



PREVENTION OF  
TRANSMISSION OF HIV AMONG DRUG USERS  
IN SAARC COUNTRIES

TD/RAS/03/H13

4

**BUPRENORPHINE SUBSTITUTION**

**INTERVENTION TOOL-KIT**  
UNDER TESTING

## **Intervention Tool-kit**

(A set of six modules)

### **UNODC-ROSA undertaking**

For the AusAID supported project 'Prevention of transmission of HIV among Drug Users in SAARC Countries' (Project code- TD/RAS/03/H13)

### **Module 4**

'Buprenorphine Substitution'

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# Intervention Tool-kit

## Module-4

### Buprenorphine Substitution



UNITED NATIONS  
*Office on Drugs and Crime*  
Regional Office for South Asia



**Australian Government**  

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**AusAID**



**EXTRACT FROM THE OPENING STATEMENT OF ANTONIO MARIA COSTA,  
UNODC EXECUTIVE DIRECTOR AT THE 48th SESSION OF THE COMMISSION  
ON NARCOTIC DRUGS, VIENNA, MARCH 7-14, 2005**

"In many countries, the current dramatic spread of blood-borne infections, from HIV/AIDS to Hepatitis C, is aggravating the suffering that comes from the chronic abuse of drugs. As a result, people at risk of HIV, or already infected by AIDS need tangible, targeted, and immediate help before this pandemic evolves into the biggest killer in history ... My office is mandated, via the UN Drugs Conventions, not just to reduce the prevalence of drug abuse, but also **to reduce the harm caused by drugs**.

The best form of dealing with the problem is, of course, abstinence and at UNODC, we've invested substantial resources in prevention and treatment. We are increasing the assistance to populations at high HIV/AIDS risk, and we work with governments so that they can reach people before they join the ranks of the HIV-positive. This is where we can make a significant difference. This is where resources are well spent, as it is always easier to attack a problem before it materialises, or spins out of control.

My office believes that greater attention and more resources should be invested in drug control programmes aimed at checking the spread of blood-borne diseases. These initiatives must not stand alone, but be part of **comprehensive efforts** aimed at reducing drug use. We unequivocally reject any initiative, well intended as it may be, that could lead to a perpetuation of drug abuse... Governments can, and must **ensure both drug control and HIV prevention**.

As stated by the INCB in its 2003 report: '*... governments need to adopt measures to reduce the demand for illicit drugs taking into account... the drug-related spread of HIV infection. At the same time... prophylactic measures should not promote and/or facilitate drug abuse*'."

**UNODC'S COMPREHENSIVE PACKAGE APPROACH**

HIV/AIDS prevention and care programmes for injecting drug users typically include a wide variety of measures (the 'package' approach), ranging from drug dependence treatment, including drug substitution treatment, outreach providing injecting drug users with information on risk reduction and referral to services, clean needles and syringes, and condoms, voluntary counselling and testing, treatment of sexually transmitted infections, antiretroviral therapy, and interventions for especially at-risk populations such as prisoners and sex workers who inject drugs. Such a comprehensive package of measures also usually includes treatment instead of punishment for persons convicted of minor offences, since drug treatment not only constitutes a humane, cost effective alternative, but also incarceration usually increases the risk of HIV transmission.



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# 1. AIMS

The United Nations Office on Drugs and Crime Regional Office for South Asia (UNODC-ROSA) has developed an intervention tool-kit comprising six modules under the project entitled 'Prevention of transmission of HIV among Drug Users in SAARC<sup>1</sup> countries' (Project code - TD/RAS/03/H13). In view of the heterogeneity that exists in the SAARC region with regard to the pattern of drug use (including injecting drug use) as well as HIV prevalence among drug users, the project has undertaken this activity to help develop capacity in the region for scaling up HIV interventions among injecting drug users (IDUs) and other opiate users.

The present document is the fourth in the series of six modules with the following aims:

- ♦ To outline the safety and effectiveness of buprenorphine in the management of heroin and other opioid dependence.
- ♦ To describe the guidelines and procedures for buprenorphine maintenance treatment for opioid dependence.
- ♦ To discuss issues relating to buprenorphine administration and a rollout plan for buprenorphine substitution clinics.
- ♦ To understand the quality assurance indicators in the operation of the buprenorphine clinics.

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<sup>1</sup> The South Asian Association for Regional Co-operation

## 2. INTRODUCTION

In South Asia, opioid use and in particular heroin use, is on the increase. The diffusion of injecting drug use is causing concern in the region (UNODC & MSJE, 2004). Heroin and other opioid dependence cause significant morbidity and mortality; it is a chronic and enduring condition that often requires long-term treatment and care. Adequate access to a range of treatment options should be offered to respond to the varying needs of people with heroin/opioid dependence.

Substitution maintenance treatment is an efficacious, safe and cost-effective modality for the management of opioid dependence. Such treatment is a valuable and critical component of the effective management of opioid dependence and the prevention of HIV among IDUs. Scientific evidence

suggests that substitution treatment can help reduce criminality, infectious diseases and drug-related deaths as well as improve the physical, psychological and social well-being of dependent users (Gibson *et al*, 1999). Provision of substitution maintenance therapy should be integrated with other HIV preventive interventions and services, as well as with those for treatment and care of people living with HIV/AIDS (WHO, UNODC & UNAIDS, 2004). A recent review recommended that the provision of substitution treatment should be supported for opioid dependence in countries with emerging HIV and injecting drug use problems as well as in countries with established populations of injecting drug users (Gowing *et al*, 2004).

Pharmacological agents used as substitution substances in the management of opioid dependence are: methadone, buprenorphine, Levo Alpha Acetyl Methadol (LAAM), Dihydrocodeine and tincture of opium (laudanum). Methadone is the most employed agent in substitution treatment around the world. There have been increasing doubts about the safety of LAAM because of the related cardiac risk. Buprenorphine is emerging as a useful complementary or alternative option to methadone.

The partial opiate-receptor agonist profile of buprenorphine is attractive, and this drug could be used to suppress heroin craving and antagonise heroin effects, while having a limited potential for dose escalation and toxicity. Buprenorphine is efficacious in comparison with other available options as shown by individual comparative studies of buprenorphine in heroin

**Drug substitution** means replacing, under medical supervision, the drug, which the drug user is taking with a similar substance. It may also mean using the same drug but taking it in a different way, for example, sublingual buprenorphine to replace injecting of buprenorphine. Substitution treatment comes either with or without psychosocial support.

dependence (Johnson *et al*, 1992; Strain *et al*, 1994; Ling *et al*, 1996; Ling *et al*, 1998; Johnson *et al*, 2000; Pani *et al*, 2000) and meta-analyses (West *et al*, 2000; Barnett *et al*, 2001). Observational data from France where buprenorphine substitution is widely used lend support to the notion of reduced toxicity (Auriacombe *et al*, 2001). Since it is a partial agonist, buprenorphine can be especially useful for patients who need only a limited degree of agonist action. The one-year retention rate for buprenorphine substitution combined with psychosocial care was 75 per cent compared with 0 per cent for a placebo group in Sweden and the treatment was safe and efficacious for heroin dependence (Kakko *et al*, 2003).

Buprenorphine also has an important role to play in the control of HIV infection among and from injecting drug users. However, the impact of buprenorphine on HIV infection in this population has been less researched than methadone. A study at Chennai in India demonstrated the potential of buprenorphine treatment in reducing injecting drug use among heroin users (Kumar *et al*, 2003). As buprenorphine reduces the number of injecting episodes, it is likely to have an effect similar to methadone on reducing the spread of HIV.

#### **Buprenorphine Substitution**

As efficacious as other available options

Reduced toxicity

Better retention in treatment

Potential for reducing HIV among heroin injectors

Buprenorphine, in sublingual tablet form (in the doses of 0.4 mg and 2 mg), has been licensed in India for the management of opioid dependence, including maintenance and detoxification, at specified drug treatment centres approved by the Ministry of Social Justice and Empowerment, Government of India. This preparation is effective in the long-term, as a maintenance treatment programme, and in the short-term for treatment of heroin withdrawals. To assist in the safe and effective implementation of buprenorphine treatment in India and other countries of the SAARC region, a protocol was developed by the All India Institute of Medical Sciences, New Delhi. The practice of substitution maintenance therapy must be guided by clinical modules and supported by adequate training and evaluation. Possible adverse consequences need to be minimised by adhering to best clinical practices, monitoring treatment quality and outcomes, and instituting adequate control measures and regulations to avoid diversion of the medicines into illicit channels. Hence, this module on buprenorphine substitution has been developed to guide maintenance programmes using buprenorphine.

### 3. WHAT NEEDS TO BE IN PLACE BEFORE INITIATING BUPRENORPHINE SUBSTITUTION

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#### **Policies and procedures for buprenorphine clinics to establish prior to initiating opioid dependence treatment**

- ✦ Establish policies and procedures for buprenorphine treatment (outpatient delivery in supervised settings - directly observed treatment)
- ✦ Plans for staff education and training
- ✦ Backup coverage for the absence or leave of the medical doctor / core team
- ✦ Assurance of the privacy and confidentiality of addiction treatment information
- ✦ Linkages with other drug treatment services, who will accept referrals for other forms of treatment (e.g., abstinence oriented approaches; psycho-social interventions)
- ✦ A referral network of medical specialists
- ✦ Timely physical examinations
- ✦ Linkages with medical treatment facilities including HIV treatment and care
- ✦ Linkages with addiction and psychiatric treatment programmes (e.g., detoxification centres, psychiatric clinics)
- ✦ Listing of community referral resources, including specific self-help groups who would welcome patients on buprenorphine substitution

Buprenorphine is listed under Schedule III of the 1971 Convention on Psychotropic Substances. Given the lax drug control measures in South Asia, there is a fear that buprenorphine used in drug maintenance treatment may be diverted to the black market. Reducing the diversion of buprenorphine to the black market can be achieved by observing certain procedures strictly. Currently, the drug is licensed and can be prescribed for heroin dependence in India by specified drug de-addiction centres notified by the Ministry of Social Justice and Empowerment, Government of India. Procedures have been laid down for procuring, storing and documenting the distribution of medication. It is essential that the agencies responsible for buprenorphine treatment are completely aware of the legal and regulatory procedures related to this drug in their respective countries and strictly adhere to them.

#### ***Assessment of the capacity of the agencies***

The capacity of the agencies that will be establishing the buprenorphine clinic has to be assessed. Given the nature of the treatment and the regulatory procedures, it is important that to begin with, the services are provided by clinics at medical colleges, university hospitals, major government hospitals and recognised drug treatment services.

## 4. IMPLEMENTATION

The implementation of buprenorphine substitution is organised into five subsections. The first subsection on 'clinical pharmacology' provides information on the safety and effectiveness of buprenorphine. Subsection II, 'assessing patients for treatment with buprenorphine', deals with the assessment of opioid dependent individuals and considers candidates for buprenorphine treatment. Subsection III describes the guidelines and procedures for maintenance treatment with buprenorphine. Subsection IV discusses the issues relating to the administration of buprenorphine and the rollout plan for delivering buprenorphine to the patients. The final subsection V focuses on training needs and ongoing support.

- I. Clinical pharmacology
- II. Assessing patients for treatment with buprenorphine
- III. Guidelines and procedures for maintenance treatment
- IV. Roll-out plan for buprenorphine administration
- V. Training and support

### **I. Clinical Pharmacology**

In this subsection, the following will be discussed: i) about buprenorphine; ii) onset and duration of response to buprenorphine; iii) buprenorphine withdrawal syndrome; iv) side effects; v) safety; vi) drug interactions; vii) properties and the clinical implications; and, viii) a comparison between buprenorphine and methadone.

#### **i) About buprenorphine**

Buprenorphine is a synthetic opioid derived from the morphine alkaloid thebaine. It has low intrinsic activity<sup>2</sup> and high affinity at the opioid receptors responsible for some properties of opioids like analgesia and euphoria.<sup>3</sup>

*Buprenorphine suppresses the craving for heroin as well as blocks the effect of additional heroin and other opioid use.*

<sup>2</sup> Buprenorphine is a partial agonist and has both agonist (opiate like) and antagonist (blocking the action of opiates) activity at the opiate receptors.

<sup>3</sup> Several opioid receptor subtypes have been described and characterised. Receptors: Classic opioids like morphine bind here preferentially. They are believed to be responsible for most analgesic properties of opiates, as well as for euphoria, sedation, constipation, respiratory depression and dependence.

## ii) Onset and duration of response to buprenorphine

Buprenorphine has poor gastrointestinal bioavailability but has a fair sublingual bioavailability. It is easily absorbed within 5-10 minutes.

Onset of effects	30 - 60 minutes
Peak clinical effects	1 - 4 hours
Duration of effects	8 - 12 hours at low dose (e.g. < 4 mg) 24 - 72 hours at high dose (e.g. >16 mg)

*Higher doses have prolonged duration of response*

The reasons for the extended action of buprenorphine are:

- ◆ Tight binding at opioid  $\mu$  receptors and slow dissociation
- ◆ Release of low levels of buprenorphine from the fat stores very slowly

*Extended duration of action helps a daily dose or thrice a week dose*

## iii) Buprenorphine withdrawal syndrome

Withdrawal effects from full agonists like heroin, morphine or methadone are marked but only a low level of withdrawal effects are observed when buprenorphine is abruptly withdrawn. The low level of withdrawal symptoms also appears delayed and for 72 hours, there may be no significant withdrawal symptoms following cessation of the drug. Its partial agonist properties, along with its slow dissociation from opioid receptors, are thought to explain why opioid withdrawal syndrome is milder.<sup>4</sup>

## iv) Side effects

The medical effects of acute buprenorphine administration are similar to those of opioid agonists. Opioid dependent individuals show tolerance to many of these effects. Since buprenorphine tablets dissolve readily in water, these can be injected. The use of combination tablets of buprenorphine and naloxone<sup>5</sup> (in doses of 2 mg of buprenorphine and 0.5 mg naloxone) will help mitigate potential diversion and abuse. This combination will also permit sublingual use without precipitating withdrawals.

### **Side effects**

Constipation  
Disturbed sleep  
Drowsiness  
Sweating  
Headaches  
Nausea

## v) Safety

Buprenorphine exerts a "ceiling effect" and as the dose of buprenorphine increases, the agonist effect reaches a peak and then reduces in magnitude. In contrast to full opioid agonists, overdose of buprenorphine (by itself) does not appear to cause lethal respiratory depression in non-compromised individuals.

*Overdose of buprenorphine (by itself) does not appear to be fatal.*

<sup>4</sup> Treatment with opioid antagonists (e.g., Naltrexone ) can be commenced within days of the cessation of low-dose buprenorphine treatment without precipitating severe opioid withdrawal. This enables patients to transfer promptly to naltrexone treatment, and avoid relapse and treatment dropout.

<sup>5</sup> Naloxone is an opiate antagonist (preventing activation of opiate receptor by an opioid); it is short acting; used in the treatment of overdose; 10-20 times more potent by injection than by sublingual route.

## vi) Drug interactions

### **Drugs**

Sedatives  
(benzodiazepines)

Opioid antagonists

Opioid agonists

Hepatic enzyme  
inhibitors<sup>6</sup>

Hepatic enzyme  
inducers<sup>7</sup>

### **Drug interactions**

Additive sedative effects

Deaths reported with combinations

High doses of naloxone required for treating overdose  
Naltrexone can precipitate a delayed withdrawal syndrome

Difficult to achieve analgesia with short-term opiate agonists in patients maintained on buprenorphine

HIV drugs like Ritonavir<sup>®</sup>, Saquinavir<sup>®</sup>;  
Ketoconazole<sup>®</sup>

HIV drugs Nevirapine<sup>®</sup>, Efaviren<sup>®</sup>;

## vii) Properties of buprenorphine and their clinical implications

<b>Property</b>	<b>Clinical implication</b>
Opioid effects	Reduces cravings for heroin
Partial agonist	Less sedating than full agonists (heroin, morphine or methadone)
Prevents or alleviates heroin withdrawal symptoms	Can be used for maintenance or withdrawal treatment of heroin dependence
Diminishes the effects of additional opioid use (e.g. heroin)	Diminishes psychological reinforcement of continued heroin use.
Long duration of action	Allows for once a day to three-times-a-week dosing schedules.
Ceiling on dose response effect	Higher doses prolong the duration of action but safer in overdose.
Preparation (sublingual)	Poorly absorbed orally. Accidental poisoning by children may not be fatal. More time required for directly observed therapy (DOT).
No severe withdrawal precipitated by opioid antagonists	Treatment with naltrexone can be commenced within days of buprenorphine.
Side effect profile similar to other opioids	Generally well tolerated, with most side effects transient.

*Lintzeris et al, 2001*

<sup>6</sup> Buprenorphine is metabolised by the hepatic enzyme system (cytochrome P450 3A4). Medications that inhibit this enzyme system may potentially increase blood levels of buprenorphine. As yet, no controlled studies have examined the pharmacokinetic interactions.

<sup>7</sup> Medications that induce the enzyme system may potentially decrease the blood levels of buprenorphine. As yet, no controlled studies have examined the pharmacokinetic interactions.

### viii) Comparison between buprenorphine and methadone

Buprenorphine	Methadone
Partial agonist and produces only a low level of euphoria.	Full agonist and can produce significant intoxication.
Has low dependence potential compared with full opioid agonists.	Potential to produce significant dependence. As tolerance increases, dose increases over time are required.
Abstinence leads to mild withdrawal symptoms.	Abstinence leads to marked withdrawal symptoms.
At high doses, there is a ceiling effect. The risk of fatal respiratory depression by overdose of buprenorphine by itself is minimal. But when combined with benzodiazepines (diazepam), alcohol and other CNS depressants, respiratory depression has been reported.	Risk of fatal overdose by respiratory depression.
Sublingual tablets are effectively absorbed. It is not orally active. Sublingual tablets can be crushed, easily dissolved and injected.	Orally active.

## II. Assessing patients for treatment with buprenorphine

To determine the appropriateness of buprenorphine substitution treatment, a comprehensive patient assessment is essential. A candidate for buprenorphine treatment should have an objectively ascertained diagnosis of opioid dependence. In this subsection, how to assess and diagnose opioid dependence through history, examination and laboratory investigations is outlined first, followed by the criteria to determine the suitability of patients for buprenorphine maintenance treatment. Additional information on the appropriateness of buprenorphine treatment is found in the Annex.

### i) How to assess and diagnose opiate dependence?

#### A) History:

Reason for presentation

- ◆ In crisis (health or economic or legal crisis).
- ◆ Brought in by a concerned parent / relative / spouse/ employer/ friend / outreach worker.
- ◆ Want help for their drug use and motivated to change their behaviour.
- ◆ Usual source of drugs not available.
- ◆ Referred from another medical practitioner.
- ◆ Pregnant.

### Past and current drug use (last 4 weeks)

- ✦ The age of starting drug use (including alcohol and nicotine).
- ✦ Types and quantities of drugs taken (including concomitant alcohol misuse).
- ✦ Frequency of use including routes of administration.
- ✦ Experience of overdose.
- ✦ Periods of abstinence.
- ✦ What triggers a relapse?
- ✦ Symptoms experienced when unable to obtain their drugs.

### History of injecting and risk of HIV and hepatitis

- ✦ Past history
- ✦ Present usage and why patient changed to injecting?
- ✦ Supply of needles and syringes
- ✦ Sharing habits including lending and borrowing injection equipment / paraphernalia
- ✦ Does the patient know how to inject safely?
- ✦ How does the patient clean equipment?
- ✦ How does the patient dispose of the used equipment / works?
- ✦ Has the patient thought or tried any other method of use?
- ✦ Knowledge of HIV, hepatitis B and C issues and transmission
- ✦ Use of condoms

### Medical history

- ✦ Complications of drug use – abscesses, thromboses, viral illnesses, chest problems
- ✦ Hepatitis B, C status if known
- ✦ HIV status if known
- ✦ History and/or diagnostics for STIs
- ✦ Last menstrual period
- ✦ Operations, accidents and head injury
- ✦ Any current medication?

### Psychiatric history

- ✦ Any psychiatric consultations?
- ✦ Any overdoses? (accidental or deliberate)

## Forensic history

- ✦ Any outstanding charges?
- ✦ Past imprisonment?
- ✦ Past custodial lock-ups?

## Social history

- ✦ Family situation
- ✦ Employment situation
- ✦ Housing situation
- ✦ Financial situations including debts

## Past contact with treatment services

- ✦ Previous efforts to reduce or stop taking drugs
- ✦ Contacts with doctors, addiction services, social services, community services
- ✦ Previous admissions, how long they lasted and the cause of any relapses

## **B) Examination**

### Assessing motivation

Is the patient motivated to stop or change their pattern of drug use or to make other changes in their life?

### Assessing general health

General - Anaemia, nutritional status, dentition and overall hygiene

Skin - Needle marks, tattoo, skin abscesses and open wounds

Route specific - Injecting (abscesses, cellulitis)

Drug related - *(See Annex A for assessing medical syndromes associated with opioid use.)*

Side effects (e.g. constipation)

Overdose (e.g. respiratory depression)

Withdrawal (e.g. irritability, pain) - *(See Annex B for opiate withdrawal scale.)*

Current medication - What drugs? If HIV status known, whether on HIV drugs?

Assessment of mental health - co-existing psychiatric problems

Assessment of social and family situation

## **C) Special investigations with full informed consent**

### Haematological investigations

- ✦ Haemoglobin
- ✦ Liver function tests
- ✦ Hepatitis B and C

Urine assessment: Opiates persist in the urine up to 24 hours

After completing a comprehensive assessment of a candidate for treatment, the physician should be prepared to

- ✦ Establish the diagnosis or diagnoses
- ✦ Determine appropriate treatment options for the patient
- ✦ Make initial treatment recommendations
- ✦ Formulate an initial treatment plan
- ✦ Plan for engagement in psychosocial treatment
- ✦ Ensure that there are no absolute contraindications to the recommended treatments
- ✦ Assess other medical / psychiatric conditions that need to be addressed

The physician then decides about the appropriateness of buprenorphine treatment for the patient. (*See Annex C for buprenorphine treatment appropriateness checklist.*)

Criteria to determine suitability for treatment with buprenorphine

#### *Patient Selection Criteria*

- ✦ Age above 18 years
- ✦ Regular opiate users (non-injecting) who have failed conventional treatment at least twice earlier or injecting opiate (injecting heroin and/or buprenorphine) users
- ✦ Persons willing for sublingual buprenorphine (provide informed consent for treatment)

#### *Contraindications*

- ✦ Patients with serious medical conditions like acute respiratory failure, acute hepatic disease, acute alcoholism, and delirium tremens.
- ✦ Patients under 15 years of age.
- ✦ Female patients who are pregnant or breastfeeding.
- ✦ Known hypersensitivity to buprenorphine.

#### *Precautions*

- ✦ Co-morbid dependence on high doses of benzodiazepines or other central nervous system depressants (including alcohol)
- ✦ Significant untreated psychiatric co-morbidity
- ✦ Significant medical complications
- ✦ Transfer from methadone maintenance

### *Intake Process*

Opiate dependant individuals - diagnosed by qualified and/or trained physician/ psychiatrist



Informed consent for treatment with buprenorphine



Treatment contract signed (see Annex D for an example of a treatment contract.)



Involvement of family member (desirable)



Decision about maintenance with buprenorphine jointly made by the physician and patient



Treatment protocols explained clearly

### **III. Guidelines and procedures for maintenance treatment**

Physicians who use buprenorphine to treat opioid dependence must consider the entire process of treatment, from induction, through stabilisation, and then maintenance. At each stage of the process, many different factors must be considered if the physician is to provide comprehensive and maximally effective opioid addiction care. The following issues are dealt with in this subsection: i) factors that need to be considered before selecting an opioid dependent person for buprenorphine substitution; ii) induction; iii) stabilisation; iv) maintenance dosing; v) frequency of dosing; and vi) withdrawal from buprenorphine.

#### **i) Before selecting an opioid dependent person for buprenorphine substitution**

*Response to treatment:* Treatment goals to be agreed upon by the patient and the provider. Additional psychosocial support is beneficial for majority of patients and improves adherence to maintenance treatment.

*Individual variation in absorption, metabolism and clearance rates* of the drug, buprenorphine should be considered.

*Adverse effects:* People complaining of sedation with methadone prefer buprenorphine.

*Logistics of participating in treatments:*

- ✦ ease of access for participants
- ✦ frequency of dispensing (alternate day or thrice weekly is attractive for working patients)
- ✦ convenient location of treatment services (located where drug users live; central location; public transportation)

- ✦ user-friendly services
- ✦ costs to patients (free or subsidized treatment is most attractive to users)

*Ease of withdrawal from maintenance buprenorphine treatment:* Though withdrawals are milder compared to methadone, the relapse to heroin following discontinuation of buprenorphine is the same for both drugs.

*General expectations of the treatment:* Some patients have unrealistic expectations about the treatment and all patients must be told clearly about the treatment benefits and limitations.

*Capacity for transfer from methadone maintenance:* Patients who cannot reduce methadone<sup>8</sup> below 60 mg are not ideal for transfer to buprenorphine.

*Additional psychosocial care with buprenorphine improves treatment adherence*

## ii) Induction

*Initial buprenorphine dose: inducting heroin users*

The first dose of buprenorphine should be administered at least 6 hours after the last heroin use to reduce the risk of a precipitated opioid withdrawal. The initial dose should be between 0.4 and 4 mg.<sup>9</sup> Induction is usually done in the first one or two days. The following must be taken into consideration when considering the initial dose:

- ✦ the degree of tolerance to opioids:
  - ▶ low or uncertain tolerance to opioids: 0.4 to 4 mg.
  - ▶ high levels of tolerance: 6 to 8 mg..
- ✦ severity of opioid withdrawal experienced by patient at first buprenorphine dose:
  - ▶ moderate to severe opioid withdrawal: 6 to 8 mg.
  - ▶ little or no opioid withdrawal: 0.4 to 4 mg, or delay initial dose.
- ✦ alcohol, sedative drug (benzodiazepines), or illicit heroin use warrants low initial buprenorphine doses, with frequent reviews.
- ✦ medical conditions may warrant the use of lower initial doses

## iii) Stabilisation

The key principles to stabilising patients are:

- ✦ review of the patient by the prescribing doctor / members of the treatment team

<sup>8</sup> Applicable in countries where both drugs (methadone and buprenorphine) are legally available for substitution treatment.

<sup>9</sup> Clinical experience in India has indicated this dosage recommendation; however rigorous studies may be required in the region to establish proper initial doses.

- ✦ titration of the buprenorphine dose by the reviewing doctor according to:
  - ▶ features of intoxication, withdrawal, cravings over preceding 24 hours
  - ▶ additional drug use (e.g., heroin, sedatives)
  - ▶ side-effects or other adverse events
  - ▶ adherence to dosing regime (attendance at the buprenorphine clinic)
  - ▶ adherence to dosing route (injecting the crushed medicines)
  - ▶ patient satisfaction with buprenorphine dose
- ✦ dose changes:
  - ▶ increases should be by increments of 0.4 - 2 mg at a time
  - ▶ allow at least 2 - 3 days between dose increases

*Patients' experience with an administered dose is relevant to determining proper dosage*

At each review, the buprenorphine dose should be titrated in the light of:

- ✦ Intoxication, or significant side effects indicate a need to reduce the dose
- ✦ Adverse events (such as overdoses) - an indication to reduce the dose
- ✦ Cravings for heroin use, use of illicit and other drugs, reported withdrawal symptoms - reasons for increasing the daily dose

The stabilisation phase takes 2-8 weeks in general and the goal of buprenorphine treatment is to treat with the optimal dose of medication needed to address target signs, symptoms and desired benefits.

*Adequate and optimal dosing helps to reduce additional illicit drug use and promote adherence to maintenance treatment*

### **Initiating and maintaining treatment with sublingual buprenorphine - a tentative schedule drawn from the experience in Chennai, India**

Day 1: The doctor gives medication under observation. It should be taken sublingually. After receipt of the buprenorphine tablet, the patient should remain in the office for at least one hour to observe for any reaction. The dosage should be slowly stepped up depending on the prevailing withdrawal symptoms. Dispense enough medication to last till the next visit. The patient may be seen every day for a period of a week and be given medication under the direct observation therapy (DOT).

The time of the first dose of sublingual buprenorphine is six hrs (range: 4 - 8 hrs) after the last dose of heroin. Initial dose is 0.4 mg to 4 mg of sub-lingual buprenorphine tablet.

Week 1: Review with the doctor regarding the patient's progress, relapse if any, symptoms or adverse effects of the medication.

Week 2-5: Mandatory to meet the doctor every week and, if necessary more often too.

Week 6: Meet with the doctor for review of your treatment. At this time the decision whether to continue buprenorphine and the benefits and limitations of treatment are discussed in detail with the counsellor. The patient has been stabilised by this time and the dose that is required for maintenance is determined. This maintenance dose will be delivered to the patient regularly under DOT by the clinic staff.

Week 7 and beyond: Since the treatment continues for a longer period, the patient meets the doctor only periodically to assess progress. Encourage participation of the patient in psychosocial intervention programmes and self-help groups. If the clinic staff members feel that the patient is experiencing any special difficulty, then the patient is shown to the doctor.

The first few days of treatment are a difficult phase. Insomnia and restlessness can be frequently encountered and it can be reduced to a great extent by reassurance and reducing the anxiety of the patient. Craving usually comes in waves and can be triggered by external cues like seeing people using drugs, frequenting places where drugs are used, paraphernalia used and internal cues like stress, anger, depression, depression, anxiety and boredom. In addition, specific strategies to reduce craving can be taught to patients.

*(Buprenorphine treatment for injecting opiate users in Chennai, India, SAHAI Trust, 1999-2002- supported by European Commission)*

#### iv) Maintenance dosing

Buprenorphine doses should be individually titrated according to the patients' response to treatment. Effective maintenance doses that result in reduced heroin use and improved treatment retention are achieved with high buprenorphine doses in the range of 8 to 24 mg buprenorphine per day in Western studies. Little is known regarding the nature of adverse events at maintenance daily doses greater than 32 mg, therefore, the maximum daily dose of buprenorphine routinely recommended is 32 mg. In India experience indicates that persons dependent on opioids require a comparatively smaller dose (4 - 8 mg/day).<sup>10</sup> For injecting buprenorphine users, the maintenance dose is approximately 2 to 4 times the dose that they are regularly administering by intramuscular or intravenous route (given the 42 per cent and 29 per cent buprenorphine bioavailability in the sublingual route relative to intramuscular and intravenous routes, respectively).

*In India, a majority of patients require a maintenance dose of about 4 - 8 mg every day*

#### v) ) Frequency of dosing

Daily dosing with buprenorphine is required during induction and stabilisation. Once the patients' daily medication dose has been stabilised (usually after 2-8 treatment weeks) either an alternate day or 3 times a week dosing may be instituted as follows:

1. A dose equal to 2 times the daily dose on alternate days, not to exceed a maximum of 32 mg.
2. A dose equal to 2 times the daily dose to be given on Mondays and Wednesdays with a dose equal to 3 times the daily dose on Fridays not to exceed a maximum of 32 mg.

Daily Buprenorphine dose (mg)	Alternate Day Buprenorphine (mg)	Three times a week dose (mg)	Buprenorphine
		Mon & Wed	Fri
2	4	4	8
4	8	8	12
8	16	16	24
16	32	32	32
20	32	32	32
24	32	32	32

<sup>10</sup>Lesser compared with the maintenance dose suggested in the Western countries. The suggested dose is based on the clinical experience from India and studies are required to determine proper maintenance dose for persons with opioid dependence in the region

Alternate day dosing and thrice weekly dosing is an option to lessen the number of visits and is usually attractive to working patients. However, some patients (up to 15 per cent) experience craving and return to heroin use if transferred to thrice weekly dosing.

#### **vi) Withdrawal from buprenorphine**

There is no reason to believe that abstinence following buprenorphine differs greatly from abstinence following methadone. Research evidence confirms that both severity of withdrawal, and relapse post-detoxification,<sup>11</sup> appear similar for methadone and buprenorphine. Withdrawal from buprenorphine should only be conducted with the consent of the patient. A graduated reduction over weeks results in better outcomes. For patients on 8 mg and below, the dose reduction is 2 mg per week or fortnight and for those receiving 8 - 16 mg, the reduction shall be 2 - 4 mg per week or fortnight.

### ***IV. Rollout plan for buprenorphine administration***

Buprenorphine is an opioid and its use is regulated. Clinicians should take special precautions in the prescribing, handling, dispensing and storage of the medication. Certain procedures have to be followed before administering the drug to the patients. It is preferable to deliver the drug in substitution programmes through directly observed treatment (DOT). Buprenorphine treatment should be part of a comprehensive treatment and care service for opioid dependents and in order to achieve this, government run community based buprenorphine clinics should work in close collaboration with non-governmental agencies as well as hospitals.

#### **i) Procedures prior to administering the dose of buprenorphine**

A psychiatrist at the substitution clinic or a physician trained in buprenorphine treatment shall prescribe the substitution substance buprenorphine. Once the treating physician has stabilised the dose, a pharmacist or nurse or a community health nurse can administer the drug subsequently.

Prior to administering the medication, staff must:

- ✦ Establish the identity of the patient
- ✦ Confirm that the patient is not intoxicated
- ✦ Check the quantity of the drug in the prescription
- ✦ Check for current prescription
- ✦ Check that the current day is a dose day on the patient's regime
- ✦ Confirm the dose for the current day if it is an alternate-day or three-times-a-week regime
- ✦ Record the dose in the recording system

<sup>11</sup>Some patients may prefer to be detoxified with buprenorphine and it is important to transfer them, following detoxification, to either naltrexone or intensive psychosocial care for relapse prevention. Drug users who have failed with buprenorphine detoxification may be considered for buprenorphine maintenance.

## **ii) Administering buprenorphine through Directly Observed Treatment (DOT)**

After recording dose details in the necessary documentation system, the following procedures should be observed. The drug is preferably given by way of Directly Observed Treatment (DOT). This will ensure that the drug is not taken away, crushed and injected by the clinic patients. There is considerable experience for the provision of buprenorphine through DOT in many centres across India.<sup>12</sup>

- 1) Count and check the buprenorphine tablets into a dry dosing cup. Double-check the number and strength.
- 2) Crush the tablets into powder
- 3) Place the powder under the tongue of the patient
- 4) Give the following instructions:
  - a) do not swallow saliva until powdered tablets have dissolved (2 - 5 minutes on average)
  - b) do not swallow the powdered tablets
  - c) once the tablets are given to you, they are your responsibility and will not be replaced.
- 5) Observe the patient until you are satisfied the tablets are not divertible (usually > 2 minutes).
- 6) Ask to see "how the powdered tablets are dissolving" enough times for this to become an acceptable part of the patient's delivery routine.
- 7) Patients should sign / affix thumb impression that they have received their dose. Offer water to rinse taste out of mouth.

The doctor should be notified if the dosing administrator has concerns that patients may be attempting to divert their medication.

## **iii) Roll-out plan for buprenorphine substitution**

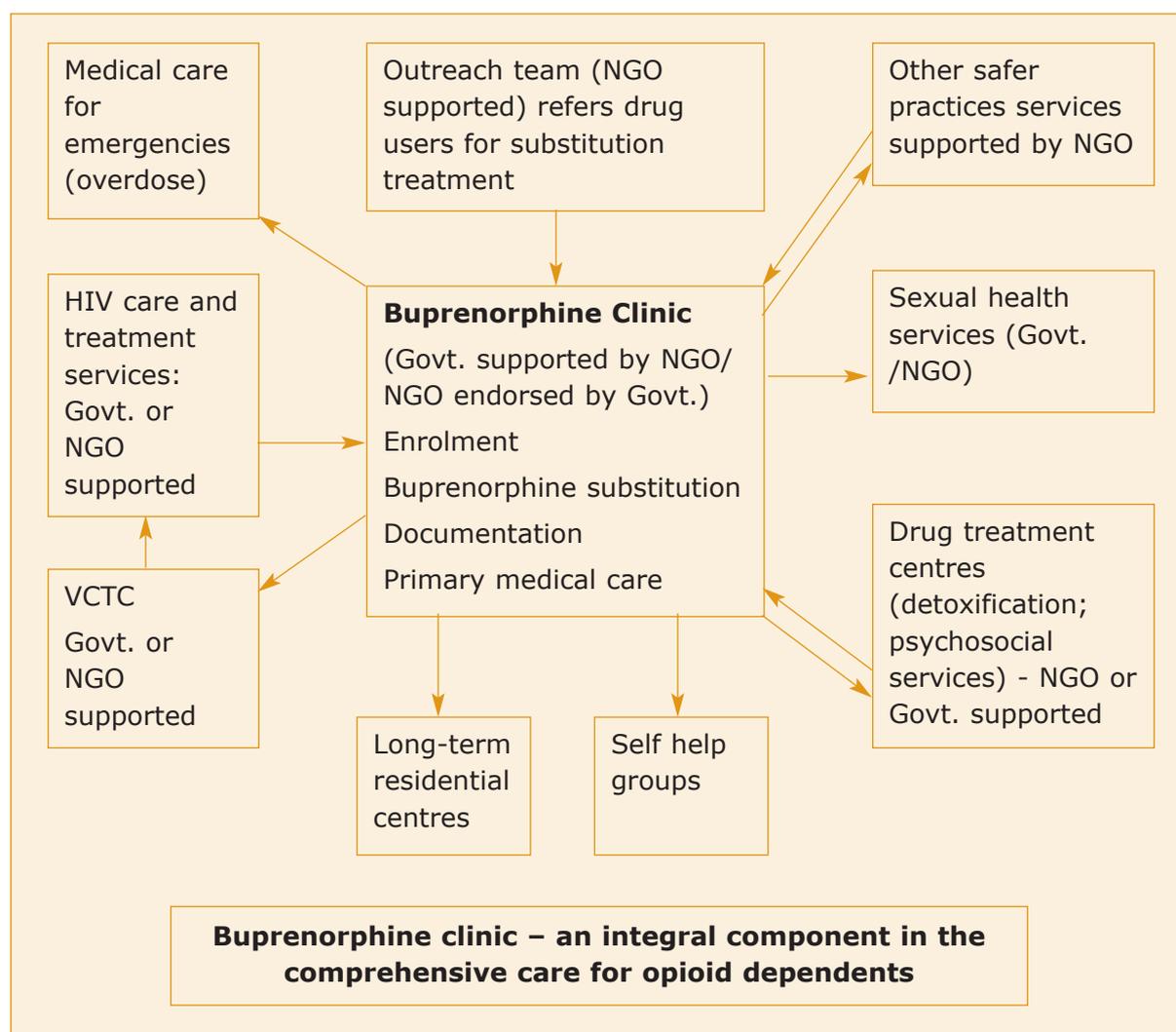
The following personnel are required to operate a buprenorphine substitution clinic serving about 300 regular patients with opioid dependence: a medical doctor; a documentation officer; six nurses; one counsellor; security staff and clinic maintenance staff. Apart from optimal dose, the effectiveness of the substitution treatment is dependent on the length of time in treatment and linkages with other services. In order to ensure that patients can receive the medication prescribed uninterrupted, it is important that the substitution programmes are supported and endorsed by the respective governments. Sudden interruptions in the supply of maintenance medication can potentially do more harm to the users. Long-term plans should be made for establishing and maintaining substitution programmes.

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<sup>12</sup>Through a European Commission supported programme, seven Indian NGOs (from the cities of New Delhi, Mumbai, Kolkata, Chennai and Imphal) provided sublingual buprenorphine substitution through DOT in community based clinics for more than 1,500 injecting opioid users / heroin users.

Community based clinics are more attractive to drug users and the government sponsored buprenorphine clinics should be community based. Both the government (supply of substitution medication, monitoring of regulatory procedures) and the non-governmental organisations (NGOs) involved in community based services, psychosocial care and support services for drug users should become partners in the delivery of treatment. The substitution programme should be integrated to existing drug treatment / rehabilitation services and should be part of a comprehensive and continuum of care for the drug users.

In places with high potential for HIV transmission among injecting opiate users, substitution treatment should become a key component of HIV prevention strategies for injecting drug users. A broad range of dosages (if possible, range of substitution substances – methadone and buprenorphine) should be offered in the clinics to match the profile of the patients. The proportion of problem opioid users to be covered by the substitution can be reviewed periodically in different geographical locations.



## V. Training and support

Staff members at the clinics need to be trained and the training should be organised before the clinics are operational. Proper training on the use of buprenorphine will be the key to successful implementation of buprenorphine substitution. The training for the staff can be assisted with the help of a) training module; b) 1-3 days training workshops; and, c) clinical placement in an existing buprenorphine clinic. Apart from the initial workshops, there should be provision for follow-up training and support. A comprehensive training module can be developed that can be field-tested and widely used in the region. It is likely that pilot projects will be established in many places in South Asia before large-scale buprenorphine programme supported by respective Governments become operational. The staff participating at the pilot projects can be brought together for a centralised workshop. For the medical doctors, the one-day workshop can address issues specifically related to patient assessment for buprenorphine treatment, clinical pharmacology - dosing, drug interactions - and, buprenorphine in the context of dependence care and HIV services. For core team members from a State/Province, an initial three days training programme conducted centrally within that State/Province can address several issues relating to maintenance treatment, patient care, administrative issues, confidentiality, regulatory issues, documentation, liaison services and linkages. Clinical placements are extremely useful and even after establishment of pilot projects, there could be exchange visits. Attendance at Harm Reduction Conferences and Drug Treatment Workshops should be encouraged for the buprenorphine clinic team members. The core team members, who have been trained in the State/Province level three days training workshops can train new members of the team with the help from local consultants periodically.

Topics for three days training workshop for the core team:

Day 1	Day 2	Day 3
Introduction to the workshop	Assessment of a patient with opioid use and criteria for buprenorphine substitution	Directly observed treatment of buprenorphine Enhancing 'quality' in patient care
Opioid dependence - concept, course and consequences	Effectiveness of buprenorphine substitution	Liaison services and linkages
Effective treatment approaches	Regulatory procedures Confidentiality	Visit to a buprenorphine clinic
Substitution treatment - definition, benefits and risks	Documentation and record keeping	

The workshops should adopt participatory training methodology and should be done by trainers well versed with the buprenorphine substitution. The workshop should address practical issues and enhance the skills of the participants.

## 5. MONITORING AND QUALITY CONTROL OF INTERVENTIONS

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### *Description*

Quality improvement is based upon measuring and monitoring the processes and outcomes of treatment, and making use of the information to improve the delivery of care. The practitioner works within a treatment system, and implements quality improvement approaches to ensure that the system delivers care in ways, which are effective and accountable.

### *Important Tasks*

- ✦ Maintenance of adequate documentation of treatment processes
- ✦ Maintenance of clear lines of responsibility and communication between different team members involved in the delivery of care
- ✦ Patient details and records are stored securely, only accessible to those who need the information

The project should take the following quality assurance indicators into consideration.

*Accessibility* - These programmes should be community based to ensure accessibility and to keep the cost low. The NGO collaborating with the community-based buprenorphine clinic can provide the psychosocial support services and while emergency services such as overdose management should be provided by a hospital.

*Safety* - Guidelines to ensure patient safety should be laid down. Adequate training of staff is required to ensure patient referral in case of an emergency.

*Preventing diversion* - There is a valid public health basis for concern over inappropriate prescribing, and a need to differentiate between patients who are likely to divert drugs to the black market and those who obtain prescribed opioids for their own use. Towards this end, all the regulatory procedures must be strictly adhered to. To minimize the risks and maximise the benefits of using opioids, they should only be prescribed in the context of a comprehensive assessment and treatment plan, with regular reviews of whether treatment is being beneficial. One of the ways of ensuring prevention of diversion by clients is to promote Directly Observed Therapy (DOT) for drug users receiving buprenorphine maintenance. DOT should be recommended for the following:

- ✦ patients who are using street heroin
- ✦ patients with evidence of current injecting drug use

- ✦ patients with continuously escalating dosage requirements
- ✦ patients who appear highly unstable: poly-drug use, overdoses
- ✦ patients over whom the practitioner has concerns — even if these are non-specific

*Efficacy* - Adequate dose of medicine should be given. It is to be recognised that a smaller dose of buprenorphine may be required for patients in this region. Wherever possible, along with the maintenance drug, psychosocial intervention should be provided to the patients. Low intensity psychosocial intervention (3-4 sessions in a group setting) with minimal staff investment should be planned.

*Intake criteria* - Specific selection criteria should be laid down (see Section 4:II and the Annex).

*User participation* - The programmes should be flexible and should involve patient participation at the level of planning and implementation. It should incorporate changes based on the requirements of the patients.

*Cost-effectiveness* - The programme can function with minimal staff (See Section 4: IV and Section 7).

*Patient coverage* - An outreach team supported by the NGO collaborating with the buprenorphine clinic can facilitate referral of patients to the clinic for assessment relating to suitability for buprenorphine substitution. By publicising the programme, adequate utilisation of services can be ensured. Various methods can be used for this purpose depending on the suitability in the particular community such as street plays, advertising in local cable in the television or in the radio, distribution of pamphlets, etc. Further recruitment can be done with the help of registered drug users using snowball technique.

*Patient retention* - This can be enhanced by using adequate doses, empathic staff, having a programme that is receptive to the patients' needs, flexibility in the programme, other adjunctive facilities for which a liaison with other local NGOs can be made. The retention of patients in a maintenance programme is related to its efficacy as well as its "user-friendly" attitude.

*Training of staff* - Training that provides basic information about opiates, concept of abuse and dependence, complications related to opioid use, history taking, psychosocial assessment, information about effective approaches and buprenorphine maintenance should be given to the staff. They should also be trained in identification of complications including intoxication and overdose (see Annex A), and should be aware of when to refer a case to the hospital. The training should also address issues relating to patient care - concern, empathy and user friendly services

## 6. CHECKLIST FOR MENTOR/S

- Number of buprenorphine clinics in the City/ State or Province/ Country
- Location and type of buprenorphine clinic
- Government - NGO partnership
- Community participation
- Training for staff
  - Proportion of trained staff
  - Qualifications / Skills
  - Ongoing training support
- Policy and procedures governing treatment delivery at the clinic in place
- Assessment and intake criteria
  - Criteria for selection defined and transparent
  - No discrimination in selecting patients for treatment
- Operational issues
  - Timing of the clinics
  - Backup coverage (for absence of key staff)
- Consent procedures
  - Informed consent
  - Treatment contracts
- Regulatory procedures
  - Strict adherence to procedures
  - Proper accounting of the medicines
  - Safe custody of medicines
- Documentation
  - Patients' records (demographic, risk behaviour and treatment characteristics)
  - Confidentiality of information
- Buprenorphine delivery
  - Range of doses
  - DOT
  - Alternate dosing schedules
- Other services provided at the clinic
  - HIV prevention education / Overdose prevention education
  - Primary medical care
- Other psychosocial support and care services
  - Liaison with other agencies providing range of services
  - Referral networks
- Retention rates
  - Number enrolled for treatment
  - Proportion of regular patients
- User participation in evaluation of services
  - Patient satisfaction
- Data gathered on potential outcome indicators
  - Crime rates among patients attending services
  - Employment among patients attending services
  - Risk behaviours (drug use, injection and sex related)
  - Community safety



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## 9. ANNEXURES

### A. Medical Syndromes Associated with Opioid Use

Syndrome (Onset and Duration)	Characteristics
Opiate intoxication	Conscious, sedated, "nodding"; mood normal to euphoric; pinpoint pupils; history of recent opiate use
Acute overdose	Unconscious; pinpoint pupils; slow, shallow respiration
Opiate Withdrawal Anticipatory* (3-4 hours after last "fix")	Fear of Withdrawal; Anxiety; Drug seeking behaviour
Early (8 - 10 hours after last "fix")	Anxiety; Restlessness; Yawning; Nausea; Sweating; Nasal stuffiness; Rhinorrhoea; Lacrimation; Dilated pupils; Stomach cramps; Drug-seeking behaviour
Fully Developed (1 - 3 days after last "fix")	Severe anxiety; Tremor; Restlessness; Piloerection**; Vomiting, Diarrhoea; Muscle spasm***; Muscle pain; Increased blood pressure; Tachycardia; Fever, Chills; Impulse-driven drug-seeking behaviour
	Protracted abstinence (indefinite duration)
*Anticipatory symptoms occur as the acute effects of heroin begin to subside	**The piloerection has given rise to the term "cold turkey".  *** The sudden muscle spasms in the legs have given rise to the term "kicking the habit".

## B. Clinical Opiate Withdrawal Scale (COWS)

For each item, circle the number that best describes the patient's signs or symptom. Rate just on the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score

Patient's name: \_\_\_\_\_ Date & time: \_\_\_\_/\_\_\_\_/\_\_\_\_: \_\_\_\_

Reason for assessment: \_\_\_\_\_

<p><b>Resting Pulse Rate:</b> ____ <b>beats/minute</b></p> <p><i>Measured after the patient is sitting or lying for one minute.</i></p> <p>0 pulse rate 80 or below 1 pulse rate 81 - 100 2 pulse rate 101 - 120 4 pulse rate greater than 120</p>	<p><b>GI Upset:</b> over last ½ hour</p> <p>0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhoea 4 multiple episodes of diarrhoea or vomiting</p>
<p><b>Sweating:</b> over past ½ hour not accounted for by room temperature or patient activity.</p> <p>0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 4 pulse rate greater than 120</p>	<p><b>Tremor:</b> observation of outstretched hands</p> <p>0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching</p>
<p><b>Restlessness:</b> Observation during assessment</p> <p>0 able to sit still 1 reports difficulty sitting still, but is able to do so 2 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds</p>	<p><b>Yawning:</b> Observation during assessment</p> <p>0 no yawning 1 yawning once or twice during assessment 2 yawning three or more time during assessment 4 yawning several times/minute</p>
<p><b>Pupil size</b></p> <p>0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible</p>	<p><b>Anxiety or Irritability</b></p> <p>0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable anxious 4 patient so irritable or anxious that participation in the assessment is difficult</p>
<p><b>Bone or Joint Aches:</b> If patient was having pain previously; only the additional component attributed to opiates withdrawal is scored.</p> <p>0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscle 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</p>	<p><b>Gooseflesh skin</b></p> <p>0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 4 prominent piloerection</p>
<p><b>Runny nose or tearing:</b> Not accounted for by cold symptoms or allergies</p> <p>0 not present 1 nasal stuffiness or unusually moist eyes 4 nose constantly running or tears streaming down cheeks</p>	<p>Total score ____ The total score is the sum of all 11 items. Score: 5-12=mild; 13-24=moderate; 25-36=moderately severe; more than 36=severe withdrawal</p> <p>Initials of persons completing Assessment</p>

### **C. Buprenorphine Treatment Appropriateness Checklist**

1. Does the patient have a diagnosis of opioid dependence?
2. Are there current signs of intoxication or withdrawal? Is there a risk for severe withdrawal?
3. Is the patient interested in buprenorphine treatment?
4. Does the patient understand the risks and benefits of buprenorphine treatment?
5. Can the patient be expected to adhere to the treatment plan?
6. Is the patient willing and able to follow safety procedures?
7. Does the patient agree to treatment after a review of the options?
8. Is the patient psychiatrically stable? Is the patient actively suicidal or homicidal; has he or she recently attempted suicide or homicide? Does the patient exhibit emotional, behavioural, or cognitive conditions that complicate treatment?
9. Is the patient pregnant?
10. Is the patient currently dependent on or abusing alcohol?
11. Is the patient currently dependent on benzodiazepines, barbiturates, or other sedative-hypnotics?
12. Does the patient have a history of multiple previous treatments or relapses, or is the patient at high risk for relapse to opioid use? Is the patient using other drugs?
13. Has the patient had prior adverse reactions to buprenorphine?
14. Is the patient taking other medications that may interact with buprenorphine?
15. Does the patient have medical problems that are contraindications to buprenorphine treatment? Are there physical illnesses that complicate treatment?
16. Are the patient's psychosocial circumstances sufficiently stable and supportive? Is there a family member who can help with in the treatment process?

***Adapted from Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction, DHSS, 2004***

#### **D. TREATMENT CONTRACT**

As a participant in the buprenorphine for opioid dependence treatment protocol, I freely and voluntarily agree to accept this treatment contract, as follows:

- (1) I agree to keep, and be on time to, all my scheduled appointments with the doctor and his/her assistant at the clinic/treatment centre.
- (2) I agree to conduct myself in a courteous manner in the clinic/treatment centre.
- (3) I agree not to arrive at the clinic/treatment centre intoxicated or under the influence of drugs. If I do, the doctor will not see me and I will not be given any medication until my next scheduled appointment.
- (4) I agree not to sell, share or give any of my medication to another person. I understand that such mishandling of my medication is a serious violation of this agreement and would result in my treatment being terminated without recourse for appeal.
- (5) I agree not to deal, steal or conduct any other illegal or disruptive activities in the clinic/treatment centre.
- (6) I agree that my medication (or prescriptions) can only be given to me at my regular clinic/treatment centre visits. Any missed clinic/treatment centre visits will result in my not being able to get medication until the next scheduled visit.
- (7) I agree that the medication I receive is my responsibility and that I will keep it in a safe, secure place. I agree that lost medication will not be replaced regardless of the reasons for such loss.
- (8) I agree not to obtain medications from any physicians, pharmacies, or other sources without informing my treating physician. I understand that mixing buprenorphine with other medications, especially benzodiazepines, such as Calmpose or Valium, and other drugs of abuse, can be dangerous. I also understand that a number of deaths have been reported among persons mixing buprenorphine with benzodiazepines.
- (9) I agree to take my medication as the doctor has instructed and not to alter the way I take my medication without first consulting the doctor.
- (10) I understand that medication alone is not sufficient treatment for my disease and I agree to participate in the patient education and relapse prevention program, as provided, to assist me in my treatment.

\_\_\_\_\_  
Patient Signature

\_\_\_\_\_  
Witness Signature

\_\_\_\_\_  
Date



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