Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Acamprosate Calcium). A white or almost white powder. Freely soluble in water; practically insoluble in alcohol and in dichloromethane. A 5% solution in water has a pH of 5.5 to 7.0.

Adverse Effects
The main adverse effect of acamprosate is dosage-related diarrhoea; nausea, vomiting, and abdominal pain occur less frequently. Other adverse effects have included pruritus, and occasionally a maculopapular rash; bullous skin reactions have occurred rarely. Depression and fluctuations in libido have also been reported. Hypersensitivity reactions including urticaria, angioedema, and anaphylaxis have been reported very rarely.

Effects on the skin. A case of erythema multiforme in a woman with cirrhosis of the liver has been attributed to use of acamprosate[1] although both the diagnosis and any association with acamprosate have been seriously challenged.[2]

1. Fortier-Beaulieu M, *et al.* Possible association of erythema multiforme with acamprosate. *Lancet* 1992; **339:** 991.
2. Potgieter AS, Opsomer L. Acamprosate as cause of erythema multiforme contested. *Lancet* 1992; **340:** 856–7.

Precautions
In the UK, acamprosate is contra-indicated in patients with severe hepatic impairment (Child-Pugh Class C). US licensed product information states that acamprosate is not metabolised via the liver and its pharmacokinetics are not altered in those with mild to moderate hepatic impairment (Child-Pugh Classes A and B); no change in dose is required in such patients. (No advice is given regarding use in those with more severe impairment.) For precautions regarding the use of acamprosate in patients with renal impairment, see under Uses and Administration, below.

Pharmacokinetics
Absorption of acamprosate from the gastrointestinal tract is slow but sustained and is subject to considerable interindividual variation. Steady-state concentrations are achieved after dosage for 7 days. Bioavailability is reduced if given with food. Acamprosate is not protein bound and although it is hydrophilic it is reported to cross the blood-brain barrier. Acamprosate does not appear to be metabolised and is excreted unchanged in the urine. The elimination half-life after oral doses has been reported to be about 33 hours.

◊ References.

1. Saivin S, *et al.* Clinical pharmacokinetics of acamprosate. *Clin Pharmacokinet* 1998; **35:** 331–45.

Uses and Administration
Acamprosate has a chemical structure similar to that of the endogenous amino acid, homotaurine, which is a structural analogue of gamma-aminobutyric acid (GABA—p.2308) and taurine (p.2395). It is given as the calcium salt to prevent relapse in alcoholics who have been weaned off alcohol. The usual oral dose is 666 mg of acamprosate calcium given three times daily. UK licensed product information also recommends that patients weighing less than 60 kg should be given a dose of 666 mg at breakfast followed by 333 mg at midday and 333 mg at night. For doses in patients with renal impairment, see below. Treatment should be started as soon as possible after alcohol withdrawal and maintained, even if the patient relapses, for the recommended period of 1 year.

Administration in renal impairment. It is considered[1] likely that accumulation of acamprosate would occur with prolonged use of therapeutic doses in patients with renal impairment. It has been reported that the mean maximum concentration of acamprosate after a single 666-mg dose was 813 nanograms/mL in 12 patients with moderate or severe renal impairment compared with 198 nanograms/mL in 6 healthy subjects; values for the plasma elimination half-life were 47 and 18 hours, respectively.

Licensed product information in the UK does not recommend the use of acamprosate in patients with renal impairment (serum creatinine greater than 120 micromoles/litre).

In the USA the use of acamprosate is contra-indicated in those with severe renal impairment (creatinine clearance (CC) less than 30 mL/minute). However, in those with moderate impairment (CC 30 to 50 mL/minute), a starting dose of 333 mg three times daily may be given.

1. Wilde MI, Wagstaff AJ. Acamprosate: a review of its pharmacology and clinical potential in the management of alcohol dependence after detoxification. *Drugs* 1997; **53:** 1038–53.

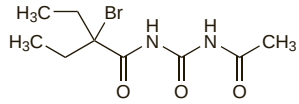
Alcohol dependence. Acamprosate is considered to be of use as an adjunct to psychotherapy in maintaining abstinence after alcohol withdrawal in patients with alcohol dependence (p.1626). Reviews[1-4] of placebo-controlled studies conclude that acamprosate helps to prevent relapse and increase the number of drink-free days during a 1-year course of treatment and possibly for up to one year thereafter. Efficacy appears to be dose related but its effects in promoting abstinence may wane during treatment. Use with disulfiram or naltrexone may improve results but a large multicentre study in the USA found that adding acamprosate to naltrexone or behavioural therapy did not produce any additional benefit, and that the drug was ineffective when used alone.[5] Several mechanisms have been proposed to account for acamprosate's action including inhibition of neuronal hyperexcitability by antagonising excitatory amino acids such as glutamate.

1. Wilde MI, Wagstaff AJ. Acamprosate: a review of its pharmacology and clinical potential in the management of alcohol dependence after detoxification. *Drugs* 1997; **53:** 1038–53.
2. Anonymous. Acamprosate for alcohol dependence? *Drug Ther Bull* 1997; **35:** 70–2.
3. Mason BJ. Treatment of alcohol-dependent outpatients with acamprosate: a clinical review. *J Clin Psychiatry* 2001; **62** (suppl 20): 42–8.
4. Overman GP, *et al.* Acamprosate for the adjunctive treatment of alcohol dependence. *Ann Pharmacother* 2003; **37:** 1090–9.
5. Anton RF, *et al.* Combined pharmacotherapies and behavioral interventions for alcohol dependence. The COMBINE study: a randomized controlled trial. *JAMA* 2006; **295:** 2003–17.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Campral†; ***Austral.:*** Campral; ***Austria:*** Campral; ***Belg.:*** Campral; ***Braz.:*** Campral†; ***Chile:*** Campral; ***Cz.:*** Campral; ***Denm.:*** Campral; ***Fr.:*** Aotal; ***Ger.:*** Campral; ***Hong Kong:*** Campral; ***Hung.:*** Campral; ***Irl.:*** Campral; ***Mex.:*** Campral; ***Neth.:*** Campral; ***Norw.:*** Campral; ***Pol.:*** Campral; ***Port.:*** Campral; ***S.Afr.:*** Besobrial; Sobrial†; ***Singapore:*** Campral†; ***Spain:*** Campral; Zulex; ***Swed.:*** Campral; ***Switz.:*** Campral; ***Turk.:*** Campral; ***UK:*** Campral; ***USA:*** Campral.

Acecarbromal *(rINN)*
Acécarbromal; Acecarbromalum; Acetcarbromal; Acetylcarbromal. *N*-Acetyl-*N*′-(2-bromo-2-ethylbutyryl)urea.

Ацекарбромал
$C_9H_{15}BrN_2O_3$ = 279.1.
CAS — 77-66-7.

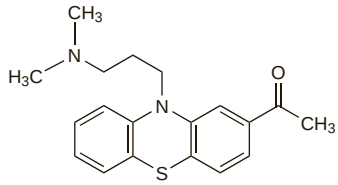


Profile
Acecarbromal is a bromureide with similar actions to those of carbromal (p.967). It has been used for its sedative properties but the use of bromides is generally deprecated.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: Cz.: Afrodor; ***Ger.:*** Afrodor; ***Hung.:*** Afrodor†; ***Rus.:*** Afrodor (Афродор).

Acepromazine *(BAN, rINN)*
Acepromazin; Acepromazina; Acépromazine; Acepromazinum; Asepromatsiini. 10-(3-Dimethylaminopropyl)phenothiazin-2-yl methyl ketone.

Ацепромазин
$C_{19}H_{22}N_2OS$ = 326.5.
CAS — 61-00-7.
ATC — N05AA04.
ATC Vet — QN05AA04.



Acepromazine Maleate *(BANM, USAN, rINNM)*
Acépromazine, Maléate d'; Acepromazini Maleas; Acetylpromazine Maleate; Asepromazin Maleat; Maleato de acepromazina. 10-(3-Dimethylaminopropyl)phenothiazin-2-yl methyl ketone hydrogen maleate.

Ацепромазина Малеат
$C_{19}H_{22}N_2OS,C_4H_4O_4$ = 442.5.
CAS — 3598-37-6.
ATC — N05AA04.
ATC Vet — QN05AA04.

Pharmacopoeias. In *US* for veterinary use only. Also in *BP(Vet)*.
BP(Vet) 2008 (Acepromazine Maleate). A yellow crystalline powder. Soluble in water and in alcohol; freely soluble in chloroform; slightly soluble in ether. A 1% solution in water has a pH of 4.0 to 4.5.
USP 31 (Acepromazine Maleate). pH of a 1% solution is between 4.0 and 5.5. Protect from light.

Profile
Acepromazine is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It has been given orally as the maleate in the treatment of anxiety disorders, hiccups, and nausea and vomiting. Acepromazine, as the base, has also been given in preparations for the management of insomnia.

Preparations
Proprietary Preparations (details are given in Part 3)
Denm.: Plegicil; ***Turk.:*** Plegicil.
Multi-ingredient: *Fr.:* Noctran.

Acetylcarbromal *(rINN)*
Acétylcarbromal; Acetylcarbromalum; Acetylcarbromal. *N*-Acetyl-*N*′-(2-bromo-2-ethylbutyryl)urea.

Ацетилкарбромал
$C_9H_{15}BrN_2O_3$ = 279.1.
CAS — 77-66-7.

Profile
Acetylcarbromal is a bromureide with similar actions to those of carbromal (p.967). It has been used for its sedative properties but the use of bromides is generally deprecated.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: Cz.: Afrodor; ***Ger.:*** Afrodor; ***Hung.:*** Afrodor†; ***Rus.:*** Afrodor (Афродор).

Acetylpromazine Maleate *(BANM, USAN, rINNM)*
Acépromazine, Maléate d'; Acepromazini Maleas; Acepromazine Maleate; Asepromazin Maleat; Maleato de acepromazina. 10-(3-Dimethylaminopropyl)phenothiazin-2-yl methyl ketone hydrogen maleate.

Ацетилпромазина Малеат
$C_{19}H_{22}N_2OS,C_4H_4O_4$ = 442.5.
CAS — 3598-37-6.
ATC — N05AA04.
ATC Vet — QN05AA04.

Pharmacopoeias. In *US* for veterinary use only. Also in *BP(Vet)*.
BP(Vet) 2008 (Acepromazine Maleate). A yellow crystalline powder. Soluble in water and in alcohol; freely soluble in chloroform; slightly soluble in ether. A 1% solution in water has a pH of 4.0 to 4.5.
USP 31 (Acepromazine Maleate). pH of a 1% solution is between 4.0 and 5.5. Protect from light.

Profile
Acepromazine is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It has been given orally as the maleate in the treatment of anxiety disorders, hiccups, and nausea and vomiting. Acepromazine, as the base, has also been given in preparations for the management of insomnia.

Preparations
Proprietary Preparations (details are given in Part 3)
Denm.: Plegicil; ***Turk.:*** Plegicil.
Multi-ingredient: *Fr.:* Noctran.

Acetylpromazine
Acépromazine; Acepromazini Maleas; Acetylpromazine Maleate; Asepromazin Maleat; Maleato de acepromazina. 10-(3-Dimethylaminopropyl)phenothiazin-2-yl methyl ketone hydrogen maleate.

Ацетилпромазина Малеат
$C_{19}H_{22}N_2OS,C_4H_4O_4$ = 442.5.
CAS — 3598-37-6.
ATC — N05AA04.
ATC Vet — QN05AA04.

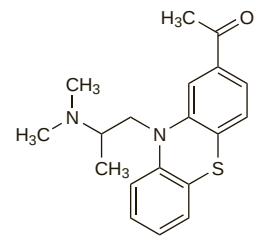
Pharmacopoeias. In *US* for veterinary use only. Also in *BP(Vet)*.
BP(Vet) 2008 (Acepromazine Maleate). A yellow crystalline powder. Soluble in water and in alcohol; freely soluble in chloroform; slightly soluble in ether. A 1% solution in water has a pH of 4.0 to 4.5.
USP 31 (Acepromazine Maleate). pH of a 1% solution is between 4.0 and 5.5. Protect from light.

Profile
Acepromazine is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It has been given orally as the maleate in the treatment of anxiety disorders, hiccups, and nausea and vomiting. Acepromazine, as the base, has also been given in preparations for the management of insomnia.

Preparations
Proprietary Preparations (details are given in Part 3)
Denm.: Plegicil; ***Turk.:*** Plegicil.
Multi-ingredient: *Fr.:* Noctran.

Acepromethazine *(rINN)*
16-64 CB; Acepromethazina; Acéprométazine; Acepromethazinum. 10-(2-Dimethylaminopropyl)phenothiazin-2-yl methyl ketone.

Ацепрометазин
$C_{19}H_{22}N_2OS$ = 326.5.
CAS — 13461-01-3.

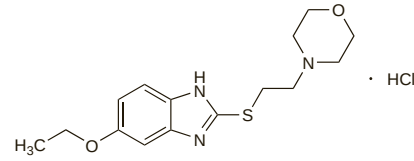


Profile
Acepromethazine is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It is available usually as the maleate in preparations for the management of insomnia.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: *Fr.:* Mepronizine; Noctran.

Afobazol
Afobazole; Aphobazole; CM-346; SM-346. 5-Ethoxy-2-{[2-(4-morpholinyl)ethyl]thio}-1*H*-benzimidazole Monohydrochloride.

Афобазол
$C_{15}H_{21}N_3O_2S.HCl$ = 343.9.
CAS — 173352-39-1.



NOTE. Afobazol has also been described as the dihydrochloride.

Profile
Afobazol is a non-benzodiazepine anxiolytic used in the treatment of anxiety disorders. It has been given orally in a usual dose of 10 mg three times daily. A maximum of 60 mg may be given daily.

◊ References.

1. Neznamov GG, *et al.* Aphobazol—new selective anxyolytic drug. *Zh Nevrol Psikhiatr Im S S Korsakova* 2005; **105:** 35–40.

Allobarbital *(USAN, rINN)*
Allobarbitaali; Allobarbitalum; Allobarbitone; Alobarbital; Diallylbarbitone; Diallylbarbituric Acid; Diallylmalonylurea; Diallymalum; NSC-9324. 5,5-Diallylbarbituric acid.

Аллобарбитал
$C_{10}H_{12}N_2O_3$ = 208.2.
CAS — 52-43-7.
ATC — N05CA21.
ATC Vet — QN05CA21.