Effective drug treatment involves a spectrum of care – from counselling and detoxification, to prescribed medication and aftercare – depending on the needs of a particular client. Prescribing medication is an important element of many drug treatment programmes.

The National Treatment Agency (NTA) established a prescribing expert group to advise the Agency on its approach and work programme on prescribing. The group consists of substance misuse specialists, general practitioners, psychiatrists, nurses and treatment service users. This briefing has been developed by the group and lead authors are identified for each section.

This briefing outlines the key findings and recommendations of the NTA’s expert prescribing group on:

- The evidence base for the pharmacological treatment of drug misuse
- Recommended guiding principles of an effective prescribing regime
- Recommended components of an effective prescribing service.

This briefing does not replace existing clinical guidelines (Department of Health, 1999). It has been produced to complement the existing guidelines and the new service framework for drug treatment – Models of care (NTA, 2002).
Pharmacological treatment for drug misusers: review of the evidence base

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In order to commission the best possible prescribing services for drug users, commissioning should be based, as far as possible, on available evidence as to which treatments are effective (1,2,3). There are recognised difficulties in developing a comprehensive and up-to-date evidence base for all forms of treatment for drug misuse, but the aim of this briefing is to demonstrate what evidence is currently available and to point out where gaps exist.

Summary

Some pharmacological treatments should be available to treat drug misuse on the basis of their strong evidence base (e.g. methadone and buprenorphine). Others should be available because of the importance or severity of the condition which they treat, even if their overall effectiveness is restricted to some groups of patients. This category includes drugs such as lofexidine and naltrexone whose relatively lower effectiveness may be due at least in part to the more stringent criteria imposed upon them in measuring outcomes. There can, however, be no doubt regarding the strength of the evidence base for oral methadone maintenance treatment.

There is a further category of drugs for whose effectiveness very little evidence exists and where there may be some contrary evidence suggesting that they should be used with caution: this group includes dihydrocodeine and the benzodiazepines. Whilst these drugs may have some place in the pharmacological treatment of drug dependence, they should be used with particular caution.

Oral methadone maintenance treatment

The best evidence for pharmacological treatments in the drugs field is for oral methadone which has been shown to provide major harm minimisation outcomes in a variety of different settings over a number of years (4,5,6). Against the reasonable assertion that oral methadone has not really been tested in the modern British primary care setting (7,8) can be set a growing body of published outcomes in this setting (9,10,11). The evidence as it stands suggests that: higher doses are better than lower doses at retaining patients in treatment and optimising outcomes (12,13,14); enforced reduction in oral methadone dose (as opposed to maintenance) is ineffective (15,16); and oral methadone treatment accompanied by some form of non-prescribing intervention is probably more effective than methadone alone (17). In view of the strength of the evidence for oral methadone treatment in reducing mortality (18), reducing injecting behaviour (19) and preventing people from being forced to commit crimes in order to obtain drugs (6), it seems essential that every area should offer accessible oral methadone maintenance treatment for those who require this as a harm minimisation intervention. Treatment provided in primary care will be appropriate for many patients.

Other maintenance treatments

There is a growing body of evidence for the efficacy of buprenorphine in the treatment of opioid dependence (20,21,22). The level of evidence does not suggest that buprenorphine should replace methadone as a substitution treatment, but rather that buprenorphine should now be considered an evidence-based addition to the range of pharmacological maintenance treatments. Much of the
emerging evidence derives from other European countries and the evidence for efficacy of this treatment in Great Britain is very limited and based on very few studies.

**Dihydrocodeine** is not generally considered to be an appropriate medication for long term maintenance (3,7) because there is a lack of evidence for its effectiveness, there are a number of practical problems in dispensing it (tablet form, not eligible for controlled drug scripts etc) and the fact that it is not licensed for this indication.

**Injectable methadone** has been found to compare favourably with oral methadone on a range of treatment outcomes but has not been demonstrated to have better results than the oral formulation, although there is some suggestion that certain subgroups of patients may benefit differentially from the injectable form (23). **Injectable diamorphine** (heroin) has also been used for maintenance in some specialist settings (see below).

**Detoxification treatments**

The evidence for success in detoxification treatments is far less compelling than the evidence for harm minimisation maintenance interventions, and this may be in part because the aim of abstinence is correspondingly harder to achieve. There is some evidence for the effectiveness of **lofexidine** (24,25), although the Cochrane review (26) concluded that whilst **clonidine** and lofexidine had similar efficacy to methadone when used for detoxification over a ten-day period, participants in fact stayed in treatment longer with methadone and experienced fewer adverse effects. Lofexidine is considered by many clinicians to be most suitable for patients using up to 50mg methadone or less than 1g heroin daily, for those with shorter drug histories, and for non-polydrug users. Methadone as an agent for detoxification is problematic for a number of reasons including its relative addictiveness and long duration of action (7) but it remains a pragmatic choice in many cases where reduction and maintenance may have become blurred. **Buprenorphine** on the other hand may overcome some of the problems of methadone for detoxification, including a milder abstinence syndrome on withdrawal from the drug, and appears to be as effective as methadone in detoxification from heroin (27,28). **Dihydrocodeine** has in the past been used by practitioners for detoxification and there is some evidence for its efficacy (29) but its advantages may well be superseded by those of buprenorphine (7).

In view of the above evidence, the expert group concluded that lofexidine, methadone and buprenorphine should all have a place in the group of pharmacological therapies used for detoxification. There are a number of newer approaches to detoxification such as rapid detoxification under sedation or anaesthetic (30,31,32,33) and whilst these are not yet generally available or widely researched and for this reason remain controversial (35,36,37), the evidence for their effectiveness should be kept under review.

**Pharmacological treatments for stimulant use**

A number of Cochrane reviews show that current evidence does not support the use of **dopamine agonists**, **carbamazepine** or **antidepressants**, with the possible exception of short-term **fluoxetine** (38,39,40,41). Seivewright (7) has also reviewed the evidence for pharmacological treatments for stimulant users and has concluded “there are precious few effective pharmacological treatment options”. There is, however, an important and large group of patients who need to be attracted into treatment in order to access harm minimisation and for specific treatment for their drug use. Harm minimisation for stimulant users, and crack users in particular, is not well developed, and local areas may want to look at the further development (and evaluation) of such initiatives. Especially in view of the potential severity of the withdrawal syndrome from these drugs, appropriate interventions for users of stimulants such as crack cocaine and amphetamine should be available in all areas in spite of the relative lack of evidence for the effectiveness of pharmacological treatments for this group. Such treatments may, in a specialist setting, include interventions such as **dextroamphetamine** (42) and amelioration of withdrawal symptoms with selective serotonin re-uptake inhibitors (SSRIs) such as **fluoxetine** and/or short term **benzodiazepines**. In some cases, inpatient treatment may be necessary.
 Whilst the evidence base for individual pharmacological treatments is still highly unsatisfactory, results from the National Treatment Outcome Research Study (NTORS) suggests that stimulant users who use stimulants both as a primary drug and as part of a range of polydrug use do, nevertheless, benefit from a range of treatment interventions, especially in rehabilitation services (43).

**Benzodiazepines**

Benzodiazepines are frequently used by drug misusers as a secondary drug, either to enhance the effect of the primary drug or to ameliorate withdrawal effects. They have strong addictive potential, the withdrawal syndrome can be dangerous, and they are known to be a major contributor to deaths from drug misuse. Whilst there is no evidence to support their use for maintenance treatment (3), in view of the major role which they occupy in the field of drug misuse, services must be able to accommodate and treat benzodiazepine use and to prescribe benzodiazepines where appropriate (3) and within their licence. In general this will mean using benzodiazepines primarily for people withdrawing from benzodiazepine dependence.

**Relapse prevention**

Reviews of the effectiveness of naltrexone, the most commonly used pharmacological treatment in relapse prevention, have not been entirely favourable (38) but effectiveness has been demonstrated by some studies, particularly for highly motivated individuals. The Cochrane review of naltrexone maintenance treatment for opioid dependence (39) concludes that the available trials do not allow a final evaluation of naltrexone maintenance treatment yet. Studies of naltrexone inevitably suffer from the high rate of relapse associated with opiate dependence and poor outcomes may reflect inappropriate outcome criteria (40). Combined use of naltrexone and psychosocial therapy has proved to be more effective than either therapy alone in improving post treatment outcomes (41).

Whilst the evidence for naltrexone does not suggest that it will be suitable for every patient, it should nevertheless be available as a treatment option to those who can benefit, not least because of the supreme importance of avoiding relapse.

**Specialist prescribing opiate maintenance options**

There is some emerging evidence for the effectiveness of prescribing intravenous diamorphine for certain groups of patients (42). Whilst there is little research on the effectiveness of injectable methadone, there is considerable agreement amongst many clinicians that this is an important specialist prescribing option for some patients (4). Other specialised drug regimens are similarly uninvestigated but may have a place in the range of treatment options available to the specialist. However, consideration of safe dispensing and avoidance of diversion are essential.

**Recommendations**

Further research and systematic reviews should be carried out in UK settings especially in the following areas:

- effectiveness of treatment in primary care settings
- treatment of stimulant use including harm minimisation
- use of buprenorphine in UK settings
- effectiveness of lofexidine and naltrexone
- treatment of benzodiazepine dependence
- use of rapid detoxification treatments.

Commissioners, planners and providers of drugs services should use the evidence as outlined in this paper when making decisions regarding the essential components of a drugs service and how these should be delivered.
Guiding principles on prescribing

Lead author: Bill Nelles, Methadone Alliance

Careful and appropriate prescribing has been shown to reduce the risks to individuals from illicit drug use. Interventions should prioritise reducing the harm of illicit drug use by offering appropriate and individualised interventions in a safe and effective manner. There is appropriate guidance on this in the Drug misuse and dependence: guidelines on clinical management (Department of Health, 1999).

Prescribing should be tailored to the needs of each individual. The effectiveness of prescribing treatments is further increased when services such as psychological and social support are also provided as appropriate.

Prescribing practices should reflect the evidence base that currently exists. The existing evidence base should also be expanded through the evaluation and research of appropriate interventions – particularly those that have shown success in other areas.

Similar models of prescribing must be available to people in all parts of the country. Each area has a responsibility to ensure all patients can access a comprehensive range of interventions (see service framework outlined in Models of care, NTA, 2002).

Ideally, doctors and patients are partners in care. When prescribing is initiated, there should be broad agreement between doctor and patient on the short and longer term goals of such treatment. Any reduction programme should be agreed with the patient, and undertaken with their active consent. Enforced reduction of methadone is rarely effective, particularly in people with a longstanding addiction to opiates.

Prescribing components of a drug treatment service

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The prescribing components outlined here are designed to complement work already developed in the new service framework for drug treatment - Models of care (NTA, 2002). Prescribing regimens will follow general principles set out in Drug misuse and dependence: guidelines on clinical management (Department of Health, 1999). Importantly, prescribing is only one part of an overall treatment package. The guidance given in Developing an integrated model of care for drug treatment (Department of Health, 2001) is a fuller discussion of the nature of a treatment episode.

Essential components

The following components must be included in a prescribing service:

- Assessment of prescribing needs.
- Safe flexible systems of assessment of appropriate dose, taking into account the risk of overdose and needs of the patient.
The duration of treatment should be:
- Short term (up to 21 days) outpatient detoxification with lofexidine, buprenorphine or other pharmacological support
- Medium term (1 to 6 months) detoxification with methadone or buprenorphine
- Inpatient detoxification with various pharmacological options available
- Longer term or maintenance treatment with oral methadone or buprenorphine.

Supervised dispensing and daily dispensing for:
- the initial stages of treatment
- for clients who fail to reduce illicit drug use or
- those whose lifestyles remain chaotic.

Detoxification treatment for individuals with concurrent alcohol dependence.

Urine or saliva testing to assist in assessing dependence initially and to monitor that the drug prescribed is being taken.

Objectives and outcome goals should be built into a prescribing episode. These objectives can be harm reduction or abstinence based ones (e.g. cessation of injecting or improvement of physical health). The prescription must be reviewed regularly by the prescriber and the goals must be monitored.

Adequately and regularly trained and supported prescribers.

Prescribing options for special groups (e.g. pregnant drug users, young people under 21 and clients in contact with criminal justice services).

Appropriate care co-ordination to ensure psycho-social and other elements of treatment are provided.

Adequate doses for those on oral methadone maintenance (e.g. on average 60–120mg daily).

Desirable components
It is desirable that a prescribing service should have the following components:
- Access to new treatment options, as they become available (e.g. emerging treatments for cocaine addiction).
- Substitute prescribing for concurrent benzodiazepine addiction in polysubstance abusers.
- High dose methadone prescribing (i.e. above 120mg).
- Opiate antagonist prescribing (e.g. naltrexone and pre-prescribing challenge).
- Inpatient stabilisation programmes.
- Specialist prescribing options (e.g. injectable methadone, injectable diamorphine and morphine sulphate).*
- Prescribing for stimulant users (e.g. antidepressants for post cocaine depression and possibly dexamphetamine prescribing for amphetamine users).**

* Research should be commissioned to clarify the role for these options. Evidence based guidance is being developed by the NTA on injectable heroin and methadone.

**Further research will soon be available which may provide more evidence on the effectiveness of dexamphetamine prescribing for amphetamine users.
References

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