National Institute for Health and Care Excellence

Single Technology Appraisal (STA/MTA)

Imlifidase for preventing kidney transplant rejection in people with chronic kidney disease ID1672

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Hansa Biopharma	Hansa believes that it is appropriate to refer this topic to NICE for appraisal; however, Hansa believes that imlifidase should be considered through the highly specialised technology route.	This was discussed at the scoping workshop, no change to scope.
	British Transplantation Society and Royal College of Physicians	Yes *(Note: in response to 'It is important that appropriate topics are referred to NICE to ensure that NICE guidance is relevant, timely and addresses priority issues, which will help improve the health of the population. Would it be appropriate to refer this topic to NICE for appraisal?')*	Noted, no change to scope.
Wording	Hansa Biopharma	Hansa feels that the draft remit was missing information that better covers the proposed indication of imlifidase, including adult population, deceased donor with a positive crossmatch and suggest the following wording: To appraise the clinical and cost effectiveness of imlifidase within its marketing authorisation for desensitisation treatment before kidney	The remit has been left broad as the technology has not yet received a marketing authorisation, but the population in the scope has been altered to reflect the age of

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		transplantation in highly sensitised chronic kidney disease adult people with positive crossmatch against an available deceased donor.	people who may be eligible for treatment, in line with the proposed indication.
	British Transplantation Society and Royal College of Physicians	Could be more in detail	The remit has been left broad as the technology has not yet received a marketing authorisation. No change to scope.
Timing Issues	Hansa Biopharma	Highly sensitised patients with chronic kidney disease currently awaiting a deceased donor kidney do not have any available options and also have a high unmet need. Imlifidase offers these patients an innovative treatment to enable them to receive the same standard of care (kidney transplantation) that non-sensitised patients currently receive. Hansa, therefore, believes that due to the benefits for these patients, with no current treatment options, that this appraisal has a high urgency and importance to the NHS.	Noted, no change to scope.
	British Transplantation Society and Royal College of Physicians	Moderate *(Note: in response to 'What is the relative urgency of this proposed appraisal to the NHS?')*	Comment noted, no change to scope.
Additional comments on the draft remit	-	None received	-

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Hansa Biopharma	We noticed a typographic error: • Paragraph 1, line 7 – reference 2 before reference 1 which is on line 8 In addition, we would like to suggest adding in caregivers to the following line: • Paragraph 2, line 4 – …patients and caregivers, strict dietary control and limited fluid intake.	Amended in scope.
	British Transplantation Society and Royal College of Physicians	Reasonable *(Note: in response to 'Consider the accuracy and completeness of this information')*	Comment noted, no change to scope.
The technology/ intervention	Hansa Biopharma	We suggest a couple of changes to the wording of the technology: Paragraph 1, line 4 – Imlifidase is administered intravenously Paragraph 2, line 2 – …highly sensitised adult kidney transplant patients… In regard to intervention, The time period in which imlifidase should be administered should reflect the proposed Summary of Product Characteristics. In the draft scope it states 'immediately prior to transplantation'; however, 'within 24 hours prior to transplantation' accurately reflects the posology of imlifidase. We therefore suggest the following wording: Imlifidase given within 24 hours prior to transplantation.	These suggested changes have been made in the scope.

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	British Transplantation Society and Royal College of Physicians	Yes *(Note: in response to 'Is the description of the technology or technologies accurate?')*	Comment noted, no change to scope.
Population	Hansa Biopharma	The population eligible for imlifidase, based on the indication, is adult patients who have a positive crossmatch to a deceased donor kidney and are highly sensitised with human leukocyte antigen (HLA) antibodies. We suggest amending to the following wording to align with the licenced indication: Adult people with chronic kidney disease awaiting a kidney transplant from a deceased donor, who have a positive crossmatch and are highly sensitised with human leukocyte antigen (HLA) antibodies	Population wording in scope changed to reflect adult patients with a positive crossmatch, as discussed in the scoping workshop.
	British Transplantation Society and Royal College of Physicians	Yes groups within this population should be considered separately.	This was explored at the scoping workshop, with possible subgroups added to the scope.
Comparators	Hansa Biopharma	The only comparator in the indicated population (highly sensitised patients with a positive crossmatch to a deceased donor kidney) is best supportive care, e.g. chronic dialysis in this case. In the absence of imlifidase and a living donor kidney, these patients will not be able to receive transplant with a deceased donor as they will be positively crossmatched, a contraindication to transplant. Unfortunately, the standard of care (kidney transplantation) is not available in these patients. Therefore, we suggest the following changes to the comparator list:	As the clinical trials for imlifidase included both living and deceased donors, no change to the scope is required.

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		Established clinical management without imlifidase, including: • Haemodialysis/haemodiafiltration (possible settings include hospital, satellite unit, or at home) • Peritoneal dialysis (continuous ambulatory peritoneal dialysis, automated peritoneal dialysis)	
	British Transplantation Society and Royal College of Physicians	Current comparators include transplanting across low level antibodies and treating rejection when it occurs. Or being on dialysis- either PD or HD This technology may not be the best alternative care to low risk groups	Transplantation for highly sensitised patients with 'low risk' levels of antibodies was discussed at the scoping workshop, and comparators added accordingly.
Outcomes	Hansa Biopharma	In the draft scope there were a number of key outcomes missing from the list. Therefore, we suggest an updated list with the following outcomes to be considered: Efficacy on crossmatch conversion (ability to create a negative crossmatch test in people who exhibit donor specific antibodies) • Kidney function (eGFR) • Death-censored graft survival rate • Patient survival • Adverse effects of treatment • Health-related quality of life	These suggested outcomes were discussed at the scoping workshop, with amendments/additions made to the outcomes in the scope.

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		• Caregiver disutility	
	British Transplantation Society and Royal College of Physicians	Will also need 1.Graft and patient survival – medium and long-term 2. Incidence of viral and bacterial infections 3. Rebound of DSA post-transplant 4. Number and Type of rejection episodes 5. Outcomes in relation to primary diagnosis	These suggested outcomes were discussed at the scoping workshop, with amendments/additions made to the outcomes in the scope.
Economic analysis	Hansa Biopharma	None	-
Equality and Diversity	Hansa Biopharma	People who are highly sensitised are currently not being provided the same access to transplantation and standard of care as non-sensitised people. This is clear in the differences in time on the waiting list when comparing these patient groups. The updated kidney allocation scheme is proof that there has historically been an equity gap between these populations. Imlifidase will help to ensure that this gap can be narrowed further in the future. Imlifidase will also offer highly sensitised patients in minority ethnic groups, who already have difficulty accessing a matched donor kidney, a desensitisation treatment option to enable access to a deceased donor kidney. These people with protected characteristics could gain access to a donor kidney sooner and, thus, are likely to have better outcomes once transplanted.	This has been captured in the Equalities Impact Assessment, no change to scope.
	British Transplantation Society and	No issues with equality legislation.	Comments noted, no change to scope.

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	Royal College of Physicians		
Other considerations	Hansa Biopharma	None	-
	British Transplantation Society and Royal College of Physicians	To be initially used only by one or two units with expertise in antibody incompatible transplants. If successful, then to be rolled out to all transplanting units.	Comments noted, no change to scope.
Innovation	Hansa Biopharma	Imlifidase is innovative in that it is able to rapidly cleave human immunoglobulin G into F(ab')2 and Fc fragments to enable transplantation in patients highly sensitised with human leukocyte antigen antibodies. Highly sensitised patients with a positive crossmatch to a deceased donor kidney have no availability to the donor pool as they have donor-specific antibodies inhibiting successful transplant. There is a clear unmet need in these patients and imlifidase offers an option for these patients where historically there has been none; thus, providing a step-change in the management of highly sensitised patients with end-stage chronic kidney disease.	Comments noted, no change to scope.
	British Transplantation Society and Royal College of Physicians	Yes *(Note: in response to 'Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?')* No	Comments noted, no change to scope.

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		(Note: in response to 'Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?')	
Questions for consultation	Hansa Biopharma	*Which treatments are considered to be established clinical practice in the NHS for desensitisation treatment before kidney transplantation in highly sensitised people with chronic kidney disease?* There is currently no approved or established clinical practice for desensitisation of highly sensitised patients in the NHS. Where practice does take place, this is for desensitisation of living donor organs, when there is time. There is no desensitisation of deceased donors. *How would people who are highly sensitised usually be treated in the NHS while waiting for a transplant?* These patients would usually be treated with chronic dialysis until a suitable donor is found. *How would people who are highly sensitised usually be treated in the NHS, if no suitable donor is found?* Patients would stay on chronic dialysis until they are deemed too sick to continue and provided palliative care. *In current NHS practice, are people who are highly sensitised eligible for kidney transplant when there is HLA mismatch (e.g. does NHS Blood and Transplant ever allow this in your area)?*	Comments noted, no change to scope based on these comments. At the scoping workshop, it was discussed that within the NHS, some highly sensitised patients already receive low risk immunologically incompatible transplantation, as these patients have been 'delisted' due to low levels of some antibodies, that clinicians believe can be managed with existing immunosuppression. There is also the potential for the marketing authorisation to include transplants from living donors. Clinical experts

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		For patients with a negative crossmatch, there is the option for transplant. For patients with a positive crossmatch there is no option for transplant with a deceased donor (in the absence of imlifidase). *Do you consider that the use of imlifidase can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* Imlifidase offers the potential to significantly and substantially improve patient mortality and quality of life, as well as the large societal impact of chronic dialysis, including the patients' ability to work and the quality of life of caregivers. *To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.* We believe that there are natural barriers that exist that will limit the extent to which imlifidase could be offered, these include: finite number of deceased donor kidneys available and limited number of transplantations that are feasibly possible to undertake per year at the limited number of licenced kidney transplant centres. For these reasons, and in light of the updated kidney allocation scheme, we believe this should form part of a highly specialised service.	explained that some desensitised patients already receive desensitisation treatment in the NHS. As a result, dialysis is not the only comparator included in the scope.
	British Transplantation Society and	Would they need any antibiotic prophylaxis? If so what and for how long? What is the estimated cost for a single injection?	First question was beyond remit of scoping workshop. The estimated cost will be

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	Royal College of Physicians		presented in the company submission.
Additional comments on the draft scope	British Transplantation Society and Royal College of Physicians	A good potential drug. Can have many further uses in transplant patients with antibodies.	Comment noted, no change to scope.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

None.