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Alcohol use disorders: sample chlordiazepoxide dosing regimens for use in managing alcohol withdrawal

February 2010

Clinical Guideline Implementation Tools

NICE clinical guidelines 100 and 115

These sample chlordiazepoxide dosing regimens accompany the clinical guideline: 'Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence' (available online at www.nice.org.uk/guidance/CG115) and 'Alcohol-use disorders: diagnosis and clinical management of alcohol-related physical complications' (available online at www.nice.org.uk/guidance/CG100).

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The purpose of this tool is to highlight some sample dosing regimens for chlordiazepoxide in managing alcohol withdrawal.

This tool is not NICE guidance. NICE is not endorsing or recommending these dosing regimens.

Implementation of the guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in the guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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Introduction

NICE clinical guidelines 100 and 115 recommend pharmacotherapy delivered via fixed and symptom-triggered protocols for assisted alcohol withdrawal. The preferred medication for assisted alcohol withdrawal is benzodiazepines and both guidelines highlight the use of chlordiazepoxide or diazepam. Chlordiazepoxide is more typically used in practice and therefore is the focus of this document.

- Offer pharmacotherapy to treat the symptoms of acute alcohol withdrawal as follows:
  - consider offering a benzodiazepine[1] or carbamazepine[2]
  - clomethiazole[3] may be offered as an alternative to a benzodiazepine or carbamazepine. However, it should be used with caution, in inpatient settings only and according to the summary of product characteristics. [recommendation 1.1.3.1 of NICE clinical guideline 100]
- Prescribe and administer medication for assisted withdrawal within a standard clinical protocol. The preferred medication for assisted withdrawal is a benzodiazepine (chlordiazepoxide or diazepam). [recommendation 1.3.5.3 of NICE clinical guideline 115]

The NICE implementation team has identified a lack of clear guidance on chlordiazepoxide dosing regimens for alcohol withdrawal brought about by generalised recommendations in the British National Formulary and a lack of national guidance. This has resulted in a current variation in practice in delivery of chlordiazepoxide dosing regimens for assisted alcohol withdrawal.

[1] Benzodiazepines are used in UK clinical practice in the management of alcohol-related withdrawal symptoms. Diazepam and chlordiazepoxide have UK marketing authorisation for the management of acute alcohol withdrawal symptoms. However, at the time of publication (February 2011), alprazolam, clobazam and lorazepam did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented. In addition, the summary of product characteristics (SPC) for alprazolam advises that benzodiazepines should be used with extreme caution in patients with a history of alcohol abuse. The SPC for clobazam states that it must not be used in patients with any history of alcohol dependence (due to increased risk of dependence). The SPC for lorazepam advises that use in individuals with a history of alcoholism should be avoided (due to increased risk of dependence).

[2] Carbamazepine is used in UK clinical practice in the management of alcohol-related withdrawal symptoms. At the time publication (February 2011), carbamazepine did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented.

[3] Clomethiazole has UK marketing authorisation for the treatment of alcohol withdrawal symptoms where close hospital supervision is also provided. However, at the time of publication (February 2011), the SPC advises caution in prescribing clomethiazole for individuals known to be addiction-prone and to outpatient alcoholics. It also advises against prescribing it to patients who continue to drink or abuse alcohol. Alcohol combined with clomethiazole, particularly in alcoholics with cirrhosis, can lead to fatal respiratory depression even with short-term use. Clomethiazole should only be used in hospital under close supervision or, in exceptional circumstances, on an outpatient basis by specialist units when the daily dosage must be monitored closely.

This document was developed to help those in practice who are looking to address this gap and establish standard fixed or symptom-triggered chlordiazepoxide dosing regimens, which are in accordance with NICE guidance, in their organisation. This document illustrates examples of fixed-dose and symptom-triggered chlordiazepoxide dosing regimens for alcohol withdrawal which compliment the recommendations in NICE clinical guidelines 100 and 115. If applicable, the direct application from the example dosing regimen to the NICE recommendation will be highlighted.

These example dosing regimens should not be used alone to inform management of people undergoing assisted alcohol withdrawal. This document should be used in practice alongside NICE clinical guidelines 100 and 115 and in accordance with your organisation’s governance policies.

Fixed-dose regimens

- When conducting community-based assisted withdrawal programmes, use fixed-dose medication regimens[4]. [recommendation 1.3.5.1 of NICE clinical guideline 115]
- Fixed-dose or symptom-triggered medication regimens[5] can be used in assisted withdrawal programmes in inpatient or residential settings. If a symptom-triggered regimen is used, all staff should be competent in monitoring symptoms effectively and the unit should have sufficient resources to allow them to do so frequently and safely. [recommendation 1.3.5.2 of NICE clinical guideline 115]
- In a fixed-dose regimen, titrate the initial dose of medication to the severity of alcohol dependence and/or regular daily level of alcohol consumption. In severe alcohol dependence higher doses will be required to adequately control withdrawal and should be prescribed according to the summary of product characteristics (SPC). Make sure there is adequate supervision if high doses are administered. Gradually reduce the dose of the benzodiazepine over 7–10 days to avoid alcohol withdrawal recurring. [recommendation 1.3.5.4 of NICE clinical guideline 115]

Example regimen one: fixed dose

The key components to this sample dosing regimen which is displayed in table 1 below are that it highlights:

- the need to assess severity of dependence before starting the regimen
- the need for doses to be titrated to severity of dependence and/or regular daily level of alcohol intake
- clear indication of the doses and duration of treatment needed for people with difference severities of dependence.

[4] A fixed-dose regimen involves starting treatment with a standard dose, not defined by the level of alcohol withdrawal, and reducing the dose to zero over 7–10 days according to a standard protocol.
[5] A symptom-triggered approach involves tailoring the drug regimen according to the severity of withdrawal and any complications. The service user is monitored on a regular basis and pharmacotherapy only continues as long as the service user is showing withdrawal symptoms.

Table 1 Example dosing regimen one: fixed dose

Daily alcohol consumption	**15–25 units**		**30–49 units**		**50–60 units**
Severity of alcohol dependence	**Moderate SADQ score 15–25**		**Severe SADQ score 30–40**		**Very severe SADQ score 40–60**
Day 1 (starting dose)	15 mg four times a day	25 mg four times a day	30 mg four times a day	40 mg four times a day[a]	50 mg four times a day[b]
Day 2	10 mg four times a day	20 mg four times a day	25 mg four times a day	35 mg four times a day [a]	45 mg four times a day [b]
Day 3	10 mg three times a day	15 mg four times a day	20 mg four times a day	30 mg four times a day	40 mg four times a day [a]
Day 4	5 mg three times a day	10 mg four times a day	15 mg four times a day	25 mg four times a day	35 mg four times a day [a]
Day 5	5 mg twice a day	10 mg three times a day	10 mg four times a day	20 mg four times a day	30 mg four times a day
Day 6	5 mg at night	5 mg three times a day	10 mg three times a day	15 mg four times a day	25 mg four times a day
Day 7		5 mg twice a day	5 mg three times a day	10 mg four times a day	20 mg four times a day
Day 8		5 mg at night	5 mg twice a day	10 mg three times a day	10 mg four times a day
Day 9			5 mg at night	5 mg three times a day	10 mg four times a day
Day 10				5 mg twice a day	10 mg three times a day
Day 11				5 mg at night	5 mg three times a day
Day 12					5 mg twice a day
Day 13					5 mg at night

SADQ = Severity of Alcohol Dependence Questionnaire

[a] Doses of chlordiazepoxide in excess of 30 mg four times a day should be prescribed only in severe alcohol dependence The patient's response to treatment should always be regularly and closely monitored.

[b] Doses in excess of 40 mg four times a day should be prescribed only if there is clear evidence of very severe alcohol dependence. Such doses are rarely necessary in women and children and never in older people or if there is liver impairment.

This sample regimen was adapted from the dosing regimen in Ghodse H. (1998), by the Guideline Development Group to bring it in line with the recommendations in NICE clinical guideline 115.

Symptom-triggered dosing regimens

- Follow a symptom-triggered regimen[6] for drug treatment for people in acute alcohol withdrawal who are:
  - in hospital **or**
  - in other settings where 24-hour assessment and monitoring are available. [recommendation 1.1.3.4 of NICE clinical guideline 100]
- Fixed-dose or symptom-triggered medication regimens[7] can be used in assisted withdrawal programmes in inpatient or residential settings. If a symptom-triggered regimen is used, all staff should be competent in monitoring symptoms effectively and the unit should have sufficient resources to allow them to do so frequently and safely. [recommendation 1.3.5.2 of NICE clinical guideline 115]

Example regimen two: symptom triggered

On days 1–4, chlordiazepoxide 20–30 mg as needed up to hourly, based on symptoms (including pulse rate greater than 90 per minute, diastolic blood pressure greater than 90 mmHg or signs of withdrawal).

Example dosing regimen two was taken from 'Alcohol-use disorders: diagnosis and clinical management of alcohol-related physical complications'. Royal College of Physicians (2010). For more information see the full guideline, page 46 (available at www.nice.org.uk/guidance/CG100). The Royal College of Physicians highlighted that when managing acute alcohol withdrawal, correctly assessing the person's symptoms is important because they guide the use of 'as-needed' treatment.

The summary of product characteristics (SPC) for chlordiazepoxide recommends 25 mg–100 mg and to repeat if necessary in 2–4 hours. Example dosing regimen two suggests a more rapid repeat (hourly) than the SPC recommendation (2-hourly). Please see the Electronic Medicines Compendium (www.medicines.org.uk) for more information on the SPC recommendations for chlordiazepoxide.

[6] A symptom-triggered regimen involves treatment tailored to the person's individual needs. These are determined by the severity of withdrawal signs and symptoms. The patient is regularly assessed and monitored, either using clinical experience and questioning alone or with the help of a designated questionnaire such as the The Clinical Institute Withdrawal Assessment – Alcohol, revised (CIWA–Ar). Drug treatment is provided if the patient needs it and treatment is withheld if there are no symptoms of withdrawal (definition from NICE clinical guideline 100).

[7] A symptom-triggered approach involves tailoring the drug regimen according to the severity of withdrawal and any complications. The service user is monitored on a regular basis and pharmacotherapy only continues as long as the service user is showing withdrawal symptoms (definition from NICE clinical guideline 115).

Further related recommendations

This section highlights the recommendations from NICE clinical guidelines 100 and 115 that are particularly relevant to these example dosing regimens. It is important to note that these dosing regimens should be used in practice alongside all of the recommendations in NICE clinical guidelines 100 and 115.

This document is directly applicable to the following recommendations in NICE clinical guideline 100:

- Healthcare professionals who care for people in acute alcohol withdrawal should be skilled in the assessment and monitoring of withdrawal symptoms and signs. [recommendation 1.1.2.1]
- Follow locally specified protocols to assess and monitor patients in acute alcohol withdrawal. Consider using a tool (such as the Clinical Institute Withdrawal Assessment – Alcohol, revised [CIWA–Ar] scale[8]) as an adjunct to clinical judgement. [recommendation 1.1.2.2]
- People in acute alcohol withdrawal should be assessed immediately on admission to hospital by a healthcare professional skilled in the management of alcohol withdrawal. [recommendation 1.1.2.3]

This document is directly applicable to the following recommendations in NICE clinical guideline 115:

- When managing alcohol withdrawal in the community, avoid giving people who misuse alcohol large quantities of medication to take home to prevent overdose or diversion[9]. Prescribe for installment dispensing, with no more than 2 days' medication supplied at any time. [recommendation 1.3.5.5]
- In a community-based assisted withdrawal programme, monitor the service user every other day during assisted withdrawal. A family member or carer should preferably oversee the administration of medication. Adjust the dose if severe withdrawal symptoms or over-sedation occur. [recommendation 1.3.5.6]

[8] Sullivan JT, Sykora K, Schneiderman J et al. (1989) Assessment of alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). British Journal of Addiction 84:1353–7

[9] When the drug is being taken by someone other than for whom it was prescribed.

- If benzodiazepines are used for people with liver impairment, consider one requiring limited liver metabolism (for example, lorazepam); start with a reduced dose and monitor liver function carefully. Avoid using benzodiazepines for people with severe liver impairment. [recommendation 1.3.5.10]

Other resources to support learning

The following versions of NICE clinical guideline 115 are available from www.nice.org.uk/guidance/CG115

- The NICE guideline – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals and patient pathway algorithms.
- 'Understanding NICE guidance' – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote reference numbers N2440 (quick reference guide) and/or N2441 ('Understanding NICE guidance').

Implementation tools

NICE has developed tools to help organisations implement this guideline, available from www.nice.org.uk/guidance/CG115

- Slide set to highlight the key messages from the guideline.
- Costing template and report to estimate the national and local savings and costs associated with implementation.
- Audit support for monitoring local practice.

Related NICE guidance

Alcohol-use disorders: preventing harmful drinking. NICE public health guidance 24 (2010). Available from www.nice.org.uk/guidance/PH24

Alcohol-use disorders: physical complications. NICE clinical guideline 100 (2010). Available from www.nice.org.uk/guidance/CG100

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References

- Ghodse H, Checinski K, Drummond C et al. (1998) St Georges Hospital Medical School Department of Psychiatry of Addictive Behaviour. Handbook. 4th edition. St George's Hospital Medical School: London.

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