SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Disulfiram 200 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg disulfiram.

Excipient(s) with known effect: Each tablet contains 34 mg of lactose and 0.175 mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

White to off-white, round, flat faced, bevelled-edge, uncoated tablets debossed with 'I 99' on one side and breakline on other side, with a diameter of 11 mm.

The tablet can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Alcohol deterrent compound. Disulfiram may be indicated as an adjuvant in the treatment of carefully selected and co-operative patients with drinking problems. Its use must be accompanied by appropriate supportive treatment.

4.2 Posology and method of administration

Posology

Adults and elderly patients only:
It is recommended that treatment with Disulfiram should be initiated only in a hospital or specialised clinic and by physicians experienced in its use. The patient should have adequate social and family support to avoid ingestion of alcohol. Suitable patients should not have ingested alcohol for at least 24 hours and must be warned that a Disulfiram-alcohol reaction is potentially dangerous.

On the first day of treatment, the patient should be given no more than 4 tablets of Disulfiram in one dose (800 mg). The next day the patient should take 3 tablets followed on the third day by 2 tablets and on the fourth and fifth days by 1 tablet. Subsequently, daily dosing should continue at 1 or half a tablet daily for as long as advised by the physician but no longer than six months without review.

In the routine management of the alcoholic it is not recommended to carry out an alcohol challenge test. If the clinician feels an alcohol challenge test is essential for the success of the therapy, full information of the procedure and risks of this test can be obtained from the company. As severe reactions can occur any alcohol challenge should be carried out in specialised units by physicians acquainted with the procedure. Full resuscitation facilities must be immediately available.

Paediatric population:
There is no relevant use of Disulfiram in the paediatric population.

Method of administration

Oral

4.3 Contraindications

- Uncompensated cardiac failure
- coronary artery disease
- previous history of CVA
- hypertension
- severe personality disorder
- suicidal risk
- psychosis
- consumption of alcohol (see section 4.4, 4.5 and 4.8)
- hypersensitivity to the active substance, disulfiram or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Caution should be exercised in the presence of

- renal failure
- reduced hepatic function
- respiratory disease
- diabetes mellitus
- hypothyroidism
- cerebral damage
- epilepsy

Alcohol must not be consumed during treatment and for up to 14 days after discontinuation, as disulfiram prevents the metabolism of ethanol, causing acetaldehyde to accumulate in the body. This can result in a “disulfiram-alcohol reaction” causing adverse effects as listed in section 4.8.

Before initiating treatment it is advised that appropriate examinations should be carried out to establish the suitability of the patient for treatment. Patients must be warned of the unpredictable and potentially severe nature of a Disulfiram-alcohol reaction as, in rare cases deaths have been reported following the drinking of alcohol by patients receiving Disulfiram. Certain foods, liquid medicines, remedies, tonics, toiletries, perfumes and aerosol sprays may contain sufficient alcohol to elicit a Disulfiram-alcohol reaction and patients should be made aware of this. Caution should also be exercised with low alcohol and “non-alcohol” or “alcohol-free” beers and wines, which may provoke a reaction when consumed in sufficient quantities. All personnel involved in the administration of Disulfiram to the patient know that Disulfiram should not be given during a drinking episode.

Disulfiram treatment may cause drug-induced liver injury. Fatal cases have been reported (see section 4.8). Liver function should be monitored before initiation of treatment and periodically thereafter; caution should be taken in patients with known reduced hepatic function. Please consider drug discontinuation if symptoms or signs of liver injury associated with jaundice occur.

Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Disulfiram blocks the metabolism of alcohol and leads to an accumulation of acetaldehyde in the blood stream. For full details of the disulfiram-alcohol reaction please refer to section 4.8.

The intensity of the Disulfiram-alcohol reaction may be increased by amitriptyline. Chlorpromazine while decreasing certain components of the Disulfiram-alcohol reaction may increase the overall intensity of the reaction.

Disulfiram inhibits the metabolism of certain benzodiazepines such as chlordiazepoxide and diazepam enhancing their sedative effect. The interaction is not indicated for oxazepam. Benzodiazepines may reduce the disulfiram-alcohol reaction.

Disulfiram inhibits the metabolism of many drugs which are converted in the liver (such as phenytoin, theophylline and warfarin) and thereby enhances efficacy. Dose adjustment may be necessary.

Animal studies have indicated similar inhibition of metabolism of pethidine, morphine and amphetamines.

A few case reports of increase in confusion and changes in affective behaviour have been noted with the concurrent administration of metronidazole, isoniazid or paraldehyde.

Potentiation of organic brain syndrome and choreoatphetosis following pimozide have occurred very rarely.

Disulfiram inhibits the oxidation and renal excretion of rifampicin.

4.6 Fertility, pregnancy and lactation

Pregnancy
The use of Disulfiram in the first trimester of pregnancy is not advised. The risk/benefit ratio in assessing adverse effects of alcoholism in pregnancy should be taken into account when considering the use of Disulfiram in pregnant patients.
There have been rare reports of congenital abnormalities in infants whose mothers have received Disulfiram in conjunction with other medicines.

Breast-feeding
Should not be used. No information is available on whether Disulfiram is excreted in breast milk. Its use during breast feeding is not advised especially where there is a possibility of interaction with medicines that the baby may be taking.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Disulfiram may cause side effects such as drowsiness or fatigue. Patients should make sure they are not affected before driving or operating machinery.

4.8 Undesirable effects

The following terms and frequencies are applied: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (frequency not known).

Psychiatric disorders
Not known: psychotic reactions; depression, paranoia, schizophrenia, mania, reduction in libido.

Nervous system disorders
Not known: drowsiness (during initial treatment), peripheral neuritis, optic neuritis, Encephalopathy.

Gastrointestinal disorders
Not known: nausea, Vomiting.

Hepatobiliary disorders
Not known: hepatic cell damage, drug induced liver injury (fatal cases have been reported).

Skin and subcutaneous tissue disorders

Not known: allergic dermatitis, rash.

General disorders and administration site conditions

Not known: fatigue (during initial treatment), halitosis.

Disulfiram-alcohol reaction:

Disulfiram irreversibly inhibits acetaldehyde dehydrogenase. Intake of ethanol during disulfiram therapy will lead to accumulation of acetaldehyde, which is considered the main contributing factor to the disulfiram-alcohol reaction. Disulfiram-ethanol reactions often develop within 15 minutes after exposure to ethanol; symptoms usually peak within 30 minutes to 1 hour, and then gradually subside over the next few hours. Symptoms may be severe and life-threatening.

The disulfiram- alcohol reaction is characterised by:

- Intense vasodilation of the face and neck causing flushing, increased body temperature, sweating, nausea, vomiting, pruritis, urticaria, anxiety, dizziness, headache, blurred vision, dyspnoea, palpitations and hyperventilation.
- In severe cases tachycardia, hypotension, respiratory depression, chest pain, QT prolongation, ST depression, arrhythmias, coma and convulsions may occur.
- Rare complications include hypertension, bronchospasm and methaemoglobinaemia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important.
It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

Disulfiram overdose

Disulfiram alone has low toxicity. Although most patients will develop symptoms within the first 12 hours, there are case reports of clinical deterioration days after an overdose, with slow recovery and long-term sequel.

Symptoms include:

- Nausea, vomiting, abdominal pain, diarrhoea, drowsiness, delirium, hallucinations and lethargy may occur.
- Tachycardia, tachypnoea, hyperthermia and hypotension. Hypotonia may be prominent, especially in children and tendon reflexes may be reduced. Hyperglycaemia, leukocytosis, ketosis (often disproportionate to the degree of dehydration) and methaemoglobinaemia have been reported.
- In severe cases there may be cardiovascular collapse, coma and convulsions.
- Rare complications include sensorimotor neuropathy, EEG abnormalities, encephalopathy, psychosis and catatonia, which may appear several days after overdose. Dysarthria, myoclonus, ataxia, dystonia and akinesia may also occur. Movement disorders may be related to direct toxic effects on the basal ganglia.

Treatment:

Treatment should be symptomatic and observation is recommended.
Supportive therapy should be available and measures may be necessary to counteract hypotension.

Gastric lavage and/or activated charcoal may be considered in cases of disulfiram overdose.

Severe vomiting might occur requiring administration of intravenous fluids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in alcohol dependence.
ATC code: N07BB01

Mechanism of Action

The effect of Disulfiram is primarily due to irreversible inactivation of liver ALDH. In the absence of this enzyme, the metabolism of ethanol is blocked and the intracellular acetaldehyde concentration rises. The symptoms of the Disulfiram-alcohol reaction (DAR) are due partly to the high levels of acetaldehyde. The conversion of dopamine to noradrenaline is also inhibited and the depletion of noradrenaline in the heart and blood vessels allows acetaldehyde to act directly on these tissues to cause flushing, tachycardia and hypotension.

In addition to its effect on acetaldehyde dehydrogenase, disulfiram inhibits other enzyme systems including dopamine-beta-hydroxylase (which converts dopamine and noradrenaline) and hepatic microsomal mixed function oxidases (which are responsible for the metabolism of many drugs). Disulfiram may thus potentiate the action of drugs which are metabolised by these enzymes.

5.2 Pharmacokinetic properties

Absorption
Following oral administration, absorption is variable.

Distribution
Distribution is primarily to the kidney, pancreas, liver, intestines and fat.

Biotransformation
Disulfiram is rapidly metabolised to diethyldithiocarbamic acid (DDC), is conjugated with glucuronic acid, oxidised to sulphate, methylated and decomposed to diethylamine and carbon disulphide.

Elimination
Excretion is primarily through the kidneys.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Lactose
Stearic acid
Sodium starch glycolate
Colloidal anhydrous silica
Magnesium stearate

6.2 Incompatibilities

None.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

HDPE bottle with a polypropylene cap. Pack size of 50 tablets.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

Brown & Burk UK Ltd
5 Marryat Close
Hounslow West
Middlesex
TW4 5DQ
United Kingdom.

8. MARKETING AUTHORISATION NUMBER(S)

PL 25298/0151

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07/10/2025

10. DATE OF REVISION OF THE TEXT

07/10/2025