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

URN	1853
POLICY TITLE	Rituximab for refractory Systemic Lupus Erythematosus (SLE) in adults and post-pubescent children
CRG:	Specialised Rheumatology
NPOC:	Internal Medicine
Date	20/11/2019

Description of comments during consultation	Extract from consultation: 'My group at University College Hospital probably has the world's largest single centre experience of using rituximab in SLE and we are about to publish our latest update review (of 165 patients given rituximab so far and; we present data on 144). The paper is in press and I would be delighted to send you a pre-print. In essence though, 85.5 % responded favourable to rituximab (median BILAG scores dropping from 17 at baseline (IQR 12-23) to 5 (IQR 2- 8) in those 124 patients in whom it worked. In the 20 patients for whom it did not work, the median score went from 8.5(IQR 6-12.7) to 11.5 (IQR 7- 13.7). My colleagues and I also reported recently on a differential clinical response in dermatological disease depending upon the precise type of skin involvement (Costa RQ et al JAMA (Dermatology) doi.10.1001/jamadermatol.2018.3793). Prof Lightstone's group and my own have also reported notable benefit at the time of diagnosis and over a 6 year follow up we reported a huge reduction in the use of concomitant steroids with all their attendant complications and costs! (see gracia-Tello et al Lupus Sci Med 2017: 4 (1) :e000182 (Also interesting to note that a fully humanised version of rituximab recently met its end int in a phase trial of lupus nephritis)' **The consultation comments above relate to and advocate the early use of Rituximab in moderate/severe SLE as part of a beta cell depletion treatment (BCDT) strategy to avoid the usual initial treatment strategy of glucocorticoids, hydroxychloroquine and immunosuppressive; e.g. Azathioprine, Mycophenolate Mofetil or cyclophosphamide as steroid sparing agent in order to avoid/minimise steroid related harm, morbidity and mortality.**

Action taken by Public Health lead	**I have reviewed the reference attached** (Gracia-Tello B, Ezeonyeji A, Isenberg D. Lupus Science & Medicine 2017;4:e000182. doi:10.1136/lupus-2016-000182). Essentially this is a small non-randomised control study of 16 newly diagnosed patients who were given an upfront treatment regimen comprising Rituximab and Cyclophosphamide. Patient outcomes during follow up (1- average of 4.5 years) were then compared with historical controls receiving conventional steroid and immunosuppressive treatment. For each active patient 3 matched controls were identified. Significant reductions compared to baseline were achieved in both groups in serological disease markers - ESR, double stranded DNA, CD19+ beta lymphocytes but not in immunoglobulin levels and a significant higher rise in C3 complement levels in the BCDT group. The BCDT group had non-significantly fewer flares/year. No significant differences between groups mean scores were seen in the SLICC-ACR scale. .However, at 5 years of follow -up the BCDT group had accumulated only one third of the total steroid dose of the conventional treatment group, a difference that was statistically significant especially as the active treatment group had higher inflammatory activity at the outset. Comments: It is difficult to draw conclusions other than hypothesis generation from such a small study with heterogenous patients with some BCDT patients having received up-front steroids and also differences in Rituximab treatment regimens and in conservative maintenance treatment. This study population i.e. newly diagnosed patient group is different from that of the current policy proposition and the positioning of Rituximab is also different within the treatment algorithm.
Outcome	**<u>Low grade evidence identified by stakeholders that does not materially affect the conclusions of the existing evidence reviews</u>**