Manchester Mental Health and Social Care Trust

Shared Care Guideline for	Reference Number
Prescription and monitoring of Disulfiram (Antabuse)	
Author(s)/Originator(s): (please state author name and department)	**To be read in conjunction with the following documents:**
Dr C Daly – Consultant in Alcohol Services Dr F Donnelly – ST5 in Alcohol Services	Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Medicines Management Committee: 10th September 2013	**Review Date: 28th February 2014**

1. Licensed Indications	Maintenance of abstinence in alcohol dependence
2. Therapeutic use & background	Disulfiram is licensed as an adjuvant for maintaining abstinence in those with chronic alcohol dependence. Disulfiram prevents the breakdown of alcohol by irreversibly blocking the enzyme acetaldehyde dehydrogenase. Within 10 minutes of consuming alcohol patients experience an unpleasant reaction mediated by facial flushing, headache, palpitations, tachycardia, dyspnoea, nausea and vomiting. The severity of the reaction varies between individuals and may occasionally become life threatening with hypotension, arrhythmias and collapse. The reaction can last for several hours with peak levels occurring at 8-12 hours. The action of disulfiram lasts for 7 days after the last dose and patients must be warned of this. Patients must be advised to avoid alcohol including low alcohol or non-alcohol beers and wines. They also need to be aware that some food, toiletries, perfumes, aerosol sprays and alcohol hand gels may contain enough alcohol to elicit a reaction. Disulfiram works by changing the expectancy of the effects of alcohol from positive to negative and aversive. In a 1992 study by Chick et al which examined supervised consumption of disulfiram against placebo showed 100 v 69 days abstinent in 6 months and reduced alcohol use 80% v 50% as well as an improvement in GGT levels. Response to treatment is better in those with a supervisor. It is not a standalone treatment it is essential that the patient is actively engaged with psychosocial interventions aimed at relapse prevention. Some patients find that they have no reaction at standard dose an may require a higher dose of up to 600mg. For these people and those who drink through the reaction they should be informed of the risk of repeated acetaldehyde toxicity leading to brain damage, liver damage and cardiac problems.

<table>
<tr><td>3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).</td><td><16
Consumed alcohol in the last 24hrs
Recent MI, angina, cardiac failure and uncontrolled hypertension
History of CVA
Pregnancy
Breastfeeding
Psychosis not absolute contra-indication but should be reviewed by specialist before decision to treat.
Severe personality disorder with associated risk of impulsivity and self harm. Not absolute contra-indication but should be reviewed by specialist before decision to treat.
Severely deranged LFT – GGT>3X normal reference limit (f=120U/L, m=180U/L)
- Bilirubin>30µmol/l
- Albumin:Globulin reversal
- ALT >150U/L
Suicide risk not absolute contra-indication but should be reviewed by specialist before decision to treat. The risk of suicide may be associated with intoxication and continued drinking and may therefore be reduced by successful treatment with disulfiram

Known hypersensitivity</td></tr>
<tr><td>4. Prescribing in pregnancy and lactation</td><td>This drug cannot be prescribed in the pregnant/breastfeeding patient In these circumstances discuss with specialist addiction psychiatrist</td></tr>
<tr><td>5. Dosage regimen for continuing care</td><td>
<table>
<tr><td>Route of administration</td><td>oral</td></tr>
<tr><td colspan="2">Preparations available
Scored White tablets of 200mg which can be partially dissolved in water</td></tr>
<tr><td colspan="2">Please prescribe:
200mg once daily or 400mg on alternate days this should be supervised by a nominated person on these occasions.</td></tr>
<tr><td>Is titration required</td><td>Yes ✓ No</td></tr>
<tr><td colspan="2">Titrate dosage up by units 800mg day1
600mg day2
400mg day3
200mg onwards</td></tr>
<tr><td colspan="2">Adjunctive treatment regime

Psychosocial interventions active involvement with an evidence based intervention e.g. Motivational Enhancement, CBT</td></tr>
<tr><td colspan="2">Conditions requiring dose reduction
e.g. impaired renal/ liver function
Over-sedation on previous use
Skin reactions related to commencement of disulfiram</td></tr>
</table>
</td></tr>
</table>

Usual response time

Starting at the above titration the patient should be informed the disulfiram alcohol effect will be present immediately and alcohol (and alcohol containing products) should be avoided from commencement on this medication

Duration of treatment
6-12 months

Treatment to be terminated by
GP or specialist

NB. All dose adjustments will be the responsibility of the initiating specialist care unless directions have been specified in the medical letter to the GP.

6.Drug Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics

The following drugs must <u>not</u> be prescribed without consultation with the specialist:

Paraldehyde

The following drugs may be prescribed with caution:

Disulfiram inhibits hepatic microsomal enzymes leading to interference of the metabolism of a variety of prescribed drugs:

- Warfarin – enhanced effect therefore careful monitoring of INR required
- Tricyclics – Disulfiram increases the plasma concentration of tricyclics by 50% risk of toxicity may need to reduce dose or use alternative antidepressant.
- Amitryptiline – increased disulfiram reaction.
- Phenytoin – metabolism inhibited increasing risk of toxicity
- Temazepam – increased risk of toxicity
- Benzodiazepines – metabolism is inhibited so increased sedative effects can be used and is often commenced during detoxification
- Theophylline – metabolism is inhibited so increased risk of toxicity.

- Metronidazole, isoniazid and paraldehyde interact with Disulfiram increasing the risk of psychotic reaction.

7. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain,

Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Adverse event System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**

consult Summary of Product Characteristics or BNF	Drowsiness, sweatiness, halitosis, alteration in taste, impotence, dizziness and headache.	Generally mild and transient if severe may require a reduction in dose.	GP or Specialist
	Hypertension	Generally mild and transient but if persists may require reduction in dose or cessation of the drug	GP or Specialist
	Dermatological reactions including acneiform eruptions, allergic dermatitis	Generally only during the first two weeks of treatment, if persists then may require reduction or cessation of the drug Treat dermatitis as per usual protocols	GP or specialist
	Allergic reaction including anaphylaxis	Generally within the first few doses treat allergy, if not confirmed consider re-challenge with specialist	Accident and Emergency
	Optic Neuritis, peripheral neuritis, polyneuritis	Late onset at 6-9 months and is progressive, disulfiram should be stopped It may be reversible on cessation of disulfiram but there may be permanent changes.	GP or specialist
	Cholestatic and Fulminant Hepatitis	Hepatotoxicity is very rare and risk peaks between 6-12 weeks but can occur anytime and may be fatal. Risk is higher with co-existent liver disease. Stop medication and refer to medical specialist. If acutely unwell advise patient to attend emergency services If confirmed will need careful monitoring and not for re-challenge unless risk benefit review by specialist	Accident and Emergency or GP

	Psychotic reactions (inc persecutory, depressive and manic presentations +/- hallucinations)	Stop medication, start antipsychotic medication if necessary and seek the advice of addiction or general adult psychiatrist	GP or specialist
	The patient should be advised to report any of the following signs or symptoms to their GP or attend local emergency department without delay: Symptoms of allergic reaction, disulfiram reaction, severe hepatotoxicity or overdose should be reported to Accident and Emergency. Symptoms of neuritis or hepatotoxicity if mild report to GP.		
	Other important co morbidities :		
	Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.		
8.Baseline investigations	List of investigations / monitoring undertaken by secondary care Baseline BP and pulse rate Baseline U+E, LFT, GGT, FBC Baseline ECG if indicated by possibility of cardiac disease		
9. Ongoing monitoring requirements to be undertaken by GP	**Is monitoring required?**	**Yes**	

Monitoring	**Frequency**	**Results**	**Action**	**By whom**
LFT and GGT	6 weeks after initiation then 3 monthly from initiation.(unless advised more frequently by specialist)	If significantly elevated cf initial bloods	Stop medication and seek expert opinion	GP
		If mildly elevated cf initial bloods	Continue medication but obtain advice from specialist Increase frequency of LFT/ GGT to 2-4 weeks	GP
Physical state	As appropriate		As indicated by physical findings	GP
Mental Health	monthly		As indicated by	CAT worker or Specialist

				assessment findings	
10. Pharmaceutical aspects	"no special considerations"				
11. Secondary care contact information	**If stopping medication or needing advice please contact:**				
	Dr _____				
	Contact number: _____				
	Hospital: _____				
12. Criteria for shared care	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements				

13. Responsibilities of initiating specialist	Identify suitable individuals Initiate treatment and prescribe until dose is stable Undertake baseline monitoring. The tests may be taken in primary care but should be reviewed by the specialist in making prescribing decisions. Dose adjustments. Monitor patient's initial reaction to and progress on the drug. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. i.e. 4/52 supply together with dose titration as appropriate Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment Provide GP with advice on when to stop this drug. Provide patient with relevant drug information to enable (see attached patient information forms) Informed consent to therapy Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action Provide patient with relevant drug information to enable understanding of the role of monitoring. Provide patient with monitoring booklet where appropriate. Provide information leaflet to nominated supervisor (see attached)
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14. Responsibilities of the GP	Initiate treatment as directed by the specialist Ensure no drug interactions with concomitant medicines To monitor and prescribe in collaboration with the specialist according to this protocol To ensure that the monitoring and dosage record is kept up to date Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. Stop medication if the patient repeatedly fails to collect prescriptions
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15. Responsibilities of the patient	To take medication as directed by the prescriber and under supervision , or to contact the GP if not taking medication Must be alcohol free for 24hrs before taking the medication To attend hospital, CAT and GP clinic appointments, Failure to attend will result in medication being stopped (on specialist advice). To report adverse effects to their Specialist or GP. To avoid alcohol, alcohol containing products and others advised by specialists To engage in psychosocial interventions

16.Additional Responsibilities	**List any special considerations**	**Action required**	**By whom**	**Date**
	Nominated supervisor	CAT team / Specialist help patient identify supervisor and give information Supervisor to reveiew the information and watch the patient take the medication ideally everyday but at least 3x per week	CAT Specialist Nominated supervisor	
17. Supporting documentation	The SCG must be accompanied by a patient information leaflet and su[pervisor information leaflet			
18. Patient monitoring booklet	None.			
19. Shared care agreement form	Attached below			

Shared Care Agreement Form

Specialist request

***IMPORTANT: ACTION NEEDED**

Dear Dr *[insert Doctors name here]*

Patient name: *[insert Patients name here]*
Date of birth: *[insert date of birth]*
Diagnosis: *[insert diagnosis here]*

This patient is suitable for treatment with *[insert drug name]* for the treatment of *[insert indication]*

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by Trust / LHB / AWMSG). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on *[insert date started]* *[insert dose].*

If you are in agreement, please undertake monitoring and treatment from *[insert date]*
NB: date must be at least 1 month from initiation of treatment.

Baseline tests: *[insert information]*

Next review with this department: *[insert date]*
You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice. The patient will not be discharged from out-patient follow-up while taking *[insert text here]*.

Please use the reply slip overleaf and return it as soon as possible.

Thank you.

Yours

[insert Specialist name]

Shared Care Agreement Form

GP Response

Dear Dr *[insert Doctors name]*

Patient *[insert Patients name]*

Identifier *[insert patient date of birth/address]*

I have received your request for shared care of this patient who has been advised to start *[insert text here]*

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

GP signature Date

GP address/practice stamp