Stakeholder Response Form
CRG Product Testing

Please complete one response form per consultation document that you wish to provide comments on.

Date	**18/12/2018**
Respondent's Name	Dr Ruth Pepper
Respondent's Organisation	The Renal Association
Replying on behalf of organisation?	Yes
Document responding to:	Clinical Commissioning Policy Statement Rituximab for the treatment of refractory Focal Segmental Glomerulosclerosis in adults (1818)
Relevant CRG	Renal Services

Do you support the proposals within the policy statement?
NO

Do you have any further comments on the proposal?
YES

If Yes, please describe below, in no more than 500 words, any further comments on the proposed changes to the document as part of this initial 'sense check'.
FSGS is a leading cause of nephrotic syndrome in adults and a significant cause of end-stage renal failure (ESRF). A significant proportion of patients will have treatment resistant or frequently relapsing disease. However, FSGS is a heterogeneous disease, classified into primary (unknown) causes as well as numerous secondary causes. In children, steroid resistant nephrotic syndrome is increasingly recognized as a genetic disease with an increasing array of causative genetic mutations demonstrated to be associated with disease. A single-gene cause of steroid resistant nephrotic syndrome (SRNS) presenting before the age of 25 years has been demonstrated in 29.5% of patients (1). Basu B et al (2) is quoted in the commissioning document. This paper included patients with minimal change (13 patients) or FSGS (11 patients) aged 2-16 years. However, genetic testing was not performed in any of the patients, and with a diagnosis of FSGS at a young age, it is probable there may be a causative genetic mutation. Therefore perhaps unsurprisingly this study resulted in non-response to all immunosuppressive treatments including rituximab. Bagga A et al (3) included 3

patients with FSGS (2 with minimal change). All had a complete or partial response. The same authors proceeded to demonstrate in a much larger group of 33 patients with SRNS that Rituximab resulted in remission in 48.5% (4). This is a significant response rate considering this cohort had exhausted all other treatment options, yet still responded to rituximab rescue therapy.

This demonstrates 2 important points, which are missing from the commissioning document. Patient selection is clearly very important when deciding upon the use of rituximab. Secondary causes of FSGS need to be excluded in which immunosuppressive treatment would be futile. Those patients presenting at a young age with a possible genetic cause will be unlikely to respond to treatment, therefore it is questionable using this population and applying this to the adult population. Adult patients who are steroid dependent, or those patients dependent on CNIs to prevent relapses resulting in renal dysfunction, would benefit from rituximab therapy.

Additionally, in patients with FSGS, even a partial remission with a decrease in proteinuria is beneficial with respect to overall renal survival and delaying the onset of ESRF (5). Several small studies and case reports have shown the benefit of rituximab in patients with refractory FSGS resulting in either complete or partial remission in which other therapies have either shown a poor or non-sustained response (6-9). Also, rituximab rescue therapy has been used in renal transplant recurrence. Those patients not responding to conventional immunosuppression are highly likely to progress to ESRF.

Therefore we would like to strongly oppose the policy statement not recommending rituximab be available for refractory FSGS. With appropriate patient selection in the small number of resistant, refractory patients, rituximab will be one of the last remaining therapeutic options demonstrated to be effective in some patients, to prevent or delay the onset of ESRF, or complications of a persisting nephrotic state as well as the loss of a renal transplant in recurrent disease.

References

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Please declare any conflict of interests relating to this document or service area.

No conflict of interest