SPECIALISED COMMISSIONING – RESPONSE TO AMENDMENTS REQUESTED TO EVIDENCE REVIEW DURING ENGAGEMENT

URN	1818
POLICY TITLE	Rituximab for the treatment of refractory Focal Segmental Glomerulosclerosis in the native kidney in adults
CRG:	Renal Services
NPOC:	[redacted]
PUBLIC HEALTH LEAD:	[redacted]

Description of comments during consultation	Additional study identified on steroid resistant nephrotic syndrome. (1) Gulati et al. Clin J Am Soc Nephrol. 2010 Dec;5(12):2207-12) Commentators suggest this presents stronger evidence of effectiveness (2) Troyanov S, Wall CA, Miller JA, Scholey JW, Cattran DC; Toronto Glomerulonephritis Registry Group. Focal and segmental glomerulosclerosis: definition and relevance of a partial remission. J Am Soc Nephrol. 2005 Apr;16(4):1061-86. Additional evidence: Pescovitz MD, Book BK, Sidner RA. Resolution of recurrent focal segmental glomerulosclerosis proteinuria after rituximab treatment. New Engl J Med. 2006;354(18):1961-3. 7. Marasa M, Cravedi P, Ruggiero B, Ruggenenti P. Refractory focal segmental glomerulosclerosis in the adult: complete and sustained remissions of two episodes of nephrotic syndrome after a single dose of rituximab. BMJ Case Rep. 2014;2014.8. Ren H, Lin L, Shen P, et al. Rituximab treatment in adults with refractory minimal change disease or focal segmental glomerulosclerosis. Oncotarget. 2017;8(55):93438-43.9. Wee Leng G, Mustafar R, Kamaruzaman L, Mohd R, Cader RA, Wei Yen K, Kiew Bing P. Intravenous Rituximab in Severe Refractory Primary Focal Segmental Glomerulosclerosis. Acta Med Indones. 2018 Jul;50(3):237-243. Further studies suggested by respondents included studies on post-

	transplant patients, importantly a prospective controlled trial (Transplantation. 2018 Mar;102(3):e115-e120. doi: 10.1097/TP.0000000000002008.)
Action taken by Public Health lead	Reviewed papers. (1) Gulati et al is indeed a larger treatment cohort than the three quoted in the policy statement. It is a retrospective case series of 33 patients with steroid resistant disease 16/33 had FSGS. Principal outcome: remission rates at 6 months Outcomes were lower (31%) for patients with FSGS than in rest of the studied cohort (65%). However, the study design is still vulnerable to the bias and confounding identified among the papers used to formulate the policy statement. (2) Troyanov et el outlines the biological plausibility and potential mechanism of action rather than treatment effectiveness. Further single case reports (Pescovitz, Wee Leng, Marasa), and small case series (Ren). A review of the field (Kronbichler) appears to confirm (from abstract only) that the field is indeed comprised of retrospective uncontrolled studies. The prospective controlled study on post-transplant patients (Alasfar) provides the highest quality evidence, but does not identify benefits to patients. I discussed with clinical PWG members on the intent of the policy, the nature of the disease in native and post-transplant patients, and the relevance of the evidence-base from one group for informing commissioned treatments in the other group. I concluded that whilst the scope of the policy was appropriate, that the suggested studies in post-transplant patients were subject to the same sources of bias as those examining people with FSGS affecting native kidneys.
Outcome	Low grade evidence identified by stakeholders that does not materially affect the conclusions of the existing evidence reviews. It should be noted that NIHR have just funded a RCT (TURING Trial) to evaluate rituximab in Minimal Change Disease and FSGS.