A.23	Osimertinib – EGFR+ non-small cell lung cancer
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Lung cancer is a global lead for cancers globally, with about 200,000+ new lung cases in US in 2017. Evidence suggests that 80% reported cancers are nonsmall cell lung cancers. There already exists drugs on the EML lists for Lung cancers.
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.	Osimertinib is a new drug (approved 2018) being proposed for treatment of NSCLC although other EGFR-TK1 drugs (first and second generation) have been used in the past. None of these are on the model list. The existing body of evidence suggests EGFR-TK1 are associated with longer survival rates and lower toxicity compared to other drugs in the market on this condition. Osimertinib is a third generation EGFR-TK1 taken orally and superior inhibitory effect on the T790M mutation
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: I found a number of reviews on the topic which were not included. Existing reviews however are not very strong and I think more could be (needs to be) done in this area. Reviews of interest are below. Liu 2020, Erickson 2020. I also think we need to GRADE the existing evidence.
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). 1. Efficacy: synthesized evidence suggests that in terms of overall survival, the patients treating with osimertinib favours a higher survival rate compared with other treatments (HR 0.56, 95% CI 0.44–0.71, P<.001). Similarly, osimertinib increased the progression free survival in comparison with other treatments (HR 0.38, 95% CI 0.33–0.44, P<.001). (Liu 2020) 2. Safety: Osimertinib does not seem to have more adverse effects compared to other agents for this indication. Adverse effects include pneumonitis, prolonged QTc interval, or decrease in cardiac contractility. 3. Cost: Osimertinib is considered expensive (5000 GBP per pack).

	Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Not completely, most available studies have been conducted in high income countries.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: the application did not place as much importance in term of review of existing literature on safety as we see in efficacy and cost.
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments: the cardiac side effects require monitoring
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Favourable: Metastatic NSCLC is life threatening and will lead to serious events if untreated. Based on best available evidence Osimertinib performs better than other agents for this indication with less side effects. Because osimertinib demonstrated an improvement over currently available therapies with a risk profile acceptable compared with the clinical benefit offered I will vote favourably however there is need for more rigorous evaluation of the existing evidence.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Moderate: more rigorous review of existing evidence for efficacy, safety, and cost should be done. These should be more representative of geographical and economic groups.
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: The need for advanced laboratory testing before treatment will also increase cost and reduce access to this treatment. There is also need to monitor heart function while treating patients.
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:

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:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The agent is expensive. Inclusion in EML will require government subsidies for access to many patients.
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.	I have doubts about the quality of existing review of evidence and will recommend a rigorous synthesis of evidence before inclusion. In addition due to high cost and associated health technologies needed to treat with this agent, poorer groups will not be able to use this medication.
References (if required)	1. Odogwu, Lauretta, et al. "FDA benefit-risk assessment of osimertinib for the treatment of metastatic non-small cell lung cancer harboring epidermal growth factor receptor T790M mutation." *The oncologist* 23.3 (2018): 353. 2. Erickson, Anders W., Priscilla K. Brastianos, and Sunit Das. "Assessment of effectiveness and safety of osimertinib for patients with intracranial metastatic disease: a systematic review and meta-analysis." *JAMA network open* 3.3 (2020): e201617-e201617. 3. Liu, Jing, et al. "The efficacy and safety of osimertinib in treating nonsmall cell lung cancer: A PRISMA-compliant systematic review and meta-analysis." *Medicine* 99.34 (2020). 4. Piper-Vallillo, Andrew J., Lecia V. Sequist, and Zofia Piotrowska. "Emerging Treatment paradigms for egfr-mutant lung cancers progressing on osimertinib: a review." *J. Clin. Oncol* (2020).