1.9	Cancer medicines for children – low-grade glioma
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments:
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	Medicines proposed are Carboplatin, Cisplatin, Cyclophosphamide, Vinblastine, Vincristine All the above 5 medicines are already listed in EMLc under 8.2.1 (cytotoxic medicines) for different indications 1. Carboplatin (all vials listed in the application are included in EMLc) 2. Cisplatin: 50 mg/50 mL; 100 mg/100 mL are listed (Application lists lower volumes as well like 10 mg/10 mL and 25 mg/25mL) 3. Cyclophospamide: Only 500 mg powder for injection is listed in addition to tablets, (Application lists other strengths as well, like 200, 750, 1000 and 2000) 4. Vincristine – EMLc has 1 mg/mL, 1 and 5 mL vials, Application: 1 mg/mL and 2 mg/mL 5. Vinblastine – No difference 1 mg/mL, 10 mg vials The question here is whether LGG can be added as an indication for all these 5 medicines in addition to the given indications
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included Application is based on SIOP-LGG-2004 trial and the work undertaken by SIOP to develop a common list of anticancer medicines that are essential to treat children and adolescents with cancer in Europe I was not able to find any other studies
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes ☐ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). The overall survival (OS) of the whole cohort was 0.95 (±0.02) at 5 years but the 5-year event-free survival (EFS) was 0.40 (±0.05) (15). For those 39 patients treated with chemotherapy, either directly after surgery (12/39) or in case of progression or relapse (27/39), the picture is very similar: 5-year OS of 0.89 ±0.05 and 5-year PFS of 0.42 ±0.08. Considering the rarity of the tumour, its varying natural history and ethical complexity in conducting rigorous clinical trials in children with cancer, I accept the data from 39 patients

	Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? NA – This is for children
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: But 1. All five medicines have been uses for a long time and their safety profile is well know 2. All five medicines are already listed in EMLc, the application is to add the LGG as another indication 3. Irrespective of indications, the safety profile will be the same
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments See my comments above
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Favourable considering multiple points though efficacy data is not very valid and not from clinical trials of high methodological quality 1. Rarity of the tumour 2. Difficulty in conducting clinical trials for paediatric oncology 3. Only a proportion will need chemotherapy 4. Known of adverse effects –Monitoring and management possible 5. All 5 medicines are already listed in EMLc
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Evidence for LGG is low, but see my earlier comments
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: As for any cancer therapy

Are you aware of 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: All these five medicines are considered as "standard" anti-cancer medicines and had been in the market for a long time Already listed in WHO Model EMLc Listed in many national EMLs as well
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☒ No ☐ Not applicable Comments: No WHO guideline approved by the Guideline Review Committee is available for LGG
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	All these five medicines are considered as "standard" anti-cancer medicines and had been in the market for a long time Already listed in WHO Model EMLc Listed in many national EMLs as well
Any additional comments	
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	RECOMMEND TO ADD LGG AS AN INDICATION FOR ALL FIVE MEDICINES WHICH ARE ALREADY LISTED IN COMPLEMENTARY LIST OF EMLc REASONS 1. All 5 medicines are already listed in EMLc 2. Application is to add LGG as an additional indication for these 5 medicines 3. All five are "standard" anti-cancer medicines and in the market for a long time 4. Oncologists are familiar with the optimal use of these medicines 5. Not adding LGG as an indication for these medicines might compromise chemotherapy of LGG for deserving children 6. It might not be possible to generate high quality data than the available data
References (if required)	