC prior to returning to MSAC. The Population will be the MSAC proposed population, the Intervention, imlifidase, is unchanged and the Outcome measures for the PICO are unchanged. The Comparator is proposed to remain the Comparator agreed in the Ratified PICO Confirmation with the rationale addressed in the Comparator section of the PICO set document.

**Select the most applicable Medical condition terminology (SNOMED CT):**

## Intervention

**Name of the proposed health technology:**

Imlifidase (IDEFIRIX®)

## Comparator

**Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This include identifying health care resources that are needed to be delivered at the same time as the comparator service:**

Current care in the absence of imlifidase: dialysis until a transplant becomes available.

## Outcomes

**Outcome description - please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:**

The intended patient outcome is a kidney transplant in a patient who would otherwise remain on dialysis. Imlifidase is a novel desensitisation therapy derived from *Streptococcus pyogenes* that cleaves immunoglobulin G (IgG) molecules, enabling kidney transplantation in highly sensitised patients. Imlifidase provides a rapid, effective, and convenient means for desensitisation within a few hours, converting patients from crossmatch positive to an available donor, to negative, enabling transplantation in a patient population who would otherwise remain on dialysis for life or die waiting for a kidney transplant. Imlifidase works consistently across different levels of sensitisation and baseline DSAs; even for the most highly sensitised patients (cPRA  $\geq 99\%$ ).

## Specified restrictions for funding

**Please add one or more items, with specified restriction for funding, for each Population / Intervention:**

**Proposed item:** AAAAA

**Is the proposed item restricted:**



Yes - restricted

**Provide a short description of the restriction:**

Highly sensitised ( $\geq$ cPRA 99%) adult kidney transplant patients with a positive crossmatch against an available deceased or living donor who are unlikely to be otherwise transplanted.

**Please draft a proposed restriction to define the population and health technology usage characteristics that would define eligibility for funding:**

For patients on the deceased donor list, highly sensitised and unlikely to be transplanted can be defined as:

- Highly sensitised (cPRA  $\geq$ 99%) adult patients, AND
- With a positive crossmatch against an available donor, AND
- Have been on the deceased donor transplant list for at least 2 years.

For patients with a living donor, high sensitised unlikely to be transplanted can be defined as:

- Highly sensitised adult patients (cPRA  $\geq$ 99%), AND
- With a positive crossmatch against an available living donor AND
- Whom desensitisation regimens for organ transplantation are contraindicated or have failed, OR
- based on clinical judgement and experience, plasmapheresis /IVIG/ rituximab base desensitisation regimens are considered unlikely to provide a sufficient decrease in antibodies to enable transplantation, OR
- plasmapheresis / IVIG / rituximab-based desensitisation regimens are not logistically compatible with the patient’s circumstance or the organization of the transplant centre.

**Proposed price of supply:**

**Redacted**

**Indicate the overall cost per patient of providing the proposed health technology:**

**Redacted**

**Provide details and explain:**

The applicant requested in the initial submission a price per vial of imlifidase (11mg power for concentrate for solution for infusion) of A\$ **Redacted**/ vial. However, the applicant will rigorously explore all the commercial terms recommended in the PSD by MSAC, within the Applicant Developed Assessment Report to be submitted in February 2024. E.g. Per patient pricing

**How is the technology / service funded at present? (For example: research funding; State-based funding; self funded by patients; no funding or payment):**

The technology is not funded.

**Please provide a cost break down attachment:**

Document type	File name
Cost breakdown attachment	1732 resubmission Cost breakdown Spreadsheet 29 Nov 2023.xlsx

## Claims

**In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?**

Superior

**Please state what the overall claim is, and provide a rationale:**

Renal failure requiring renal replacement therapy is an important cause of morbidity and mortality in Australia. In Australia in 2022, 29,025 patients received renal replacement therapy (overall prevalence of 902 per one million). End-stage kidney disease is defined by partial or complete failure of kidney function. Patients with end-stage kidney disease need regular dialysis or a kidney transplant to survive. A kidney transplant gives patients a greater chance of survival and a better quality of life than remaining on dialysis.

## Estimated utilisation

**Estimate the prevalence and/or incidence of the proposed population:**

Per the presentation provided in camera at the MSAC meeting in July 2023: In 2021, approximately 11% (n = 153) of the 1,338 people on the kidney transplant waitlist had cPRA of 99% or more, and 140 of those had been on the waitlist for two or more years. The applicant is reaching out to ANZDATA and OrganMatch for data to support the prevalent and incident populations. The applicant per the PSD from MSAC is also working with RTAC on the place and potential utilisation of Imlifidase in Australian clinical practice. In the meantime, the applicant expects the following uptake.

**Provide the percentage uptake of the proposed health technology by the proposed population:**

**Year 1 estimated uptake (%):**

Redacted

**Year 2 estimated uptake (%):**

Redacted

**Year 3 estimated uptake (%):**

Redacted

**Year 4 estimated uptake (%):**

Redacted

**Estimate the number of patients who will utilise the proposed technology for the first full year:**

Redacted

**Optionally, provide details:**

Availability of kidneys for transplantation is the biggest restraint. Despite annual growth in the number of transplants performed, similar increases in the number of candidates waitlisted have prevented any reduction in the size of the waitlist. In 2022 there were greater than 1,300 people active on the kidney transplant waitlist, largely unchanged from the 1338 in 2021 (ANZDATA Registry), with approximately 140 patients highly sensitised, unlikely to be transplanted who have been on the waitlist for two or more years. On the ANZKX there are 75 living donor pairs annually (Organ and Tissue Authority, 2021) of whom around 40% are unlikely to be transplanted at the end of two years. (Cantwell et al., 2015).

A system constraint is the number of specialist adult transplant centres (n=15) able to provide appropriate post-discharge care. System performance in organ donation and transplantation depends on successful coordination across systems, designated authorities, hospitals, and individuals involved





in donor detection and management, organ procurement, allocation, donor and recipient follow-up, monitoring and surveillance, and regulation. The Australian Organ and Tissue Authority (OTA), and programmes to assist with allocations such as OrganMatch, ANZKX are crucial to the efficient running of the transplant services, especially in the highly sensitised group of patients.

**Will the technology be needed more than once per patient?**

No, once only

**Provide references to support these calculations:**

Document type	File name
Estimated utilisation references	2022-ANZDATA-Australia-Summary-Consumer-Infographic-v2.pdf; Chapter-6-Australian-Transplant-Waiting-List-ANZDATA-Annual-Report-2022.pdf





## Consultation

**List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the health technology/service:**

**Professional body name:**

American Society of Histocompatibility and Immunogenetics (ASHI)

**Professional body name:**

TRANSPLANTATION SOCIETY OF AUSTRALIA & NEW ZEALAND INC.

**List all appropriate professional bodies / organisations representing the group(s) of health professionals that may be impacted by the health technology/service:**

**List the patient and consumer advocacy organisations or individuals relevant to the proposed health technology:**

**Number of organisations listed:** 2

**Professional body name:**

Kidney Health Australia

**Number of organisations listed:** 2

**Professional body name:**

Transplant Australia Limited

**List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed service or health technology:**

**Professional body name:**

AUSTRALIAN AND NEW ZEALAND SOCIETY OF NEPHROLOGY

**Professional body name:**

Dialysis Clinics

**Professional body name:**

RENAL SOCIETY OF AUSTRALASIA LIMITED





## Regulatory information

**Would the proposed health technology involve the use of a medical device, in-vitro diagnostic test, radioactive tracer or any other type of therapeutic good?**

No