World Health Organization

ACCESS TO MEDICINES AND HEALTH PRODUCTS DIVISION

Scoping Document

WHO Guideline on ensuring balanced national policies for access and safe use of controlled medicines

Scope and key questions

I. Background

Access to medicines is a key component of the attainment of universal health coverage, which is central to the health-related Sustainable Development Goal.[1] Controlled medicines include narcotics, such as opioids, and psychotropic substances that have an effect on the central nervous system, such as benzodiazepines, barbiturates and amphetamines. WHO recognises that these medicines are needed as pre- and post-operative medication, for sedation, for the management of both acute and chronic pain, for palliative care, as anticonvulsants (anti-epileptics), for the management of anxiety disorders, and for the management of substance use disorders, including as opioid agonist therapies. Because these medicines may be associated with risks of non-medical use, misuse and diversion to illicit supply chains, they are subject to international control according to the 1961 Single Convention on Narcotic Drugs and the 1971 Convention on Psychotropic Substances. The guideline is proposed to cover all controlled medicines containing substances listed in Schedules I, II, III and IV of the 1961 Single Convention and Schedules I, II, III and IV of the 1971 Convention which have identified or emergent medical applications.

The preambles to both the 1961 and 1971 Conventions recognise that psychoactive substances with medical use are necessary for the provision of healthcare. The 1961 Single Convention recognises that “the medical use of narcotic drugs continues to be indispensable for the relief of pain and suffering and that adequate provision must be made to ensure the availability of narcotic drugs for such purposes”. The 1971 Convention recognises that “the use of psychotropic substances for medical and scientific purposes is indispensable and that their availability for such purposes should not be unduly restricted”.

The need for a balanced approach is implicit in the Conventions themselves. For example, The Conventions require countries to limit exclusively to medical and scientific purposes the production, manufacture, export, import, distribution of, trade in, use and possession of drugs, to allow medical use only on medical prescription, and to take measures to prevent diversion for non-medical use. The 1961 Convention also requires countries to provide estimates of annual consumption for medical and scientific purposes to the International Narcotics Control Board (INCB).

The need for a balanced approach was noted in the United Nations General Assembly Special Session Resolution in 2016.[2] The need to ensure access to controlled medicines while preventing their diversion and misuse has been endorsed by Member States in a number of World Health Assembly Resolutions such as those on palliative care medicines (WHA 67.19), on surgical care and anaesthesia (WHA 68.15) and on epilepsy (WHA 68.20).[3]

In line with its mandate for monitoring countries compliance with the Conventions, the INCB issues regular reports on the extent of access to controlled medicines.[4] The most recent summary of the global situation noted persistent disparities in consumption, which refers to medical and scientific use, as reported to the INCB:[5]

- "Recent data on the availability for consumption of opioid analgesics for medical use show that, despite global increases, global disparity and imbalance remain evident."
- "The availability for consumption of some essential psychotropic substances (diazepam, midazolam, lorazepam and phenobarbital) has declined or has remained stable in the majority of countries for which data on the consumption of psychotropic substances was provided to INCB, despite an increasing number of people living with anxiety disorders and epilepsy."

The 2011 WHO guidance document *"Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines"* was developed to assist policy makers as well as programme managers and experts in countries in the formulation and implementation of balanced policies that ensure access to and safe use of controlled medicines while preventing their diversion, misuse and harm to health. This guideline was also meant to be used in emergency situations where national regulatory authority and supply chain do not function efficiently or have collapsed. Model guidelines were issued by WHO in 1996 to assist national authorities in applying simplified export-import control measures in emergencies.[6]

In June 2019, WHO announced that it was discontinuing two guidelines ("*Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines*" issued in 2011, and "*WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses*" issued in 2012) and that they would be revised "in light of new scientific evidence that has emerged since the time of their publication"[7] and that the experts involved in their revision would comply with WHO's new policy for the management of conflicts of interest that had been in place since 2014 . WHO emphasised, however, that it "remains fully committed to ensuring that people suffering severe pain have access to effective pain relief medication, including opioids". WHO expressed concern "that there is very low access to medication for moderate and severe pain, particularly in low and middle-income countries." Nonetheless, WHO also recognised that "the need for access to pain relief must be balanced with concerns about the harm arising from the misuse of medications prescribed for the management of pain, including opioids."

This document describes the scope of a fundamental and thorough revision of the 2011 guideline "*Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines*", in accordance with WHO guidance on the development of evidence-based guidelines.[8]

II. Review of the latest evidence

A: Access to and safe use of controlled medicines

The global burden of health-related suffering from serious life-threatening and life-limiting illnesses is expected to almost double by 2060, requiring far greater access to appropriate palliative care, including access to controlled medicines.[9] Controlled medicines are needed to treat a number of the non-fatal causes of years lived with disability that are part of a growing global burden.[10] A number of

medicines containing controlled substances, listed in the various Schedules to the United Nations Conventions that provide an international framework for appropriate control and access, are included in the WHO Model List of Essential Medicines.[11,12]

Drawing on INCB data, the Lancet Commission on Palliative Care and Pain Relief has noted that "people living in low-income and middle-income countries (LMICs) have little or no access to pain relief or palliative care".[13] The Commission therefore recommended that a "well-functioning and balanced global system must both prevent non-medical use and misuse of medicines and ensure effective access to essential medicines for palliative care, including opioids for pain relief." Likewise, the Johns Hopkins–Lancet Commission on Drug Policy and Health emphasised the need for access to controlled medicines.[14] Also based on INCB data, it was reported that, although the use of opioid analgesics has increased at a global level, it remains low in Africa, Asia, Central America, the Caribbean, South America, and eastern and south eastern Europe.[15]

In some parts of the world, and within particular patient populations, there are concerns with overuse of controlled medicines, including opioids and benzodiazepines.[16,17] Increased consumption of these medicines, however, has not always been associated with negative health outcomes such as overdose-related deaths.[18] For example, increased utilisation of opioids, in countries such as Germany, Austria, Belgium, Denmark and the Netherlands, has not always been associated with negative health outcomes, whereas increased use has been associated with increased overdose-related deaths in the United States, Canada, Sweden, Norway, Ireland, and parts of the United Kingdom. The OECD Health Policy Studies report noted that "an appropriate use and regulatory environment for prescription opioids can be compatible with having a higher availability of these drugs for medical use".

B: Factors influencing access to and use of controlled medicines positively and negatively

Factors influencing access to and use of controlled medicines, whether positively (by addressing barriers) or negatively (resulting in increased non-medicinal, inappropriate use or diversion to illicit channels) operate at the level of the entire health system.

Some of these factors can be seen as common to all categories of medicines and involve factors related to healthcare financing, service delivery, medicine pricing, medicine selection and procurement, prescribing and dispensing practices, information systems and accountability mechanisms.[19] The Lancet Commission on Essential Medicines Policies provided a review of such factors and made specific recommendations on interventions that can improve access and appropriate use of medicines.[20] The WHO Roadmap for Access 2019-2023 addresses many of the systemic barriers to access to medicines and vaccines.[21]

In addition, specific barriers apply to controlled medicines compared to other/regular medicines, such as higher levels of control for the supply, prescribing and dispensing; caution/fear in prescribing and dispensing these substances with potential for misuse and dependence as well as for the risk of being punished in case of diversion.

In the 2011 version, and in the literature, attention has been focused on factors that inhibit access to controlled medicines in central and eastern European countries, and in particular on legal and regulatory barriers.[22,23,24,25,26,27] Far less is documented about how these identified factors are hampering access in other settings, both in high-income and low-and middle-income countries. Earlier survey data on formulary access and regulatory barriers have been reported for various

regions by the Global Opioid Policy Initiative (GOPI).[28,29,30,31,32,33] Differences in national evidence-based guidelines, prescribing culture, regulatory policies and costs were identified as some of the factors that could explain differences in opioid use in The Netherlands and Australia.[34] A positive association between the intensity of opioid marketing and overdose mortality has been demonstrated in the United States, where such marketing practices are the subject of intense litigation.[35] In response to the opioid crisis in the United States, various authorities have issued new clinical guidelines on pain management.[36,37] More recently, data from low-income countries and relief organisations have identified particular barriers to access to controlled medicines, including weaknesses in procurement processes, administrative complications specific to controlled medicines (such as when annual national estimates are exceeded, or delays in obtaining import authorisations).[38]

WHO has updated its guidelines on the management of cancer pain in adults and adolescents,[39] and has commenced the process of revising its guidelines on the management of persisting pain in children.

III. Analytical framework or logic model

The scope of the guideline and the overarching research questions will be agreed upon by the WHO Guideline Steering Group and the Guideline Development Group, and subjected to external comment prior to finalisation. Searches will be tailored to the research question and will not be restricted to those indexed in bibliographic databases. The scope of the searches is likely to include evidence that may not be published in peer-reviewed publications (i.e. grey literature). Where possible, evidence summaries will be created using the GRADE system to provide a clear description of benefits and harms and a rating of the certainty of the evidence on an outcome-by-outcome basis. The literature reviews carried out so far have shown that the available evidence includes a number of qualitative studies, for example studies that have used interviews to document the barriers to accessing controlled opioids and proposals for managing these barriers. Qualitative evidence synthesis to inform specific recommendations within the updated guidelines will be done using the CERQual approach.[40,41] The WHO-INTEGRATE evidence-to-decision framework will be relied upon in this area of complex policy.[42]

IV: Key questions

The guideline is intended to assist Member States in developing and implementing balanced national policies for access and safe use of controlled medicines. The controlled medicines included will be those containing substances listed in Schedules I, II, III and IV of the 1961 Single Convention and Schedules I, II, III and IV of the 1971 Convention which have identified or emergent medical applications. The scope will also consider the role of national control measures and the placement of medicines therein.

The following issues will be out of the scope of the guideline: psychosocial interventions, non-psychotropic or non-narcotic medicines, and non-pharmacological strategies for managing acute or chronic pain.

The following background questions will be addressed:

1) What are controlled medicines; why and how are they handled differently than other medicines at global and country level?
2) What are the differences and trends between countries and over time in accessing and using, including misusing, controlled medicines?
3) What are the impacts of the lack of access to controlled medicines on the health of populations?
4) What are the impacts associated with medical overuse and misuse of controlled medicines on the health of populations?
5) What are the most important pharmacological classes of controlled medicines; which controlled medicines (as defined in the scope) are included in the WHO Model List of Essential Medicines and in national EMLs? What are the classes that are the most harmful and what type of harm do they cause?
6) Which indications for controlled medicines (as defined in the scope) are listed in current WHO clinical practice guidelines, and which indications require systematic review and the development of clinical practice guidelines?[43]

The key research questions, which will inform the guideline content will be:

1) What are the main barriers to access to, and appropriate use of controlled medicines:
    a. at international, national, and local levels; and
    b. what are the consequences of these barriers?
2) What are the main factors that have been demonstrated to contribute to medical overuse and misuse of controlled medicines?
3) What are the policies or interventions that have been successfully implemented for improving access to controlled medicines, including:
    a. international regulations;
    b. national regulations;
    c. educational interventions;
    d. clinical practice guidelines; and
    e. prescription monitoring systems?
4) What are the policies or interventions that have been successfully implemented for improving the safe use of controlled medicines, including:
    a. minimising diversion;
    b. improving appropriate use of controlled medicines, limiting overuse and misuse; and
    c. minimizing the risk of harm?

References and notes

[1] SDG3 is “Ensure healthy lives and promote well-being for all at all ages”. Target 3.8 is “Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.” (https://www.un.org/sustainabledevelopment/health/)

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2015. Resolution WHA68.20 Global burden of epilepsy and the need for coordinated action at the country level to address its health, social and public knowledge implications. Geneva, 2015.

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