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# THE PRACTICES AND CONTEXT OF PHARMACOTHERAPY OF OPIOID DEPENDENCE IN CENTRAL AND EASTERN EUROPE

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## Abstract

This publication presents an overview of the practices and the context of pharmacotherapy of opioid dependence in selected countries in Central and Eastern Europe and the Newly Independent States. Based on reports provided by professionals involved in the treatment of opioid dependence in these regions, this document describes the current situation with opioid use in Central and Eastern Europe and the Newly Independent States, the role of pharmacological treatment of opioid dependence in public health responses to opioid dependence and associated health consequences in the region, as well as priorities and recommendations for development of treatment services and responses. The publication contains key informant reports from Belarus, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Kyrgyzstan, Hungary, Latvia, Lithuania, Poland, Russian Federation, Slovakia and Ukraine. This publication has been prepared in conjunction with another WHO document that is focused on pharmacotherapy of opioid dependence in selected countries of South-East Asia and Western Pacific regions and both documents are a part of the global activity on treatment of opioid dependence which is currently being implemented by the WHO Department of Mental Health and Substance Abuse.

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# PART ONE

## Pharmacotherapy of Opioid Dependence in Central and Eastern Europe

### INTRODUCTION

The explosive epidemic of HIV/AIDS among injection drug users (IDUs) in Eastern Europe coupled with the epidemic of opioid use necessitate the implementation of effective interventions. There is substantial evidence for the effectiveness of drug dependence treatment in HIV/AIDS prevention and care. Agonist pharmacotherapy of opioid dependence has proven to be effective in HIV/AIDS prevention by attracting IDUs into various drug treatment programmes, and thus reducing participation in risk behaviours and the subsequent health and social consequences of drug dependence. In spite of the rapidly evolving HIV epidemic among injection opioid users, access to effective pharmacological treatment for opioid dependence in this region is very limited. Lack of research activity on the effectiveness of pharmacological treatment of opioid dependence in certain cultural contexts, and in the framework of particular treatment systems, hamper further development of such programmes. In response to the need for a review of current treatment practices in the region and to establish a scientific basis for their development, the WHO Department of Mental Health and Substance Abuse, in consultation with the WHO Regional Office for Europe, convened a meeting of experts from selected countries of Central and Eastern Europe (CEE). This meeting took place in Ljubljana, Slovenia in September 2001.

The key objectives of the meeting were as follows:

- To review the role and place of pharmacotherapy in the management of opioid dependence in the region.
- To review currently available programmes of pharmacological treatment of opioid dependence and their legal, professional and institutional context in CEE countries.
- To identify needs and priorities for further development of pharmacological treatment of opioid dependence in this region, with a particular focus on opioid agonist pharmacotherapy in the countries with rapidly evolving epidemics of HIV/AIDS among drug users.
- To explore the possibility of establishing a research network incorporating a WHO multi-site evaluation study of pharmacological treatment of opioid dependence in this region.

The aim of this publication, based largely on the results of the WHO meeting in Ljubljana, is to compare the practices and context of pharmacological treatment of opioid dependence across Central and Eastern Europe, in the general framework of pharmacotherapy of opioid dependence. The overview on the implementation of substitution therapy in the region in Part One of this publication represents the situation in the year 2003 for the countries represented at the meeting in Ljubljana.

## RANGE OF PHARMACOLOGICAL APPROACHES TO OPIOID DEPENDENCE•

The two primary pharmacological treatment approaches used in managing opioid dependence are detoxification methods (with or without subsequent relapse prevention using naltrexone) and substitution maintenance therapy using synthetic opioids such as methadone and buprenorphine. Substitution maintenance therapy, when administered appropriately, can reduce the spread of infectious diseases, such as HIV/AIDS and hepatitis, lower consumption of illegal drugs, reduce rates of criminality and prostitution, increase chances of psychosocial rehabilitation and employment, and retain patients in treatment for longer periods of time.

A number of different opioid agonists are used in substitution pharmacotherapy, including methadone, levo-alpha acetyl methadol (LAAM), slow-release morphine, and buprenorphine (Table 1). Findings have consistently demonstrated significant benefits associated with both methadone maintenance and, more recently, buprenorphine maintenance treatment. Several recent studies also report that slow-release morphine is as efficacious as methadone, and the use of a sublingual buprenorphine/naloxone combination tablet (dosing ratio of buprenorphine:naloxone – 2 mg:0.5 mg) in opioid maintenance therapy was well-accepted and tolerated by patients.

*Table 1. Types of synthetic opioids used in substitution therapy of opioid dependence*

| *Name / Type* | *Opioid-Effect* | *Peak* | *Duration of effect* | *Half-Life* |
|---|---|---|---|---|
| **Methadone**<br>• **μ opioid receptor agonist**<br>• **Oral administration** | > 40 minutes | 4 hours | 36 hours | 15-22 hours |
| **Slow-release (sustained) morphine**<br>• **μ opioid receptor agonist**<br>• **Oral administration**<br>• **Good bioavailability**<br>• **Controlled slow-release system** | > 60 minutes | 8-9 hours | 24 hours | 3-4 hours |
| **Levo-alpha-acetyl-methadol (LAAM)**<br>• **μ opioid receptor agonist**<br>• **Oral administration**<br>• **Sufficient oral bioavailability** | > 90 minutes | 4 hours | 72 hours | 48-72 hours |
| **Buprenorphine**<br>• **Partial μ-agonist/κ-antagonist**<br>• **Sublingual administration**<br>• **Sufficient sublingual bioavailability** | 20 minutes | 2 hours | 72 hours | 6-7 hours |

The goals of opioid agonist maintenance treatment, as mentioned earlier, are to lower levels of illicit drug use, to reduce risk behaviours concerning the transmission of blood borne viruses such as HIV and hepatitis B and C, to improve treatment retention, to reduce criminality and to improve overall well-being for the individual, their family and society as a whole. Currently there is moderately robust

• Based on presentation of Professor Gabriele Fischer (Austria)

evidence that this type of treatment can make a substantial contribution to these goals, but that such interventions required the development of training, monitoring, support and supervision to ensure good quality treatment.

## TREATMENT DOCUMENTATION AND EVALUATION RESEARCH•

Comprehensive documentation and evaluation are considered an essential component of treatment programme management. Documentation should involve the maintenance of records for each patient, including baseline data (prior to commencing treatment), projected treatment plan and rationale, and appropriate recording of adverse or other events throughout the treatment programme. Documentation of treatment may be classified according to three broad areas, which are outlined in Table 2. These records may serve as tools for internal controls, supervision, and evaluation purposes, and may be of importance should legal disputes arise.

*Table 2. Main areas of documentation*

| *Area of Documentation* | *Main Items* |
|---|---|
| **Client/Patient Description** | • Entry Data<br>– Demographic data<br>– Education, professional activities, income<br>– Family history, personal history, social network<br>– Substance use, patterns of use<br>– Past treatment experiences<br>– Convictions, legal status<br>• Data at discharge<br>– Type of discharge, follow-up treatment<br>– Changes from entry data |
| **Service Description** | • Structural Description<br>– Legal basis, funding, responsible organization<br>– Orientation, objectives, target population<br>– Therapeutic programme<br>– Rules, controls, sanctions<br>– Staff, training, supervision<br>– Networking, collaboration<br>• Annual Description<br>– Staff turnover<br>– Conceptual changes |
| **Treatment Description** | • Basic Items<br>– Diagnostic assessment<br>– Treatment plan<br>– Intervention records<br>– Consultations, medical/psychiatric care<br>• Special Aspects in Substitution Therapy<br>– Goals of substitution treatment<br>– Dosages, urine controls, take home possibility |

• Based on presentation by Professor Ambros Uchtenhagen (Switzerland)

The objectives of treatment evaluation are to improve service delivery, to assess the quality of treatment, to test therapeutic approaches and methods, to monitor treatment policy, and to assess the adequacy of the programme to meet treatment needs. According to these various objectives, there are different types of evaluation, focusing on:

- the results of treatment (outcome evaluation)
- aspects of service delivery and programme structure, such as client and staff satisfaction (process evaluation)
- the capacity of the service to reach target groups and meet the needs of these individuals (utilisation evaluation, needs assessment)
- the relation of resources to outcome (economic evaluation, especially cost-effectiveness).

Treatment evaluation has rapidly developed in the last decade, on the basis of an increased interest in evidence-based treatment policy. The main trends include developing national documentation systems, systematic and comparative evaluation, improving economic evaluation and needs assessment, evaluating service quality and implementing quality management systems. Overall it is considered that good monitoring and evaluation may have a significant impact on policy and may support the further development of this approach to treatment.

## BACKGROUND AND CURRENT PRACTICES OF SUBSTITUTION THERAPIES IN WESTERN EUROPE

The number of opioid users in substitution treatment throughout Western Europe tripled between 1993 and 1999. This dramatic rise is considered to have largely been in response to the HIV epidemic emerging during this time. It is estimated that there were, by 1999, 300 000 opioid dependent individuals accessing substitution treatment, which was provided by a number of service delivery models, including general practitioners, dedicated treatment centres, “methadone buses”, and pharmacies. While substitution treatment was primarily with methadone, several alternatives became available with the introduction of buprenorphine, dihydrocodeine and slow-release morphine.

It was estimated that the number of inhabitants between the ages of 15 and 64 using heroin ranged from 2 (in Germany and Finland) to over 6 (in Italy and Luxembourg) per 1000. The problem of HIV among IDUs had been significantly contained in most countries through the use of an extensive network of treatment and prevention strategies. There continued to be variation between countries in the balance between maintenance and detoxification approaches. Some countries placed greater emphasis on detoxification, but the overall trend was towards greater use of maintenance as experience was gained in the use of opioid agonist pharmacotherapies. Over the past five years, general consensus has emerged in Western Europe regarding the role of substitution therapy as an essential component of treatment options available to opioid-dependent individuals.

There remained, however, considerable variation between countries in terms of treatment delivery and service structure. Some countries employed a combination of service delivery by general practitioners and dedicated treatment centres, while others either primarily used specialist treatment centres or