R.2	Proposal to amend square box listings in the EML and EMLc
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.	Not applicable. The 'square box' symbol has been used in the Model Lists since 1983 to indicate that the listed medicine is representative of therapeutically equivalent alternatives, any of which would be suitable for selection at country level for inclusion on national Essential Medicines Lists. The 2019 Model Lists include 108 entries (involving 93 unique medicines or fixed-dose combinations). There is considerable heterogeneity in the way these listings are presented – some name the specific alternatives, others do not, and others refer to acceptable alternatives, without having a square box listing. Amendments fall into the following groups: • Group 1: Listed medicines without a square box but with an asterisk denoting accepted alternatives – proposed to be converted to qualified square box listings. • Group 2: Listed medicines without a square box but with an asterisk denoting accepted alternatives – independent listings are proposed for the alternatives. • Group 3: Unrestricted square box listings where accepted alternatives are described in the Technical Report of the meeting where the listing was recommended – proposed to be converted to qualified square box listings. • Group 4: Unrestricted square box listings where the Secretariat proposes specific alternatives for qualified square box listings. • Group 5: Unrestricted square box listing where alternatives can be defined by pharmacological class at the ATC4 level. • Group 6: Unrestricted square box listing where the Secretariat proposes removal of the square box due to the absence of suitable alternatives. • Group 7: Unrestricted square box listings proposed for review of suitable alternatives • Group 8: Qualified square box listings for which no amendments are proposed.
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:

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). Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)?
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☐ No ☒ Not applicable Comments: The heterogeneity of the uses of the square box symbol (SqB) in the EML to indicate that therapeutic equivalents could be selected at the national level was highlighted in a recent article. The application presents an analysis that was conducted in order to characterize the extent of that heterogeneity and proposes a change in the uses and nomenclature of the square box, with the focus on the new e-EML and its expected added value and performance.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☐ No ☒ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	The standardization of classification would reduce confusion.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	Not applicable.
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:
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: These medicines are already denoted with an * or a square box in the current WHO EML and EMLc
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Not applicable
Any additional comments	Simplifying categorization assist national selection committees with decision making and finding cost effective or cheaper alternatives. The case set out in attachments 1 and 2 are compelling and call for the need to have more clarity and consistency in the designation and use of the square box symbol.
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.	The reviewer, based on the analyses conducted in attachments 1 and 2, recommends that the proposal by the secretariat be accepted as follows: • ***Group 1:*** Listings without square box but with asterix (*) denoting accepted alternatives - propose convert these to qualified square box listings • ***Group 2:*** Listings without square box but with asterix (*) denoting accepted alternatives - propose add independent listings for accepted alternatives • ***Group3:*** Unrestricted square box listings where accepted alternatives are described in TRS recommendations - propose convert to qualified square box listings • ***Group 4:*** Unrestricted square box listings where a qualified square box listing for specific limited alternatives is proposed • ***Group 5:*** Unrestricted square box listings where qualified square box listings with alternatives defined by ATC4 are proposed • ***Group 6:*** Unrestricted square box listings where removal of the square box is proposed • ***Group 7:*** Unrestricted square box listings proposed for a review of suitable alternatives at future EML and EML reviews • ***Group 8:*** Qualified square box listing - no changes proposed
References (if required)	