SPECIALISED COMMISSIONING - CLINICAL EVIDENCE EVALUATION CRITERIA FOR A PROPOSITION FOR A CLINICAL COMMISSIONING POLICY FOR ROUTINE COMMISSIONING

URN: A13X03
TITLE: Rituximab for Primary Sjorgens Syndrome (PSS)

CRG: Specialised rheumatology
NPOC: Internal medicine
Lead: Ursula Peaple

Date: 17/2/16

The panel were presented a policy proposal for routine commissioning

Question	**Conclusion of the panel**	**If there is a difference between the evidence review and the policy please give a commentary**
<u>The population</u> 1. Are the eligible and ineligible populations defined in the policy consistent with the evidence of effectiveness, and evidence of lack of effectiveness; and where evidence is not available for the populations considered in the evidence review?	The eligible population(s) defined in the policy is not the same or similar to the population(s) for which there is evidence of effectiveness that considered in the evidence review	The panel noted that many studies are relatively small case series. An RCT of 120 patients did not meet the primary outcome target (that is, the predetermined degree of improvement in fatigue at week 24). The panel noted that there was greater improvement at earlier time points but was concerned that these earlier measures were not the primary end points. Another RCT of 30 patients showed mixed results regarding improved saliva production. A recently completed and not yet published UK RCT of over 100 patients is understood not to have shown significant benefit. The panel noted that the studies included patients with a range of severity of PSS. This added to the difficulty of demonstrating effectiveness of rituximab in the those more severely

		affected as described in the eligibility criteria of the policy. The panel recognised the significant morbidity in this group of patients and the lack of treatment options. The panel noted that the population defined in the policy were severe cases (that is ESSDAI>=14) and that the evidence in this patient group is undeveloped. In addition, patients only received two doses of rituximab in most studies (doses differed but most commonly used was 1g given twice) whereas policy allows for subsequent doses for which there is very limited evidence.
<u>Population subgroups</u> 2. Are any population subgroups defined in the policy and if so do they match the subgroups considered by the evidence review?	There is a difference between the population subgroups defined in the policy and the populations for there is evidence in the evidence review	No other evidence related to a sub group. There is a sub population defined as those who cannot have cyclosporin who have severe systemic disease. This sub group is not defined in any of the evidence presented
<u>Outcomes - benefits</u> 3. Are the clinical benefits demonstrated in the evidence review consistent with the eligible population and/or subgroups presented in the policy?	The clinical benefits demonstrated in the evidence review do not support the eligible population and/or subgroups presented in the policy	Some benefit has been shown in some of the case series studies and variable but inconsistent benefit in the RCTs. It is unclear if rituximab is effective. The evidence does not support use in a particular patient sub group and the dosing schedules are also unclear and not supported by evidence of effectiveness.

		A number of the studies including the RCTs - did not show clinically significant improvement in primary endpoints.
<u>Outcomes – harms</u> 4. Are the clinical harms demonstrated in the evidence review reflected in the eligible and / or ineligible population and/or subgroups presented in the policy?	The clinical harms demonstrated in the evidence review are reflected in the eligible population and/or subgroups presented in the policy	The harms are well recognised.
<u>The intervention</u> 5. Is the intervention described in the policy the same or similar as the intervention for which evidence is presented in the evidence review?	The intervention described in the policy the same or similar as in the evidence review	The dosing regime is similar to that uses in some studies but not strongly evidence based. There is no evidence regarding repeated dosing.
<u>The comparator</u> 6. Is the comparator in the policy the same as that in the evidence review? 7. Are the comparators in the evidence review the most plausible comparators for patients in the English NHS and are they suitable for informing policy development.	The comparator in the policy is not the same as that in the evidence review. N/A	B: Comparator in the RCTs was placebo. Some patients took other drugs with rituximab. It could be argued that it should be compared against current active treatment options, although in the severely affected patients alternative treatments have usually been tried and been ineffective. Not Applicable
<u>Advice</u> The Panel should provide advice on matters relating to the evidence base and policy development and		There was insufficient evidence of effectiveness to support a routine commissioning proposition If further published evidence

prioritisation. Advice may cover: • Uncertainty in the evidence base • Challenges in the clinical interpretation and applicability of policy in clinical practice • Challenges in ensuring policy is applied appropriately • Issues with regard to value for money • Likely changes in the pathway of care and therapeutic advances that may result in the need for policy review.		comes forward the evidence base could be reviewed.

<u>Overall conclusions of the panel</u>

Proceed to CPAG as non-routine commissioning policy.

Report approved by:
David Black
Clinical panel Chair (panel B)
14/3/16