Proposal to the WHO Expert Committee on Selection of Medicines

**A request to place medicines for palliative care in a separate highest level section of the Model List of Essential Medicines for Children**

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1. **Summary statement**

   This proposal requests that the WHO Expert Committee on Selection of Medicines changes the 3rd WHO Model List of Essential Medicines for Children dated March 2011 (hereafter referred to as the “EMLc”)\(^1\) so that medicines for palliative care are located in a separate highest-level section of the list. Such a repositioning of the list will help to end the lack of access, especially in low- and middle-income countries, to essential medicines for palliative care and will avoid unequal and impaired access for patients with a similar health status in other care settings.

   The recently published *WHO Guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illnesses*\(^2\) highlight the need for changes to the EMLc and so do the WHO policy guidelines *Ensuring Balance in National Policies on Controlled Substances, Accessibility and Availability of Controlled Medicines*\(^3\). Some of the changes needed relate to individual preparations and will be addressed in separate applications to the Expert Committee. This application relates to the structure of the list, which needs improvement in order to advance availability and accessibility of opioid analgesics and of palliative care medicines.

   Currently the WHO has no analogue guideline for persisting pain in adults, but it is obvious that the arguments presented in this application equally apply to the EML for adults\(^4\), and the Committee may therefore want to draw similar conclusions for the latter.
Because this is not an application for the addition of specific medicines to the EMLc, the standard format for applications did not seem suitable; therefore, this application has a format deviating from the format provided by the Committee.

2. **Focal point in WHO**

Willem Scholten, WHO Team Leader, Access to Controlled Medicines, Medicines Access and Rational Use, Department of Essential medicines and Health Products, World Health Organization.

Correspondence after 31 October 2012: wk.scholten@bluewin.ch.

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

The following organizations were requested to comment on the draft application and to support the final application:

a. European Association of IASP Chapters, EFIC, Christel Geevels, Executive Secretary (secretary@efic.org) (Please see letter of support)

b. Human Rights Watch, Mr Diederik Lohman (lohmand@hrw.org) (Please see letter of support)

c. International Association for Hospice and Palliative Care, Executive. Director, Dr Liliana de Lima (lidelima@iahpc.com) (Please see letter of support)

d. International Association for the Study of Pain, Dr Kathy Kreiter, Executive Director, (Kreiter@iasp-pain.org) (IASP Special Interest Group on Pain in Childhood, contact: Dr Gary Walco, gary.walco@seattlechildrens.org) (Please see letter of support)

e. International Children’s Palliative Care Network, Dr Joan Marston, Executive Director (joan.icpcn@gmail.com) (Please see letter of support)

f. International Union Against Cancer (UICC), Ms Julie Torode, Deputy CEO (torode@uicc.org) (Please see letter of support)

g. World Institute of Pain, Dianne Willard, Executive Officer, (dianne.willard@worldinstituteofpain.org) (Please see letter of support)

h. World Health Organization, Cancer Control Programme, Department of Chronic Diseases Prevention and Management, Dr Cecilia Sepulveda Bermedo, Senior Adviser (sepulvedac@who.int) (No reaction received)

i. World Health Organization, Department of Child and Adolescent Health, Dr Lulu Muhe, Technical Officer (muhel@who.int) (Please see e-mail of support)

j. World Wide Palliative Care Alliance, Dr Stephen R. Connor Ph. D., Senior Fellow (sconnor@thewpca.org) (Please see letter of support)

4. **Current status of palliative care on the EMLc**

Medicines for palliative care are currently included in the EMLc as Subsection 8.4 in Section 8, titled: *Antineoplastic, Immunosuppressives and Medicines used in Palliative Care*. Some of the medicines in Subsection 8.4 are also included in
other sections of the EMLc, according to their therapeutic use, e.g. opioid analgesics are listed in Section 2.2. Other medicines are exclusively listed in Subsection 8.4.

5. Public-health rationale for this application

Introduction

From a public-health perspective, currently many patients are without access to essential medicines for pain and palliative care. WHO policies and international drug conventions require that countries make medicines controlled under these conventions readily available to those in need. Opioid analgesics like morphine are among these controlled medicines. Palliative care is promoted by WHO policies and is becoming more important as the burden of NCDs increases. Positioning of the medicines for palliative care on the Model List in a way that indicates secondary importance can negatively affect access. The optimal positioning of the palliative care list is therefore of the utmost importance.

Importance of improving access to opioid analgesics in global public health

It has been well documented that in most countries of the world, patients do not have adequate access to opioid analgesics. The various barriers are described in the World Medicines Report and in the WHO policy guidelines Ensuring Balance in National Policies on Controlled Substances, Accessibility and Availability of Controlled Medicines. Legal and policy barriers are important reasons why these medicines are not available in many countries. Seya et al. estimate that in 2006 only 464 million people had adequate access to opioid analgesics, and 4.7 billion people had virtually no access.

The World Health Assembly in its resolution 58.22 “On Cancer prevention and control” (2005), called on WHO to address access to opioid analgesics. Other international bodies such as the International Narcotics Control Board (e.g. in a special report on the availability of internationally controlled drugs) and the UN Commission on Narcotic Drugs, have called for greater access for patients to these medicines.

In addition, the International Association for the Study of Pain adopted the World Pain Declaration, the Union for International Cancer Control published the World Cancer Declaration and a consortium of 60 international and national organizations initiated by Pallium India launched the Morphine Manifesto. All these declarations call for adequate access to pain medicines and treatment of pain worldwide.

Importance of promoting palliative care in global public health

In recent years it has become clear that palliative care will become more and more important. This is most clear for cancer control strategies, but palliative care is also important to treat patients with HIV/AIDS, multiple and extensively drug resistant tuberculosis (M/XDR TB), severe congenital disease and many other conditions. In WHA resolution 58.22 “On Cancer prevention and control”, the Assembly called also on WHO to establish cost-effective standards that include palliative care. WHO published in 2006 the WHO guide for effective programmes for Cancer control: Knowledge into action. In this guide, consisting of a series of guidelines on various topics of cancer
control, it has been made clear that palliative care is an essential part of cancer control. WHO strongly promotes that countries include palliative care as a part of their health care systems.

A parallel development was that WHO added a section on medicines used in palliative care to the EMLc. This was done at the request of the International Association for Hospice and Palliative Care that initially organized a consensus meeting for the drafting of a list\textsuperscript{19,20}. From this consensus list, several medicines were included in the EMLc, but not all.

6. Disadvantages of current listing

Current listing is misleading

The purpose of the List is to be a guide for development of national and institutional essential medicine lists and treatment policies. The current placement of palliative care medicines together with antineoplastic and immunosuppressive medicines gives the impression that palliative care medicines are intended for cancer patients only and thereby validates laws and regulations in some countries that permit opioid analgesics to be prescribed only for late-stage cancer patients.

Current listing lacks adequate guidance about indication

In Section 8.4, medicines are classified by the speciality of the health-care workers. There is no other section exclusively bringing together medicines for a specific type of care: the basic organizing principle used in the EMLc is to group medicines according to their general effect on the body by organ system (e.g. cardiovascular medicines, gastrointestinal medicines, dermatologic medicines) or by pharmacokinetic activity (e.g. anaesthetics, analgesics, anti-neoplastic medicines). This structure permits listing of sub-categories that identify specific indications. Because Medicines Used in Palliative Care currently is a subsection, it does not give indications for any medicines. For example, there is no sub-section on “medicines for nausea and vomiting” that would include ondansetron. This lack of specific indications will result in reduced access to the proper palliative medicines.

The exclusive listing of medicines in this section can lead to the denial of access for patients with an identical or similar health status as patients in palliative care and who equally qualify for these medicines, but who are treated by other specialities. Therefore, there should be a clear justification for exclusively listing any medicine in this (sub)section of the EMLc only. For instance, for opioid analgesics the WHO Guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illnesses\textsuperscript{2} point out that the clinically correct manner of treating pain does not depend on etiology but on the pathophysiological mechanism of the pain.\textsuperscript{21} Therefore, pain patients with a similar type and level of pain should be treated equally, regardless of the type of service providing the treatment. The current differences between Section 8.4 and other sections related to pain treatment are therefore unjustified.
Another negative consequence of the current structure of the EMLc is that medicines listed in other sections of the EMLc do not appear in the section on palliative care (e.g. essential medicines listed as anti-neoplastics, anti-retrovirals and anti-tuberculosis medicines). This may cause the misunderstanding that patients in palliative care do not qualify for access to these other medicines, and policy makers may conclude that hospices and palliative care institutions do not need these medicines.

**Principle of Non-Discrimination**

Non-discrimination in health services is one of the core principles of the World Health Organization’s Constitution, as well as of the international legal regime. Regretfully, the current structure of the EMLc may unintentionally lead to violations of this principle, as health policy makers may erroneously conclude that palliative care medicines are intended for cancer patients only. This could lead to unjustifiable failure to treat non-cancer patients with medicines listed in the section—especially controlled medicines—despite a medical need. United Nations and WHO policies indicate clearly that access to controlled substances should not be restricted to certain groups only.

Furthermore, in the case of pain treatment, not treating patients for their pain by neglect, is a violation of the right to the highest attainable standards of health and wellbeing as illustrated in the memorandum on the right to health and access to medicines for pain and palliative care.\(^2\)

WHO policy as enunciated in its policy guidelines *Ensuring balance in national policies on controlled substances*\(^3\) is found in Guideline 7. It states:

“**Guideline 7: Governments should include the availability and accessibility of controlled medicines for all relevant medical uses in their national pharmaceutical policy plans. They should also include the relevant controlled medicines and relevant services in specific national disease control programmes and other public health policies.**

**Planning for availability through the formulation of policy plans is essential for defining and realizing the health policy objectives of a country. It is also essential for the realization of a country’s international obligations with respect to the international drug conventions and human rights conventions.**

The objective to make controlled medicines available and accessible for all medical and scientific purposes in the national medicines policy plan should be stipulated at the outset. Policies should also address availability of controlled medicines for scientific purposes, as research with these substances may be necessary for such use.

**Only after establishing this general policy should specific policy plans be developed for individual diseases. As a minimum, countries should ensure that availability and accessibility of controlled medicines is addressed for the following disease-specific policies:**... [the table that follows includes cancer
control, HIV/AIDS, mental health including substance abuse or other disorders, and maternal health."

Thus clearly, medicines for palliative care are not only for cancer patients, but also for HIV/AIDS patients, M/XDR TB, severe congenital disease and other conditions. The Guidelines clearly recommend that countries adopt a general policy on accessibility of controlled medicines before developing policies for specific conditions. The current EMLc is organized the opposite way. It only lists palliative care medicines as related to cancer, without providing a general list of essential palliative care medicines for all conditions that require such health services. Thus, for patients with exactly the same pain, the structure of the essential medicines list may result in negligence of their pain, a result that cannot be justified medically nor under the Guidelines. This could constitute discrimination by health status, and thus a violation of international human rights norms.

Examples of countries where discrimination of pain patients occurs in practice

It is important to avoid introducing rights for certain groups that could be construed as withholding this right to other patient groups. Indeed in practice this is happening. For example in the Russian Federation and Japan, it is not allowed to prescribe strong opioid analgesics for patients other than terminal cancer patients. In the State of Kerala, India, after the introduction of a state policy to make strong opioids available to cancer patients, access was denied to patients suffering severe pain from HIV, because the policy did not state such use. Even recently in Kerala, a non-cancer patient in pain was requested to present a biopsy report.

7. Technical corrections for inconsistencies

If the Expert Committee decides to reorganize the list, this may be an opportune time to address the following items for technical correction:

Updating to new guidelines

There is a question as to whether the analgesics on the list are adequate to meet the needs of the growing demand that will result from NCDs. The EML and EMLc should be aligned with pharmacological treatment guidelines for adults and children. (Based on the new persisting pediatric pain guidelines, separate preparation-specific applications for the EMLc will be submitted)

Lack of listing the indication or intended use in the palliative care list

The intended use of the medicines in the palliative care section is not specified.

Unjustified differences between the general part and the palliative care list

- Some medicines in the palliative care subsection are not listed in the general part

In principle every preparation on the palliative care list should also be on the main list, unless there is a sound justification why patients with a similar symptom should not receive the treatment outside a palliative care setting. There are 13 medicines in the palliative care list but only 7 appear elsewhere. Examples are the laxatives docusate sodium and lactulose.
Some medicines needed in palliative care not listed in the specific PC section

The existence of a section with a limited number of medicines for palliative care can easily lead to misinterpretation. There is a risk that policy makers will withhold medicines not on the list to palliative care services and hospices (e.g. essential medicines listed as anti-neoplastics, anti-retrovirals and anti-tuberculosis medicines). Being admitted to palliative care does not necessarily mean that the treatment of the patient’s specific disease should be interrupted. Antiretrovirals, antituberculosis medicines and many other treatments should be continued and in many cases the treatment can be provided by the palliative care service.

Examples of the problems mentioned above:
Issues with laxatives

Together with any opioid administration, laxatives should be given concurrently. This is a "mandatory" treatment approach that goes back for decades. It was already mentioned in the WHO guidelines Cancer Pain Relief in 1986. The WHO guidelines Cancer Pain Relief in Children (p 40) mention: “constipation is an expected side-effect of opioid administration and it does not resolve. It can be avoided by giving a suitable diet (increased fluids and bulk) and by the daily administration of stool softeners, such as docusate, combined with a stimulant, such as senna.” The WHO guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illnesses, mention “Long-term opioid use is usually associated with constipation and patients should also receive a combination of a stimulant laxative and a stool softener prophylactically.” (p 41) Therefore, laxatives are essential medicines in any treatment with opioid analgesics, regardless whether the patient is treated in a palliative care setting or in any other setting. However, in the EMLc, laxatives are only mentioned in Section 8.4 (Palliative Care), which section lists docusate sodium, lactulose and senna. As a result, patients treated with opioids in a different setting than a palliative care setting may not receive the treatment they need.

Issues with morphine

The EMLc lists morphine for palliative care. Although not mentioned in the EMLc, the listing of morphine in Section 8.4 is obviously intended for the treatment of pain and not as a pre-operative agent. It is not clear that oral morphine solution is also intended for the palliation of dyspnoea.

Issues with ibuprofen and morphine

The WHO guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illnesses do not make any distinction between the treatment of pain in a palliative care setting or in another setting. However, several dosage forms and strengths are exclusively mentioned in Section 8.4 of the EMLc: ibuprofen tablet 600 mg, and morphine granules (modified release; to mix with water): 20 mg; 30 mg; 60 mg; 100 mg; and 200 mg. This range of granule capsules gives access to children who cannot swallow solid preparations and to children who can swallow but who have a need for
higher strengths, as the highest slow release tablet on the EMLc is only 60 mg. As a result, patients treated for pain with ibuprofen or morphine in a different setting than a palliative care setting may not receive the treatment they need.

The recent publication of the guidelines on persisting paediatric pain leads to the need for making the EMLc consistent with the new guidelines. There will be new dosage forms and new opioid analgesics. The additions need to be accurately added in the same manner to all parts that relate to pain control, both in the general part and the palliative care section in order not to create new inconsistencies. Based on the new persisting pediatric pain guidelines, several separate applications for the addition of preparations of opioid analgesics to the EMLc will be submitted.

8. Timeliness of this application

The Committee noted in its 2011 report that the WHO guidelines for palliative care are in need of update. The guidelines for Cancer pain relief and Palliative Care in Children have been replaced now by the new pediatric guidelines on persisting pain and WHO has issued numerous policy statements with reference to chronic and other specific diseases. This proposal offers an opportunity to bring the EMLc in alignment with WHO treatment and policy guidelines and with human rights practice.

This request makes no suggestion on the particular content of the palliative care part of the EMLc; the precise content of the list is not what this application is about. Rather this application refers to the headings under which these medicines are grouped and the system in use. It is hoped this application may assist the Committee in organizing medicines for pain and palliative care in an up-to-date, user friendly manner. All that is needed is to group all medicines for palliative care under one highest-level section with appropriate subsections and as deletions and additions are made these changes would be included in the new section and subsequent subsections the Committee deems appropriate. Unlike for other sections, the section title does not indicate the use of the medicines in the palliative care section and therefore such an indication needs to be added. By creating a highest-level section for medicines for palliative care, the Committee will highlight the importance of palliative care and avoid the impression that other patients are not entitled to be relieved of avoidable.

9. Application/Request

Today, palliative care is not (yet) integrated in the health care system in many countries and does not exist in other countries. Given the great importance of palliative care in current global public health, a special position in the EMLc is justified, as already explained above under *Importance of promoting palliative care in global public health*. Such a positioning of the palliative care section should not lead to discriminate against any patients with similar or identical medical needs for the medicines listed on this list and it should also not impede access to other medicines listed for patients admitted to palliative care.

*We request* that an appropriate separate highest-level section is created for the content of Section 8.4. A short introduction in the explanatory notes of the EMLc will be
needed to clearly define the meaning of this highest-level section. An example of how such an introduction may look like is presented in Annex 1.

By the creation of a separate highest-level section on medicines for palliative care, the full impact of WHO policy can be made clear, and the availability of these medicines improved. Highlighting such medicines in this manner will provide an up-to-date presentation of medicines for palliative care reflecting best medical practices, human rights, and WHO policies. By establishing a new highest-level section in the EMLc, and possibly also in the EML, the utility of the EML(c) to serve as a guide for the development of national and institutional essential medicine lists will be strengthened and provide robust guidance to national medicines policies.

10. Acknowledgements

Dr Willem Scholten has been assisted by Michele Forzley, JD, MPH, Professor of Global Public Health Law Widener School of Law, USA when drafting this application. Mr Diederik Lohman (Human Rights Watch) and Dr Erik Krakauer (Harvard Medical School; on behalf of UICC) reviewed the manuscript.

Additional Reading


- Rajagopal M. Disease, dignity and palliative care. Indian J Palliat Care. 2010 May;16(2):59-60.


Annex 1
Proposed text for the Explanatory Notes (to be inserted after the 2nd paragraph on the complementary list):

The **palliative care list** (Section [X]) contains those medicines that are essential for palliative care. With the increasing burden of non-communicable diseases, the importance of providing adequate palliative care services is rising around the world. This list highlights those medicines that are always needed for palliative care. In addition, palliative care services may need additional essential medicines from other sections to treat the specific diseases of the patients cared for by palliative care services.

References

19 The International Association for Hospice and Palliative Care list of Essential Medicines for Palliative Care (background document), accessible at:
20 The International Association for Hospice and Palliative Care list of Essential Medicines for Palliative Care (list), accessible at: http://www.hospicecare.com/resources/pdf-docs/iahpc-essential-meds-en.pdf