I.8	Rituximab – Burkitt lymphoma – EMLc
Draft recommendation	☒ Recommended ☐ Not recommended **Justification:** The application is a request to extend the indications listed on the current WHO EMLc 2021 for Rituximab by mature aggressive B-cell lymphoma/leukemia (Burkitt lymphoma/leukemia). The current evidence supports the use of Rituximab for BL[1] with good prognosis and outcomes
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable **Comments:** Non-Hodgkin lymphoma (NHL) is the fourth most common type of cancer in children and adolescents with an incidence of about 0.7 – 1.5 per 100,000 per year in Europe. It has been reported that over 80% of paediatric cancers globally occur in children who live in low and middle income countries (LMICs); it is estimated that 90% of children diagnosed with NHL live in LMIC.[2] Burkitt Lymphoma (BL) is the most frequent non-Hodgkin lymphoma (NHL) in children and accounts for 50%-60% of childhood NHL. It is endemic in the area known as the Burkitt belt, where it represents > 50% of childhood cancers in sub-Saharan Africa

[1] Zhen Z, Zhu J, Wang J, Lu S, Sun F, Huang J, Sun X. Rituximab is highly effective in children and adolescents with Burkitt lymphoma in Risk Groups R2 to R4. Pediatr Hematol Oncol. 2020 Sep;37(6):489-499. doi: 10.1080/08880018.2020.1759741. Epub 2020 May 4. PMID: 32364412.

[2] Gross TG, Biondi A. Paediatric non-Hodgkin lymphoma in low and middle income countries. Br J Haematol. 2016 May;173(4):651-4. doi: 10.1111/bjh.14030. Epub 2016 Apr 20. PMID: 27098084; PMCID: PMC4862913

Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable **Comments:** The following studies support the use of rituximab in BL: • Zhen Z, Zhu J, Wang J, Lu S, Sun F, Huang J, Sun X. Rituximab is highly effective in children and adolescents with Burkitt lymphoma in Risk Groups R2 to R4. Pediatr Hematol Oncol. 2020 Sep;37(6):489-499. doi: 10.1080/08880018.2020.1759741. Epub 2020 May 4. PMID: 32364412. • Pfreundschuh, M., et al., CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MInT) Group. Lancet Oncol, 2006. 7(5): p. 379-91. • Meinhardt, A., et al., Phase II window study on rituximab in newly diagnosed pediatric mature B-cell non-Hodgkin's lymphoma and Burkitt leukemia. J Clin Oncol, 2010. 28(19): p. 3115-21. • Minard-Colin, V., et al., Rituximab for High-Risk, Mature B-Cell Non-Hodgkin's Lymphoma in Children. N Engl J Med, 2020. 382(23): p. 2207-2219. • Goldman, S., et al., Rituximab and FAB/LMB 96 chemotherapy in children with Stage III/IV B-cell non-Hodgkin lymphoma: a Children's Oncology Group report. Leukemia, 2013. 27(5): p. 1174-7. In addition, two treatment protocols are currently open in Europe including Rituximab in the treatment of patients with Burkitt Lymphoma: The LBL 2018 trial (NCT04043494) and the B-NHL 2013 (NCT03206671).
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable **Comments:** This medicine is already included in the EML and EMLc for other indications.
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable **Comments:** Treatment with Rituximab comes along with adverse events, including anaphylactic reactions or hypogammaglobulinaemia, which bears the risk of infections and fever episodes and so requires close monitoring

Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable **Comments:** Diagnostic capabilities are required as are skills in identifying the condition and managing side effects and toxicities.
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☐ Yes ☒ No ☐ Not applicable **Comments**: Rituximab has been on the market for a while and biosimilars are available
Are there any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable **Comments**: This medicine is already included in the EML and EMLc for other indications, and is registered with MRAs globally.
Is the proposed medicine recommended for use in a current WHO guideline? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable **Comments:** Rituximab is already included in the EML and EMLc for other indications: Follicular lymphoma; Chronic lymphocytic leukaemia or small lymphocytic lymphoma; Diffuse large B-cell lymphomas.