

Reports of advisory bodies

Expert committees and study groups¹

Report by the Secretariat

SELECTION AND USE OF ESSENTIAL MEDICINES

**Twentieth meeting of the Expert Committee on the Selection and Use of Essential Medicines
Geneva, 20–24 April 2015²**

19th WHO Model List of Essential Medicines and the 5th WHO Model List of Essential Medicines for Children

1. The twentieth meeting of the Expert Committee on the Selection and Use of Essential Medicines was held at WHO headquarters in Geneva from 20 to 24 April 2015. The Expert Committee reviewed 77 applications.

2. An open session was held on 20 April 2015, at which the Secretariat and stakeholders made presentations on the role and decision-making criteria of the WHO Model List of Essential Medicines. Presenters included representatives of IMS Institute for Healthcare Informatics (on behalf of the International Federation of Pharmaceutical Manufacturers and Associations), Médecins sans Frontières, the Union for International Cancer Control, Knowledge Ecology International, and the Youth Commission on Essential Medicines Policies.³

Main recommendations

3. As a result of a comprehensive review of cancer medicines recommended at the nineteenth meeting of the Expert Committee in 2013, the Committee recommended the addition of 16 new medicines for the treatment of specific cancers, including monoclonal antibodies (trastuzumab and rituximab) and targeted therapies (imatinib). A comprehensive review was undertaken, which focused

¹ The Regulations for Expert Advisory Panels and Committees provide that the Director-General shall submit to the Executive Board a report on meetings of expert committees containing observations on the implications of the expert committee reports and recommendations on the follow-up action to be taken.

² WHO Technical Report Series, No. 994.

³ The presentations are available at: http://www.who.int/selection_medicines/committees/expert/20/en/ (accessed 8 October 2015).

on cancers with high incidence and where treatment produced a clinically relevant survival benefit and on rare cancers for which the goal of systemic treatment is cure or long-term remission. As a result, 29 applications were considered. In making its recommendations, the Committee considered the magnitude of clinical benefit associated with treatment, however, a specific threshold for benefit was not identified. The cancer medicines section of both Model Lists was updated to include specific indications for which each medicine was recommended.

4. The Committee recommended the addition to the WHO Model List of Essential Medicines of various direct-acting antiviral medicines, including fixed-dose combinations for the treatment of chronic hepatitis C, based on evidence supporting their substantial therapeutic benefit, satisfactory safety profile, and shorter treatment duration. These medicines have very high prices and are currently considered unaffordable in many countries. The Committee recommended the listing of all the proposed direct-acting antiviral medicines, to promote competition and to allow for the selection of optimal combination treatment regimens.

5. The Committee added entecavir and tenofovir to the WHO Model List of Essential Medicines for the treatment of chronic hepatitis B, given the clear evidence from clinical trials on their role in hepatitis B treatment regimens recommended in current WHO guidelines.¹

6. The Committee added four new medicines to the complementary list of the WHO Model List of Essential Medicines for the treatment of multidrug-resistant tuberculosis: bedaquiline, delamanid, linezolid and terizidone (as a specific alternative to cycloserine). Linezolid was also added to the complementary list of the WHO Model List of Essential Medicines for Children. Rifapentine was added to the core list of both Model Lists for the treatment of latent tuberculosis infection. These new medicines are included in WHO treatment programmes and are supported by WHO guidelines. The Committee recommended ongoing review of these medicines and consideration at the next Expert Committee meeting. The monitoring of their use and the establishment of an active pharmacovigilance programme was recommended in order to ensure that more evidence is made available for their efficacy and safety.

7. Other medicines that were added to the WHO Model List of Essential Medicines and/or the WHO Model List of Essential Medicines for Children include: abacavir+lamivudine fixed-dose combination, darunavir and new formulations of efavirenz and nevirapine for treatment of HIV; valganciclovir for treatment of cytomegalovirus retinitis; desmopressin for certain rare bleeding disorders; enoxaparin for prophylaxis and treatment of venous thromboembolism and treatment of acute coronary syndromes; clopidogrel for acute coronary syndromes and following percutaneous coronary intervention; three new contraceptive formulations and alcohol-based hand rub. The recommended indications for misoprostol tablets were extended to include treatment of post-partum haemorrhage. Atenolol was reinstated as an antihypertensive treatment alternative to bisoprolol.

8. The Committee did not recommend addition to the WHO Model List of Essential Medicines of ranibizumab for the treatment of neovascular eye diseases. Independent evidence supports equivalent efficacy and safety of bevacizumab and ranibizumab for these indications. Ranibizumab is considerably more expensive than off-label bevacizumab (currently included on the WHO Model List of Essential Medicines) and would not offer any additional clinical benefit. The Committee considered

¹ See the guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection, available at: http://apps.who.int/iris/bitstream/10665/154590/1/9789241549059_eng.pdf?ua=1 (accessed 13 October 2015).

that inclusion only of the less expensive bevacizumab on the WHO Model List of Essential Medicines might serve to facilitate its use (albeit off-label) for this indication.

9. The Committee did not recommend addition to the WHO Model List of Essential Medicines of novel oral anticoagulants for stroke prevention in patients with atrial fibrillation, as there was no relevant clinical advantage demonstrated over warfarin in patients established and stable within the therapeutic range with warfarin therapy. The Committee also noted that, unlike for bleeds related to warfarin, there are currently no specific antidotes for reversing the effects of novel oral anticoagulants in case of emergencies.

10. The Committee did not recommend addition to the WHO Model List of Essential Medicines of “polypill” fixed-dose combinations for secondary prevention of cardiovascular disease on the basis of limited evidence of relevant differences in clinical outcomes and concerns regarding adverse events, and the management of dose titration or the cessation of individual medicines.

11. The Committee did not recommend addition to the WHO Model List of Essential Medicines of dopamine agonists for the treatment of Parkinson’s disease, as there was insufficient evidence to demonstrate a clinically relevant advantage over the existing medicines included in the WHO Model List of Essential Medicines.

Significance for public health policies

12. In the decision-making process for the review of cancer medicines, the Committee gave particular consideration to the magnitude of clinical benefit; however, there was no specific endorsement of a threshold for benefit. This remains an area requiring further work for WHO. The Expert Committee acknowledged the importance of establishing strategies and actions to make highly priced cancer medicines more affordable, taking into account their public health relevance.

13. The decision made by the Expert Committee, to include all proposed direct-acting antiviral medicines, aims at promoting competition among available alternatives. Since new treatment regimens for hepatitis C are still being developed, an independent clinical research agenda to determine optimal combinations is important from a health system and public health perspective. The suitability of treatments in paediatric patients should also be investigated.

14. With respect to the listing of medicines for off-label indications, the Committee based its decisions on available clinical evidence, and noted that labelling is the responsibility of national regulatory authorities and could also be a commercial decision of pharmaceutical manufacturers.

15. Despite their high price, several new medicines were included on the WHO Model List of Essential Medicines. These decisions were made on the basis of their public health relevance and the evidence available, showing that these medicines were both highly effective and safe. It is expected that their addition to the WHO Model List of Essential Medicines will require global and country strategies, and interventions for reducing prices and facilitating their access.

Implications for the Organization’s programmes

16. The continued updating of the Model Lists provides WHO, other United Nations agencies with relevant programmes and Member States with a robust tool for the selection, use, procurement and reimbursement of medicines and related supplies.

17. The establishment of ad hoc working groups that meet between Expert Committee meetings is considered an efficient way to conduct comprehensive reviews of important medicines classes (such as for cancers), and to facilitate the work of the Expert Committee.

18. The methods for the assessment of medicines proposed for addition to the WHO Model List of Essential Medicines, and the use of reliable evidence to guide the decision-making process, are promoted in countries as a model for achieving optimal selection and use of medicines.

19. The recent updates of the WHO Model List of Essential Medicines, in areas such as cancer, hepatitis C and tuberculosis, suggest the importance of both the new, effective and safe medicines for treating such conditions, and the contribution of the WHO Model List of Essential Medicines to WHO global programmes in these priority areas. The Committee recommended that, in addition to its leading role for the selection and use of effective and safe medicines, WHO engages with its Member States and its partners in order to develop strategies to ensure better affordability and improved access to highly priced essential medicines.

ACTION BY THE EXECUTIVE BOARD

20. The Board is invited to note the report.

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