

Indication: Maintenance of abstinence in alcohol dependence

General guidance

This protocol sets out details for the shared care of patients taking **disulfiram** and should be read in conjunction with the General Guidelines for Shared Care. Sharing of care requires communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **The doctor who prescribed the medication legally assumes responsibility for the drug and the consequences of its use.** The prescriber has a duty to keep themselves informed about the medicines they prescribe, their appropriateness, effectiveness and cost. They should also keep up to date with the relevant guidance on the use of the medicines and on the management of the patient's condition.

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.

Disulfiram works by changing the expectancy of the effects of alcohol from positive to negative and aversive. Response to treatment is better in those with a supervisor. It is not a stand alone treatment it is essential that the patient is actively engaged with psychosocial interventions aimed at relapse prevention.

Responsibilities

A. Consultant responsibilities

1. When treatment is **initiated** send Shared Care request form with Shared Care Protocol to GP.
2. Counsel the patients on avoiding alcohol including low alcohol or non-alcohol beers and wines. Ensure that patient is aware that some food, toiletries, perfumes, aerosol sprays and alcohol hand gels may contain enough alcohol to elicit a reaction. Patients should avoid alcohol for 24 hours before taking disulfiram and be aware that the action of disulfiram lasts for 14 days after the last dose.
3. Help patient identify and give information to a supervisor on supervising patient self administration of disulfiram (supervisor to review the information and watch the patient take the disulfiram ideally every day but at least three times a week)
4. Inform patients who drink alcohol while taking disulfiram of the risk of repeated acetaldehyde toxicity leading to brain damage, liver damage and cardiac problems.

5. Check LFTs at baseline and at 4 and 8 weeks post commencement of disulfiram. Continue monitoring clinical parameters, and biochemical markers if necessary (see monitoring section). The most recent LFTs should be sent to the GP. Where these results are abnormal the baseline bloods should be sent for the purposes of comparison, to show a reduction. Patients with worsening LFTs, likely to be related to disulfiram (usually a rapid rise in transaminases from baseline within the first 4 to 8 weeks) are not suitable for shared care and need careful and close monitoring.
6. Initiate therapy following full discussion with the patient of benefits and risks.
7. Counsel the patient to report immediately to the GP if onset of any feature of liver toxicity (e.g. nausea, vomiting, abdominal discomfort, dark urine, jaundice) or optic neuritis or neuritis (usually experienced as one of: pain on moving affected eye, blurring, glare, or blackening of vision, loss of colour vision)
8. Commence disulfiram, adjusting dose as appropriate and undertake monitoring of clinical response (and adverse effects)
9. When a GP positive response to SC has been received and patient has been stabilised send a letter to GP “handing over” the Shared Care of the patient to the GP.
10. Respond to any request from GP to review the patient due to adverse effects of therapy.
11. Advise the GP on continuing or stopping disulfiram following medical review of the patient and associated drug therapy
12. Notify GP if patient is failing to attend clinic and advise GP on appropriate action

B. GP responsibilities.

1. Prescribe disulfiram as part of the shared care agreement.
2. Monitor the general health of the patient
3. Report adverse effects of therapy to the consultant and the Medicines and Health Care products Regulatory Agency (MHRA).
Disulfiram may be stopped by GP if patient is repeatedly drinking alcohol while taking medication or is not collecting prescriptions or attending specialist centre clinic appointments.

C. Patient responsibilities

1. Consent to treatment with disulfiram
 2. Attend regular appointments with specialist centre and GP.
 3. Report any side effects to the specialist or GP whilst taking disulfiram.
 4. To avoid alcohol and alcohol containing products as advised by specialists.
 5. To engage in psychosocial interventions*
 6. To self administer medication as directed by the specialist centre (supervised by nominated lay or specialist supervisor), and to contact the GP if not taking medication.
- Disulfiram should be seen as an adjunct to active involvement with psychosocial interventions, for example AA or Smart Recovery. Patient failure to maintain psychosocial interventions is not usually seen as a reason to stop treatment, provided the patient remains alcohol free

Dosage Regimen

200mg od. Dose may be increased to 400mg od if no/inadequate aversive reaction seen with 200mg od. All dose adjustments will be the responsibility of the initiating specialist.

The supervision of self administration by a specialist centre, or by a spouse/family member is recommended- and will normally be arranged by the specialist centre on commencement of disulfiram.

- Daily dosing maybe adjusted, under specialist guidance, to allow supervision of self administration (e.g. 200mg od may be taken as 400mg on Mondays and Wednesdays, and 600mg on Fridays). Although this is an unlicensed dosing schedule it allows more reliable disulfiram supervision: the evidence base strongly support supervised administration of disulfiram.

Supervised administration details should be clearly detailed in any correspondence from specialist to GP.

- Treatment is usually continued for 6-12 months in the first instance. Longer term prescribing is supported but with a clear undertaking from the patient to attend specialist reviews-usually at six month intervals.

Monitoring

Baseline- Blood pressure, pulse rate, creatinine and electrolytes, LFTs (including GGT) FBC. Baseline ECG if any symptoms suggestive of cardiac disease.

Continued monitoring-by specialist

LFTS – at four weeks and at eight weeks.

Further LFT monitoring is only indicated for the monitoring of disulfiram if bloods have worsened between onset and 4-8 week review, or if signs of liver disease (see point 5, consultant responsibilities, page 2)

Physical state- offer every six months

Mental health – offer every six months

Adverse effects

Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Drowsiness, sweatiness, halitosis, alteration in taste, impotence, dizziness and headache.	Generally mild and transient if severe may require a reduction in dose. If drowsiness or fatigue avoid driving or operating machinery
Hypertension (occurs rarely)	Generally mild and transient but if persists may require reduction in dose or cessation of the drug

Dermatological reactions including acneiform eruptions, allergic dermatitis (occurs rarely)	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
Allergic reaction including anaphylaxis	Generally occurs within the first few doses: treat allergy depending on presentation Unconfirmed mild reactions may warrant cautious rechallenge in a specialist setting.
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.
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
Psychotic reactions (inc persecutory, depressive and manic presentations +/- hallucinations)	Stop medication, and seek the advice of addiction or general adult psychiatrist. Antipsychotic medication maybe necessary
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	

Contraindications

- Age less than 16 years
- Consumption of alcohol in the last 24 hours (prior to first dose of disulfiram)
- Recent MI, angina, cardiac failure and uncontrolled hypertension
- History of stroke
- Pregnancy and lactation
- Known hypersensitivity
- Severely deranged LFTs > 3 times the upper limit of normal
- Hypersensitivity to disulfiram or any of its excipients

Psychosis, severe personality disorder or suicide risk are not absolute contraindications but should be reviewed by specialist before decision to treat.

Interactions

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.
- Tricyclic antidepressants (TCAs)- plasma concentrations increased by 50%- may need to reduce TCA dose or use an alternative antidepressant.
- Amitriptyline- increased disulfiram reaction
- Phenytoin –metabolism inhibited increasing risk of toxicity,
- Benzodiazepines–metabolism 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.

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