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THERAPEUTIC PRODUCTS DIRECTORATE GUIDELINES

THE USE OF OPIOIDS IN THE MANAGEMENT OF OPIOID DEPENDENCE

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1 BACKGROUND

Guidelines for the use of methadone in the treatment of narcotic dependence were prepared in 1971 by a joint committee of the Canadian Medical Association and Health and Welfare Canada. In 1988, an expert advisory committee was convened to review the guidelines; its report was published in April 1990 and comments were received from interested groups and individuals. The following guidelines are based on the committee's report, on the comments received, and on discussions with medical and pharmacy licensing authorities.

2 BASIC PRINCIPLES

The use of drugs in the treatment of opioid abuse and dependence requires careful consideration of many factors relating to the person being treated and to the nature and context of the treatment. Several treatment alternatives, including drug-free residential and out-patient therapies, must be explored prior to initiating a drug therapy such as methadone.

Pharmacotherapy may assist the opioid abuser in re-establishing life along more constructive lines by promoting rehabilitation, reducing health risks and costs to the community. Support services addressing the psychological, social, and physical health issues in an abuser's life must be available in order that he or she may achieve and maintain the goal of abstinence.

3 DEFINITIONS

These definitions are to be used in the context of this document.

Buprenorphine: a synthetic mixed opioid agonist-antagonist (morphine-like and naloxone-like actions) with good oral/sublingual absorption, reduced dependence liability and improved therapeutic index compared to morphine.

Detoxification: the progressive termination of opioid use **by a person who is not on a methadone program**. Detoxification must be completed within 180 days when using an opioid in decreasing doses (see section 4.3, Pharmacological management).

Dependence syndrome: a cluster of physiological, behavioural and cognitive phenomena in which the use of a drug or a class of drugs takes on a much higher priority than other previously valued behaviours. Dependence syndrome is characterized by the desire (often strong, sometimes overpowering) to take drugs (which may or may not have been medically prescribed).

Levo-alpha-acetylmethadol (LAAM): a long-acting methadone derivative.

Methadone: a synthetic opioid agonist (morphine-like actions) with good oral bio-availability, equipotency with morphine and long duration of action.

Methadone maintenance: the daily oral administration of methadone over a prolonged period as an oral substitute for heroin or other morphine-like drugs. Generally, the dosage is stable.

Methadone withdrawal: the gradual cessation of methadone maintenance.

Opiate: refers to naturally occurring opioids such as morphine and codeine.

Opioid: refers to all substances, both naturally occurring and synthetic, with morphine-like actions.

Opioid agonists: substances with morphine-like actions.

Opioid antagonists: substances which block the effects of morphine and other opioid agonists, and which can precipitate an abstinence syndrome in an opioid-dependent person.

Naloxone: an opioid antagonist which can precipitate an abstinence syndrome in an opioid-dependent person.

Naltrexone: a synthetic long-acting opioid antagonist with good oral bio-availability which blocks the effects of morphine and other opioid agonists.

Opioid agonist and antagonists: substances with morphine-like and naloxone-like actions.

Physiological dependence to opioids: a state where the regular administration of an opioid is required to avoid the onset of withdrawal symptoms and signs such as mydriasis, piloerection, vomiting, restlessness and rhinorrhea.

4 DETOXIFICATION

4.1 Introduction

In general, opioid detoxification is not life threatening and can often be accomplished safely with simple therapeutic support. Many opioid-dependent persons do not require detoxification with opioids. When specific opioids (see section 4.3, Pharmacological management) are used, detoxification must be completed within 180 days.

The treatment of a pregnant opioid-dependent person is an exception, addressed separately in section 7 of these guidelines (page 16).

4.2 Criteria for detoxification with drug therapy

a) Voluntary informed consent must be obtained.

b) A complete medical examination with emphasis on signs and symptoms of drug use and its complications must be performed.

c) Appropriate laboratory testing should be completed as clinically indicated (e.g. hepatitis B, HIV and pregnancy tests).

d) A psychosocial evaluation, including substance abuse history, should be undertaken and repeated as necessary.

e) A treatment plan should be established, outlining objectives, methods, conditions/expectations, and a progress monitoring system (e.g. urine testing).

4.3 Pharmacological management

Drugs to suppress withdrawal symptoms (such as clonidine) or, in specific circumstances, psychoactive agents, may be necessary in the pharmacological management of detoxification from opioids. Specific opioids **may only be used orally** for detoxification purposes.

These opioids are: methadone; codeine (for codeine dependence or where a short-acting opioid is required); pentazocine (for pentazocine dependence); propoxyphene (for propoxyphene dependence). Tincture of opium may be used in the treatment of an opioid-dependent neonate.

4.4 Urine drug testing

a) For assessment purposes, a minimum of one urine screen is required prior to or on admission to a detoxification program.

b) During detoxification, urine drug screening must be carried out no less than twice per month.

c) Urine should be tested for the presence of commonly abused drugs, as well as drugs known to be abused in the specific community.

4.5 Carry privileges

No carry privileges (take-home medication) are recommended during the detoxification stage except for weekends.

4.6 Formulation

Methadone should be dispensed in "Tang" or a similar preparation. (See methadone guidelines for pharmacists.)

Codeine, propoxyphene, and pentazocine **must be administered in oral form only.**

5 METHADONE MAINTENANCE

5.1 Introduction

Methadone maintenance involves the daily oral administration of methadone over a prolonged period as an oral substitute for heroin or other morphine-like drugs, for an individual dependent on heroin or other morphine-like drugs. Generally, the dosage is stable.

Drug-free out-patient therapies or detoxification should be offered to the patient prior to consideration of methadone maintenance.

Support services stressing psychosocial rehabilitation should be included as part of the total treatment plan for those prescribed a maintenance regimen of methadone.

The treatment of a pregnant opioid-dependent person is an exception, addressed separately in section 7 of these guidelines (page 16).

5.2 Objectives

The use of methadone in conjunction with treatments aimed at improving the mental, social and physical well-being of the opioid-dependent person, may result in:

- a reduction in the use of illicit drugs, especially opioids;

- a reduction in mortality rates among opioid users;

- a reduction in the spread of infections associated with needle-sharing such as AIDS, and/or

- improved psychosocial functioning and reduced criminal activity.

5.3 Criteria for admission to and monitoring of methadone maintenance

a) There should be evidence of extensive past opioid use and/or failed treatment attempts.

b) Voluntary informed consent must be obtained.

c) A complete medical examination must be performed with emphasis on signs and symptoms of drug use and its complications. Appropriate laboratory testing should be completed as clinically indicated (e.g. hepatitis B, HIV and pregnancy tests).

d) A psychosocial evaluation, including substance abuse history, should be undertaken and repeated as necessary.

e) A treatment plan must be established, outlining objectives, methods, conditions/expectations, and a progress monitoring system (e.g. urine testing).

f) A treatment contract must be established between the patient and treatment staff, outlining specific treatment expectations and consequences for expectations not fulfilled, e.g. a written document which details the consequences for positive* urine tests, such as loss of carry privileges.

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* Presence of unacceptable drugs and/or unexplained absence of methadone or its metabolites.

g) Where possible, the psychiatric co-morbidity should be monitored.

NOTE: Less stringent criteria apply when the opioid-dependent person is a) pregnant or b) has a life-threatening illness such as AIDS, or is HIV-positive and abusing opioids by injection.

5.4 Pharmacological management

In Canada, methadone is currently the only authorized opioid for long-term (more than 180 days) out-patient pharmacological treatment of opioid-dependent persons.

5.5 Urine drug testing

a) The urine collection process should be done at least twice per week during the first three months of treatment. In some instances, it may be advisable to supervise the urine collection.

b) A minimum of one urine drug screen is advised prior to initiation of methadone maintenance.

c) Urine drug screening must be carried out **no less than once per week at random for the first three months** of treatment and **at least twice per month at random thereafter.**

NOTE: Collecting urine samples on a more frequent basis than they are tested has economic advantages and can be a deterrent to illicit drug use. Not knowing which urine sample will be tested may serve as a deterrent.

d) Urine specimens should be screened for methadone and its metabolites, commonly abused drugs, and any other drugs known to be abused in the community.

e) It is expected that illicit drugs will not be used during treatment. Positive drug screening results (the presence of an unacceptable drug and/or the unexplained absence of methadone or its metabolites) should lead to the adjustment of the treatment plan. Repeated positive urine tests require **mandatory review of treatment** and/or consideration of withdrawal of methadone.

f) In cases where urine drug testing results indicate treatment noncompliance, it is advisable to confirm the initial screening procedure by a second method based on a different chemical principle.

5.6 Carry privileges

In view of the risks associated with methadone diversion, carry privileges must be limited. Appropriate dispensing facilities (such as pharmacies, hospitals, or treatment centres) should be used for dispensing and administering methadone **under supervision** on a daily basis, except for weekends.

a) In all instances, carry privileges must be limited to a maximum period of **four days** or a maximum total dosage of **400 mg**, whichever is least.

b) No carry privileges, except for weekends, will be granted to patients receiving more than 100 mg of methadone per day.

NOTE: Carry privileges should be used as a therapeutic tool which is granted as a reward for satisfactory adherence to the treatment contract and is revoked for non-compliance. These conditions should be clearly specified in the treatment contract drawn up at the initiation of treatment.

5.7 Dosage

Dosage should be individualized. The majority of patients can be treated at a dose lower than 80 mg/day. Doses of more than 100 mg/day must be justified and the reasons clearly documented on the patient's file. Consultation must have taken place with the medical licensing authority, and Health and Welfare Canada must be informed in writing.

5.8 Formulation

Methadone should be dispensed in "Tang" or a similar preparation. (See methadone guidelines for pharmacists.)

5.9 Administration

Except for carry privileges, daily doses of methadone must be ingested under the direct supervision of a health professional.

5.10 Substance abuse treatment centre

Methadone maintenance therapy should be initiated in a specialized multidisciplinary treatment centre offering, at a minimum, the following services to opioid-dependent persons:

- initial medical, psychiatric and psychosocial assessment;

- ongoing psychosocial treatment (e.g. counselling on an individual, group or family basis) and aftercare;

- ongoing medical management; and

- provision for appropriate methadone dispensing and administration, and urine drug testing according to the guidelines.

Treatment centres or acceptable alternatives must be approved by provincial medical licensing authorities.

5.11 Private practitioner

a) Patient case load: The number of patients a private practitioner may treat with methadone maintenance depends on the professional and therapeutic involvement each patient will require. The maximum case load will be determined by the medical licensing authority and/or Health and Welfare Canada.

b) Affiliations: The private practitioner must have established a formal affiliation with a substance abuse treatment centre, as defined above, to ensure a level of care consistent with the clinical management expectations outlined in this guideline.

c) Qualifications: The necessary qualifications for a private practitioner undertaking the treatment of opioid dependency are determined by the provincial medical licensing authority.

6 ADMINISTRATIVE PROCEDURES

Health and Welfare Canada is responsible for the administration of the methadone control program which consists of giving authorizations to prescribe methadone, monitoring and surveillance, and renewing or revoking authorizations. Methadone prescriptions are reviewed on a regular basis to ensure compliance with the guidelines and the conditions of authorization.

6.1 Authorizations

Authorization for prescribing methadone may be granted by Health and Welfare Canada after submission of acceptable protocol. The provincial medical licensing authority will also be consulted.

6.2 Compliance

Authorized practitioners must adhere to these guidelines, as well as to the conditions of authorization stipulated by Health and Welfare Canada. Non-compliance is sufficient cause for revocation or non-renewal of the authorization.

6.3 Reporting requirements

Authorized physicians must provide, on request, to the Minister of National Health and Welfare Canada information necessary to determine compliance with these guidelines.

6.4 Revocation

Non-compliance with these guidelines or the conditions of authorization constitutes grounds for the revocation of the authorization to prescribe methadone.

6.5 Authorization for other opioids

Physicians who wish to carry out detoxification using codeine, pentazocine, or propoxyphene must be authorized in the same manner as for methadone.

7 PREGNANCY

Opioid dependence in pregnancy is associated with an increased risk of fetal growth retardation, prematurity, neonatal withdrawal and Sudden Infant Death Syndrome. Withdrawal in pregnancy has been associated with fetal compromise and stillbirth. For these reasons, treatment of pregnant opioid-dependent women should be based on the principles outlined below.

Diagnosis should be based on a full history and a physical which should include an examination for evidence of recent drug use or withdrawal symptoms. A urine drug screen is necessary to evaluate the impact of multi-drug use on the fetus. The naloxone challenge test or detoxification are not recommended since both may compromise the fetus. Should detoxification be requested by the patient, it should only be performed on an in-patient basis under intensive fetal monitoring conditions. The patient should sign a release form indicating that detoxification is performed against medical advice.

For opioid-dependent pregnant women, methadone maintenance should be provided at the lowest accepted dose which prevents withdrawal symptoms (usually less than 80 mg/day). In later pregnancy, an increase by 10-20 mg and/or a divided dose may be required.

Treatment should be provided throughout pregnancy to protect the fetus and for a minimum of six months post-partum.

If the drug of dependence is codeine or pentazocine, out-patient or in-patient maintenance during pregnancy with the drug of dependence is recommended, with detoxification at approximately six months postpartum.

In labour, the optimal method of pain control is epidural anaesthesia.

It is recommended that no carry privileges be provided in pregnancy, except in emergencies **(a four-day supply or a maximum total dosage of 320 mg, whichever is least)**, or in situations where the patient has no easy access to a distribution centre and public health services cannot provide a daily supply.

At least two random urine drug screens per week should be performed throughout the treatment, and one on admission in labour.

Since women may be more receptive to lifestyle changes during pregnancy than at any other time in their life, it is essential that all efforts at psychosocial rehabilitation be made.

Special care is required for the infant born to a mother who has been dependent on methadone and/or other opioids. Newborn infants who have been exposed to opioids in utero within four weeks of delivery must be considered potentially dependent and closely observed for withdrawal symptoms for two weeks (irritability, seizures, poor feeding, diarrhoea and/or a high-pitched cry). Treatment should occur in a hospital equipped with specially trained staff and intensive care facilities, and may include detoxification with tincture of opium.

There may be a second withdrawal experience within the first six months. Clinical management should be similar to that for the first episode.

Breast-feeding may result in the passage of opioids or other substances into the breast milk. The evaluation of the risks and benefits of breast-feeding while on methadone should be done jointly by the physician and the patient.