1. Introduction
Disulfiram (Antabuse®) is an adjunct in the treatment of alcohol dependence (under specialist supervision).

It acts by blocking the activity of the liver enzyme aldehyde dehydrogenase, which leads to an accumulation of acetaldehyde in the body when alcohol has been consumed, even in small amounts. This gives rise to an unpleasant systemic reaction which includes flushing, headache, tachycardia, nausea and vomiting. The disulfiram-alcohol reaction begins within 10 minutes of
alcohol consumption and lasts typically 30-60 minutes; longer if large amounts have been taken. [1]

NICE Guideline 115 (Alcohol-use disorders) [2] recommends the use of disulfiram in combination with a psychological intervention for patients who have successfully withdrawn from moderate to severe alcohol dependence and want to achieve abstinence, and for whom acamprosate or naltrexone are not suitable or preferred.

2. **Scope**
Pennine Care NHS Foundation Trust

3. **Clinical Condition being treated**
Disulfiram is licensed as an alcohol deterrent compound [3]. By producing extremely unpleasant physical symptoms whenever even a small amount of alcohol is taken, it helps the co-operative and well-motivated patient to achieve abstinence. It should be prescribed in combination with appropriate psychosocial interventions. [4]

Disulfiram does not prevent the harmful effects of continuous alcohol abuse.

Disulfiram does not constitute treatment for the symptoms of alcohol withdrawal.

Disulfiram is to be used only when total abstinence is the goal. It is inappropriate for patients who wish merely to attenuate their drinking.

NICE Guidelines [2] recommend if possible a family member or carer should oversee the administration of the drug.

4. **Product information and treatment regimen to be used**
Disulfiram (Antabuse®) is presented in 200mg tablets.

It is recommended [3] that disulfiram treatment should be initiated in a hospital or specialised clinic and by physicians experienced in its use. Within Pennine Care, it may also be initiated by a General Practitioner with a Special Interest (GPwSI) working within the national Enhanced Guidelines for Alcohol. The disulfiram may be initiated by the GP on the advice of the secondary care service where that service is not commissioned to initiate treatment. Disulfiram may be initiated within a tertiary service detoxification programme and this service will liaise closely with Pennine Care NHS Foundation Trust and the GP.
It must be started at least 24 hours after the last alcoholic drink was consumed. [2]

The recommended initiation regime is as follows. To be taken as a once daily dose.

Day 1: 4 tablets (800 mg)
Day 2: 3 tablets (600mg)
Day 3: 2 tablets (400mg)
Day 4: 1 tablet (200mg)
Day 5: 1 tablet (200mg)

Thereafter, dosage may continue at 1 or half a tablet (200mg or 100mg) daily, for no longer than 6 months without review. [3]

For people who continue to drink, if 200mg taken regularly for at least a week does not cause a sufficiently unpleasant reaction to deter drinking, an increase in dosage may be considered in consultation with the person. [2]

After initiation, patients should be monitored every two weeks for the first two months, then monthly for the following four months, thereafter every 6 months.

If relapse occurs, disulfiram treatment should be discontinued; however, a disulfiram reaction can occur up to 14 days after discontinuation of the drug.

5. Regimen Management

Aspects of care for which the Consultant psychiatrist /GPwSI / specialist team is responsible

Assessment and liaison

- To make a diagnosis, and assess the suitability of the patient for disulfiram treatment
- To discuss with the patient, and their family or carers the proposed treatment, including the possible side effects and toxic effects, and to obtain their agreement and commitment to proceed. In particular to ensure the patient/carer is aware of the rare complication of hepatotoxicity and recognises the symptoms which would indicate a need to stop disulfiram and seek urgent medical attention
- To arrange for complementary psychological treatment
- To explain that the reaction between disulfiram and alcohol may cause flushing, nausea, palpitations, and, with larger quantities of alcohol, more serious symptoms such as arrhythmias, hypotension and collapse. [1]
- To warn the patient and their family or carers that disulfiram may also react with alcohol in food, perfume, aerosol sprays etc.
• To provide the patient and family or carers with written information about the drug. Suitable information may be found at http://www.choiceandmedication.org/penninecare/medications/136

Treatment initiation
• To arrange for liver function and urea and electrolytes tests to assess for liver or renal impairment.
• To ensure that the patient is not currently taking any medication which would interact with disulfiram. (See below)
• To prescribe and oversee the initial ‘loading’ dosing of the patient on days 1-5 (see above) or provide instructions to the GP for initiation and/or titration to a suitable dose where this has been agreed.
  NB Appropriate action must be taken if the patient changes care setting during the loading phase eg is taken into an Accident and Emergency department. [5]
• To establish the appropriate maintenance dose
• To continue care of the patient, performing the required assessments, until the maintenance dose is achieved and their condition is stable.

Liaison with General Practitioner (GP)
• To ask the GP whether they are willing to participate in shared care
• To provide details of dosage, and nature and frequency of monitoring
• To ensure that there are clear arrangements in place for specialist back-up and advice.
• To advise the GP of any dosage adjustments required, when to refer back, and when and how to stop treatment (if appropriate).

Adverse reaction reporting
• To report any unexpected adverse drug reactions to the medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card Scheme https://yellowcard.mhra.gov.uk

Aspects of care for which the GP is responsible

Liaison with Secondary care/GPwSI
• To reply to the request for shared care as soon as possible
• To refer to the consultant/GPwSI /specialist team in the event of
  • a problem with the patient’s treatment concordance
  • intolerable side effects
  • an unexpected adverse reaction to disulfiram
  • a suspected relapse
In the event that a patient continues to drink because a 200mg daily dose, taken for at least a week, does not provide a sufficiently unpleasant response, to consider, in consultation with specialist services, an appropriate increase in dosage.

Patient care
- To prescribe the disulfiram at appropriate intervals
- To ensure no interacting medicines are concurrently prescribed (See below)
- To continue monitoring as agreed with specialist service
- To provide the patient with information and advice

Adverse reaction reporting
- To report any unexpected adverse drug reactions to the medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card Scheme https://yellowcard.mhra.gov.uk

6. Contra-indications, cautions, side-affects etc.

Contraindications [3]
- presence of cardiac failure
- coronary artery disease
- previous history of cerebrovascular accident
- hypertension
- severe personality disorder
- suicidal risk
- psychosis
- consumption of alcohol
- pregnancy
- breast feeding
- hypersensitivity of disulfiram tablets or any of its excipients

Cautions [3]
Caution should be exercised in the presence of
- renal failure
- hepatic disease
- respiratory disease
- diabetes mellitus
- hypothyroidism
- cerebral damage
- epilepsy

Side effects [3]
Commonly
- drowsiness and fatigue (during initial treatment)
- nausea
- vomiting
- reduced libido
- halitosis

Rarely
- psychotic reactions, depression, paranoia, schizophrenia, mania
- allergic dermatitis
- peripheral neuritis
- hepatic cell damage
- encephalopathy
- optic neuritis

7. Drug Interactions [1]
- alcohol (may be present in liquid medicines, sprays, lotions)
- antibacterials: psychotic reaction with metronidazole, CNS effects of disulfiram possibly increased by isoniazid
- anticoagulants: enhances anticoagulant effect of warfarin and acenocoumarol
- antidepressants: amitriptyline increases disulfiram reaction to alcohol, disulfiram increases plasma levels of tricyclics
- antiepileptics: increases plasma levels of phenytoin
- anxiolytics and hypnotics: increases plasma levels of benzodiazepines
- paraldehyde: increased risk of toxicity
- theophylline: increased risk of toxicity

8. Back-up care available to GP from Drug and Alcohol services, including emergency contact procedures and help line numbers

Drugs and Alcohol services (Monday to Friday 9.00am – 4.45pm)

Rochdale Drug and Alcohol Service
11 – 13 St Chad’s Court
Rochdale
OL16 1QU
Tel: 01706 676500

Oldham Drug and Alcohol Service
First Step and The Gateway
5 Horsedge Street
Oldham
OL1 3SXTel: 0161 716 3666

Stockport Drug and Alcohol Service
Cirtek House
Higher Hillgate
Stockport
9. Statement of agreement
This guideline is a request by the consultant/specialist services to share the suggested care pathway for the patient.

if the GP is unable to agree to the sharing of care and prescribing this should be made known to the consultant/specialist service with in 14 days, stating the specific nature of the concern.

10. Written information provided to the patient

Manufacturer’s leaflet
http://www.medicines.org.uk/emc/medicine/3048/XPL/Antabuse+Tablets++200mg
Pennine Care Choice & Medication
http://www.choiceandmedication.org/penninecare/medications/136

11. Supporting References

1. British National Formulary (BNF) 65 Mar-Sep 2013

2. NICE Clinical Guideline CG 115 Alcohol-use disorders February 2011
www.nice.org.uk

3. Summary of Product Characteristics Antabuse
http://www.medicines.org.uk/emc/medicine/519/SPC/Antabuse+Tablets++200mg

4. Pennine Care MM0086 Community Alcohol Detoxification Guidelines

5. Pennine Care MM069 Guidelines for the Prevention of Fatalities from Medication Loading Doses