



**World Health  
Organization**

**Executive Summary:**

**The Selection and Use of  
Essential Medicines (2015)**

Report of the 20<sup>th</sup> WHO Expert Committee on the  
Selection and Use of Essential Medicines

**20-24 April 2015**

**WHO headquarters, Geneva**



## Table of contents

	page numbers
Executive Summary: The Selection and Use of Essential Medicines (2015)	
• Executive Summary	1-3
• Expert Committee Members and Temporary Advisers	4-5
• Participants from UN Agencies, WHO Regions and WHO Secretariat	6
• Declarations of Interests for Expert Committee Members, Temporary Advisers and WHO Secretariat	7-9

## ANNEXES

Annex 1: 19 <sup>th</sup> WHO Model List of Essential Medicines List (EML 2015)	1–51
Annex 2: 5 <sup>th</sup> WHO Model List of Essential Medicines for Children (EMLc 2015)	1–38



## Executive summary

The 20th meeting of the WHO Expert Committee on the Selection and Use of Essential Medicines took place in Geneva, Switzerland, from 20 to 24 April 2015. The goal of the meeting was to review and update the 18th WHO Model List of Essential Medicines (EML) and the 4th WHO Model List of Essential Medicines for Children (EMLc).

In accordance with approved procedures<sup>1</sup>, the Expert Committee evaluated the scientific evidence on the basis of the comparative effectiveness, safety and cost-effectiveness of the medicines. Both lists went through major revisions this year, as the Committee considered 77 applications, including 29 treatment regimens for cancer and innovative hepatitis C and TB medicines.

The Expert Committee:

- recommended the addition of 36 new medicines to the EML (15 to the core list and 21 to the complementary list); and
- recommended the addition of 16 new medicines to the EMLc (five to the core list and 11 to the complementary list).

The following are the main recommendations in order of their appearance on the Model Lists:

### Section 6.2.4 Antituberculosis medicines

For the treatment of multi-drug resistant tuberculosis (MDR-TB), extensively drug resistant tuberculosis (XDR) and pre-XDR, the Expert Committee recommended the addition of bedaquiline, delamanid and linezolid to the complementary list, and the addition of terizodone (as an alternative to cycloserine) to the core list. Similarly, linezolid and terizidone were recommended for the EMLc. The Committee supports the use of these medicines recommended in WHO guidelines, with careful selection of patients, close monitoring to control adverse events and active pharmacovigilance. The Committee also recommended the addition of rifapentine to the core list of EML and EMLc for the treatment of latent TB infection.

### Section 6.4.2 Antiretrovirals

The Expert Committee considered applications for the addition and deletion of antiretrovirals, and noted the recommendations in the *WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach*, published in 2013. The Committee recommended the addition of darunavir,

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<sup>1</sup> See: [http://www.who.int/selection\\_medicines/committees/subcommittee/2/eeb1098%5b1%5d.pdf](http://www.who.int/selection_medicines/committees/subcommittee/2/eeb1098%5b1%5d.pdf)

new formulations of efavirenz, nevirapine and a fixed-dose combination of abacavir + lamivudine. The Committee did not recommend listing the fixed dose combinations of cobicistat + elvitegravir + emtricitabine + tenofovir and emtricitabine + rilpivirine + tenofovir.

The Committee recommended the deletion of 30 antiretroviral formulations from the EML and EMLc, as these are no longer recommended by WHO guidelines.

#### **Section 6.4.4 Antihepatitis medicines**

The Expert Committee recommended that a new section be inserted to the core EML to include medicines for the treatment of viral hepatitis infections, with sub-sections for hepatitis B, and hepatitis C. The Committee recommended the addition of entecavir and tenofovir for the treatment of hepatitis B, and the addition of six oral direct-acting antiviral medicines including daclatasvir, ledipasvir + sofosbuvir, ombitasvir + paritaprevir + ritonavir with or without dasabuvir, simeprevir, and sofosbuvir, for the treatment of hepatitis C. The recommendations for inclusions were based on the comparative efficacy, increased tolerability and the potential public health impact of these medicines. The very high cost of hepatitis C medicines was considered and the Committee recommended that WHO take actions at global level to make these medicines more accessible and affordable.

#### **Section 8.2 Cytotoxic and adjuvant medicines**

Following a review requested by the previous Expert Committee in 2013, the Committee recommended the addition of 16 new medicines and endorsed the use of 30 medicines listed currently as part of proven clinically effective treatment regimens. These medicines will be included on the complementary list of the EML for the treatment of specific cancers. The Committee recommended that the Model Lists should specify the cancers for which use of each medicine is recommended. Among the medicines recommended are some high-cost medicines including imatinib, trastuzumab and rituximab. The Committee also recommended, among others, the addition of aromatase inhibitors, bendamustine, capecitabine, cisplatin, oxaliplatin and transretinoic acid.

#### **Section 10.2 Medicines affecting coagulation**

The Expert Committee recommended the addition of enoxaparin to the core EML with a square box symbol representative of the pharmacological class of low molecular weight heparins (with alternatives to be limited to nadroparin and dalteparin) for the prophylaxis and treatment of venous thromboembolism, and in the treatment of acute coronary syndromes. The Committee did not recommend the addition of the novel oral anticoagulants (NOACs, including dabigatran, rivaroxaban and apixaban) for use in stroke prevention in patients with non-valvular atrial fibrillation. The Committee found that NOACs provide no overall clinically relevant advantage compared to warfarin for patients who are established and stable on warfarin therapy. The Committee emphasized the need for further research to define unmet needs for anticoagulation in patients who cannot be stabilized with warfarin and also for use in for clinical settings where access to warfarin monitoring is not reliable or available.

## **Section 12 Cardiovascular medicines**

The Expert Committee did not recommend the addition of fixed-dose combination therapy for secondary prevention of cardiovascular disease. The Committee based its recommendation on the lack of evidence on clinical outcomes, the higher number of adverse events reported with the use of combinations and difficulties associated with dose titration of the components as proposed in the various fixed dose combinations.

## **Section 18 Hormones, Other Endocrine Medicines & Contraceptives**

The Expert Committee recommended the addition of three new contraceptive products to the EML: the etonogestrel-releasing implant, the levonorgestrel-releasing intrauterine system and the progesterone contraceptive vaginal ring.

## **Section 21.6 Anti-vascular endothelial growth factor (anti-VEGF) eye medicines**

The Expert Committee did not recommend the addition of ranibizumab to the EML for the treatment of neovascular (proliferative) eye diseases. The Committee concluded that the available evidence shows similar effectiveness and safety between ranibizumab and bevacizumab. In cost-effective analyses, bevacizumab is the preferred option as ranibizumab is offered at a greater cost with no additional clinical benefits. The Committee was concerned that the inclusion of ranibizumab for the treatment of these eye diseases might detract relevant resources from other interventions.

## **Section 22.1 Oxytocics**

Two applications related to misoprostol were considered by the Expert Committee. The Committee recommended listing misoprostol for the additional indication of post-partum hemorrhage, when oxytocin is not available or cannot be used safely, but it did not recommend deletion of misoprostol for the post-partum hemorrhage prevention indication. The Committee noted that no new clinical trial data to support deletion has been presented compared to the same application in 2013.

## **Additional recommendations**

The Expert Committee recommended the addition of valganciclovir, desmopressin, clopidogrel, omeprazole IV formulation and alcohol-based hand rub. The Committee did not recommend the addition of dopamine agonists for Parkinson's disease, a new strength formulation of ferrous salt + folic acid and gadolinium-based radiocontrast media.

All applications and documents reviewed by the Expert Committee are available on the WHO website at: [http://www.who.int/selection\\_medicines/committees/expert/20/en/](http://www.who.int/selection_medicines/committees/expert/20/en/)

## Expert Committee Members and Temporary Advisers

### Expert Committee Members

Hany Abdel-Aleem Aly, Department of Obstetrics and Gynecology, Women's Health Hospital, Assiut University Hospital, Assuit, Egypt

Gitanjali Batmanabane, Head of the Department of Medical Education at the Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India

Lisa Bero (Chair), Chair of Medicines Use and Health Outcomes, Charles Perkins Centre, The University of Sydney, Australia

Vittorio Bertelé, Internal Medicine Physician, Drug Regulatory Policies Laboratory, Mario Negri Institute for Pharmacological Research, Milan, Italy

Franco Cavalli, Scientific Director, Oncology Institute of Southern Switzerland, Ospedale San Giovanni, Bellinzona, Switzerland

Graham Cooke, Clinical Senior Lecturer in Infectious Diseases, Imperial College, London, United Kingdom

Margareth Dalcolmo, Professor of Respiratory Medicine and Clinical Researcher at the Reference Centre Helio Fraga, FIOCRUZ, Rio de Janeiro, Brazil

Paul Garner (Rapporteur), Medical Epidemiologist, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Mohammed Hassar, Internist and Clinical Pharmacologist, Rabat School of Medicine and Pharmacy, Rabat, Morocco

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Michael Link, Pediatric Oncologist, Professor of Pediatrics, Stanford University, California, United States of America

Thamizhanban (Anban) Pillay (Vice-Chair), Deputy Director General for Health Regulation and Compliance, National Department of Health, and Honorary Senior Lecturer, University of KwaZulu Natal, Republic of South Africa

Shalini Sri Ranganathan, Professor of Pharmacology and Specialist in Pediatrics, University of Colombo, Sri Lanka

Robyn Ward, Oncologist, Deputy Vice Chancellor (Research), University of Queensland, Brisbane, Australia

### Temporary Advisers

Carla Coffin, Assistant Professor, Cumming School of Medicine and Director of the Viral Hepatitis Clinic, University of Calgary, Alberta, Canada

Robert Mvungi, Cardiologist, Department of Cardiovascular Medicine, Muhimbili National Hospital, Dar es Salaam, Tanzania

Francis Ofei, Internal Medicine Physician, Associate Professor of Medicine, University of Cape Coast, Ghana

Edith Okeke, Consultant Gastroenterologist, Faculty of Medical Sciences, University of Jos, Jos University Teaching Hospital, Nigeria

## Participants from UN Agencies, WHO Regions and WHO Secretariat

### UN Agencies

*United Nations Population Fund (UNFPA)*

Kabir U Ahmed, Technical Adviser, Technical Division, New York, NY, USA

*United Nations Children's Fund (UNICEF)*

Henrik Nielsen, Technical Specialist, Essential Medicines Unit, Medicines and Nutrition Centre, UNICEF Supply Division, Copenhagen, Denmark

### WHO Regions

*WHO Regional Office for Europe*

Hanne Bak Pedersen, Programme Manager, Health Technologies and Pharmaceuticals, Copenhagen Denmark

*WHO Regional Office for the Americas / Pan American Health Organization*

Jose Luis Castro, Advisor, Rational Use of Medicines, Washington DC, United States of America

### WHO Secretariat

Kees de Joncheere, Director, Essential Medicines and Health Products Department (EMP), Health Systems and Innovation Cluster (HIS)

Gilles Forte, Coordinator, Policy, Access and Use (HIS/EMP/PAU)

Nicola Magrini, Secretary of the Expert Committee on Selection and Use of Essential Medicines, Policy, Access and Use (HIS/EMP/PAU/EML)

Bernadette Cappello, Technical Officer, EML Secretariat, Policy, Access and Use (HIS/EMP/PAU/EML)

Lorenzo Moja, Technical Officer, EML Secretariat, Policy, Access and Use (HIS/EMP/PAU/EML)

Jane Robertson, Temporary Adviser, Policy Access and Use (HIS/EMP/PAU/EML)

Suzanne Hill, Senior Adviser, Policy, Access and Use (HIS/EMP/PAU/EML)

Peter Beyer, Senior Adviser, Public Health, Innovation and Intellectual Property (HIS/EMP/PHI)

Jeanne-Marie Scott, Administration and Web Support, EML Secretariat, Policy Access and Use (HIS/EMP/PAU/EML)

## Declarations of Interests for Expert Committee Members, Temporary Advisers and WHO Secretariat

Competing interests may occur in health care. This results in the potential for conflict of interest. These can lead to biased generation or assessment of evidence and lead to misinformed healthcare policies. The WHO has stringent policies to avoid, or at best limit, conflict of interest, particularly in the development of official guidance documents that affect health care. As declaration of conflict of interests is insufficient to neutralize potentially harmful effects, WHO has accurate mechanisms to identify relevant conflict of interests and suggest approach to manage them (e.g. excluding members, recusing participation from meeting sessions, restricting participation) ensuring the validity and transparency of the decision-making process of the credibility of the Expert Committee Member decisions. Declarations of interest of Expert Committee Members and Temporary Advisers were assessed by the WHO Compliance and Risk Management and Ethics Office (CRE).

### Conflicts of Interest for Expert Committee Members and Temporary Advisers

In reviewing and assessing the conflicts of interest of the Members of the 20th Expert Committee on the Selection and Use of Essential Medicines, the WHO Essential Medicines and Health Products Department sought the advice of the CRE. The following conclusions were reached:

#### **Financial and intellectual conflicts of interest**

All Members and Temporary Advisers of the 20th Expert Committee on the Selection and Use of Essential Medicines submitted written disclosures of competing interests that might cause a conflict of interest when making decision related to the Essential Medicines List. These included employment by a commercial entity, consultancy, board or advisory board membership, lecture fees, expert witness income, industry-sponsored grants including contracted research, patents received or pending, royalties, stock ownership or options, other personal financial interests; whether the institution or employer has a financial relationship with a commercial entity that has an interest in medicines evaluated by the Expert Committee. Committee Members and Temporary Advisers were also asked to disclose academic or scientific activities that created the potential for an attachment to a specific point of view that could unduly affect an individual's judgment about a specific decision. These included authorship of original studies or grant applications directly bearing on a decision about a medicine.

Members who did not declare financial conflict of interests that were above the acceptable WHO monetary threshold were: Hany Abdel-Alem Aly, Gitanjali Batmanabane, Lisa Bero, Vittorio Bertelé, Franco Cavalli, Graham Cooke, Margareth Dalcolmo, Paul Garner,

Mohammed Hassar, Kalle Hoppu, Youping Li, Michael Link, Thamizhanban Pillay, Shalini Sri Ranaganathan, Robyn Ward, Carla Coffin, Robert Mvungi, Francis Ofei and Edith Okeke.

Members who did not declare any relevant intellectual conflict of interests were: Hany Abdel-Aleem Aly, Gitanjali Batamanabane, Lisa Bero, Vittorio Bertelé, Franco Cavalli, Graham Cooke, Margareth Dalcolmo, Paul Garner, Mohammed Hassar, Kalle Hoppu, Youping Li, Michael Link, Thamizhanban Pillay, Shalini Sri Ranaganathan, Robyn Ward, Carla Coffin, Robert Mvungi, Francis Ofei, and Edith Okeke. Several Expert Committee Members and Temporary Advisers had participated in previous guideline panels, other expert committees, narrative or systematic reviews that provided reviews or recommendations about a medicine under evaluation.

Vittorio Bertelé declared that he had co-authored a Cochrane systematic review about the safety of ranibizumab and bevacizumab for neovascular macular degeneration. The systematic review pooled together the results of all previous RCTs that compared bevacizumab and ranibizumab. All RCTs and the systematic review had been funded through public money (non-industry-sponsored). This was not considered a conflict of interest with respect to the evaluation of ranibizumab. Lorenzo Moja, now a WHO staff member, was the first author on this systematic review.

Lisa Bero declared that she co-authored an editorial accompanying the above-mentioned Cochrane systematic review in collaboration with Nicola Magrini, now a WHO staff member and Secretary of the Expert Committee. This was not considered a conflict of interest with respect to the evaluation of ranibizumab.

All the above-mentioned situations were considered disclosures not reaching the statutorily-set thresholds for direct intellectual conflicts of interests or material effect. It was determined that all Expert Committee Members and Temporary Advisers should have the opportunity to engage in the discussion on the evaluation of all medicines.

Expert Committee Members were appraised of the declared conflict of interests of all other participants before the deliberations of the EML meeting began.

Conflicts of Interest of each Expert Committee Member and Temporary Adviser were acknowledged and fully disclosed, as well as decisions and reasons to abstain from any topic discussion, have been acknowledged and fully disclosed.

Additional conflicts were not declared at the meeting.

None of the Expert Committee Members and Temporary Advisers reported having been approached by any one of the applicants.

### Conflicts of Interest for Members of the WHO Secretariat

Conflicts of Interest of the WHO Secretariat of the Essential Medicines List were reviewed as well (though this was not mandatory) with guidance was sought from the CRE with respect to potential conflicts.

Bernadette Cappello, Suzanne Hill, Nicola Magrini, Lorenzo Moja, Jane Robertson, did not have any financial and relevant intellectual conflict of interest. Lorenzo Moja had authored several systematic reviews and meta-analyses about medicines under evaluation (ranibizumab, trastuzumab, anti-thrombotic agents). Nicola Magrini had authored an editorial accompanying the above-mentioned Cochrane systematic review and was also called to testify by the Italian Antitrust Authority in a case against Roche and Novartis for anticompetitive activities in respect of one medicine (ranibizumab) under evaluation. In this respect, it is noted that Nicola Magrini had conducted detailed discussions with CRE on this matter and, while it was determined that he did not have any direct conflict of interest with respect to the evaluation of ranibizumab, he was advised he might consider, of his own volition, to recuse himself from this part of the evaluation in order to avoid a perception of conflict of interest. Nicola Magrini did decide to recuse himself from participating in the discussions and formulation of the recommendation on ranibizumab.

