NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

Draft remit/appraisal objective

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

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, which requires strict dietary control and limited fluid intake. People with CKD may spend a lot of time having dialysis, and may require carer assistance. 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 potential transplant recipient 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 plasma exchange and intravenous immune globulin treatments[6]) typically need repeated dosing before a planned transplant, so this is rarely an option for people who are highly sensitised and waiting for a transplant from a deceased donor, as transplants have to take place within hours of the donor's death.[7] In the UK, some people on the waiting list for a kidney

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who are highly sensitised may be deemed as low risk in terms of immunologic incompatibility with a donor. This means they have low levels of some antibodies, which could be removed by desensitisation, usually via plasma exchange. In these cases, the clinician may amend the person's profile on the waiting list so that the presence of these low level antibodies is no longer a barrier to matching with a donor who also has the antibodies. This is sometimes referred to by clinicians as 'delisting'. This is because the treating doctor believes desensitisation or immunosuppressive treatment will overcome issues presented by low level antibodies, allowing the transplant to be successful, despite the transplant being immunologically incompatible.[8]

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. Imlifidase is given intravenously prior to transplantation.

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

Intervention(s)	Imlifidase in addition to an immunosuppressive regimen
Population(s)	Adults with chronic kidney disease awaiting a kidney transplant from a donor, who are highly sensitised with human leucocyte antigens (HLA) and have a positive crossmatch with the donor
Comparators	Established clinical management without imlifidase: • Kidney transplant (may include plasma exchange) • Haemodialysis/haemodiafiltration or peritoneal dialysis
Outcomes	The outcome measures to be considered include: • Efficacy on crossmatch conversion (ability to create a negative crossmatch test in people who exhibit donor specific antibodies) • Mortality • Kidney function (eGFR) • Time to graft failure • Time to rejection; type of rejection; number of rejection episodes • Time to next renal replacement therapy; type of next renal replacement therapy • Time to rebound concentration of donor specific antibodies post-transplant; proportion of patients who

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	require treatment of rebound antibodies post-transplant • Incidence of viral and bacterial infections • Hospitalisation days • Adverse effects of treatment • 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. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows, the following subgroups will be considered. These include: recipients of kidneys from living donors; recipients of kidneys from deceased donors; low risk ('delisted') recipients of donor kidneys, non-delisted recipients of donor kidneys; degree of sensitisation in terms of antibody levels (e.g. positive microbead test, flow cytometry (FC) crossmatch, positive complement dependent cytotoxic (CDC) crossmatch). The availability and cost of biosimilar and generic products should be taken into account. 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: Immunosuppressive therapy for kidney transplant in adults (2017). NICE Technology Appraisal 481. Review date TBC. Machine perfusion systems and cold static storage of kidneys from deceased donors (2009). NICE Technology Appraisal 165. Reviewed April 2013. Related Guidelines:

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	Renal replacement therapy and conservative management (2018). NICE guideline 107. Review date TBC. Guidelines in development: Chronic kidney disease in adults: assessment and management (updated 2015). NICE clinical guideline 182. Reviewed April 2017, publication expected March 2021. Related Interventional Procedures: Laparoscopic insertion of peritoneal dialysis catheter (2007). NICE interventional procedures guidance 208. Robot-assisted kidney transplant (2018). NICE interventional procedures guidance 609. Related Quality Standards: Chronic kidney disease in adults (updated 2017). NICE quality standard 5. Renal replacement therapy services for adults (updated 2018). NICE quality standard 72. Related NICE Pathways: Chronic kidney disease NICE pathway https://pathways.nice.org.uk/pathways/chronic-kidney-disease
Related National Policy	NHS England (2017) Adult Kidney Transplant Services Service Specifications NHS England (2015) Clinical Commissioning Policy: Bortezomib for the treatment of refractory antibody mediated rejection post kidney transplant NHS England (2015) Clinical Commissioning Policy: Eculizumab for the treatment of refractory antibody mediated rejection post kidney transplant The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019), Chapter 15, NHS manual for prescribed specialist services (2018/2019). 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

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References

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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

8 British Transplantation Society (2016) Guidelines for antibody incompatible transplantation (third edition). Available from: https://bts.org.uk/wp-content/uploads/2016/09/02_BTS_Antibody_Guidelines-1.pdf

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