NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA114; Methadone and buprenorphine for the management of opioid dependence

This guidance was issued in January 2007
The review date for this guidance is March 2010

Recommendation

- A review of the guidance should be transferred to the 'static guidance' list. That we consult on this proposal.

Consideration of options for recommendation:

Options	Comment
A review of the guidance should be planned into the appraisal work programme.	The absence of significant new evidence suggests that this would be a poor use of NICE resources.
The decision to review the guidance should be deferred [to a specified date].	No new evidence to suggest the guidance should be deferred.
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	No appropriate related technology appraisals have been found. Technology Appraisal 115 ' Naltrexone for the management of opioid dependence' addresses a different place in the pathway of care.
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No new appraisal has been identified
A review of the guidance should be incorporated into an on-going clinical guideline.	No new information suggests the guidance should be updated.
A review of the guidance should be updated into an on-going clinical guideline.	No new information suggests the guidance should be combined with a related technology
A review of the guidance should be transferred to the 'static guidance list'.	**No new evidence suggests the guidance should be reviewed.**

Original remit(s)

To appraise the clinical and cost effectiveness of oral methadone and sublingual buprenorphine as substitute opiates for the management of opiate

misusers and to identify those groups of misusers (in the community and prison settings) who are most likely to benefit from being prescribed oral methadone and those most likely to benefit from sublingual buprenorphine. Also to advise on the optimum doses and context of care required to secure effective outcomes, and to provide guidance to the NHS in England and Wales.

Current guidance

1.1 Methadone and buprenorphine (oral formulations), using flexible dosing regimens, are recommended as options for maintenance therapy in the management of opioid dependence.

1.2 The decision about which drug to use should be made on a case by case basis, taking into account a number of factors, including the person's history of opioid dependence, their commitment to a particular long-term management strategy, and an estimate of the risks and benefits of each treatment made by the responsible clinician in consultation with the person. If both drugs are equally suitable, methadone should be prescribed as the first choice.

1.3 Methadone and buprenorphine should be administered daily, under supervision, for at least the first 3 months. Supervision should be relaxed only when the patient's compliance is assured. Both drugs should be given as part of a programme of supportive care.

Relevant Institute work

Published

Clinical guidelines CG52 Drug misuse: opioid detoxification, published July 2007. Expected review date July 2010

Clinical guidelines CG51 Drug misuse: psychosocial interventions. Published July 2007. Estimated review date July 2010

Public health guidance PH4 Interventions to reduce substance misuse among vulnerable young people. Published, March 2007 Expected review date March 2010

Public health guidance PH18 Needle and syringe programmes: providing people who inject drugs with injecting equipment. Published February 2009. Expected review date February, 2012

Technology appraisals TA115 Naltrexone for the management of opioid dependence. Published January 2007. Review date March 2010

In Progress

Clinical guideline Psychosis in conjunction substance misuse. Expected issue date March 2011

In Topic Selection

[redacted]

Details of new products

Drug (manufacturer)	Details
Suboxone (Schering-Plough)	Suboxone®, a fixed dose combination of buprenorphine hydrochloride and naloxone hydrochloride dihydrate at a ratio of 4:1 (ratio of the bases) was made available in the UK in January 2007.

On-going trials

Trial name and contact	Details
Buprenorphine and Integrated HIV Care (NCT00317460)	The purpose of this study is to examine the efficacy of providing two levels of psychosocial support along with buprenorphine/naloxone (BUP) maintenance to opioid dependent patients receiving their care in an HIV clinical care setting. Estimated Study Completion Date: June 2010
Prescription Opioid Addiction Treatment Study (POATS) (NCT00316277)	The purpose of this study is to determine whether treatment outcome for subjects dependent on prescription opioid analgesics can be improved by adding individual drug counselling to the prescription of buprenorphine/naloxone with standard medical management. This will be examined during: a) an initial four-week treatment with taper; b) a 12-week stabilization treatment for those who do not respond successfully to the initial treatment; and c) a long-term follow-up assessment at 1.5 years, 2.5 years, and 3.5 years after treatment. Estimated Study Completion Date: May 2012
Counseling for Office-Based Buprenorphine (NCT00632151)	The major goal is to determine whether adding cognitive behavioral therapy to physician management will increase the efficacy of buprenorphine/naloxone treatment in an office-based primary care setting. Estimated Study Completion Date: July 2012
Counseling for Primary Care Office-based Buprenorphine (NCT00595764)	The major goal is to determine whether adding cognitive behavioral therapy to physician management will increase the efficacy of buprenorphine/naloxone treatment in an office-based primary care setting. Estimated Primary Completion Date: July 2010
Prison Buprenorphine (NCT00574067)	This five-year study examines the effectiveness of buprenorphine treatment provided to previously-addicted inmates(N=320; 160 males, 160 females) initiated in prison and continued in the community. The study also examines the extent to which the setting of post-release buprenorphine is provided.It is expected that participants receiving in-prison buprenorphine will have superior outcomes compared to participants who did not receive in-prison buprenorphine. Estimated Study Completion Date: July 2012
Relapse Prevention to Reduce HIV Among Women Prisoners (NCT00763958)	This study is a feasibility and acceptability study assessing whether providing buprenorphine for women under criminal justice supervision leaving a controlled environment and returning to the community would prevention opioid relapse.

	Estimated Study Completion Date: September 2010

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from 2005 onwards were reviewed.

Implementation

A submission from Implementation is attached at the end of this paper.

Equality and diversity issues No issues identified.

Appraisals comment:

There is no further evidence to indicate that a review of the guidance is appropriate at this time. A new formulation of buprenorphine – suboxone, which is a combination of buprenorphine and naloxone – became available in January 2007, after the publication of Technology Appraisal 114. However, the emergence of this combination therapy does not necessitate a review. Firstly, the European Public Assessment Report (EPAR) for suboxone indicates that the combination of an opioid antagonist (naloxone) with a mu-opioid analgesic (buprenorphine) is an established strategy to reduce the potential for intravenous misuse. As an established strategy, the new formulation would not necessarily require appraisal. Secondly, the EPAR for suboxone indicates that the activity of buprenorphine in combination with naloxone is likely to be bioequivalent to buprenorphine alone, which limits the scope to provide any recommendation preferring the use one to the other. Lastly, suboxone (a sublingual tablet) could be considered to fall under the 'oral formulations' listed in section 1.1 of the current recommendations and is thus unlikely to change the guidance as it stands.

Technology Appraisal 114 included the following recommendations for further research: randomised controlled trials conducted in the UK comparing methadone and buprenorphine using flexible dosing; randomised controlled trials conducted in the UK comparing high-dose methadone and high-dose buprenorphine; and research examining the impact of supervised consumption on the prevention of overdose. No studies of this nature have been identified.

Summary

A review of methadone and buprenorphine should be transferred to the 'static guidance' list.

GE paper sign off:

Elisabeth George, 29 07 2010

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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

IMPLEMENTATION DIRECTORATE

Guidance Executive Review

Technology appraisal 114: Methadone and buprenorphine for managing opioid dependence

1. National Prescribing

1.1 Data showing trends in prescribing costs and volume are presented below. Unfortunately this data does not link to diagnosis so needs to be treated cautiously in relation to the specific recommendations of the guidance. Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Figure 1 Trend in volume of prescribing methadone and buprenorphine in hospitals in England

Commercial in confidence information is highlighted in black

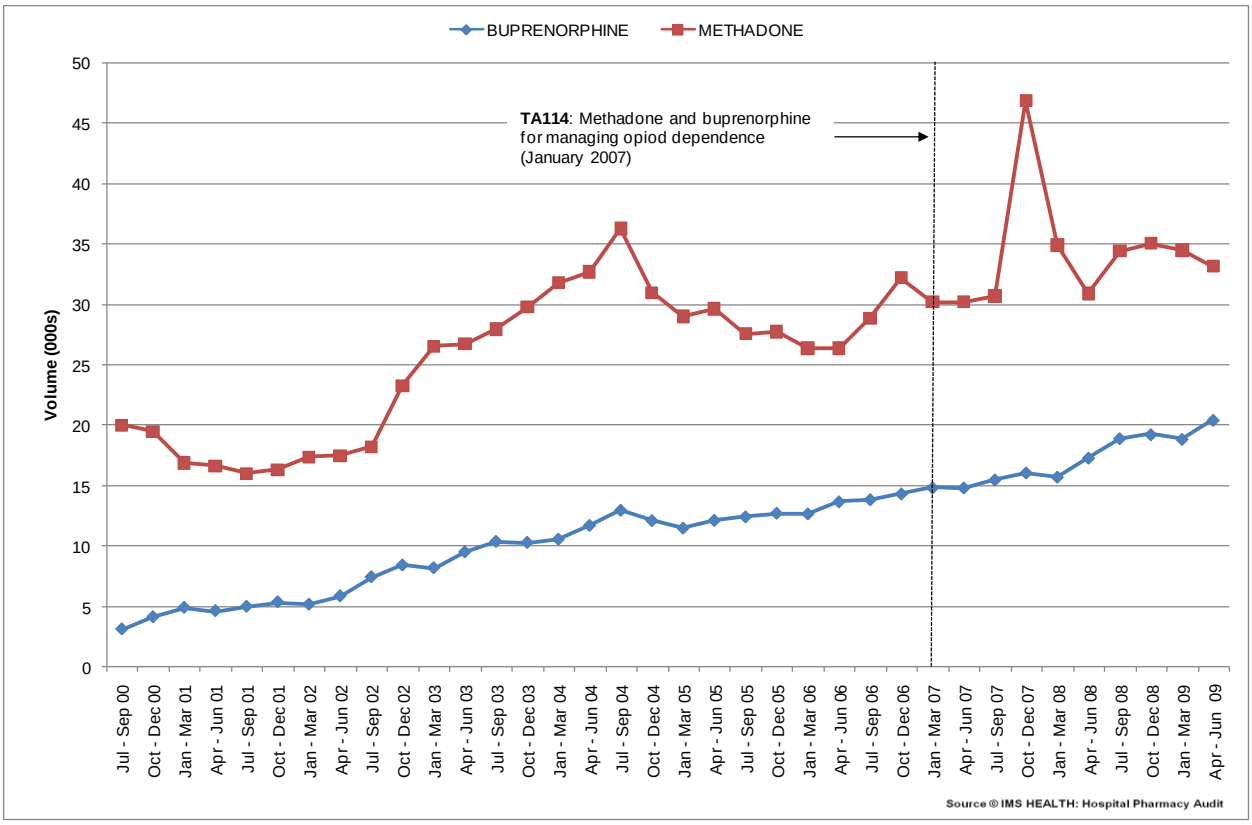
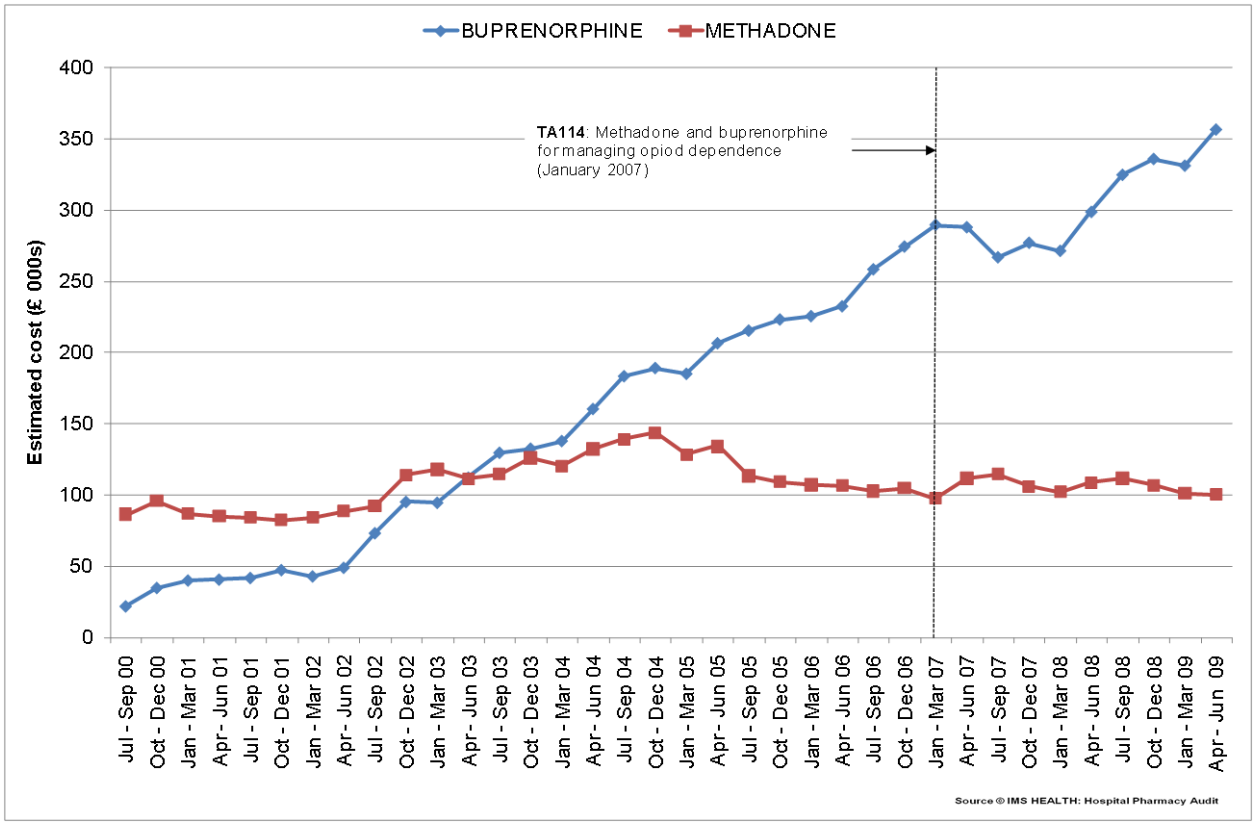


Figure 2 Trend in cost of prescribing methadone and buprenorphine in hospitals in England

Commercial in confidence information is highlighted in black



This section provides information on prescribing cost and volume for methadone and buprenorphine dispensed in the community in England. The data are obtained from the Prescription Cost Analysis (PCA) system, supplied by the Prescription Services Division of the NHS Business Services Authority, and is based on a full analysis of all prescriptions dispensed in the community. Also included are prescriptions written in Wales, Scotland, Northern Ireland and the Isle of Man but dispensed in England. The data do not cover drugs dispensed in hospitals, including mental health trusts, or private prescriptions. All costs stated are based on net ingredient cost (NIC).

Commercial in confidence information is highlighted in black

Figure 3 Items prescribed and dispensed in the community in England of methadone and buprenorphine

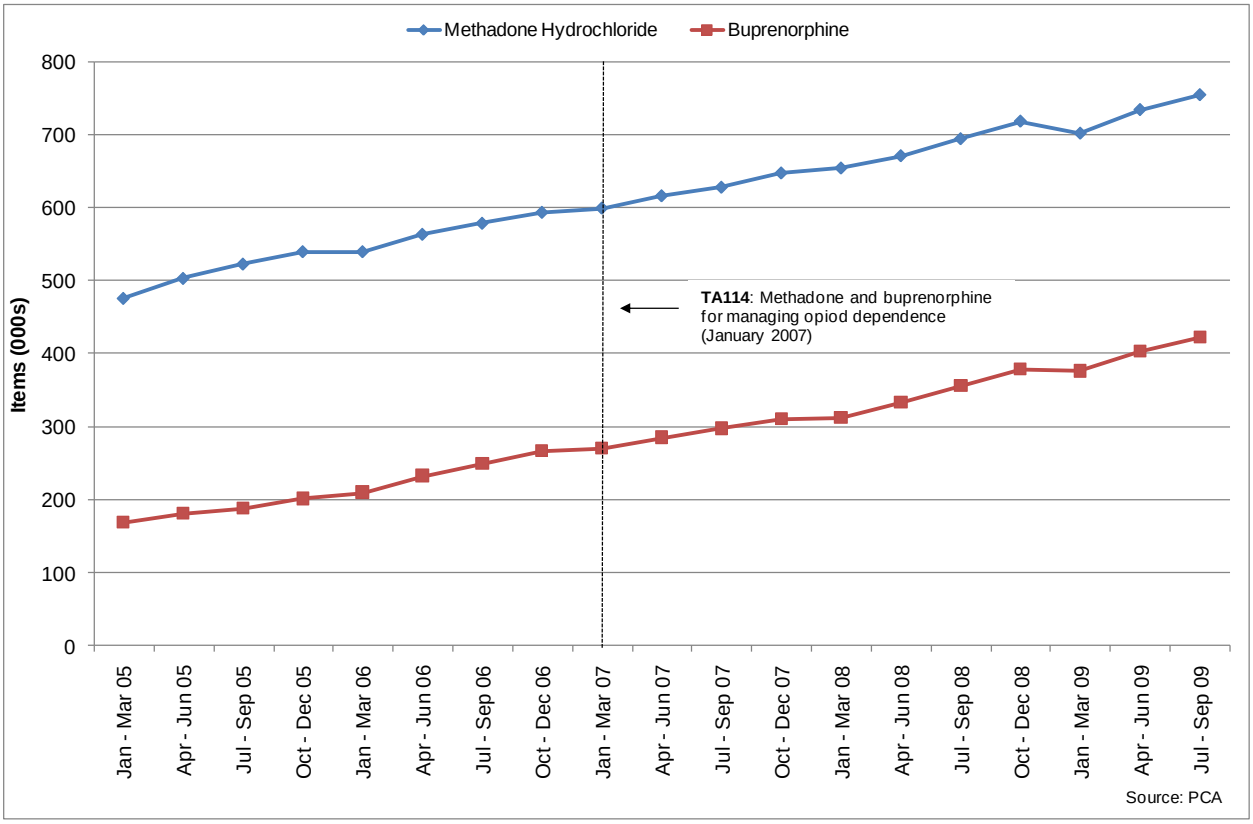
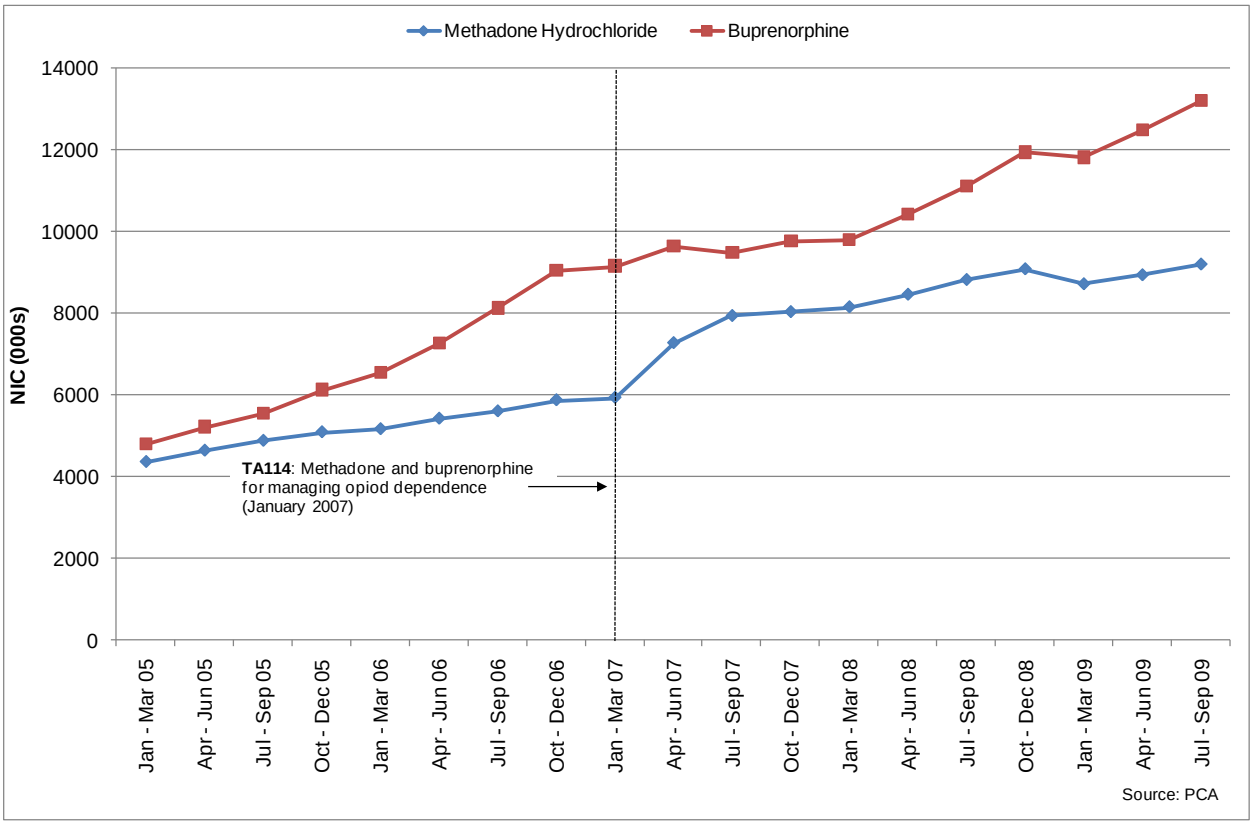


Figure 3 Prescribing costs of methadone and buprenorphine in the community in England



2. External literature

2.1 ERNIE

2.1.1Healthcare Commission and National Treatment Agency for Substance Misuse (2009) Improving services for substance misuse: Diversity, and inpatient and residential rehabilitation services London: Healthcare Commission

Description: A joint service review of inpatient and residential rehabilitation services. The vast majority (86%) routinely used methadone or buprenorphine as their primary medications in detoxification, in line with the NICE clinical guidance.

2.1.2 The Information Centre for Health and Social Care (2009) Hospital Prescribing, 2008: England

http://www.ic.nhs.uk/webfiles/publications/Primary%20Care/Prescriptions/hospre08/Hospital_prescribing_2008_report2.pdf

Cost (£000s)	Primary care	% growth primary	FP10HP*	% growth	Hospital	% growth hospital	Total	% growth total
Buprenorphine (excluding combination with naxolone)	**39,010.6**	**19.9**	**4,192.5**	**-23.5**	**1,230.3**	**9.7**	**44,433.3**	**13.5**
Methadone	**27,857.9**	**29.3**	**6,609.0**	**-13.0**	**428.9**	**-0.1**	**34,895.9**	**18.0**

*FP10HP = prescriptions written in hospitals but dispensed in the community

The data shows that the majority of prescribing for buprenorphine and methadone is carried out in a primary care setting.