

Instructions for applicants preparing a
submission for the 2025 meeting of the
WHO Expert Committee on Selection
and Use of Essential Medicines

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Preface

The 25th 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 in at WHO headquarters in Geneva, Switzerland in April 2025.

This document describes the mandatory format and key information requirements for submissions for the inclusion of new medicines and for inclusion of new indications of currently listed medicines for consideration by the Expert Committee.

New medicines are those that have not previously been evaluated for inclusion on the Model Lists, or those that were once included and have subsequently been removed. New indications are indications of an already listed essential medicine that are different to the indications for which the medicine(s) have been previously recommended for inclusion (e.g. a new disease or disease stage).

For submissions relating to the deletion of currently listed medicines and the inclusion or deletion of individual dosage form(s) and/or strength(s) of currently listed medicines for existing indications, please contact the EML Secretariat for further information.

Prospective applicants are strongly encouraged to contact the EML Secretariat for guidance on preparing submissions well in advance of the submission deadline. During the submission period, the EML Secretariat is available to provide information, feedback, and support to applicants, to ensure submissions adequately address the mandatory requirements.

The deadline for submissions is 1 November 2024, 18h00 UTC. Final submissions must be emailed in both PDF and Word formats to the EML Secretariat at emlsecretariat@who.int.

Following final submission, applicants will receive a confirmation email that their submission has been received by the EML Secretariat. This does not imply that the submission has or will be accepted for consideration by the Expert Committee.

Applicants will be notified by email whether their submission has been accepted for consideration by the Expert Committee in January 2025.

Please direct all enquiries to:

The Secretary

WHO Expert Committee on Selection and Use of Essential Medicines

Department of Health Products Policy and Standards

World Health Organization, Geneva

emlsecretariat@who.int

IMPORTANT

Submissions must adhere to the mandatory format described in these instructions and must address all sections with the relevant information / evidence.

Submissions may not be accepted by WHO for consideration by the Expert Committee if they do not adequately conform to the required format and meet minimum standards for evidence requirements and quality.

Acknowledgements

This publication was prepared by Bernadette Cappello, Lorenzo Moja and Rehab Rayan, WHO Essential Medicines team, and under the supervision of Deusdedit Mubangizi, Director, WHO Department of Health Product Policy and Standards.

Abbreviations and glossary

ATC code	Anatomical Therapeutic Chemical (ATC) classification system code. Active pharmaceutical substances are classified in a hierarchy with five different levels based on to the anatomical organ or system on which they act and their therapeutic, pharmacological, and chemical properties. The fifth level code corresponds to the individual chemical substance (medicine).
Core list	The core list presents essential medicines needed for a basic health care system. In most cases these are medicines used in the primary care setting.
Complementary list	The complementary list presents essential medicines for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. Essential medicines may also be listed as complementary because of higher cost or less favourable cost-effectiveness. In most cases these are medicines used in secondary or tertiary care settings.
EDL	WHO Model List of Essential In Vitro Diagnostics
EML	WHO Model List of Essential Medicines
EMLc	WHO Model List of Essential Medicines for Children. The EMLc lists medicines for children up to and including 12 years of age.
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
ICD-11	International Classification of Diseases, 11th Revision
INN	International non-proprietary name. Medicines are listed in the EML and EMLc using their international nonproprietary names. Each INN is a unique name that is globally recognized and is public property.
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
Square box listing	Square box listings are identified with the symbol “□” next to the listed medicine. This symbol indicates that therapeutic alternatives to the listed medicine may be considered for selection at the national level. Alternatives may be individual medicines, or multiple medicines within a pharmacological class or chemical subgroup, defined at the 4th level of the Anatomical Therapeutic Chemical (ATC) classification, which have similar clinical effectiveness and safety. The listed medicine should be the example of the class or subgroup for which there is the best evidence for effectiveness and safety or has some advantage in a relevant evaluation dimension (e.g., price). A square box is not used to indicate alternative generic brands of the same small molecule medicines, nor alternative biosimilars of biological medicines.

Information to be included in submissions for inclusion of a medicine or a new indication for an existing medicine in the WHO Model Lists of Essential Medicines

Submissions must follow the format described below and include and address all sections with the relevant information / evidence. Submissions that do not conform to these requirements may not be accepted for consideration by the Expert Committee.

- Title page
- Section 1: Summary statement of the proposal
- Section 2: Consultation with WHO technical departments
- Section 3: Other organizations(s) consulted and/or supporting the submission
- Section 4: Key information summary table for the proposed medicine(s)
- Section 5: Listing as an individual medicine or as representative of a pharmacological class or therapeutic group ('square box' listing)
- Section 6: Information supporting the public health relevance
- Section 7: Treatment details
- Section 8: Review of evidence for benefits and harms
- Section 9: Summary of recommendations in current clinical guidelines
- Section 10: Summary of available data on comparative cost and cost-effectiveness
- Section 11: Regulatory status, market availability and pharmacopeial standards
- Section 12: References

➤ A note about confidentiality and copyright.

All submissions accepted for consideration by the Expert Committee will be published on the WHO website and be available in the public domain. Therefore, submissions should not include any commercially protected information to avoid disclosure of potentially sensitive information.

All information included in a submission that is copied or reproduced from another source must appropriately reference the source and have permission to reproduce such content where necessary.

Title page

All submissions must have a separate title page clearly stating:

- A title indicating the purpose of the submission
 - inclusion, change, deletion, new indication
 - international non-proprietary name(s) of the medicine(s)
 - proposed indication(s) for use
 - proposed population(s) for use (adults and/or children)
 - proposed listing on the EML and/or EMLc
- the name(s) of the applicant(s)
- the name(s), and affiliation(s) and contact information (email) of the individual(s) responsible for the submission
- submission date

See Box 1 for an example of the title page.

Box 1. Example title page for submissions (illustrative purpose only).

PROPOSAL FOR THE ADDITION OF FLUOXETINE TO THE WHO MODEL LIST OF ESSENTIAL MEDICINES FOR THE TREATMENT OF ADULTS WITH OBSESSIVE COMPULSIVE DISORDER

Applicant:

WHO Collaborating Centre for Research and Training in Mental Health and Service Evaluation
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Name Surname, MD
Email: name@emailaddress.com
Phone: + XX XX XX XX XX

Date of submission:

16 December 2022

Section 1: Summary statement of the proposal

The submission must include a concise summary statement that provides an overview of key details of the request (maximum 500 words).

For inclusion of new medicines or new indications for currently listed medicines, briefly describe the proposal in terms of clinical indication(s), target population(s) and role in therapy for the requested medicine(s).

In all cases, specify whether the proposal relates to listing on the EML and/or EMLc, the core or complementary list, and of an individual medicine or as a representative of a pharmacological class or therapeutic group (square box listing). In the case of a square box listing, the therapeutic alternatives should also be specified.

Examples of summary statements are presented in Box 2.

Box 2: Summary statement examples (illustrative purpose only)

This submission advocates the inclusion of daratumumab as an individual medicine in the complementary list of the EML for the treatment of adult patients with newly diagnosed and relapsed or refractory multiple myeloma in transplant and non-transplant settings.

Multiple myeloma is the second most common haematological malignancy with a global incidence of approximately 140 000 and an age-standardized incidence rate of 2.1 per 100 000 population in 2016. Since 1990, the incidence rate increased by 126% worldwide.

Results of the evidence syntheses indicate that adding daratumumab to standard combination regimens probably leads to clinically important gain of overall survival, yet a higher number of people experiencing adverse events or serious adverse events. Evidence further suggests that more people receiving daratumumab may have a clinically important gain of quality of life, than people no receiving daratumumab.



This submission is made in support of the inclusion of calcipotriol on the core list of the EML and EMLc, for the treatment of plaque type psoriasis in adults and children. This proposal is being made because there are currently no topical alternatives to the use of topical corticosteroids for the treatment of psoriasis included on the Model Lists. Listing is proposed for calcipotriol as the representative of topical vitamin D analogues, with therapeutic alternatives limited to calcitriol and tacalcitol.

Psoriasis is increasingly recognized as a disabling skin disease and has a worldwide distribution. Effective treatment of patients with mild to moderate plaque type psoriasis with calcipotriol has been reported in different clinical environments and in different age groups. Inclusion of calcipotriol on the Model Lists for the proposed indication would widen access to appropriate medications for the treatment of psoriasis and provide an effective alternative for the many patients with mild to moderate forms of this chronic condition who comprise the majority of cases.



The application proposes the addition of fluoxetine on the core list of the EML for the treatment of adults with obsessive-compulsive disorder (OCD). Listing is proposed for fluoxetine with a square box as a representative of the selective serotonin reuptake inhibitors (SSRI) citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline.

OCD is the fourth most common mental disorder and the tenth cause of disability worldwide. Although the prevalence of OCD may be lower than that of depression, it constitutes a common and disabling set of conditions. In the general population, lifetime prevalence of OCD is estimated between 1-3%, with higher incidence in the female population.

In this application, we consider the best available evidence on efficacy and acceptability of selective serotonin reuptake inhibitors (SSRIs), as compared to placebo or alternative pharmacological interventions, for the treatment of adults with obsessive-compulsive disorder (OCD). Additionally, we discuss availability, cost, and cost-effectiveness of SSRIs in this population group.

Section 2: Consultation with WHO technical departments

External applicants are strongly encouraged to consult with relevant WHO technical departments early in the submission preparation process to facilitate alignment with WHO strategies and priorities.

For submissions made following consultation with the relevant WHO technical department, the submission must provide details the following details:

- name of the technical department
- name(s) of focal point(s) consulted
- date(s) of consultation
- whether the submission is being made in collaboration with the WHO technical department. A description of the collaborative efforts between applicants and the WHO technical department or written advice from the WHO technical department of their support of the submission should be included in an Annex.

If no consultation has been made with WHO technical departments in the preparation of the submission, the reason(s) why must be stated. Note that WHO may not have a relevant technical focal point or department for all therapeutic areas. In such situations, applicants should consult the EML Secretariat.

For submissions made solely by WHO technical departments, this section may be marked as not applicable.

For submissions made by external applicants at the request of and/or in collaboration with a WHO technical department, the department and focal point(s) concerned could be listed among the applicants.

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

➤ IMPORTANT

Consultation with a WHO technical department does not necessarily imply that the submission is or will be endorsed or supported by the technical department.

Section 3: Other organization(s) consulted and/or supporting the submission

The submission should indicate any other organization(s) that have been consulted in relation to the submission and who contributed to its development. The relationship between the applicant and the organization(s) consulted should be specified.

Letters of support from other organizations who support the submission, but who did not participate in its development, may be included in an Annex.

There will be a further opportunity, independent of the submission process, for interested stakeholders to provide comments on the submissions during a public consultation phase following publication of all submissions on the WHO website. This is independent from the submission process. All comments received during the public consultation phase will also be published on the WHO website in association with the submissions to which they refer.

Consultation and/or seeking support from other organization(s) for the submission by the applicant is not a mandatory requirement. When consultation and/or support has not been sought or obtained, this should be indicated in this section of the submission.

Section 4: Key information summary for the proposed medicine(s)

Key information for the proposed medicine(s) must be presented in tabular format and include:

- the international non-proprietary name (INN);
- the Anatomical Therapeutic Chemical (ATC) code;
- the indication(s) proposed for use and corresponding code from the International Classification of Diseases, 11th Revision (ICD-11). If an exact ICD-11 code is not available, the code that most appropriately matches the proposed indication(s) should be selected and be accompanied by a clear rationale for its selection;
- the dosage forms and strengths proposed for listing;
- whether listing is proposed for the EML, EMLc or both.

Examples of key information summary tables are presented in Box 3.

International non-proprietary name (INN)

Medicine(s) must be described using International Non-proprietary Names (INN) throughout the submission. INNs facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognised. Brand or proprietary names of medicines should not be used.

➤ A searchable database of INNs is available [here](#).

Anatomical Therapeutic Chemical (ATC) code

The Anatomical Therapeutic Chemical (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. The submission must indicate the ATC code specific to the medicine and proposed indication for use.

➤ A searchable version of the complete ATC index is available [here](#).

Indication(s)

The indication(s) for which the medicine(s) is proposed for inclusion must be clearly specified. When available, the appropriate code for the proposed indication using the International Classification of Diseases, 11th Revision (ICD-11) must be included.

- A searchable database of ICD-11 codes is available [here](#).
-

Dosage form(s) and strength(s)

The submission must identify the specific dosage forms(s) and strength(s) of the medicine(s) being proposed for inclusion.

If the submission relates to medicines for inclusion on the EMLc, the submission must address the availability of suitable, age-appropriate dosage forms and strengths for administration to infants and children up to 12 years of age.

-
- Applicants should perform a systematic assessment of the age-appropriateness of the proposed dosage forms and strengths of medicines for children using the paediatric quality target product profile (pQTPP) assessment tool described [here](#). The findings of the assessments should be included in an annex to the submission.
-

Box 3: Key information summary table examples (illustrative purpose only)

INN	Dolutegravir		
ATC code	J05AJ03		
Indication	Treatment of HIV infection in adults and children		
ICD-11 code	1C62.Z Human immunodeficiency virus disease without mention of associated disease or condition, clinical stage unspecified		
Dosage form	Strength	EML	EMLc
Tablet (dispersible, scored)	10 mg	No	Yes
Tablet	50 mg	Yes	Yes



INN	Levetiracetam		
ATC code	N03AX14		
Indication	Treatment of epilepsy in adults and children		
ICD-11 code	8A6Z Epilepsy or seizures, unspecified		
Dosage form	Strength	EML	EMLc
Oral solution	100 mg/mL	Yes	Yes
Tablet	250 mg, 500 mg, 750 mg, 1000 mg	Yes	Yes
Indication	Treatment of status epilepticus in adults and children		
ICD-11 code	8A66 Status epilepticus		
Dosage form	Strength	EML	EMLc
Concentrate for solution for infusion	500 mg/5mL in 5 mL vial	Yes	Yes
Solution for infusion:	5 mg/mL, 10 mg/mL, 15 mg/mL in 100 mL bag	Yes	Yes



INN	Pembrolizumab		
ATC code	L01FF02		
Indication	Treatment of non-oncogene- addicted (EGFR, ALK, and ROS1 wild type) locally advanced and metastatic non-small cell lung cancer (NSCLC) in adults		
ICD-11 code	2C25.Y Other specified malignant neoplasms of bronchus or lung		
Dosage form	Strength	EML	EMLc
Concentrate for solution for infusion	25 mg/mL in 4 mL vial	Yes	No

Section 5: Listing as an individual medicine or representative of a pharmacological class / therapeutic group

- A square box symbol (□) is used in the Model Lists to indicate that other medicines are acceptable therapeutic alternatives to the listed representative for selection at the national level.
 - More information about the square box listing concept on the WHO Model Lists is available [here](#).
-

The submission must indicate if the proposal relates to listing of an individual medicine or listing for one medicine as the representative of one or more therapeutic alternatives ("square box" listing).

When listing for an individual medicine is proposed, and other medicines within the same pharmacological class or therapeutic group for the same indication are not, the submission must provide justification for why the other medicines are not being proposed for listing as therapeutic alternatives.

When square box listing is proposed for a medicine to be representative of therapeutic alternatives in a pharmacological class or therapeutic group, the application must:

- justify the choice of the representative medicine based on best evidence for effectiveness and safety; or on price and availability data (where there is no difference in effectiveness and safety data)
- specify the proposed therapeutic alternative(s) (using INN and ATC code)
- present supporting evidence that the alternative(s) have similar efficacy and safety (e.g., similar pharmacological class effects).

Section 6: Information supporting the public health relevance

Submissions for inclusion of new medicine(s) and/or indication(s) must include information and evidence supporting the public health relevance of the proposed medicine(s), including:

- Proposed indication(s) and target population(s)
- Epidemiological data of the global disease burden, including data specific for WHO regions and country income settings.
 - E.g., incidence, prevalence, mortality, disability-adjusted life years, etc.
- Alternative medicines currently included on the Model Lists for the proposed indication(s).

Links to useful resources:

- Institute for Health Metrics and Evaluation Global Burden of Disease study data are available [here](#).
 - Global Cancer Observatory data are available [here](#).
 - WHO Global health observatory data are available [here](#).
 - The 2023 WHO Model List of Essential Medicines is available [here](#).
 - The 2023 WHO Model List of Essential Medicines for Children is available [here](#).
 - The electronic EML (eEML) database is available [here](#).
-

Section 7: Treatment details

Dosage regimen and duration of treatment

The submission should provide information on medicine delivery, focusing on elements at the point of care, describing the proposed therapeutic dosage regimen and duration of treatment for each medicine and indication. This should be informed by clinical evidence, regulatory, and real-world data.

Requirements to ensure appropriate use of the medicine(s)

The submission should outline the requirements for the appropriate use of the medicine including:

- Patient eligibility criteria (e.g., age and/or weight restrictions)
- Diagnostic and/or monitoring test requirements
- Treatment administration requirements (e.g., compounding) and setting (e.g., ambulatory, primary care, specialized treatment facilities etc.)
- Required skill levels of healthcare providers and their availability.

If companion *in vitro* diagnostic tests are required for appropriate use of the medicine(s), the submission must provide details of any such tests, with reference to their availability, and whether they are currently included on the WHO Model List of Essential In Vitro Diagnostics.

➤ The WHO Model List of Essential In Vitro Diagnostics is available [here](#).

Section 8: Review of evidence for benefits and harms

Summary of available evidence for comparative effectiveness and comparative safety

Submissions must include a summary of the best available clinical evidence to support the comparative effectiveness and comparative safety of the proposed medicine(s) for the proposed indication(s) versus relevant alternative therapies in current clinical practice.

- If the proposed medicine(s) will potentially replace a medicine already included on the Model Lists for the same indication in clinical practice, evidence for comparative effectiveness and safety versus the listed medicine must be presented.
- If the proposed medicine(s) is intended for use for an indication or target population for which no alternative medicines are currently included on the Model Lists, evidence for comparative effectiveness and safety versus the current recognized standard of care must be presented. The current standard of care may be another medicine(s), surgical treatment, best supportive care, or no treatment/placebo.

Search strategy and selection criteria

The inclusion of medicines on the WHO Model Lists of Essential Medicines is rooted in evidence-based evaluation.

Full transparency about the choice of evidence included in the application is critical. Therefore, all applicants must undertake a systematic literature search to identify the relevant evidence. The submission must include a description of the search strategy and be transparent about the selection criteria used to include or exclude identified studies.

A brief summary of the search methods (databases and other sources interrogated (e.g., reference lists, grey literature) and search terms and filters (e.g., types of studies, participants, interventions, outcome measures, language restrictions and time frame etc.) must be presented.

Priority should be given to including study types that deliver the highest level of evidence. Cumulative evidence (e.g., systematic reviews and meta-analyses) is preferred over evidence originating from single randomized studies; randomized studies are preferred over non-randomized studies.

Systematic reviews and meta-analyses

Wherever possible, evidence from recent systematic reviews and meta-analyses, including network meta-analyses and individual patient meta-analyses, should be presented. This must include a narrative summary of the evidence including information on the number of included studies and number of participants, assessment of bias of the included studies, treatment details (intervention and comparison groups), and outcomes investigated. Key outcomes should also be presented in a 'summary of findings' table and report

the magnitude of effects in relative and absolute terms, and the amount and certainty of the available evidence for the comparison(s).

Systematic reviews and meta-analyses may identified be from the published literature or conducted *de novo* by the applicant(s). When systematic reviews and meta-analyses are conducted by applicants for the purpose of the submission, this should be clearly indicated.

When several systematic reviews and meta-analyses are identified through the literature search, priority should be given to the most comprehensive and high-quality systematic review and meta-analysis. Reasons why one or more systematic reviews were selected should be clearly reported. Long lists of narrative and systematic reviews accompanied by a brief description of the results are not appropriate in this context. Older meta-analyses can be referenced in an Annex.

It is important that results and conclusions of high-quality systematic reviews and meta-analyses that contradict the request made in the submission are reported, along with possible reasons for the divergent findings.

Conducting a *de novo* systematic review / meta-analysis may be necessary if recent, relevant, and high-quality existing ones are not available in the published literature. Presenting a list and narrative review of the results of individual trials should be avoided unless there are clear reasons to do so (see below).

Applicants are encouraged to check with the EML Secretariat early in the submission preparation process if a *de novo* systematic review will be required.

Summaries of evidence from key trials using *Grading of Recommendations, Assessment, Development and Evaluation* (GRADE) tables should be included in the submission 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 [here](#). Software for producing GRADE tables can be downloaded [here](#).

Randomized controlled trials

Evidence from individual randomized controlled trials can be presented when:

- Published relevant high-quality systematic reviews and meta-analyses are not available; and
- Identified studies are insufficient in number and/or too heterogeneous to perform a *de novo* systematic review / meta-analysis. In which case, the reasons why a systematic review and meta-analysis could not be performed should be discussed with the EML secretariat and must be elaborated in the submission.

The submission must include a narrative summary of the included trial(s) including trial design, sponsor (industry-sponsored versus other), setting (including geographic location), study period, patient eligibility

criteria, randomization, patient characteristics (demographic and clinical including representation of different genders / sexes and ethnicities), treatment details (intervention and comparison groups), duration of treatment and follow-up, outcomes investigated (direct and/or indirect) and findings specific to the populations analysed (e.g. per protocol, intention to treat etc.).

The submission must also include an assessment of the risk of bias of individual studies.

Non-randomized studies

Evidence from non-randomized studies may be presented and summarized to supplement included evidence from the study types described above. Examples include large observational studies, post-marketing studies, case reports and case series, and narrative reviews.

If only non-randomized studies are presented in the submission, the submission must provide an explanation as to why evidence from experimental trials is not included, available or is not appropriate.

In consideration of safety, submissions must also include:

- An estimate of the total patient exposure to the proposed medicine(s) to date.
- Descriptions of adverse effects known to be causally related to the proposed medicine(s) and estimates of their frequency and grading of severity.
- Information on any variation in safety that may relate to health systems or patient factors.
- Information on any warning or safety issues identified by regulatory authorities (e.g., black box warnings, safety alerts etc).
- Information on any risk-minimization plans with regulatory agencies, including monitoring, warnings, use restrictions etc.
- Information on any additional strategies to mitigate or reduce medicine toxicity and adverse events (e.g., dose reduction), particularly in low-resource settings.
- Consideration of the potential for and consequences of inappropriate use or use outside the proposed indication.

Assessment of applicability of the available evidence across diverse populations and settings

Evidence from a variety of clinical settings, including settings with different income levels and resources should be included, whenever available.

Submissions must evaluate evidence for both adults and children (when applicable to the proposed medicine), and for different patient populations (e.g., patients of different genders and ethnicities, pregnant and breastfeeding patients, elderly patients etc.)

Where such evidence is not available or is limited, this should be clearly stated, and the submission should present an assessment of the applicability of the available evidence to these different populations and settings.

Section 9: Summary of recommendations in current clinical guidelines

Recommendations in existing WHO guidelines

The submission must summarize the recommendations for the medicine(s) and indication(s) in current WHO guidelines, if available, including the strength and the quality of evidence.

-
- A searchable repository of WHO guidelines is available [here](#).
-

Recommendations in other current clinical guidelines

The submission must summarize the recommendations for the medicine(s) and indication(s) in other current critically appraised clinical guidelines, if available, including the strength and quality of evidence.

Section 10: Summary of available data on comparative cost and cost-effectiveness

The submission must include information on the comparative cost of the medicine(s) in different markets and the estimated budget impact to patients and health systems.

The submission must present data on the price of the medicine(s) from a range of settings where the medicine is available. Information on any special pricing arrangements, licensing agreements, and/or access programmes, where they exist, should be included. The source(s) of the price information must be specified in the submission.

The submission should present a range of comparative costs per routine outcome for the proposed medicine(s) compared to alternative medicines currently included on the Model Lists and/or other relevant alternative pharmacological or therapeutic interventions (e.g., cost per case, cost per cure, cost per course of treatment, cost per case prevented, cost per clinical event prevented etc.). To justify the potential inclusion of medicines that incur greater costs to patients and health systems than currently listed medicines, the submission must have clearly demonstrated the advantages of the proposed medicine relative to any currently listed medicines in key dimensions such as benefits, harms, compliance, ease of use, patient values and preferences, as an alternative for patients with allergies or other contraindications to already listed medicines, or non-responders to already listed medicines, etc.

The submission must include information on the average cost per patient and the eligible treatment population (taking into consideration differences in incidence and/or prevalence) in different settings (geographic, income level). This information is required to assist with determining the likely overall budget impact to health systems of making the proposed medicine(s) available.

Data from economic analyses performed at national level (e.g., cost-effectiveness, cost-utility studies, health technology assessment) of the proposed medicine(s) versus other relevant alternative pharmacological or therapeutic interventions should also be included in the submission to provide information on whether the proposed medicine(s) provides value for money compared to alternative treatments already listed in the given setting.

Economic analyses must be identified using a systematic literature search. The submission must include a description of the search strategy and be transparent about the selection criteria used to include or exclude identified studies.

A brief summary of the search methods (databases and other sources interrogated (e.g., reference lists, grey literature)) and search terms and filters (e.g., population(s), intervention(s), types of studies, outcome measures, language restrictions and time frame etc.) must be presented.

The submission must include a narrative summary of the included studies including study design, time horizon, population characteristics, data sources, study setting and perspective, willingness-to-pay thresholds, outcome measures and results (base-case and sensitivity analyses).

Section 11: Regulatory status, market availability and pharmacopoeial standards

The submission must provide a summary of the regulatory status of the medicine(s) proposed and including the indication(s) for which the medicine(s) has regulatory approval.

Off-label indication(s) may be considered where off-label use is supported by evidence.

Regulatory status of the proposed medicine(s)

Submissions should include details of the regulatory status of the medicine(s) from national regulatory authorities.

➤ Information regarding designated and transitional WHO-Listed Regulatory Authorities (WLAs), is available [here](#).

Market availability of the proposed medicine(s)

The submission must provide information regarding the global market availability of the medicine(s), including availability of generics and/or biosimilars, patent status and, where appropriate, any existing or planned licencing agreements with generic/biosimilar manufacturers and/or the Medicines Patent Pool.

The submission should describe any actual or anticipated shortages, supply-chain issues and/or barriers to availability that may exist in various settings.

Reference to existing or planned inclusion of the proposed medicine(s) on the WHO List of Prequalified Finished Pharmaceutical Products, should be included, where appropriate.

➤ Information regarding finished pharmaceutical products and active pharmaceutical ingredients eligible for WHO Prequalification is available [here](#).

Pharmacopoeial standards

The submission must indicate the availability of pharmacopoeial standards for the medicine(s) proposed in the British, European, International and United States Pharmacopoeias.

Section 12: Reference list

The submission must be clearly referenced with in-text citations using reference management software (e.g. EndNote™, Mendeley™, Zotera™ etc). The World Health Organization (WHO) Editorial Style Guide (2024) output style must be used.

Electronic reference library files must be exportable from the Word version of the submission document or be provided separately in RIS file format. Submissions that do not provide exportable or separate reference library files cannot be accepted.

The full text of cited references must be provided in PDF format if they are not available as open access in the public domain.

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- World Health Organization (WHO) Editorial Style Guide (2024) output style for EndNote™ can be downloaded [here](#).
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