NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Belatacept for the prevention of organ rejection in kidney transplantation

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of belatacept, within its licensed indication, for the prevention of organ rejection in kidney transplantation in adults.

Background

Established kidney failure is the result of progressive disease of the kidneys leading to irreversible loss of function. Kidney transplantation is the preferred treatment option for patients with established kidney failure. The only alternative is dialysis.

Standard immunosuppressive therapy in kidney transplantation consists of maintenance therapy to prevent rejection, and short courses of additional therapy as necessary to treat episodes of acute rejection. The overall aim of therapy is to prevent acute rejection and chronic graft dysfunction – thereby prolonging graft survival – without exposing the patient to the risks of excessive immunosuppression or other toxicity related to the use of immunosuppressant drugs.

In 2008 there were around 42,000 patients receiving immunosuppression after kidney transplantation in England and Wales, with a prevalence rate of 767 per million population in England and 827 per million population in Wales. The total number of kidney transplants performed in the UK in 2008 was 2,486 compared to 2,218 in 2007 and 2,067 in 2006. The numbers of kidney transplants in the UK are limited by the availability of donor organs.

Initial immunosuppressive therapy following kidney transplantation involves different combinations of drugs which can include a calcineurin inhibitor (ciclosporin or tacrolimus), an antiproliferative agent (azathioprine or mycophenolate mofetil/sodium) and a corticosteroid (prednisolone). Maintenance therapy is the long term immunosuppression which is often identical to initial therapy but at lower doses. In some cases induction therapy, a short course of immunosuppressive therapy given in addition to the initial therapy immediately following transplant, is also given and usually involves polyclonal antibodies (e.g. rabbit anti-human thymocyte immunoglobulin) or monoclonal antibodies (e.g. basiliximab).

Current NICE guidance on immunosuppression for kidney transplantation in adults (TA85) gives guidance on the use of basiliximab, mycophenolate mofetil, sirolimus and tacrolimus in adults who receive a kidney transplant.

Daclizumab was also recommended in technology appraisal guidance 85 but it no longer has a marketing authorisation. This guidance recommends that the choice of calcineurin inhibitor is based on the relative importance of their side-effect profiles for individual people, while mycophenolate mofetil is recommended only where there is proven intolerance to calcineurin inhibitors or a very high risk of nephrotoxicity necessitating minimisation or avoidance of a calcineurin inhibitor. TA85 also recommends sirolimus as an option in cases of proven intolerance to calcineurin inhibitors (including nephrotoxicity) but only where this necessitates complete withdrawal of these treatments.

The technology

Belatacept (brand name unknown, Bristol Myers Squibb) is a soluble chimeric protein designed to selectively inhibit CD28-mediated co-stimulation of T-cells. Belatacept is an intravenous preparation which could potentially be administered in the home, in specialist hospitals, transplant centres, or associated clinics for example local nephrology units

Belatacept does not currently hold a UK marketing authorisation. In clinical studies, it has been compared with ciclosporin or tacrolimus for the prophylaxis of organ rejection in adults undergoing kidney transplantation.

Intervention(s)	Belatacept (dual therapy in combination with a corticosteroid and/or triple therapy in combination with both a corticosteroid and an antiproliferative agent)
Population(s)	Adults undergoing or who have already undergone kidney transplantation

Comparators	• Standard calcineurin inhibitor based dual or triple therapy.
	• For people who calcineurin inhibitors are inappropriate:
	  ○ mycophenolate [mofetil or sodium] based regimens, or;
	  ○ sirolimus-based regimens.

Outcomes	The outcome measures to be considered include: • patient survival • graft survival • graft functioning (serum creatinine / glomerular filtration rate) • time to and incidence of acute rejection • severity of acute rejection • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. When presenting the evidence, risk factors as reported in the studies should be listed and may include: country of origin, ethnicity of recipient, the degree of HLA histocompatibility between the recipient and donor and donor type (e.g. cadaveric or living donors).
Related NICE recommendations	Related Technology Appraisals: Technology appraisal No. 85, September 2004, The clinical and cost effectiveness of immuno-suppressive therapy for renal transplantation Technology appraisal No. 99, April 2006, Immunosuppressive therapy for renal transplantation in children and adolescents Related Guidelines: Clinical Guideline No. 73, September 2008, 'Chronic Kidney disease; early identification and management of chronic kidney disease in adults in primary and secondary care'. Review date: September 2011

Questions for consultation

Have the most appropriate comparators for belatacept for kidney transplantation been included in the scope?

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

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider belatacept 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 belatacept 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

Should belatacept be appraised as part of the review of technology appraisal guidance 85?

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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)