SPECIALISED COMMISSIONING - CLINICAL EVIDENCE EVALUATION CRITERIA FOR CLINICAL COMMISSIONING POLICY PROPOSITION
URN: 1742
TITLE: Allogeneic haematopoietic stem cell transplant (HSCT) for primary immunodeficiencies (PID) (all ages)

CRG: Allergy and Immunology
NPOC: Blood & infection
Date: 12/12/18

This policy is being considered for:	For routine commissioning	X	Not for routine commissioning	
Is the population described in the policy similar to that in the evidence reviewed, including subgroups?	The policy proposition requires some minor amendments so that it is clear that PID includes a range of disease severity. The proposition must state that many patients have a PID which is appropriately managed medically. The proposition must also state that HSCT is clinically inappropriate for many patients where medical management is a better option that HSCT and the significant mortality and risk of complications associated with it. Panel requested that the criteria relating to autoimmune disorders is amended to clarify that it is patients with a PID who, as a result develop autoimmune disease, who are eligible for treatment. The reason for this is to ensure that there is no possible misinterpretation that patients with autoimmune disease not clearly caused by PID would be eligible for HSCT.			
Is the intervention described in the policy similar to the intervention for which evidence is presented in the evidence review?	Yes.			
Are the comparators in the evidence reviewed plausible clinical alternatives within the NHS and are they suitable for informing policy development?	Panel recognised the limitations of the evidence base which consisted largely of uncontrolled studies. However, Panel took account of the relatively small population who would likely be eligible for this treatment and noted the very poor expected outcomes and high mortality for these patients with alternative treatments.			
Are the clinical benefits described in the evidence review likely to apply to the eligible population and/or subgroups in the policy?	The evidence was limited, although survival and mortality rates in the studies were described for subjects treated with HSCT. Panel noted that HSCT is a high risk intervention with a significant mortality and Panel reiterated the importance of patient selection in order to ensure only patients expected to receive an overall net benefit are selected for HSCT.			
Are the clinical harms described in the	See above.			

evidence review likely to apply to the eligible and /or ineligible population and/or subgroups in the policy?	
The Panel should provide advice on matters relating to the evidence base and policy development and prioritisation. Advice may cover: • Balance between benefits and harms • Quality and uncertainty in the evidence base • Challenges in the clinical interpretation and applicability of policy in clinical practice • Challenges in ensuring policy is applied appropriately • Likely changes in the pathway of care and therapeutic advances that may result in the need for policy review.	The policy proposition extends existing treatment to 'all ages' as there is existing policy regarding children. At the last presentation of the proposition at Panel, the evidence base identified in the evidence review almost exclusively included only children. The additional evidence presented now includes some evidence regarding use in adults. Although, the evidence presented is entirely made up of uncontrolled studies and there is very little reporting of changes in symptoms that would be important for patients. However, the evidence does demonstrate a likely improvement in survival for very carefully selected patients at high risk of death from PID. Some patients surviving HSCT and avoiding significant adverse effects (such as graft versus host disease) appear to achieve a very good outcome and are effectively cured. The Panel requested that the Policy Working Group (PWG) consider the following amendments to the proposition: • There is a description of the criteria of patients who would be eligible for this intervention. The criteria relating to autoimmune disease should emphasise that this is only where this is as a result of PID. Criteria 7 on page 19 should be clarified to reflect this. • Section 3 includes patients with 'Immune dysregulation' and Panel were concerned that this was a potentially broad and ill-defined group. The PWG should consider removing or making this much more specific. The proposition must not be interpreted as supporting the routine commissioning of HSCT for severe autoimmune disease. • The opening definition of Section 4 should also be amended to clarifying that PID has a range of severity and that this proposition concerns only patients with severe disease. This is a cohort of patients with autoimmune conditions. • The PWG may wish to consider whether the title should be changed to include 'severe'. • It would be helpful to state what proportion of total patient PID population are likely to be affected 'very severely' and likely to be eligible for the intervention.

	• There is no detail provided on how the estimated number of eligible patients has been arrived at. It would be helpful to have further information on how these have been calculated. Panel were informed the estimated eligible population in the proposition may have been based upon numbers on the waiting list / treated via existing urgent policy statements. • Remove markings on whether the criteria are based upon evidence or consensus. The first sentence in section 8 making reference to this should also be removed. • Section 8 should be amended to remove AND/OR between each criteria on the list. Instead, the criteria list should be prefaced with 'any of the following'. The 'Or' within eligibility criteria 6 may remain. • The CPAG Summary Report is very long and could be shorter and clearer. The CPAG summary report should be reviewed by the evidence review providers to be made more concise and to provide a summary of the evidence, its limitations and potential benefits and harms, This will assist CPAG to understand the overall conclusions which can be reached from the evidence, (which it is recognised is of limited quality) and ensure that prioritisation is as well informed as possible. Panel welcomed the Proposed Governance Arrangements. Panel suggested that the PoC and CRG should monitor outcome data at 2 years to ensure that these are satisfactory and to prompt review of the commissioning position if outcomes give cause for concern. The BMT CRG will review the BSBMT data and provide this data to regional commissioners so that they are aware of a particular issue relating to individual providers. The policy can then progress to stakeholder testing.		
Overall conclusion	This is a proposition for routine commissioning and	Should proceed for routine commissioning	X
		Should be reversed and proceed as not for routine commissioning	
		Should proceed for	

	This is a proposition for not routine commissioning and	not routine commissioning	
		Should be reconsidered by the PWG	

Overall conclusions of the panel
Report approved by:
David Black
Clinical Panel Co-Chair
21/12/18

Post meeting note:
[Input how actions requested by Clinical Panel have been addressed]