



PRESCRIPTION OF INJECTABLE
DIACETYLMORPHINE (HEROIN)
IN CASE OF OPIOID DEPENDENCE;
Rules of guidance no. 9240, May 11th 2009

2009



Prescription of injectable diacetylmorphine (heroin) in case of opioid dependence; Rules of guidance no. 9240 of May 11th 2009

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1 Introduction

Article 1 paragraph 2, of Act on Controlled Substances, cf. Consolidation Act no. 748 of 1. July 2008¹ provides that the Minister for Health and Prevention may decide that controlled substances covered by section 1 of the Act may be used for medical purposes as part of the medical treatment of persons for substance abuse.

Article 2 paragraph 2, cf. list A no 3 in Executive Order no. 749 of 1. July 2008 provides that diacetylmorphine² (heroin) may be used for medical purposes as part of the medical treatment of persons for substance abuse.

Article 41 paragraph 1 and 2 in Act no. 1350 of 17. December 2008 on the Authorization of Health Care Professionals and Health Care Practise³ specifies which doctors may prescribe dependence producing medicine, and section 41 subsection 3 provides that the National Board of Health shall lay down rules on prescription etc.

Article 142 paragraph 1 and 2 in the Health Act, cf. Consolidated Act no 95 of 7. February 2008⁴ specifies that the municipality shall provide treatment with dependence producing medicine free of charge for substance abusers and lays down how the municipality may secure the provision of this treatment.

In Executive Order no. 125 of 18. February 2009 on the prescription of diacetylmorphine (heroin) as part of the medical treatment of persons for substance abuse⁵ the National Board of Health has laid down rules on the prescription of and treatment with heroin.

In the present Rules of guidance the National Board of Health lays down guidelines for the prescription of heroin as part of the medical treatment of persons for substance abuse and on the responsibility for heroin treatment incumbent on the doctors in charge of treatment. In this connection the Rules of guidance specifies among other things the care and conscientiousness which pursuant to section 17 in Act no. 1350 of 17. December 2008³ on the authorization of Health Care Professionals and Health Care Practice is to be exercised in connection with prescription and treatment by authorised health care professionals, including doctors in charge of treatment.

The present Rules of guidance supplements National Board of Health Guidance no. 42 of 1. July 2008 on the medical treatment of drug abusers in substitution treatment for opioid dependence⁶.

This Rules of guidance solely concerns the use of injectable diacetylmorphine (heroin).

2 Legal framework for substitution treatment in cases of opioid dependence and the special requirements with regard to organisation and health professional competence in connection with treatment with injectable heroin

2.1 Responsibility of the municipalities for overall substitution treatment

The legal framework for the organisation of the treatment appears from the Health Act⁴ the Authorization Act³, the Social Services Act⁷ and the Administration of Justice Act⁸.

As from 1. January 2007 Municipal Councils are under obligation to provide medical treatment with controlled substances for drug abusers (substitution treatment). This obligation is laid down in the Health Act section 142 subsection 1. The municipal council continues to be responsible for the social treatment of substance abuse, cf. the Social Services Act section 101.

2.2 Medical treatment

It is a medical task to decide on the need for medical treatment of opioid dependence. Therefore an individual patient, who is assumed to be in need of abstinence or substitution treatment, may not be referred by a municipality for such treatment without medical assessment.

The medical treatment is presupposed to be an integrated part of the overall treatment and care services for drug abusers provided by the individual municipality. Thus there must be coherence between the medical treatment and the services that address the social problems of the individual drug abuser. Therefore treatment with medically prescribed heroin will have to be accompanied by services provided pursuant to the Social Services Act, i.e. both social treatment according to section 101 of the Social Services Act as well as other social support e.g. to solve any maintenance and housing problems that the substance abuser may have. It is the responsibility of the Municipal Council to secure the necessary coherence between the medical treatment and the social services provided in connection with this treatment.

The required coherence between the medical treatment and the social care implies that treatment with medically prescribed heroin will need to take place in close cooperation with the social authorities. In addition the medical treatment plan that is to be established for each single case by the doctor in charge of treatment will have

to form part of the overall action plan that the social authorities are required to establish pursuant to the Social Services Act

The medical treatment and the social treatment as well as other social support which is to be attached to the treatment with medically prescribed diacetylmorphine (heroin) play a very central role with regard to the positive results that may be achieved from this form of treatment. The results are due rather to the comprehensive treatment and support that is attached to the treatment with medically prescribed heroin than to the heroin as such.

It follows from this that medically prescribed diacetylmorphine (heroin) cannot in any way stand alone. The positive results can only be achieved if treatment services are holistic and thus also address the individual drug abuser's social problems.

As regards the medical treatment plan and the overall action plan as well as the cooperation on and the coherence of treatment, cf. National Board of Health Guidance no. 42 of 1. July 2008 on the medical treatment of drug abusers in substitution treatment for opioid dependence.

2.3 Approval of doctors authorised to prescribe injectable heroin as part of substitution treatment of opioid dependence

Treatment with injectable diacetylmorphine is a specialised health care task involving special requirements as to treatment and patient safety.

Intravenous treatment with diacetylmorphine is more complex and involves more risks than conventional oral methadone treatment, and for this reason there are specific requirements as to professional competence and staffing.

The National Board of Health must approve the doctors in charge of treatment who are allowed to prescribe injectable diacetylmorphine as part of substitution treatment in cases of opioid dependence, cf. Executive Order no. 125 of 18. February 2009 on the prescription of diacetylmorphine (heroin) as part of the medical treatment of persons for substance abuse.

The doctor in charge of treatment must have thorough experience of drug abuse treatment. The doctor must be a specialist doctor within a relevant specialty (e.g. general medicine, psychiatry, social medicine, internal medicine) and must be able to document solid clinical experience from substance abuse treatment. Clinical experience must include thorough knowledge of substitution treatment in cases of opioid dependence, somatic and psychiatric comorbidity in connection with substance abuse and experience with multidisciplinary approach to drug abuse treatment as well as the interface with social treatment services.

Initiation of treatment with injectable diacetylmorphine may only take place in connection with treatment services for treatment of opioid dependence with a doctor in charge of treatment and with sufficient medical staff in relation to the number of substance abusers treated.

Application form for authorisation to prescribe injectable diacetylmorphine as part of the medical treatment of persons for substance abuse can be found at www.sst.dk.

Following further agreement the doctor in charge of treatment may hand over prescription rights to other doctors employed by the institution, cf. Executive Order no. 125 of 18. February 2009 on the prescription of diacetylmorphine (heroin) as part of the medical treatment of persons for substance abuse.

Treatment with injectable diacetylmorphine as part of substitution treatment for opioid dependence may not be undertaken within the hospital sector unless this takes place in structured cooperation with an existing treatment institution.

Treatment with injectable diacetylmorphine as part of substitution treatment for opioid dependence may not be undertaken within the Prison and Probation Service.

2.4 Requirements with regard to doctor's assistants in connection with injection treatment

The doctor in charge of treatment may use other authorised health care professionals as assistants.

Treatment with injectable diacetylmorphine as part of substitution treatment in cases of opioid dependence may only be undertaken by authorised health care professionals with a thorough knowledge of substitution treatment and of somatic and psychiatric comorbidity in connection with substance abuse. Moreover, the health care staff must be able to assist patients in connection with injections and undertake acute treatment in the case of life threatening conditions (anaphylaxis, overdose etc.)

The doctor in charge of treatment is responsible for securing that the doctors concerned and other authorised health care staff have undergone a relevant training programme.

2.5 Requirements as to size of target group and organisational resources

A certain size of the target group is required as a precondition for uniform and acceptable quality in the running of an injection clinic (clinic for treatment with injectable heroin).

It is assumed that about 10 per cent of the overall number of persons in long term substitution treatment with oral methadone will meet the criteria for treatment with injectable diacetylmorphine (heroin).

Against the background of experiences from other countries the National Board of Health estimates that a patient base of minimum 20 persons per injection clinic is justifiable.

2.6 Requirements as to health care preparedness

Treatment with injectable diacetylmorphine requires the presence/availability of a doctor and the presence of at least two authorised persons with health care training throughout the clinic's opening hours.

3 Criteria for the initiation of treatment with injectable diacetylmorphine in cases of opioid dependence

3.1 Indication

Indication for treatment with injectable diacetylmorphine is continued intravenous abuse of prescribed or illegal opioids in spite of long term substitution treatment with oral methadone and when the patient has or is threatened by serious health complications.

Medical indication for treatment with injectable diacetylmorphine as part of substitution treatment for opioid dependence must as a minimum be assessed every six months.

3.2 Inclusion criteria

Treatment with injectable diacetylmorphine as part of substitution treatment in cases of opioid dependence presupposes the following:

- Above 18 years of age
- Regular intravenous abuse of prescribed or illegal opioids in spite of oral methadone treatment within the preceding 12 months.
- No active or untreated severe psychiatric condition which would mean that the patient cannot participate in the injection treatment.
- No severe somatic disorder that contra-indicates treatment (e.g. liver insufficiency or kidney disorder).
- No significant alcohol abuse; i.e. the patient must be able to appear in person twice daily without symptoms of severe intoxication or withdrawal.
- No significant abuse of benzodiazepine over the preceding three months. Patients in stable treatment with benzodiazepine are not excluded from injection treatment.
- No pregnancy, breast-feeding or current plans to become pregnant.
- Acceptance of the requirement to appear in person and undertake supervised self-administration of injection treatment.

3.3 Referral for treatment with injectable diacetylmorphine

Referral for treatment with injectable diacetylmorphine may only take place following concrete assessment by the doctor employed by the municipality who is responsible for the patient's oral substitution treatment.

Final indication for treatment with injectable diacetylmorphine as part of substitution treatment for opioid dependence may only be established by the doctors in charge of treatment who have been entered on the National Board of Health list of doctors authorised to take care of this form of treatment.

4 Discontinuation of or interruption of treatment with injectable diacetylmorphine

4.1 Discontinuation of treatment

If the patient wishes to discontinue injection treatment, the patient is transferred to oral methadone treatment with a view to subsequent transfer to relevant treatment services.

In addition it may be necessary to discontinue injection treatment if the patient is not able to cooperate, e.g. if the requirement to appear in person and undertake supervised self-administration is not complied with. In such a case the patient is also transferred to methadone with a view to subsequent transfer to relevant treatment services.

4.2 Interruption of treatment

Interruption of injection treatment will always take place in connection with holidays, trips abroad etc. In addition it will always be necessary to switch to oral methadone substitution treatment in connection with hospital admission or imprisonment in the institutions of the Prison Service.

5 Assessment and examination during treatment with injectable heroin

Concerning abuse history and assessment of somatic and psychiatric comorbidity in drug abusers in substitution treatment reference is made to National Board of Health Guidance no. 42 of 1. July 2008 on the medical treatment of drug abusers in substitution treatment for opioid dependence.

Prior to the initiation of treatment with injectable heroin the patient's status should be clarified with regard to hepatitis A, B and C, HIV, liver and kidney function as well as ECG.

Furthermore examination must be carried out with regard to earlier injection damage and the blood vessels that are considered suitable for injection treatment with heroin.

6 Reporting to the National Board of Health database for injectable heroin and methadone

With a view to individual as well as overall evaluation of this form of treatment, the doctor in charge of treatment shall take care of reporting to the National Board of Health database on injectable heroin and methadone, cf. section 19 of the Authorization Act.

Reporting of data to the National Board of Health database on injectable heroin and methadone shall be undertaken at the initiation of treatment and subsequently every six months. The database covers issues on substance abuse, risk behaviour, occurrence of abuse related somatic and psychiatric diseases, self-assessed health condition and questions on social vulnerability and crime.

Reporting is carried out electronically via the National Board of Health web-site, www.sst.dk.

Data may be printed out and become part of the patient record in which way it may form the basis for continuing assessment of the treatment. In connection with reporting scores are automatically generated against the background of the data entered.

The data reported will form part of a register in the National Board of Health according to the rules pertaining to storage of confidential data and will be used for national evaluation of this form of treatment.

Regarding the ordinary medical reporting obligation concerning substitution treatment for opioid dependence reference is made to National Board of Health Guidance no. 42 of 1. July 2008 on the medical treatment of drug abusers in substitution treatment for opioid dependence.

7 Clinical pharmacology

Diacetylmorphine is a semi-synthetic morphine derivate with a pronounced tolerance development and potential for habituation. It penetrates the blood-brain barrier considerably faster than morphine which results in a more intense and more rapid effect. Diacetylmorphine in itself has only a modest effect, but it is soon transformed into a number of pharmacologically active breakdown products. Of these 6-monoacetylmorphine (which is 3 to 10 times as potent as morphine) is ascribed the acute effect ("rush"), whereas morphine-3- β -glucoronide and morphine-6- β -glucoronide are believed to cause continued euphoria and sedation.

The sedating effect of diacetylmorphine is enhanced through concurrent intake of alcohol, benzodiazepines and barbiturates. The break-down products of diacetylmorphine are primarily excreted via urine for which reason accumulation may be seen in connection with severely affected kidney function. Reduced liver function is of no considerable significance.

Effects and side effects are similar to what is seen in the case of other opioids, cf. National Board of Health Guidance no. 42 of 1. July 2008 on the medical treatment of substance abusers in substitution treatment for opioid dependence. Symptoms in the case of poisoning may be impaired consciousness increasing to a state of coma, hypotension, respiratory failure, pulmonary oedema, hypoxia, cardiac arrest. In non-habituated persons intravenous administration of even minor amounts of heroin (30 mg) may be lethal.

8 Dosage guidance for treatment with injectable diaectylmorphine

8.1 Initiation of treatment with injectable diacetylmorphine

Treatment with injectable heroin will always be preceded by long term methadone substitution treatment.

8.2 Transfer from oral methadone to injectable diacetylmorphine

The pharmacodynamic effect of oral methadone is different from the pharmacodynamic effect of injectable diacetylmorphine. In general the oral methadone dose reflects what is needed to avoid withdrawal symptoms, reduce craving and possibly also to block the effect of other opioids. When in stable substitution treatment with methadone, a patient will not experience being under the influence. This is different from long term substitution treatment with injectable diacetylmorphine where most often the patient experiences an acute effect of the substance at each injection of diacetylmorphine ("rush" and euphoria). When transferring from oral methadone to injectable diacetylmorphine generally a total heroin 24-hour dose is calculated which may secure the absence of withdrawal symptoms over a period of 24 hours.

8.2.1 Transfer from treatment with oral methadone to combination treatment with injectable diacetylmorphine and oral methadone

The four phases in transfer from treatment with oral methadone to combination treatment with injectable diacetylmorphine and oral methadone:

1) *Stabilisation of oral methadone dose prior to initiation of treatment with injectable diacetylmorphine*

The patient must be stabilised for at least 10 to 14 days on an oral methadone dose that is taken under supervision.

2) *Transfer of total oral methadone dose to combination treatment with injectable diacetylmorphine and oral methadone*

Combination treatment with diacetylmorphine and methadone involves a number of advantages. Diacetylmorphine prevents withdrawal symptoms for 6 to 8 hours in tolerant persons, and therefore it can be administered up to two times within ordinary day opening hours. The background for supplementing diacetylmorphine treatment with oral methadone is based on the assumption that injection clinics will not be open 24 hours. By supplementing with an oral methadone dose for the night, withdrawal symptoms may be prevented as well as craving out of the opening hours of the injection clinic.

In addition combination treatment will ease transition between injectable diacetylmorphine and oral methadone during periods when the patient cannot come to the injection clinic (e.g. sickness, holidays).

The total dose of methadone or diacetylmorphine will vary for each individual. Attention should be paid to the fact that in the case of methadone doses of > 80 mg there will be a certain degree of blockage of the effect of diacetylmorphine, and therefore methadone doses of > 80 mg will not be suitable for a number of patients.

In general the injectable diacetylmorphine will replace 60 to 80 per cent of the original oral methadone dose. This means that 20 to 40 per cent of the original methadone dose is maintained as oral methadone in connection with the day's second diacetylmorphine dose or for self-administration at night. E.g: A patient who

initially is in treatment with 100 mg oral methadone may be transferred to injectable diacetylmorphine corresponding to 70 mg methadone (cf. table 1) in which way the remaining 30 mg of methadone is maintained. It should be noted, though, that there is no linear relation between equipotent doses of oral methadone and injectable diacetylmorphine. The conversion factor from oral methadone dose (total 24 hour dose) to injectable diacetylmorphine (total 24 hour dose) increases gradually from about 1:3 at low methadone doses to about 1:6 at large methadone doses (cf. table 1). There is, however, considerable individual variation, among other things because of differences in metabolism rates and drug interaction for which reason the final dose will always depend on concrete clinical assessment. Attention is drawn to the fact that drugs that affect methadone metabolism to a lesser extent affect diacetylmorphine metabolism.

Table 1 below shows transfer from total 24 hour dose of oral methadone to total 24 hour dose of injectable diacetylmorphine.

Table 1: Transfer from oral methadone to injectable diacetylmorphine

Oral methadone 24 hour dose (mg)	Injectable diacetylmorphine 24 hour dose (mg)	Oral methadone 24 hour dose (mg)	Injectable diacetylmorphine 24 hour dose (mg)
20	20-60	95	321-340
25	61-80	100	341-360
30	81-100	105	361-400
35	101-120	110	401-460
40	121-140	115	461-500
50	141-160	120	500-550
60	161-180	125	551-600
65	181-200	130	601-650
70	201-220	135	651-700
75	221-240	140	701-750
80	241-280	145	751-800
85	281-300	150-170	801-900
90	301-320		

Treatment with injectable diacetylmorphine is initiated through a splitting of the total 24 hour dose into two daily doses. The table below shows instances of the relation between oral methadone dose (1 x daily) and injectable diacetylmorphine dose (2 x daily) when about 30 per cent of total methadone dose from before transition has been maintained.

Table 2: Instances of dosage in connection with transition from oral methadone to injectable diacetylmorphine and oral methadone

Prior to transfer Oral methadone dose (mg)	After transfer Total 24 hour dose (mg)		After transfer Dosage schedule (mg) (D = diacetylmorphine, M = methadone)	
	Methadone (oral)	Diacetylmorphine (injectable)	Morning	Afternoon
50	15	110	55 D	55 D + 15 M
60	20	120	60 D	60 D + 20 M
70	25	140	70 D	70 D + 25 M
80	25	160	80 D	80 D + 25 M
90	30	170	85 D	85 D + 30 M
100	35	190	95 D	95 D + 35 M
110	40	210	105 D	105 D + 40 M
120	40	240	120 D	120 D + 40 M
130	45	280	140 D	140 D + 45 M
140	45	320	160 D	160 D + 45 M
150	50	340	170 D	170 D + 50 M
160	50	400	200 D	200 D + 50 M
170	55	460	230 D	230 D + 55 M
180	60	500	250 D	250 D + 60 M
190	65	540	270 D	270 D + 65 M
200	70	600	300 D	300 D + 70 M

3) Assessment of dose and dose adjustment

Methadone and diacetylmorphine doses should be adjusted according to clinical effect and dosage schedule. Dose adjustment presupposes frequent assessment. Dose assessment must be undertaken in relation to the occurrence of withdrawal symptoms and intoxication, serious side effects (sedation, hypotension, respiratory depression, severe allergic reactions), and abuse of non-prescribed opioids and other sedatives.

During dose adjustment and in connection with any dose increase the patient's clinical condition must always be assessed immediately prior to the administration of each diacetylmorphine dose and again at least 15 minutes following administration.

If a patient appears to suffer from withdrawal prior to the intake of diacetylmorphine, medication may be regulated against the background that an increase of methadone dose has the greatest effect with regard to the prevention of withdrawal symptoms in dose intervals, whereas an increase of diacetylmorphine dose has the greatest effect with regard to reducing craving/abuse of illegal diacetylmorphine.

Patients who experience satisfactory effect of medication during the day, but who complain of withdrawal symptoms during the night/early morning may benefit from an increase of oral methadone dose.

- 24 hour diacetylmorphine dose may be increased up to 30 mg per day. Because of the modest accumulation of diacetylmorphine (short half-life), dose may be increased daily in connection with clinical assessment.
- Methadone dose may be increased by no more than 10 mg per 24 hours. Because of the considerable accumulation of methadone (long half-life) dose increase may only be undertaken every 2 to 3 days and at a rate of no more than a total of 30 mg per week.
- Patients must always be monitored at least 15 minutes following increase of diacetylmorphine dose.

4) Establishing of fixed dosage schedule

At the onset of treatment with injectable diacetylmorphine most patients will take diacetylmorphine twice daily supplemented with an oral methadone dose in connection with the second dose.

During certain periods some patients may want to appear for administration of diacetylmorphine only once per day. In such cases the patient may take the whole 24 hour diacetylmorphine dose at one time. The maximum single diacetylmorphine dose may, however, not exceed 450 mg, and the supplementing oral methadone dose must be adjusted accordingly.

8.2.2 Transfer from injectable methadone to injectable diacetylmorphine

For some patients in treatment with injectable methadone it may be relevant to switch to treatment with injectable diacetylmorphine combined with oral methadone. Reasons for this may among other things be side effects from injectable methadone, continued abuse of illegal diacetylmorphine in spite of adequate methadone dose, or the patient's wish for this change.

Patients in treatment with injectable methadone may be transferred to full or part treatment with injectable diacetylmorphine according to the same principles that apply to transfer from oral methadone.

- The patient is stabilised on injectable methadone which is taken under supervision for 10 to 14 days.
- Prior to transfer to diacetylmorphine about 1/3 of injectable methadone is converted to oral methadone.
- When calculating the ratio between oral and injectable methadone the difference in bio accessibility must be taken into account. It is 100 per cent for injectable methadone and is considered to be about 80 per cent for oral methadone.

$$\text{injectable methadone} \times 1,25 \text{ (mg)} = \text{oral methadone (mg)}$$

or in the opposite direction

$$\text{oral methadone} \times 0,8 \text{ (mg)} = \text{injectable methadone (mg)}$$

The equations are only intended as a guide, and therefore it may be necessary to adjust the dose over the following days.

8.3 Maintenance treatment with injectable diacetylmorphine

8.3.1 Maintenance doses of injectable diacetylmorphine

Maintenance dose of injectable diacetylmorphine depends on the individual. Experience from abroad shows that most patients may be treated with 24 hour doses in the interval 200 to 600 mg injectable diacetylmorphine with an average 24 hour dose of 400 to 500 mg. Few patients may, however, need higher 24 hour doses (>600 mg injectable diacetylmorphine).

Maximum doses:

- 24 hour dose of injectable diacetylmorphine 900 mg
- Single dose of injectable diacetylmorphine 450 mg (in the case of single doses > 450 mg side effects in the form of respiratory depression and convulsions are seen more often)

After a long stable period without abuse of illegal opioids, it will often be possible to reduce the prescribed amount of injectable diacetylmorphine and/or oral methadone without the patient experiencing withdrawal symptoms, craving.

8.3.2 Flexible dosage

Supervised medication is a demanding treatment form which for some patients will at times be very difficult or impossible to take part in.

Therefore the patients should on a current basis and daily be offered a flexible dosage schedule which will allow varying parts of the diacetylmorphine treatment to be converted to oral methadone treatment.

Dose and form of administration must be currently documented for each single dose of injectable diacetylmorphine and oral methadone, cf. 12,2 below.

In order to secure flexibility in the dosage schedule, it is recommended that correlated doses for 24 hour dose in the following forms of administration are calculated at the outset for each single patient:

- Schedule A: Injectable diacetylmorphine + injectable diacetylmorphine + oral methadone
- Schedule B: Injectable diacetylmorphine + oral methadone

Schedule C: Oral methadone

Table 1 is used for calculating the ratio between injectable diacetylmorphine and oral methadone.

When the table is used, it should be noted that 24 hour doses of both diacetylmorphine and methadone are used as a basis for calculation.

Conversion of injectable diacetylmorphine to oral methadone is calculated by adding the two individual doses of diacetylmorphine to a total amount of diacetylmorphine and then calculating the equipotent dose of oral methadone.

E.g: $200 + 230 = 430$ mg injectable diacetylmorphine = 110 mg oral methadone.
 Note that the calculation must not be based on conversion of single diacetylmorphine doses, in which case the result in this instance would be: (Injectable diacetylmorphine 200 mg = 65 mg oral methadone) + (injectable diacetylmorphine 230 mg = 75 mg oral methadone) = 140 mg oral methadone.

9 Focus areas/issues

9.1 Multiple abuse

As in the case of other patients who receive substitution treatment for opioid dependence a concurrent abuse of intoxicants such as alcohol, benzodiazepines and cocaine will occur in the group of patients in treatment with injectable diacetylmorphine. Multiple abuse is treated according to existing guidelines, cf. National Board of Health Guidance no. 42 of 1. July 2008 Part 9 on the medical treatment of drug users in substitution treatment.

9.2 Non-appearance/missed doses

Patients who fail to appear for treatment will soon lose their achieved tolerance of the substances concerned. Missed doses should be dealt with according to table 3 below.

Table 3: Guidelines for dosage in the case of missed doses

No. of consecutive days when dose has been missed	Diacetylmorphine dose on resumption of treatment in per cent of former dose	Methadone dose on resumption of treatment in per cent of former dose
1	100	100
2	75	100
3	50	50
>3	Resumption of treatment	Resumption of treatment

When treatment is resumed following non-appearance which has resulted in missed intake of one or several doses, careful observation is required in connection with the following dosage.

9.3 Medication of intoxicated patients

Patients who to a severe degree are under the influence of alcohol or other intoxicants must not be given medication but should await further observation of their condition and renewed assessment.

10 Injection technique

Supervised administration of injectable diacetylmorphine is meant to secure correct injection technique, reduce the risk of infection and increase the patients' knowledge of the importance of clean utensils and personal hygiene through health education.

10.1 Supervised injection

Injection may only take place at the clinic where the patient carries out the injection of the dose dispensed.

Injection of diacetylmorphine must always be supervised by authorised health care staff that can provide the guidance required. The doctor in charge of treatment must establish instructions that describe principles with regard to hygiene and injection technique.

It is important to assist the patient with regard to choice of site of injection and to supervise the occurrence of any infection or vein inflammation. In order to prevent superficial instances of phlebitis it is useful to establish a rotation plan for injection site.

Injection in the groin area, armpit or head and neck area should as a main rule be avoided and may only take place following medical assessment. If at a given time the patient has no suitable veins, diacetylmorphine dose must be converted to oral methadone. By way of exception intramuscular/subcutaneous injection may be accepted after medical assessment.

Patients must be monitored at least 15 minutes after injection.

11 Acute, possibly life threatening side effects

The doctor in charge of treatment is responsible for establishing instructions and for training of the authorised health care staff with a view to acute treatment of potentially life threatening conditions such as

- overdose
- anaphylactic shock
- convulsions
- perforation of artery.

Necessary medication must be available with a view to initial treatment of the above conditions including relevant forms of antidotes. The injection clinics must have equipment for assisted ventilation with oxygen as well as defibrillator.

12 Handling of medicine

The treatment facility must be authorised by the Danish Medicines Agency to receive, handle and store diacetylmorphine, cf. executive order no. 346 of 11 May 2009 on companies' dispensing of and drug abuse treatment facilities' receipt and handling of diacetylmorphine⁹. The authorisation specifies the safety requirements for storage, receipt and record-keeping, etc.

For further information about the general provisions for the handling of medicine and the doctor's application of an assistant, please see executive order no. 1222 of 7 December 2005 on the handling of medicinal products at hospital departments and other treatment institutions¹⁰ as well as the National Board of Health's Guidance no 9429 of 30 June 2006 on Prescription and Handling of Pharmaceuticals¹¹.

The treatment facility must keep local guidance documents which describe the handling of medicine and procedures for injection therapy. The doctor responsible for the treatment must ensure that the guidance is observed and that the doctor's assistant is familiar with its content.

For further information about ordering, storage and record-keeping of diacetylmorphine (heroin), please see the Danish Medicines Agency's guidance on treatment facilities' ordering, receipt, handling and storage of diacetylmorphine for the treatment of drug abusers and companies' import and dispensing thereof¹².

12.1 Preparation and dispensing

Preparation of injectable diacetylmorphine must observe the manufacturer's recommendations.

Dispensing of injectable medicine must be carried out in compliance with the local medicine instructions.

12.2 Registration and accounts

A detailed record must be kept of injectable diacetylmorphine. The record must specify stocks and consumption on the level of patients and clinics, respectively.

Record-keeping and registration at clinic level

Dose of diacetylmorphine must be recorded for each patient on a daily basis. The level of detail must be such that both the quantity prescribed and taken, including any waste, are accounted for. The records must be supplemented by physical counts of the medicine stock.

Reference must be made to the general rules on record-keeping provided by the authorisation act and section 21 of executive order no. 1373 of 12 December 2006 on the patient records of doctors, dentists, chiropractors, midwives, clinical dieticians, dental technicians, dental hygienists, opticians and contact lens opticians (record-keeping, storage, dissemination and transfer, etc.)¹³.

Record-keeping at clinic level

The requirements for record-keeping of spillage and destruction are regulated by the Danish Medicines Agency. For further information, please see the Danish Medicines Agency's guidance no. 32 of 15 May 2009 on treatment facilities' ordering, receipt and storage of diacetylmorphine for the treatment of drug abuse and companies' import and dispensing hereof¹².

12.3 Quality control and monitoring

The quality of injection treatment depends on safety and precision in the handling of medicine. For this reason there must be detailed instructions that are known by the health care staff at the individual injection clinic.

Adverse events must be registered on a current basis and form the background of possible adjustments of practice.

Accounts of medicine stock both at individual and at institutional level must be accessible to National Board of Health surveillance at all times

The Danish Medicines Agency supervises the treatment facilities to ensure compliance with the requirements and conditions laid down in the authorisation granted by the Danish Medicines Agency.

13 National Board of Health evaluation of injection treatment

The National Board of Health monitors the use of injectable diacetylmorphine as part of substitution treatment for opioid dependence both at the general level and at patient level.

Every 6 months on a current basis the National Board of Health will calculate the number of patients that receive this form of treatment.

On the basis of its monitoring the National Board of Health will evaluate the effect of the treatment and against this background decide whether there is any need for adjustment of the present Guidance.

14 Coming into force

This Guidance comes into force on May 11th, 2009

National Board of Health, May 11th, 2009

Anne Mette Dons

Head of Departement, MD

Department of Supervision

Helle Petersen

Senior Medical Officer

15 References

1. Consolidation Act no. 748 of 1. July 2008
2. Executive order no. 749 of 1. July 2008
3. The Authorization Act, Act on the authorization of health care professionals and on the practise of health care, nor. 546 of 24. June 2006
4. The Health Act, Act. no. 95 of 7. February 2008
5. Executive Order no. 125 of 18. February 2009 on the prescription of diacetylmorphine (heroin) as part of the medical treatment of persons for substance abuse
6. Guidance no. 42 of 1. July 2008 on medical treatment of drug abusers in substitution treatment for opioid dependence
7. The Social Service Act, no. 979 of 1. October 2008
8. Consolidation Act no. 877 of 3. September 2008 on legal protection and administrations in social matters
9. Executive order no. 346 of 11. May 2009 on companies' dispensing of and drug abuse treatment facilities' receipt and handling of diacetylmorphine
10. Executive order no. 122 of 7. December 2005 on the handling of medicinal products at hospitals departments and other treatment institutions
11. Guidance no. 9429 of 30. June 2006 on Prescription and Handling of Pharmaceuticals
12. Guidance no. 32 of 15. May 2009 on the treatment facilities' ordering, receipt, handling and storage of diacetylmorphine for the treatment of drug abusers and companies' import and dispensing thereof
13. Executive order no. 1373 of 12 December 2006 on the patient records of doctors, dentists, chiropractors, midwives, clinical dieticians, dental technicians, dental hygienists, opticians and contact lens opticians (record-keeping, storage, dissemination and transfer, etc.)