# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Proposed Health Technology Appraisal

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

## Draft scope (pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of imlifidase within its marketing authorisation for desensitisation treatment before kidney transplantation in highly sensitised people with chronic kidney disease.

### Background

In chronic kidney disease (CKD), the kidneys can't remove waste products from the body as well as they should, and blood and protein may leak into the urine. People with CKD are at higher risk of developing other health conditions including cardiovascular disease. As kidney function decreases, this renal disease can lead to symptoms including weight loss and poor appetite, swollen ankles, feet or hands, shortness of breath, tiredness, feeling sick and itchy skin as the disease progresses[2]. Moderate to severe CKD affects approximately 5.5% of adults and is more common in older people.[1]

End-stage renal disease is sometimes called advanced CKD or kidney failure. Many people at this stage will have regular dialysis treatment, to filter waste products out of the blood, but this requires a high time commitment from patients, strict dietary control and limited fluid intake. Dialysis does not replace all of the kidney's functions, so kidney transplant is considered the treatment of choice in end-stage renal failure.[3] There were 4,647 adults on the UK kidney transplant waiting list in March 2019, and 3,280 adult kidney-only transplants in the UK in 2018/19 (of which 71% were from deceased donors).[4]

Many people on the waiting list for organ transplantation carry antibodies to human leukocyte antigen (HLA), which is known as being 'sensitised.' People who are highly sensitised may find it difficult getting a donor and may not be able to have a transplant because of increased risk of kidney rejection.[5] The immune system recognises 'non-self' HLA on the cells of the transplanted kidney and attacks the organ, which may lead to rejection. Transplantation rates are low for those classed as 'highly sensitised', representing around 26% of people on the UK waiting list.[5] In the UK, this is defined as having a calculated reaction frequency (cRF) of at least 85%, meaning the potential transplant recipient has pre-formed HLA antibodies in their body against at least 85% of deceased donors (they have a 'positive crossmatch' with these potential donors, so the donors and patient are incompatible).[5]

Desensitisation is the process of removing hazardous preformed donor-specific antibodies (DSA) against HLA in order to safely proceed with transplantation.[6] Current approaches to desensitisation (such as


 

plasmapheresis and intravenous immune globulin treatments[6]) need repeated dosing for weeks or months before a planned transplant, so this is rarely an option for highly sensitised patients waiting for a transplant from a deceased donor, as transplants have to take place within hours of the donor's death.[7]

## The technology

Imlifidase (Idefirix, Hansa Biopharma) is an enzyme which inactivates donor-specific antibodies to HLA. By breaking down these antibodies, imlifidase could prevent the immune system from attacking the transplanted kidney, and may reduce the risk that the organ will fail. It is given intravenously.

Imlifidase does not currently have a marketing authorisation in the UK for desensitisation treatment of highly sensitised kidney transplant patients with positive crossmatch against an available deceased donor. It has been trialled in observational studies investigating imlifidase (non-comparative), with an ongoing follow up study to monitor graft survival in people who have had kidney transplantation after imlifidase administration.

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| **Intervention(s)** | Imlifidase given immediately prior to transplantation, in addition to an immunosuppressive regimen |
| **Population(s)** | People with chronic kidney disease awaiting a kidney transplant from a deceased donor, who are highly sensitive to human leucocyte antigens (HLA) |
| **Comparators** | Kidney transplant with established clinical management without imlifidase.<br><br>Established clinical management without imlifidase or kidney transplant. May include:<br><br>• Haemodialysis/haemodiafiltration (possible settings include hospital, satellite unit, or at home)<br>• Peritoneal dialysis (continuous ambulatory peritoneal dialysis, automated peritoneal dialysis) |


 

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| **Outcomes** | The outcome measures to be considered include:<br>• Incidence of transplanted kidney rejection after transplant<br>• Efficacy on crossmatch conversion (ability to create a negative crossmatch test in people who exhibit donor specific antibodies)<br>• Mortality<br>• Requirement for dialysis<br>• Adverse effects of treatment<br>• Health-related quality of life |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br>Immunosuppressive therapy for kidney transplant in adults (2017). NICE Technology Appraisal 481. Review date TBC.<br>Machine perfusion systems and cold static storage of kidneys from deceased donors (2009). NICE Technology Appraisal 165. Reviewed April 2013.<br><br>Related Guidelines:<br>Renal replacement therapy and conservative management (2018). NICE guideline 107. Review date TBC.<br><br>Guidelines in development: |


 

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| | Chronic kidney disease in adults: assessment and management (updated 2015). NICE clinical guideline 182. Reviewed April 2017, publication expected July 2020.<br><br>Related Interventional Procedures:<br>Laparoscopic insertion of peritoneal dialysis catheter (2007). NICE interventional procedures guidance 208.<br>Robot-assisted kidney transplant (2018). NICE interventional procedures guidance 609.<br><br>Related Quality Standards:<br>Chronic kidney disease in adults (updated 2017). NICE quality standard 5.<br>Renal replacement therapy services for adults (updated 2018). NICE quality standard 72.<br><br>Related NICE Pathways:<br>Chronic kidney disease NICE pathway<br>https://pathways.nice.org.uk/pathways/chronic-kidney-disease |
| **Related National Policy** | NHS England (2017) Adult Kidney Transplant Services Service Specifications<br><br>NHS England (2015) Clinical Commissioning Policy: Bortezomib for the treatment of refractory antibody mediated rejection post kidney transplant<br><br>NHS England (2015) Clinical Commissioning Policy: Eculizumab for the treatment of refractory antibody mediated rejection post kidney transplant<br><br>The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018/2019), Chapter 15, NHS manual for prescribed specialist services (2018/2019).<br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1&2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 |

**Questions for consultation**

Have all relevant comparators for imlifidase been included in the scope? 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? How would people who are highly sensitised usually be treated in the NHS while waiting for a transplant? How would people who are highly sensitised usually be treated in the NHS, if no suitable donor is found? 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)?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom imlifidase is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider imlifidase will fit into the existing NICE pathway, chronic kidney disease?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which imlifidase will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider imlifidase 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)?

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?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.


 

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.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

**References**

1 Nitsch D, Caplin B, Hull S and Wheeler DC on behalf of the National CKD Audit and Quality Improvement Programme in Primary Care (2017) First National CKD Audit Report 2017. Available from: https://www.lshtm.ac.uk/files/ckd_audit_report.pdf

2 NHS (2019) Chronic kidney disease: Symptoms. Available from: https://www.nhs.uk/conditions/kidney-disease/symptoms/

3 NHS (2018) Dialysis. Available from: https://www.nhs.uk/conditions/dialysis/

4 NHS Blood and Transport (2019) Annual report on kidney transplantation. Report for 2018/2019 NHS Blood and Transport (2019) Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/16778/nhsbt-kidney-transplantation-annual-report-2018-19.pdf

5 Manook et al. (2017) Post-listing survival for highly sensitised patients on the UK kidney transplant waiting list: a matched cohort analysis. The Lancet, 389(10070):727-734. Available from: https://doi.org/10.1016/S0140-6736(16)31595-1

6 Lonze et al. (2018) IdeS (imlifidase): A novel agent that cleaves human IgG and permits successful kidney transplantation across high-strength donor-specific antibody. Annals of Surgery, 268(3):488–496. Available from: https://dx.doi.org/10.1097/sla.0000000000002924

7 NIHR (2019) Health technology briefing July 2019: Imlifidase for kidney transplantation in highly sensitised patients with chronic kidney disease. Available from: http://www.io.nihr.ac.uk/wp-content/uploads/2019/07/11428-Imlifidase-for-Kidney-Transplantation-V1.0-JUL2019-NONCONF.pdf


 