South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference	**145**
Intervention:	**Rituximab intravenous injection for the treatment of refractory autoimmune hepatitis in adults** (Rituximab is an anti-lymphocyte monoclonal antibody)
Date of Decision	**April 2023**
Date of Issue:	**June 2023 (time limited approval for 12 months)**
Recommendation:	**RED – suitable for prescribing, supply and administration by hospital only**
Further Information	• Refractory autoimmune hepatitis (AIH) is a chronic inflammatory disease which if untreated can lead to cirrhosis and liver failure. Rituximab intravenous injection is accepted for use in South East London as a **third line add on treatment** for refactory cases of AIH where: - **First line treatment** with steroids (prednisolone or budesonide) plus azathioprine are ineffective or contraindicated **OR** - **Second line treatment** with steroids plus mycophenolate, ciclosporin or tacrolimus are ineffective or contraindicated • Rituximab is recommended at a dose of 1g for 2 doses, given on day 1 and day 15. • A second 2 dose course of rituximab may be provided after a minimum of 6 months in cases where a reduction in baseline medication has been successful and the patient may benefit from further treatment to maintain response. • Rituximab is **not licensed** for use in this indication (off-label use). Informed consent should be gained from the patient before treatment is initiated. • This recommendation only supports use of the best value rituximab product for AIH, taking into account any locally negotiated prices. • This approval is **time limited to 12 months,** to enable experience of use with rixuximab in AIH. A report summarising outcomes with rixuximab over this period will be presented back to the committee after 12 months. This report will be **coordinated across all Trusts in SEL by the original formulary applicant** and will include: - The total number of patients initiated on rituximab across SEL for the management of AIH - Whether the use of rituximab is in line with this recommendation and the rationale for any deviation - The proportion of patients requiring a second 2 dose course of rituximab - Phased reporting over time on patient related outcomes, including: (i) Biochemical response to treatment and adverse effects after 1 year of treatment (ii) Steroid reduction rates & an assessment of relapse rates after 2 years of treatment (iii) Reduction in the development of longer term outcomes such as cirrhosis, liver failure and progression to liver transplantation, and other steroid related side effects. At time of writing, this is expected to be from year 5 onwards.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• It is estimated 15 patients will be eligible for treatment with rituximab in this setting per annum. Aproximately 80% of these patients will be from SEL (12 patients) • Treatment is based on one 500mg rituximab vial of best value rituximab preparation (biosimilar), therefore a 2 dose course of 1g is £628.64. • Asssuming approximately 12 patients overall for SEL are treated annually with rituximab in this setting, and if 50% (6 patients) require a repeat course at 6 months this equates to ~ £11,300 (or £595 per 100,000 population).

	• The costs of using rituximab could potentially be offset by a reduction in liver transplantation and associated costs in the longer term.
Usage Monitoring & Impact Assessment	**Acute Trusts:** • Monitor and audit usage and outcomes from use of rituximab in this setting as outlined in the "For information" section and report back the Committee in 12 months (data to be collated and presented no later than **June 2024**)
	SEL Borough Medicines Teams: • Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care
Evidence reviewed	**References (from evidence review)** 1. Gleeson D, Heneghan M. British Society of Gastroenterology (BSG) guidelines for the management of autoimmune hepatitis. Gut 2011 60 p1611-1629. 2. EASL Clinical Practice Guidelines: Autoimmune hepatitis. Journal of Hepatology 2015 63 p971-1004. 3. Mack C, Adams D, Assis D et al. Diagnosis and Management of Autoimmune Hepatitis in Adults and Children: 2019 Practice Guidance and Guidelines From the American Association for the Study of Liver Diseases. Hepatology, 2020 VOL . 72, NO. 2, p671-722. 4. Lohse A, Sebode M, Jørgensen M et al. Second-line and third-line therapy for autoimmune hepatitis: A position statement from the European Reference Network on Hepatological Diseases and the International Autoimmune Hepatitis Group. Journal of Hepatology 2020 vol. 73 j 1496–1506. 5. Burak K, Swain M, Santodomino-Garzon T et al. Rituximab for the treatment of patients with autoimmune hepatitis who are refractory or intolerant to standard therapy. Canadian Journal of Gastroenterology 2013 27 (5) p273-280. 6. Than N, Hodson J, Schmidt-Martin D et al. Efficacy of rituximab in difficult to manage autoimmune hepatitis: results from the International Autoimmune Hepatitis Group. JEHP Reports 2019 1 p437-444. 7. Mabthera, Summary of Product Characteristics. Available here [Accessed 27 Jan 2023] 8. Gautam N, Than N, Nizamuddin M et al. Use of rituximab in resistant autoimmune hepatitis – Birmingham Experience. Gut 2014 63 (Suppl 1)A1-A288 pA93.

NOTES:

a) SEL IMOC recommendations and minutes are available publicly via the website.

b) This SEL IMOC recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.

c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS**