I.8	Rituximab – Burkitt lymphoma – EMLc
Draft recommendation	☒ Recommended ☐ Not recommended Justification: I support the inclusion of Rituximab and quality assured biosimilars on the EMLc for the treatment of patients with Mature B-cell lymphoma/ leukemia (Burkitt Lymphoma/Burkitt Leukemia). I acknowledge the high cost of Rituximab but noted that these costs are dropping with the approval of several biosimilars, and also noted the potential for cost-savings of using less Rituximab doses (BFM study ongoing) without significantly compromising benefit. I noted that treatment with Rituximab plus chemotherapy was associated with high response rates and significant improvements in event-free and overall survival compared to chemotherapy alone, and has a slightly more toxic profile.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable Comments: Non-Hodgkin lymphomas(NHL), which have an annual incidence of 0.7 to 1.5 per 100,000 children and adolescents in Europe, are the fourth most prevalent group of malignancies. Within the NHLs, three main subtypes can be distinguished: Mature aggressive B-cell lymphoma (58%), lymphoblastic lymphoma (LBL) (21%), and anaplastic large cell lymphoma (ALCL) (13%). Burkitt lymphoma/leukaemia is the most prevalent subtype of mature aggressive B-celll lymphomas, accounting for 80% of cases; other, less common subtypes include diffuse large B cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMLBCL).
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: Rituximab added to standard LMB chemotherapy markedly prolonged event-free survival and overall survival among children and adolescents with high-grade, high-risk, mature B-cell non-Hodgkin's lymphoma. Event-free survival at 3 years was 93.9% (95% confidence interval [CI], 89.1 to 96.7) in the rituximab–chemotherapy group and 82.3% (95% CI, 75.7 to 87.5) in the chemotherapy group (hazard ratio for primary refractory disease or first occurrence of progression, relapse after response, death from any cause, or second cancer, 0.32; 95% CI, 0.15 to 0.66; one-sided P = 0.00096, which reached the significance level required for this analysis).

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: Rituximab added to standard LMB chemotherapy was associated with a higher incidence of hypogammaglobulinemia and, potentially, more episodes of infection. The incidence of acute adverse events of grade 4 or higher was 33.3% in the rituximab–chemotherapy group and 24.2% in the chemotherapy group (P = 0.07); events were related mainly to febrile neutropenia and infection.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
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: Rituximab is already in the EML for other indications (Follicular lymphoma, Chronic lymphocytic leukaemia or small lymphocytic lymphoma, Diffuse large B-cell lymphomas).
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☐ Yes ☒ No ☐ Not applicable Comments: Rituximab is already in the EML for other indications (Follicular lymphoma, Chronic lymphocytic leukaemia or small lymphocytic lymphoma, Diffuse large B-cell lymphomas). On 25 May 2020, the World Health Organization prequalified its first rituximab biosimilar medicine in an attempt to make this expensive, life-saving treatment more affordable and available globally. WHO has invited manufacturers to submit rituximab dossiers for prequalification to facilitate access to biotherapeutic products, including similar biotherapeutic products (SBPs), at affordable prices. Like generic medicines, biosimilars can be much less expensive versions of innovator biotherapeutics while keeping the same quality, safety and efficacy. They are usually manufactured by other companies once the patent on the original product has expired.

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: Rituximab is already in the EML for other indications (Follicular lymphoma, Chronic lymphocytic leukaemia or small lymphocytic lymphoma, Diffuse large B-cell lymphomas).
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: