January 19th, 2016

Dr Margaret Helliwell
Vice chair
National Institute for Health and Care Excellence
10 Spring Gardens
London SW1A 2BU

Dear Margaret

Re: Final Appraisal Determination - Immunosuppressive therapy for kidney transplant in adults (review of technology appraisal guidance 85)

The British Kidney Patient Association would like to appeal against the Final Appraisal Determination for the above mentioned technology appraisal guidance 85 on the following grounds:

Ground 2: The recommendation is unreasonable in the light of the evidence submitted to NICE

2.1 Recommendation 1.4 that 'Rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus, mycophenolate sodium, sirolimus, everolimus and belatacept are **not recommended** to prevent organ rejection in adults having a kidney transplant' is unreasonable as it has not taken into account the resultant reduction in transplants, which would lead to more dialysis. The recommendation is significant for the future of transplantation in this country. By not recommending rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus, mycophenolate sodium and sirolimus in particular, effective options for the 20-30% of patients who are intolerant of, or unsuitable for, the interventions recommended in

section 1.1-1.3 of the FAD are severely limited. These drugs have been used and embedded in clinical practice for 10 years, and in the case of Rabbit ATG for 30 years.

2.3 Recommendation 1.4 does not take into account the quality of life impact resulting from lost transplants for people who are unable to tolerate immediate release tacrolimus, basiliximab or mycophenolate mofetil, who experience acute rejection at initiation or chronic rejection over time and who are then unable to access alternative agents.

2.4 Recommendation 1.4 does not take into account the increased mortality of those who will be unable to access transplantation and are taken off the transplant waiting list because alternative treatments are not available.

2.5 The cost comparator does not take into account the additional costs of dialysis and/or failed transplant operations as a result of the inability to prescribe alternative therapies. As we pointed out in our original submission the true comparator is the costs of dialysis (at approximately £30,000 pa not including patient transport and certain drugs) and the costs of a failed transplant at approximately £17,000.

2.6 Recommendation 1.4 does not provide/enable any alternative pathway for those who are unable to use the recommended drugs in a timely manner. The recommendation does not appreciate that drugs to treat rejection may be needed in a matter of hours and that therefore a process of applying for funding through commissioners in an IFR process is unfeasible.

2.7 Recommendation 1.4, by preventing access to drugs which are in common practice and reducing the numbers of transplants possible for the 20% who are unsuitable for Basiliximab (3.2), those unable to tolerate the gastro-intestinal effects of mycophenolate mofetil and those who are much more likely not to adhere to the twice a day regimen of tacrolimus, gives a very negative message about the value of organ transplantation to the general public and potential donors. One person dies every day whilst waiting for a

kidney transplant; recommendation 1.4 will be counterproductive in respect of regular activity by patient charities and arms-length bodies such as NHSBT to increase access to increase donation rates.

2.8 Recommendation 1.4 reduces effective options for patients who are intolerant of mycophenolate mofetil by not recommending mycophenolate sodium (section 1.3). Gastrointestinal adverse reactions to mycophenolate mofetil are common and disabling despite dose modification and are less for mycophenolate sodium. For those patients who have already experienced a rejection episode there is also a risk of further rejection and poor outcomes.

2.9 Recommendation 1.4 reduces effective options for the subgroup of patients who have poor adherence or marked variability of drug levels with immediate release tacrolimus (1.2) by not recommending prolonged release tacrolimus. There is plenty of evidence that non-adherence and high variability are associated with worse outcomes, generally graft loss. Evidence given to the Appraisal Committee on this by patient representatives has not been accounted for.

2.10 Recommendation 1.4 reduces effective options for future patients who would benefit from sirolimus treatment. The Committee has not taken into consideration the current ways in which sirolimus is used e.g. to prevent further malignancy or to alleviate the gastro-intestinal effects of mycophenolate mofetil if mycophenolate sodium is also not tolerated.

2.11 Recommendation 1.4 reduces effective options for future patients who are not suitable for basiliximab induction therapy (section 1.1) by not recommending rabbit ATG. There was no compelling evidence presented showing the safety and effectiveness of using Basiliximab outside the marketing authorisation and NICE is being inconsistent in the use of evidence, as it uses lack of evidence as a reason not to recommend other drugs.

2.12 The Appraisal Committee acknowledge that there are limitations in the available evidence and of the consequent clinical and cost-effectiveness

analysis which raises concerns about the robustness of the recommendations. Nevertheless the risks in this process are disregarded and a set of recommendations, which we believe will lead to extremely poor outcomes for transplanted kidney patients and result in significantly increased cost, has been made.

2.13 An examination of the NICE guidance and planned review process does not show that a similar review is being planned in the case of recipients of other organs, apart from the recent non-recommendation for use of belatacept and everolimus in liver transplantation. As a result, kidney patients are not being treated consistently with recipients of other organs, who can continue to use rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus and mycophenolate sodium to prevent organ rejection.

Conclusion

The BKPA asks the Committee to change its wording from 'Rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus, mycophenolate sodium, sirolimus, everolimus and belatacept are **not recommended** to prevent organ rejection in adults having a kidney transplant' to '**It is not possible to make recommendations** on the use of rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus, mycophenolate sodium, and sirolimus to prevent organ rejection in adults having a kidney transplant'. We are asking NICE to retain an effective alternative treatment path for patients who will otherwise remain on dialysis or die.

This approach is entirely consistent with NICE's wording in the note in the following paragraph that 'The Appraisal Committee **was unable to make recommendations** on these technologies for…biopsy proven nephrotoxicity…'

The BKPA would like to state that the impact of this recommendation from NICE on the small heterogeneous population with kidney failure has not been fully considered by NICE and to ask that it reconsider the wording of the technology appraisal. We estimate that the appraisal will affect between 485-

730 patients a year, being the 20-30% who are unable to tolerate the recommended drugs and will develop rejection or would no longer be suitable to have a kidney transplant. This is based on the latest transplant figures available from NHS Blood and Transplant https://nhsbtdbe.blob.core.windows.net/umbraco-assets/1070/england.pdf

The BKPA wishes this appeal to proceed at an oral appeal.

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