National Institute for Health and Care Excellence

Multiple Technology Appraisal (MTA)

Immunosuppressive therapy for kidney transplantation in children and adolescents (review of technology appraisal guidance 99)

Response to consultee and commentator comments on the draft scope

Section	Consultee/ Commentator	Comments	Action
Background information	Astellas Pharma	Astellas believes the background information should include the issues for children and some adolescents with swallowing capsules. Modigraf provides a solution to this problem by being formulated as granules for oral suspension.	Comment noted. The background section is intended to be a brief introduction to the clinical area and treatment pathway. No action required.
	British Association For Paediatric Nephrology	Accurate.	Comment noted. No action required.
	Renal Association	No comments.	No action required.
	Sandoz	No comments.	No action required.
The technology/ intervention	Astellas Pharma	No comments.	No action required.
	British Association For	Yes, but please also consider the use of methylprednisolone at	Comment noted. The technologies to be appraised

Section	Consultee/ Commentator	Comments	Action
	Paediatric Nephrology	induction and rituximab for ABO incompatible transplants.	are those: - that were included in technology appraisal guidance 99; or - that have obtained a relevant marketing authorisation in the UK since the publication of technology appraisal guidance 99; or - that have been referred to NICE by the Department of Health for appraisal. Methylprednisolone and rituximab did not meet these conditions, so they have not been added to the list of interventions. In response to consultation, NICE was advised that the use of methylprednisolone as an induction therapy is considered to be established practice in the NHS. Accordingly, methylprednisolone has been added to the list of comparators. In response to consultation,

Section	Consultee/ Commentator	Comments	Action
			NICE did not receive consistent advice that the use of rituximab as an induction therapy is considered to be established practice in the NHS. Accordingly, rituximab was not included as a comparator. Please see section 6.2.2 of NICE's Guide to the methods of technology appraisal 2013: http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9
	Renal Association	No comments.	No action required.
	Sandoz	See below.	No action required.
Population	Astellas Pharma	The population is defined appropriately. Astellas believes the following subgroups should also be considered: • Those children and adolescents unable to swallow capsules	Comment noted. The draft scope stated that, if evidence allows, adherence to treatment will be considered. As part of this consideration, the Appraisal Committee could examine treatments for children and adolescents who have difficulty swallowing capsules. If a manufacturer

Section	Consultee/ Commentator	Comments	Action
		• Those children and adolescents that have difficulty adhering to treatment regimen	has evidence that a technology is especially effective or cost-effective in a subgroup, it is encouraged to include this evidence in its submission to NICE. No action required.
	British Association For Paediatric Nephrology	Yes, but please also consider ABO and HLA incompatible transplants.	The draft scope stated that, if evidence allows, the following subgroup will be considered: 'level of immunological risk (including human leukocyte antigen compatibility and blood group compatibility).' No action required.
	Renal Association	It is not clear what age group the scope applies to. Is this Birth to 16 or up to 18. Many adolescents (16+) are transplanted in adult services or transferred shortly after.	In general, 'children and adolescents' refers to people under the age of 18 years. When making recommendations for individual technologies, the committee will consider the marketing authorisation and the age range of participants in the clinical trials. No action required.
	Sandoz	Agree	Comment noted. No action required.

Section	Consultee/ Commentator	Comments	Action
Comparators	Astellas Pharma	The draft scope mentions the use of ciclosporin and azathioprine for maintenance therapy which are often used in combination regimens with or without corticosteroids. However, neither ciclosporin, azathioprine or Modigraf granules (for oral suspension) have been specifically included as technologies for maintenance therapy alongside tacrolimus, belatacept, mycophenolate mofetil, mycophenolate sodium, sirolimus and everolimus.	Comment noted. The technologies to be appraised are those: - that were included in technology appraisal guidance 99; or - that have obtained a relevant marketing authorisation in the UK since the publication of technology appraisal guidance 99; or - that have been referred to NICE by the Department of Health for appraisal. Immediate-release formulations of tacrolimus are included as interventions in the scope and therefore Modigraf is included as a technology to be appraised. No action required. Ciclosporin and azathiopine did not meet the criteria listed above and are therefore not included as interventions. The relevant comparators are therapies that are considered

Section	Consultee/ Commentator	Comments	Action
			part of established NHS practice. Therefore, ciclosporin and azathioziopine are included as comparators. Please see sections 2.2.4-2.2.6 and 6.2.1-6.2.4 of the NICE guide to the methods of technology appraisal 2013: http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9 No action required.
	Astellas Pharma	The correct comparator for Modigraf (granules for oral suspension) is 'specials' liquid suspension.	Comment noted. NICE understands that the manufacturer is referring to a 'specials' liquid suspension of immediate-release tacrolimus that is produced for a named patient and that does not have a UK marketing authorisation. Immediate-release formulations of tacrolimus that **do** hold a UK marketing authorisation are included as an intervention in the appraisal. There is an exceptional

Section	Consultee/ Commentator	Comments	Action
			directive from the Department of Health stating that the Appraisal Committee may consider making recommendations about the use of drugs **outside the terms of their marketing authorisation** where there is compelling evidence of their safety and effectiveness. However, this directive does not cover technologies that do not have a UK marketing authorisation for any indication. For this reason, 'specials' preparations of tacrolimus are not included as interventions in the appraisal. The relevant comparators are therapies that are considered part of established NHS practice (see sections 2.2.4-2.2.6 and 6.2.1-6.2.4 of the NICE guide to the methods of technology appraisal). Based on the MHRA Drug Safety Update in 2010 regarding unlicensed preparations of tacrolimus (see page 12), NICE does not consider the

Section	Consultee/ Commentator	Comments	Action
			use of 'specials' preparations to be routine clinical practice in the NHS. Therefore, 'specials' preparations of tacrolimus are not included as a comparator. Comments received during consultation advised that the comparators in the scope are appropriate. No action required.
	British Association For Paediatric Nephrology	Azathioprine is not specified in the comparator arm for maintenance treatment and this should be clarified	Comment noted. The comparators in the draft scope included 'a calcineurin inhibitor and an anti-proliferative agent with or without corticosteroids.' This phrase is intended to include azathioprine, which is mentioned in the background section as an antiproliferative used in clinical practice. No action required.
	Renal Association	No comments.	No action required.
	Sandoz	Immediate release and prolonged release formulations of tacrolimus should be assessed separately as they are not equivalent in terms of	Comment noted. The list of interventions has been

Section	Consultee/ Commentator	Comments	Action
		dosing and drug levels. Advagraf is not licensed in children and adolescents under the age of 18.	changed to include: • Immediate-release tacrolimus • Prolonged-release tacrolimus Under an exceptional directive from the Department of Health, the Appraisal Committee may consider making recommendations about the use drugs outside the terms of their marketing authorisation where there is compelling evidence of their safety and effectiveness. No action required.
		Sandoz is planning to launch to novel strengths of immediate release tacrolimus (Adoport) during this appraisal period. The new strengths will have patient benefits in terms of reduction in pill burden and alternative dosing increments for patients who are on small doses.	Comment noted. The manufacturer is invited to provide evidence on the innovative nature of the technology in its submission. No action required.
Outcomes	Astellas Pharma	No comments	No action required.
	British Association For	Yes	No action required.

Section	Consultee/ Commentator	Comments	Action
	Paediatric Nephrology		
	Renal Association	No comments.	No action required.
	Sandoz	Treatment of acute rejection episodes should be included.	Comment noted. The aim of the appraisal is to review and update (where necessary) the recommendations in technology appraisal guidance 99. Technology appraisal guidance 99 did not make recommendations for the treatment of acute rejection. Accordingly, the forthcoming appraisal will not consider treatments for acute rejection.
Economic analysis	Astellas Pharma	Astellas supports the use of the NICE reference case in demonstrating the cost-effectiveness of tacrolimus. A new model will be commissioned to represent the patient flow following successful kidney transplantation through a number of different health states. This Markov model will describe a one year life cycle and will support time horizons of between 5 and 25 years to estimate incremental cost per quality adjusted life years (QALYs) gained. We believe that all important differences in costs and outcomes will be reflected within this time horizon.	Comment noted. The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared. See section 5.1 of NICE's Guide to the methods of technology appraisal. 2013: http://publications.nice.org.uk/

Section	Consultee/ Commentator	Comments	Action
			guide-to-the-methods-of-technology-appraisal-2013-pmg9 No action required.
	British Association For Paediatric Nephrology	None	No action required.
	Renal Association	No comments.	No action required.
	Sandoz	No comment	No action required.
Equality and Diversity	Astellas Pharma	No comments	No action required.
	British Association For Paediatric Nephrology	No issues.	No action required.
	Renal Association	No comments.	No action required.
	Sandoz	No comment.	No action required.
Innovation	Astellas Pharma	Astellas believes Modigraf to be innovative for the following reasons: • The flexibility of dosing provided by Modigraf allows fine-tuning	Comment noted. The manufacturer is invited to provide evidence on the

Section	Consultee/ Commentator	Comments	Action
		to provide an optimised individualised dose • Unlike capsules, Modigraf does not have the safety issues related to the opening of capsules and possible inhalation of tacrolimus by healthy individuals (e.g. patients, carers) • Modigraf allows more accurate dosing compared to other alternatives such as 'specials' due to the availability of the 0.2 mg strength formulation	innovative nature of the technology in its submission.
	British Association For Paediatric Nephrology	No comments .	No action required.
	Renal Association	No comments.	No action required.
	Sandoz	No comments.	No action required.
Other considerations	Astellas Pharma	An MHRA-Drug Safety Update 2010 referred to the use of unlicensed tacrolimus formulations as such: • Patients unable to swallow Prograf capsules may have previously been given the contents of the capsules in water before swallowing or may have used extemporaneously prepared or unlicensed liquid preparations ('specials') • The bioavailability of such manipulations or preparations is unknown and may vary between manufacturers or from batch to batch. Special care must be taken when converting patients from unlicensed 'special' oral liquid preparations to licensed	Comment noted. For the reasons described on pages 6–8, 'specials' preparations of tacrolimus are not included as interventions or comparators in this appraisal. The Appraisal Committee will take account of the MHRA safety update when formulating its recommendations. No action required.

Section	Consultee/ Commentator	Comments	Action
		formulations of tacrolimus • A transplant specialist should closely supervise the transfer of patients from any unlicensed treatment to Modigraf • Before using an unlicensed medicine or a licensed medicine off-label, prescribers should satisfy themselves that an alternative, licensed medicine such as Modigraf would not meet the patient's needs. Advice for healthcare professionals: • Consider use of the licensed oral liquid formulation of tacrolimus (Modigraf) for paediatric patients and others with swallowing difficulties	
	British Association For Paediatric Nephrology	No comments.	No action required.
	Renal Association	No comments.	No action required.
	Sandoz	No comments.	No action required.
Questions for consultation	*Would a review of the recommendations in NICE technology appraisal guidance 99 provide value to the NHS?*		
	Astellas Pharma	Yes	Comment noted. This topic has been scheduled into the NICE work programme. Please see: http://www.nice.org.uk/guidan

Section	Consultee/ Commentator	Comments	Action
			ce/indevelopment/GID-TAG255
	British Association For Paediatric Nephrology	Yes	Comment noted. This topic has been scheduled into the NICE work programme.
	Sandoz	Sandoz believes a full review is necessary and would be beneficial as it is likely to lead to a change in current recommendations, which will reflect current clinical practice	Comment noted. This topic has been scheduled into the NICE work programme.
	Should all of the current recommendations be reviewed, or is it only appropriate to review some of the recommendations (that is, undertake a partial review)?		
	Astellas Pharma	Astellas believes all current recommendations should be reviewed since the current NICE guidance is out of date, and does not match current therapy in England and Wales. There is currently NICE UK guidance (NICE TA99) and guidance produced by the UK Renal Association (Clinical practice guidelines, 2011) recommending treatment for induction therapy, initial maintenance therapy, and long term maintenance therapy. However although these guidelines exist, centre specific variation occurs within clinical practice and a review of all recommendations will help make it clearer as to which treatments and treatment regimens should be adhered to.	Comment noted. All of the current recommendations will be reviewed. No action required.
	British Association For Paediatric	All	Comment noted. All of the current recommendations will be reviewed. No action

Section	Consultee/ Commentator	Comments	Action
	Nephrology		required.
	Sandoz	Sandoz believes a full review is necessary	Comment noted. All of the current recommendations will be reviewed. No action required.
	Is it anticipated that the evidence that has emerged since the publication of technology appraisal guidance 99 would lead to a change in the recommendations?		
	Astellas Pharma	In line with the use of immunosuppressives in adults, practice in the UK changed following the publication of the Symphony study in 2007 (Ekberg et al), and tacrolimus is now the cornerstone of immunosuppressive treatment.	Comment noted. A systematic review of the evidence will be conducted as part of the appraisal by the Assessment Group. The manufacturer is invited to provide evidence on the clinical and/or cost effectiveness of the technologies in its submission.
		Additionally the availability of Modigraf, since 2009 should be considered in guidance.	Immediate-release tacrolimus formulations are included as an intervention in the scope. The manufacturer is invited to provide evidence on the clinical and/or cost effectiveness of the technology in its submission.

Section	Consultee/ Commentator	Comments	Action
			No action required.
	British Association For Paediatric Nephrology	Yes	Comment noted. No action required.
	Sandoz	Sandoz believes a full review … is likely to lead to a change in current recommendations, which will reflect current clinical practice	Comment noted. No action required.
	Are immunosuppressive treatments frequently used outside of their marketing authorisations in the NHS? Would an appraisal that only considers the use of immunosuppressive treatments within their marketing authorisations reflect current clinical practice and would it be of value to the NHS?		
	Astellas Pharma	No comments	No action required.
	British Association For Paediatric Nephrology	*Are immunosuppressive treatments frequently used outside of their marketing authorisations in the NHS?* Yes *Would an appraisal that only considers the use of immunosuppressive treatments within their marketing authorisations reflect current clinical practice and would it be of value to the NHS?* No to both.	Comments noted. Under an exceptional directive from the Department of Health, the Appraisal Committee may consider making recommendations about the use of drugs outside the terms of their existing marketing authorisation where there is compelling evidence of their safety and effectiveness. No action required.

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	Pfizer	Pfizer considers that medicines regulation has been developed in Europe to assess how medicines should be authorised for use and there is clearly a need to ensure that the special position of the regulatory bodies is recognised. We are concerned to ensure that NICE guidance that is inconsistent with the marketing authorisation cannot be seen to undermine the regulatory framework by inappropriately influencing clinicians' professional obligation to act in the best interests of their patients.	Comment noted. Although NICE acknowledges these concerns, under an exceptional directive from the Department of Health, the Appraisal Committee may consider making recommendations about the use of drugs outside the terms of their existing marketing authorisation. Such recommendations will only be made where there is compelling evidence of the drug's safety and effectiveness.
	Sandoz	Use of medications outside of their product licence should remain as exceptions within the NICE process. It may however be relevant in this review to reflect current clinical practice and to determine future best clinical practice.	Comment noted. Although NICE acknowledges these concerns, under an exceptional directive from the Department of Health the Appraisal Committee may consider making recommendations about the use of drugs outside the terms of their existing marketing authorisation. Such recommendations will only be made where there is

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			compelling evidence of the drug's safety and effectiveness.
	Should immunosuppressive treatment for episodes of acute rejection also be included in the appraisal? If so, which interventions and comparators should be considered for this?		
	Astellas Pharma	No comments	No action required.
	British Association For Paediatric Nephrology	Yes. Intervention = rituximab, plasma exchange (+/- Methylprednisolone); comparator = Methylprednisolone	Comment noted. The aim of the appraisal is to review and update (where necessary) the recommendations in technology appraisal guidance 99. Technology appraisal guidance 99 did not make recommendations for treatment of acute rejection. Accordingly, the forthcoming appraisal will not consider treatments for acute rejection. No action required.
	Sandoz	Treatment of acute rejection episodes should be included.	Comment noted. The aim of the appraisal is to review and update (where necessary) the recommendations in technology appraisal guidance 99. Technology appraisal guidance 99 did not make recommendations for

Section	Consultee/ Commentator	Comments	Action
			treatment of acute rejection. Accordingly, the forthcoming appraisal will not consider treatments for acute rejection. No action required.
	Have the most appropriate interventions and comparators used in immunosuppressive therapy for kidney transplantation in children and adolescents been included in the scope? Are the comparators listed routinely used in clinical practice?		
	Astellas Pharma	Yes.	Comment noted. No action required.
	British Association For Paediatric Nephrology	Please also consider the use of rituximab for ABO incompatible transplants.	The relevant comparators are therapies that are considered part of established NHS practice. Please see sections 2.2.4-2.2.6 and 6.2.1-6.2.4 of the NICE guide to the methods of technology appraisal 2013: http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9 In response to consultation, NICE did not receive consistent advice that rituximab is currently established practice in the NHS. Accordingly, rituximab

Section	Consultee/ Commentator	Comments	Action
			was not included as a comparator.
	Are belatacept, mycophenolate sodium, prolonged-release tacrolimus, sirolimus, and everolimus routinely used in clinical practice, despite not having a specific marketing authorisation for kidney transplantation in children and adolescents?		
	Astellas Pharma	There is use of (and evidence for the use of) Advagraf (prolonged release tacrolimus) in adolescent patients where a once daily regimen is favoured in order to promote adherence (Harden P et al, 2012). Adolescent patients present a particular problem with regards to adherence. This is outside the marketing authorisation for Advagraf.	Comment noted. The draft scope stated that, 'if evidence allows, adherence to treatment will be considered.' No action required. Comment noted. Under an exceptional directive from the Department of Health the Appraisal Committee may consider making recommendations about the use of drugs outside the terms of their existing marketing authorisation. Such recommendations will only be made where there is compelling evidence of the drug's safety and effectiveness. No action required.
	British Association For Paediatric	Yes, although these particular agents may not be used 1st line	Comment noted. No action required.

Section	Consultee/ Commentator	Comments	Action
	Nephrology		
	Is azathioprine routinely used in clinical practice as part of immunosuppressive regimens?		
	Astellas Pharma	Yes.	Comment noted. No action required.
	British Association For Paediatric Nephrology	Yes	Comment noted. No action required.
	Should any other induction therapies be considered as comparators for induction therapy?		
	Astellas Pharma	No comments.	No action required.
	British Association For Paediatric Nephrology	Yes - methylprednisolone	Comment noted. The list of comparators has been amended to include: 'Induction regimens without monoclonal or polyclonal antibodies, for example regimens that include methylprednisolone'
	Renal Association	However, it would be appropriate to include assessment of the induction agent Alemtuzumab-although it is currently not licensed in this area there are many studies in paediatric and young adult groups.	Comment noted. The relevant comparators are therapies that are considered part of established NHS practice. Please see sections 2.2.4-

Section	Consultee/ Commentator	Comments	Action
			2.2.6 and 6.2.1-6.2.4 of the NICE guide to the methods of technology appraisal 2013: http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9 In response to consultation, NICE did not receive consistent advice that alemtuzumab is currently part of established clinical practice in the NHS. Accordingly, alemtuzumab was not included as a comparator.
	Should the different tacrolimus formulations (immediate- and prolonged-release) be considered separately? Should the different brands of immediate-release tacrolimus be considered separately?		
	Astellas Pharma	Yes to both questions. See comments above regarding use of prolonged release tacrolimus in adolescents. MHRA indicated in 2012 that tacrolimus products should be prescribed and dispensed by brand name: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON155756	Comment noted. The list of interventions has been changed to include: • Immediate-release tacrolimus • Prolonged-release tacrolimus
	British Association For	Yes to both questions.	Comment noted. The list of interventions has been

Section	Consultee/ Commentator	Comments	Action
	Paediatric Nephrology		changed to list the tacrolimus formulations separately.
	Sandoz	Immediate release and prolonged release formulations of tacrolimus should be assessed separately as they are not equivalent in terms of dosing and drug levels. Advagraf is not licensed in children and adolescents under the age of 18. *[List of references supplied but not reproduced here.]* Tacrolimus should be prescribed by brand as per the recommendations of the MHRA.	Comment noted. The list of interventions has been changed to list the tacrolimus formulations separately. Comment noted. Under an exceptional directive from the Department of Health the Appraisal Committee may consider making recommendations about the use of drugs outside the terms of their existing marketing authorisation. Such recommendations will only be made where there is compelling evidence of the drug's safety and effectiveness. No action required. Comment noted. No action required.
	Should the different mycophenolate formulations be considered separately?		

Section	Consultee/ Commentator	Comments	Action
	Astellas Pharma	No comments.	No action required.
	British Association For Paediatric Nephrology	Yes.	Comment noted. The list of interventions has been changed to include: • Mycophenolate mofetil • Mycophenolate sodium
	Sandoz	The different mycophenolate formulations produce different clinical outcomes and should therefore be assessed separately.	Comment noted. The list of interventions has been changed to list the mycophenolate formulations separately.
	In clinical practice is an induction therapy always used? Or should the comparator of 'no induction therapy' be considered?		
	Astellas Pharma	No comments.	No action required.
	British Association For Paediatric Nephrology	Yes – many paediatric centres do not routinely use induction following the RCT - Grenda R et al. A prospective, randomized, multicenter trial of tacrolimus-based therapy with or without basiliximab in pediatric renal transplantation. American Journal of Transplantation, July 2006, vol./is. 6/7(1666-1672)	Comment noted. A comparator has been added to the scope: 'Regimens without monoclonal or polyclonal antibodies, for example regimens that include methylprednisolone'.
	Sandoz	A comparator of no induction therapy should be included	Comment noted. A comparator has been added to the scope: 'Regimens

Section	Consultee/ Commentator	Comments	Action
			without monoclonal or polyclonal antibodies, for example regimens that include methylprednisolone'.
	Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom the technologies are expected to be more clinically effective and cost effective or other groups that should be examined separately?		
	Astellas Pharma	Astellas believes the following subgroups should also be considered: • Those children and adolescents unable to swallow capsules • Those children and adolescents that are unable to adhere to treatment regimen – as above	Comment noted. The draft scope stated that, if evidence allows, adherence to treatment will be considered. As part of this consideration, the Appraisal Committee could examine treatments for children and adolescents who have difficulty swallowing capsules. If a manufacturer has evidence that a technology is especially effective or cost-effective in a subgroup, it is encouraged to include this evidence in its submission to NICE. No action required.
	British Association For Paediatric	Please also consider ABO and HLA incompatible transplants.	The draft scope stated that, if evidence allows, the following subgroup will be considered: 'level of immunological risk

Section	Consultee/ Commentator	Comments	Action
	Nephrology		(including human leukocyte antigen compatibility and blood group compatibility).' No action required.
	Does immunosuppressive treatment differ depending on donor type (cadaveric or living donor)? Should this be considered as a subgroup?		
	Astellas Pharma	No comments.	No action required.
	Sandoz	Where the evidence allows for comparison, donor influences on outcomes should be assessed.	NICE did not receive any other responses recommending that the appraisal should consider separately subgroups defined by donor type (cadaveric or living donor). Accordingly, this subgroup has not been added to the scope. If a manufacturer has evidence that a technology is especially effective or cost-effective in a subgroup, it is encouraged to include this evidence in its submission to NICE. No action required.
	Questions on equalities		
	Astellas Pharma	No comments.	No action required.

Section	Consultee/ Commentator	Comments	Action
	Questions on innovation		
	Astellas Pharma	If Modigraf is not used, administrators including healthcare professionals, carers or parents may open tacrolimus capsules in order to facilitate administration to children. This presents a health risk to administrators that doesn't exist for Modigraf administration. This benefit of Modigraf is not captured in the QALY calculation.	Comment noted. The manufacturer is invited to provide evidence regarding this benefit of the technology in its submission.
Additional comments on the draft scope	British Association For Paediatric Nephrology	Please also consider management strategies for delayed graft function	Comment noted. The aim of the appraisal is to review and update (where necessary) the recommendations in technology appraisal guidance 99. Technology appraisal guidance 99 did not make recommendations for management strategies for delayed graft function. Accordingly, the forthcoming appraisal will not consider management strategies for delayed graft function.
	Renal Association	The remit of this Re-scope Consultation falls mainly under the remit of the Paediatric Nephrologists and [redacted] is coordinating a response from the paediatric perspective. I am aware that the British Transplant society is also responding. Young adults 16y+ are transplanted in adult units or are transitioned to adult Units following transplantation. As such the Renal Association will	Comments noted. The technologies to be appraised are those: - that were included in technology appraisal guidance 99; or

Section	Consultee/ Commentator	Comments	Action
		briefly comment. The draft scope for the appraisal appears appropriate. However, it would be appropriate to include assessment of the induction agent Alemtuzumab-although it is currently not licensed in this area there are many studies in paediatric and young adult groups. The Matrix of organisations involved appears complete.	- that have obtained a relevant marketing authorisation in the UK since the publication of technology appraisal guidance 99; or - that have been referred to NICE by the Department for Health for appraisal. Alemtuzumab did not meet these conditions, so it has not been added to the list of interventions.

The following consultees/commentators indicated that they had no comments on the draft scope:

Department of Health, Novartis Pharmaceuticals, Peninsula Technology Assessment Group, Royal College of Nursing, Royal College of Paediatrics and Child Health, Teva.

NATIONAL INSTITUTE FOR HEALTH CARE EXCELLENCE

Multiple Technology Appraisal (MTA)

Immunosuppressive therapy for kidney transplantation in children and adolescents (review of technology appraisal guidance 99)

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
1.	Add ESPRIT	Astellas		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. ESPRIT has been added to the matrix of consultees and commentators under 'professional groups'.

2.	Remove Commissioning Support Appraisals Service	NICE Secretariat		Removed	This organisation's interests are not closely related to the appraisal topic and as per our inclusion criteria. Commissioning Support Appraisals Service has been removed from the matrix of consultees and commentators.
3.	Remove Chemidex Pharma	NICE Secretariat		Removed	This organisation's interests are not closely related to the appraisal topic and as per our inclusion criteria. Chemidex Pharma has been removed from the matrix of consultees and commentators.
4.	Remove National Clinical Guidelines Centre for Acute and Chronic Conditions	NICE Secretariat		Removed	This organisation is now part of the National Clinical Guidelines Centre.

5.	Add National Clinical Guideline Centre	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. National Clinical Guideline Centre has been added to the matrix of consultees and commentators under 'associated guideline groups'.
6.	Add Hospital Information Services (Jehovah's Witnesses)	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. Hospital Information Services (Jehovah's Witnesses) has been added to the matrix of consultees and commentators under 'patient groups'.