INFORMATION FOR APPLICANTS
2021 WHO Expert Committee on the Selection and Use of Essential Medicines

The 23rd meeting of the WHO Expert Committee on the Selection and Use of Essential Medicines to revise and update the WHO Model List of Essential Medicines (EML) and Model List of Essential Medicines for Children (EMLc), will take place at WHO Headquarters, Geneva, Switzerland on 19 – 23 April 2021. The application period for the Expert Committee meeting is now open.

Applications for inclusion of new medicines, and changes to or deletion of currently listed medicines in the Model Lists should be emailed to the WHO Essential Medicines List Secretariat at emlsecretariat@who.int in both PDF and Word formats **by 30 November 2020**. The application period is intended to allow applicants to interact and engage with the Secretariat to ensure applications adequately address the critical elements for selection: public health relevance, clinical efficacy and safety of the proposed medicine. The full requirements for information to be included in an application are described below.

Please note that the Secretariat may not accept an application if it does not meet necessary requirements for content and quality.

All applications will be published on the WHO Department of Essential Medicines and Health Products webpage for public comment and review.

Please direct any enquiries to:
The Secretary

Expert Committee on the Selection and Use of Essential Medicines
Essential Medicines Team
Medicines Selection, IP and Affordability (MIA)
Department of Health Products Policy and Standards (HPS)
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Information to be included in an application for inclusion, change or deletion of a medicine on the WHO Model List of Essential Medicines (EML) and Model List of Essential Medicines for Children (EMLc)

General items

1. Summary statement of the proposal for inclusion, change or deletion.
For inclusion of new medicines or changes to the listing of existing medicines: briefly describe the proposal in terms of clinical indication(s), target population and role in therapy for the requested medicine (1-2 paragraphs).

NOTE: *Where a medicine is relevant for the treatment of children, the application must contain a proposal to add the medicine to the EMLc and include available paediatric data.*

For deletion of existing listed medicines, strengths and/or formulations: briefly describe the proposal, providing clear rationale and justification for the proposed deletion. Identify alternative treatments available on the Model Lists and any foreseeable consequences of the deletion.

The summary statement should also specify whether listing/deletion is being sought for the EML and/or EMLc, whether listing is sought on the core or complementary list.

The summary statement should also specify whether listing/delisting is intended for the core or complementary list. The core list presents a list of minimum medicine needs for a basic healthcare system, listing the most efficacious, safe and cost–effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment.

The complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. Medicines may also be listed as complementary on the basis of consistent higher costs or less attractive cost-effectiveness in a variety of settings.

2. Relevant WHO technical department and focal point (if applicable).

Applicants are encouraged to engage with and seek support from the relevant WHO technical department as part of the application process.

Applications received that have not been submitted by or in collaboration with WHO technical departments will be forwarded to the relevant department(s) for review and comment.

3. Name of organization(s) consulted and/or supporting the application.

Specify if other organization(s) have been consulted in relation to the application and/or support the application. Please specify the affiliation of the applicant with the organization(s).

4. International Nonproprietary Name (INN) and Anatomical Therapeutic Chemical (ATC) code of the medicine.

The medicine(s) must be described by its International Nonproprietary Name (INN). INNs facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognised. A searchable database of INNs is available at: https://mednet-communities.net/inn/ (registration required).

Include the ATC code for the medicine for the relevant indication. The ATC system classifies medicines according to the anatomical organ or system upon which they act and by therapeutic, pharmacological and chemical subgroups. A single medicine may have more than one ATC code, depending on the indications for use. A searchable version of the complete ATC index is available at: http://www.whocc.no/atc_ddd_index/.

5. Dose forms(s) and strength(s) proposed for inclusion; including adult and age-appropriate paediatric dose forms/strengths (if appropriate).

The application must identify the specific dose forms(s) and strength(s) of the medicine for which inclusion on the Model Lists is sought.

For listing of medicines on the EMLc, applications must address the availability of suitable, age-appropriate dose forms and strengths for administration to infants and children.

Details of the current market availability of the proposed formulation(s) and strength(s) must be included.

6. Whether listing is requested as an individual medicine or as representative of a pharmacological class.

The application must specify if the request for inclusion is for an individual medicine, or a medicine with a square box symbol, representing a pharmacological class.

A square box symbol (□) is used to indicate that there are a number of agents within a pharmacological class with therapeutic equivalence. The listed medicine should be the example of the class for which there is the best evidence for effectiveness and safety. Where there is no difference in terms of efficacy and safety data, the listed medicine should be the one that is generally available at the lowest price, based on international drug price information sources.

Square box listings may be unrestricted or qualified. Unrestricted square box listings include all alternatives within the pharmacological class, whereas qualified square box listings specify the alternatives to which the square box should apply, that are supported by available evidence.

Treatment details, public health relevance and evidence appraisal and synthesis

7. Treatment details (requirements for diagnosis, treatment and monitoring).
The application should specify the proposed therapeutic dosage regimen and duration of treatment.

Reference to current WHO guidelines (if available) is recommended. Reference to other evidence-based clinical guidelines may be made, however it may be necessary to address any potential conflict of interest issues that might relate to alternative guidelines.

Consideration must also be given to any additional requirements associated with treatment with the medicine, such as diagnostic tests, specialized treatment facilities, administration requirements, monitoring requirements and skill levels of health care providers.

NOTE: *Items 8, 9 and 10 are critical elements upon which Expert Committee judgments are made. The available evidence for public health relevance (item 8), clinical benefits (item 9) and harms (item 10) should be presented separately.*

8. Information supporting the public health relevance.
The application should include information on the public health need for the medicine, including:

- Epidemiological information on disease burden
- Assessment of current use
- Target population(s)
- Likely impact of treatment on the disease

9. Review of benefits: summary of evidence of comparative effectiveness.

- Identification of clinical evidence (search strategy, systematic reviews identified, reasons for selection/exclusion of particular data)
- Summary of available data (appraisal of quality, outcome measures, summary of results)
- Summary of available estimates of comparative effectiveness

10. Review of harms and toxicity: summary of evidence of safety.

- Estimate of total patient exposure to date
- Description of the adverse effects/reactions and estimates of their frequency
- Summary of available data (appraisal of quality, summary of results)
- Summary of comparative safety against comparators
- Identification of variation in safety that may relate to health systems and patient factors

The application must evaluate data for both adults and children (when applicable to the proposed medicine). Where possible, systematic reviews should be presented.

If data for certain populations (e.g. paediatric patients, pregnant patients, elderly patients) are not available, this must be clearly stated in the application.

Summaries of evidence from key trials using ***Grading of Recommendations, Assessment, Development and Evaluation (GRADE)*** *tables should be included in the application to support the comparative effectiveness and comparative safety of the proposed medicine(s). More information regarding the GRADE approach for assessment of evidence quality and strength of recommendations is available at http://www.gradeworkinggroup.org/. Software for producing GRADE tables can be downloaded from http://gradepro.org/.*

There are alternative ways of presenting available evidence either from systematic reviews or single trials. The most relevant comparative trials (randomised controlled trials, RCTs) can be presented showing patients characteristics, baseline risk for the main relevant outcomes in the standard treatment arm, absolute differences and measures of association. If this alternative approach is chosen (especially when only one or two trials are available), ensure there is adequate consideration given to the quality of the studies (or risk of bias of individual study) together with comments on applicability /generalizability of the trial data (population, interventions, outcomes chosen), and on inconsistency among studies which may reduce the quality of the evidence.

11. Summary of available data on comparative cost and cost-effectiveness of the medicine.
Show medicine prices from a range of settings where the medicine is available.

All cost analyses should specify the source of the price information.

The application should present a range of estimated cost per routine outcome such as cost per case, cost per cure, cost per month of treatment, cost per case prevented, cost per clinical event prevented.

Information from cost-effectiveness analyses performed at national level should be included where available to provide general guidance on whether the intervention provides good value for money compared to alternatives.

Where possible applicants should also consider the financial impact of making the drug available, in terms of the average cost per patient (globally) and the population in need (average or differences in prevalence) to assist with the development of budget impact calculations.

Information on any special pricing arrangements, where they exist, should be included.

Regulatory information

12. Summary of regulatory status and market availability of the medicine.
The application must provide a summary of the regulatory status of the medicine(s) proposed for inclusion and specify the indications for which the medicine has regulatory approval.

This should include the regulatory status in the country of origin, other countries and according to stringent regulatory authorities including:

- US Food and Drug Administration (FDA): http://www.accessdata.fda.gov/scripts/cder/drugsatfda/
- European Medicines Agency (EMA): http://www.ema.europa.eu/ema/
- Australian Government, Department of Health, Therapeutic Goods Administration: http://www.tga.gov.au/search/artg
- Japanese Pharmaceuticals and Medical Devices Agency: http://www.pmda.go.jp/english/index.html
- Health Canada: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/index-eng.php

The application must provide information regarding the market availability of the medicine, including where appropriate, any existing or planned licencing agreements with generic manufacturers and/or the Medicines Patent Pool; and reference to existing or planned listing of the proposed medicine on the WHO List of Prequalified Medicinal Products[1].

13. Availability of pharmacopoeial standards (British Pharmacopoeia, International Pharmacopoeia, United States Pharmacopoeia, European Pharmacopeia).
The application should address whether the proposed medicine is included in at least one of the following Pharmacopeia:

- The British Pharmacopoeia
- The International Pharmacopoeia
- The United States Pharmacopoeia
- The European Pharmacopoeia

References

14. Comprehensive reference list and in-text citations.
The application should be clearly referenced with in-text citations using the Vancouver style.

Where possible, a copy of the electronic reference library files should be provided in EndNote™.

[1] The WHO List of Prequalified Medicinal Products contains medicinal products used for HIV/AIDS, tuberculosis, malaria and other diseases, and for reproductive health, which have been assessed as part of the WHO Prequalification Programme and found to be acceptable, in principle, for procurement by UN agencies. The list of WHO prequalified medicines can be found at: https://extranet.who.int/prequal/