MANAGEMENT IN CONFIDENCE

CLINICAL PRIORITIES ADVISORY GROUP
04 June 2019

Agenda Item No	03.1
National Programme	Internal Medicine
Clinical Reference Group	Renal Services
URN	1818

Title
Rituximab for the treatment of refractory Focal Segmental Glomerulosclerosis in the native kidney in adults

Actions Requested	1. Support the adoption of the policy statement
	2. Recommend its approval as an in-year service development

Proposition
This is a policy statement proposition recommending not for routine commissioning of this rituximab for refractory primary Focal Segmental Glomerulosclerosis (FSGS) in the native kidney in adults. The treatment is not currently available for this indication and therefore does not alter the NHS England commissioning position for adults. It is noted a new NIHR trial - “TURING” will fund a Randomised Control Trial to address the lack of evidence of rituximab in rare nephrotic syndromes including FSGS.

Clinical Panel recommendation
The Clinical Panel recommended that policy statement development progressed to confirm that the treatment was not commissioned.

The committee is asked to receive the following assurance:	
1.	The Head of Clinical Effectiveness confirms the proposal has completed the appropriate sequence of governance steps and includes an: Evidence Review and Clinical Panel Report.
2.	The Head of Acute Programme confirms the proposal is supported by a: Rapid Impact Assessment; Stakeholder Engagement Report; Equality Impact and Assessment Report; Clinical Policy Statement. The relevant National Programme of Care Board has approved these reports.

3.	The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.
4.	The Clinical Programmes Director (Specialised Commissioning) confirms that the service and operational impacts have been completed.

The following documents are included (others available on request):	
1.	Clinical Policy Statement Proposition
2.	Evidence Review comprising three supporting papers
3.	Clinical Panel Report
4.	Stakeholder Engagement Report
5.	Equality Impact and Assessment Report

No	*Metric*	*Summary from evidence review* *Stopping or minimising the symptoms and complications of FSGS is a key goal of treatment. Although there is some evidence for the effectiveness of rituximab it is very limited and mainly applies to children.*
1.	Survival	Not assessed.
2.	Progression free survival	Not assessed.
3.	Mobility	Not assessed.
4.	Self-care	Not assessed.
5.	Usual activities	Not assessed.
6.	Pain	Not assessed.
7.	Anxiety / Depression	Not assessed.
8.	Replacement of more toxic treatment	Not assessed.
9.	Dependency on care giver / supporting independence	Not assessed.
10.	Safety	Rituximab is a licensed treatment for autoimmune diseases such as rheumatoid arthritis and ANCA associated vasculitis, where it has an excellent safety profile. None of the studies reported significant side effects in patients.

11.	Delivery of intervention	Not applicable.

Other health outcome measures determined by the evidence review		
No	Metric	Summary from evidence review
1.	Remission from FSGS	Basu B et al (2015): This study was a retrospective analysis of 24 children with refractory idiopathic steroid resistant nephrotic syndrome (SRNS). Follow up was 24 months. Children were treated with an initial course of 2-4 infusions of rituximab and at 3 months follow up received a second course of the drug along with mycophenolate mofetil (MMF). 40% of the children (11/24) had FSGS. After the initial course of treatment 21% of children (5/24) had complete remission. Only one of these children had FSGS. 4/5 of these children relapsed at a median interval of 53 days (range 46-72 days). 15 children started MMF at 3 months. By 24 months 33% of children sustained a complete remission after MMF maintenance therapy compared to rituximab therapy alone ($p<0.001$). The study had very small numbers of patients with even smaller numbers in each sub-group which may cast doubt on the applicability of the statistical analysis. There was no comparator group to assess effectiveness compared to best practice. A retrospective design increases the risk of selection bias and recall bias and may not adequately control for potential confounding factors. Patients were given varying doses and regimen of rituximab and had differing levels of exposure to previous therapies. The study was conducted in children which limits its applicability to adults. Bagga A et al (2007): This case series describes five children with SRNS, two of whom had FSGS. All children had previously received multiple different medications (including calcineurin inhibitors) for varying periods with episodes of partial or complete remission. Participants received a rituximab infusion and continued on calcineurin inhibitors, prednisolone or both. At six months complete remission was maintained in three patients with tapering of steroids and calcineurin inhibitors. It is not clear from the study whether the patients with sustained remission were those with FSGS. This is a small descriptive study but the population being studied had differing baseline characteristics, exposure to previous medications and duration of disease. The study was conducted in children which limits its applicability to adults.

		Varwani (2017): This case report was of a 76 year old male with steroid resistant FSGS who was treated with rituximab and remained in remission at 6 months. A case study is useful for generating a hypothesis and this is an adult patient but the study design and outcome has limited value in proving efficacy.

Considerations from review by Rare Disease Advisory Group
Not applicable.

Pharmaceutical considerations
This would have been an off label use of rituximab which is excluded from tariff. Rituximab is administered as an intravenous infusion.

Considerations from review by National Programme of Care
The proposal received the full support of the Internal Medicine National Programme of Care on 25 April 2019. It was noted the policy statement is to provide clarity on the not for routine commissioning position to support clinicians and commissioners on an interim basis.