diazepam is ineffective or poorly tolerated include baclofen or sodium valproate but benefit may be less evident. There have been isolated anecdotal reports of improvement with vigabatrin, tiagabine, and gabapentin. Antiepileptics or baclofen may sometimes be combined with benzodiazepines. Cortico-steroids may be of benefit, although any response may take several weeks, and the chronic nature of the disorder and the high incidence of type 1 diabetes mellitus may make their use problematic. Other attempts at immunomodulation such as plasmapheresis have yielded variable results; there is some evidence of the efficacy of immunoglobulins.

References.

1. Toro C, *et al.* Stiff-man syndrome. *Semin Neurol* 1994; **14:** 154–8.
2. Gerhardt CL. Stiff-man syndrome revisited. *South Med J* 1995; **88:** 805–808.
3. Stayer C, Meinck H-M. Stiff-man syndrome: an overview. *Neurologia* 1998; **13:** 83–8.
4. Levy LM, *et al.* The stiff-person syndrome - an autoimmune disorder affecting neurotransmission of γ-aminobutyric acid. *Ann Intern Med* 1999; **131:** 522–30.
5. Meinck H-M. Stiff man syndrome. *CNS Drugs* 2001; **15:** 515–26.
6. Dalakas MC, *et al.* High-dose intravenous immune globulin for stiff-person syndrome. *N Engl J Med* 2001; **345:** 1870–6.
7. Vasconcelos OM, Dalakas MC. Stiff-person syndrome. *Curr Treat Options Neurol* 2003; **5:** 79–90.

Nausea and vomiting. Benzodiazepines, particularly lorazepam, are used as adjuncts in the management of nausea and vomiting induced by cancer chemotherapy (p.1700), particularly anticipatory emesis.

Premenstrual syndrome. For mention of the limited role of benzodiazepines in the management of premenstrual syndrome, see p.2099.

Schizophrenia. Benzodiazepines may be useful adjuncts to antipsychotics in the initial management of schizophrenia (p.955).

Sleep-associated movement disorders. Sleep-associated movement disorders (p.958) rarely require treatment other than the symptomatic treatment of sleep-related medical problems. A number of such conditions, including restless legs syndrome, sleepwalking, and night terrors, have been reported to respond to benzodiazepines. Although the muscle relaxant and anxiolytic action of a benzodiazepine can be helpful in bruxism (teeth grinding) it has been recommended that they should only be prescribed on a short-term basis during the acute phase.

References.

1. Schenck CH, Mahowald MW. Long-term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults. *Am J Med* 1996; **100:** 333–7.

Substance dependence. The benzodiazepines are used in the management of symptoms of *alcohol* withdrawal (p.1626), of *opioid* withdrawal (p.101), and of *cocaine* withdrawal (p.1860).

Vertigo. Although intravenous diazepam has been used to abort acute attacks of vertigo of peripheral origin (p.565), it can prolong compensation and recovery from vestibular lesions.[1]

1. Rascol O, *et al.* Antivertigo medications and drug-induced vertigo: a pharmacological review. *Drugs* 1995; **50:** 777–91.

Preparations

BP 2008: Diazepam Injection; Diazepam Oral Solution; Diazepam Rectal Solution; Diazepam Tablets;
USP 31: Diazepam Capsules; Diazepam Extended-release Capsules; Diazepam Injection; Diazepam Tablets.

Proprietary Preparations (details are given in Part 3)

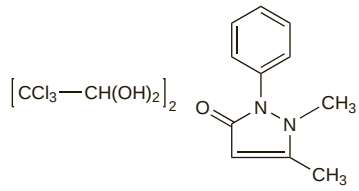
Arg.: Cuadel; Daiv; Dezepan; Diactal; Dipezona; Fabotranil; Glutasedan†; Lembrol; Plidan; Plidex T; Rupediz†; Saromet; Timab; Valium; ***Austral.:*** Antenex; Ducene; Valium; Valpam; ***Austria:*** Gewacalm; Psychopax; Stesolid; Umbrium; Valium; ***Belg.:*** Valium; ***Braz.:*** Ansilive; Calmociteno; Compaz; Diazefast; Diazepan†; Dienpax; Kiatrium; Letansil; Menostress; Noan; Pazolini; Relapax; Somaplus; Uni Diazepax; Valium; Valix†; Vetansil; ***Canad.:*** Diastat; Diazemuls; Novo-Dipam; Valium; ***Chile:*** Cardiosedantol; Elongal†; Pacinax; ***Cz.:*** Apaurin; Seduxen†; Stesolid; ***Denm.:*** Apozepam; Hexalid; Stesolid; Valaxona; Valium; ***Fin.:*** Diapam; Medipam; Stesolid; ***Fr.:*** Novazam†; Valium; ***Ger.:*** Diazep; Faustan; Lamra; Stesolid; Tranquase†; Valiquid; Valium; Valocordin-Diazepam; ***Gr.:*** Apollonset; Atarviton; Stedon; Stesolid; ***Hong Kong:*** Diazemuls; Kratium; Stesolid; Valpam; ***Hung.:*** Seduxen; Stesolid; ***India:*** Anxol; Calmpose; Elcion; Paxum; Placidox; Rec-DZ; Valium; Zepose; ***Indon.:*** Mentalium; Stesolid; Trazep; Valdimex; Valisanbe; Valium; ***Irl.:*** Anxicalm; Diazemuls; Stesolid; Valium; ***Israel:*** Assival; Diaz; Stesolid; ***Ital.:*** Aliseum; Ansiolin; Diazemuls; Micronoan; Noan; Tranquirit; Valium; Vatran; ***Malaysia:*** Diapine; Diapo; Valium; ***Mex.:*** Alboral; Arzepam; AT-V†; Benzyme; Diacepam†; Diapanil†; Diatex†; Freudal†; Ifa-Fonal; Laxyl; Onapan; Ortopsique; Prizem†; Relazepam; Tandial†; Valium; Zepan; Zeprat†; ***Neth.:*** Diazemuls; Stesolid; Valium; ***Norw.:*** Stesolid; Valium; Vival; ***NZ:*** D-Pam; Diazemuls; Propam; Stesolid; ***Philipp.:*** Nixtensyn; Trankil; Valium; ***Pol.:*** Relanium; Relsed; ***Port.:*** Bialzepam; Metamidol; Stesolid; Unisedil; Valium; ***Rus.:*** Apaurin (Апаурин); Relanium (Реланиум); Relium (Релиум); Seduxen (Седуксен); ***S.Afr.:*** Benzopin; Betapam; Calmpose; Doval; Pax; Tranject; Valium; ***Singapore:*** Diapine; Diapo; Stesolid; ***Spain:*** Aneurol; Aspaserine B6 Tranq†; Complutine; Gobanal; Pacium; Sico Relax†; Stesolid; Valium; Vincosedan; ***Swed.:*** Apozepam†; Stesolid; ***Switz.:*** Paceum; Psychopax; Stesolid; Valium; ***Thai.:*** Azepam; Diano; Diapam; Diapine; Dizan; Dizepam†; Sipam; Stesolid†; V Day Zepam†; Valenium†; Valium; Zopam; ***Turk.:*** Diapam; Diazem; Lizan; Nervium; ***UK:*** Dialar; Diazemuls; Rimapam; Stesolid; Tensium; Valclair; ***USA:*** Diastat; Valium; ***Venez.:*** Talema; Telsomet†; Valium†.

Multi-ingredient: ***Arg.:*** Arnol; Dafne; Dislembral†; Faradil; Pasminox Somatico; Plidex†; Tratobes; ***Austria:*** Betamed; Harmomed; ***Braz.:*** Dialudon; Dobesix†; Moderine; ***Chile:*** Calmosedan; Diapam; Mesolona†; Multisedil; Promidan; Sedantol; Sedilit; ***Cz.:*** Seduxen RG†; ***Fin.:*** Gastrodyn comp; Relapamil; Vertipam; ***Gr.:*** Distedon; ***India:*** Depsonil-DZ; Dericip Plus; ***Indon.:*** Analsik; Cetalgin; Danalgin; Hedix; Neurodial; Neuroval; Opineuron; Proneuron; ***Ital.:*** Gamibetal Plus; Spasen Somatico; Spasmeridan; Spasmomen Somatico; Valpinax; Valtrax; ***Mex.:*** Adepsique; Esbelcaps; Numencial; Qual; Redotex; ***Port.:*** Gamibetal Compositum†; ***Rus.:*** Reladorm (Реладорм); ***Spain:*** Ansium; Tepazepan; Tropargal; ***Turk.:*** Spazmo-Valibrin; ***USA:*** Emergent-Ez; ***Venez.:*** Tepazepam†.

Dichloralphenazone *(BAN)*

Dicloralfenazona; Dikloraalifenatsoni; Dikloralfenazon.

$C_{15}H_{18}Cl_6N_2O_5$ = 519.0.
CAS — 480-30-8.
ATC — N05CC04.
ATC Vet — QN05CC04.



Pharmacopoeias. In *US.*
USP 31 (Dichloralphenazone). A white microcrystalline powder with a slight odour characteristic of cloral hydrate. Freely soluble in water, in alcohol, and in chloroform; soluble in dilute acids. It is decomposed by dilute alkalis liberating chloroform.

Profile

Dichloralphenazone dissociates when given, to form cloral hydrate and phenazone. It has the general properties of cloral hydrate (p.979), although it is less likely to cause gastric irritation after oral doses. Phenazone-induced skin eruptions may, however, occur (see p.116). Dichloralphenazone is used in some countries in combination preparations mainly for the treatment of tension and vascular headaches.

Porphyria. Dichloralphenazone has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Preparations

USP 31: Isometheptene Mucate, Dichloralphenazone, and Acetaminophen Capsules.

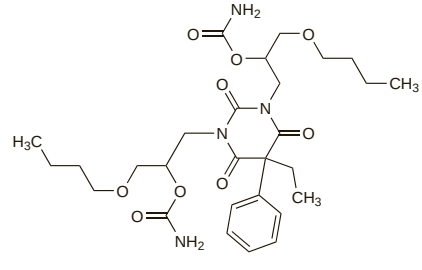
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***USA:*** Duradrin†; Midrin; Migratine†.

Difebarbamate *(rINN)*

Difébarbamate; Difebarbamato; Difebarbamatum. 1,3-Bis(3-butoxy-2-hydroxypropyl)-5-ethyl-5-phenylbarbituric acid dicarbamate ester.

Дифебарбамат

$C_{28}H_{42}N_4O_9$ = 578.7.
CAS — 15687-09-9.



Profile

Difebarbamate is a barbiturate with general properties similar to those of amobarbital (p.961). Tetrabamate, a complex of difebarbamate, febarbamate, and phenobarbital, has been used in the management of anxiety disorders and alcohol withdrawal syndrome but was also associated with the development of hepatitis. Furthermore barbiturates are not considered appropriate in the management of these conditions.

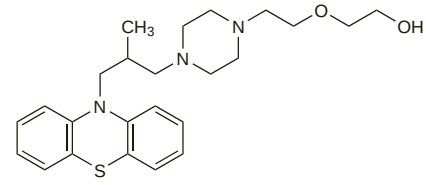
Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Hung.:*** Atrium†.

Dixyrazine

Diksyratsiini; Dixirazina; Dixyrazin; Dixyrazinum; UCB-3412. 2-(2-{4-[2-Methyl-3-(phenothiazin-10-yl)propyl]piperazin-1-yl}ethoxy)ethanol.

$C_{24}H_{33}N_3O_2S$ = 427.6.
CAS — 2470-73-7.
ATC — N05AB01.
ATC Vet — QN05AB01.



Profile

Dixyrazine is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It has a piperazine side-chain. It is given for its antipsychotic, antiemetic, and sedative properties in oral doses ranging from 20 to 75 mg daily. Dixyrazine has also been given by injection.

◊ References.

1. Larsson S, *et al.* Premedication with intramuscular dixyrazine (Esucos): a controlled double-blind comparison with morphine-scopolamine and placebo. *Acta Anaesthesiol Scand* 1988; **32:** 131–4.
2. Karlsson E, *et al.* The effects of prophylactic dixyrazine on postoperative vomiting after two different anaesthetic methods for squint surgery in children. *Acta Anaesthesiol Scand* 1993; **37:** 45–8.
3. Oikkonen M, *et al.* Dixyrazine premedication for cataract surgery: a comparison with diazepam. *Acta Anaesthesiol Scand* 1994; **38:** 214–17.
4. Feet PO, Götestam KG. Increased antipanic efficacy in combined treatment with clomipramine and dixyrazine. *Acta Psychiatr Scand* 1994; **89:** 230–4.
5. Kokinsky E, *et al.* Postoperative nausea and vomiting in children using patient-controlled analgesia: the effect of prophylactic intravenous dixyrazine. *Acta Anaesthesiol Scand* 1999; **43:** 191–5.
6. Glaser C, *et al.* Dixyrazine for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2004; **48:** 1287–91.

Porphyria. Dixyrazine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Preparations

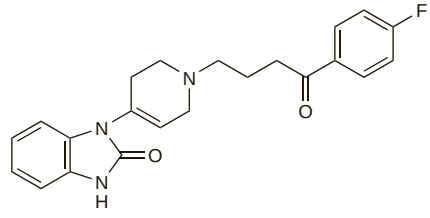
Proprietary Preparations (details are given in Part 3)
Austria: Esucos; ***Fin.:*** Esucos; ***Ital.:*** Esucos; ***Norw.:*** Esucos; ***Swed.:*** Esucos.

Droperidol *(BAN, USAN, rINN)*

Dropéridol; Droperidoli; Droperidolis; Droperidolum; McN-JR-4749; R-4749. 1-{1-[3-(4-Fluorobenzoyl)propyl]-1,2,3,6-tetrahydro-4-pyridyl}-benzimidazolin-2-one.

Дроперидол

$C_{22}H_{22}FN_3O_2$ = 379.4.
CAS — 548-73-2.
ATC — N01AX01; N05AD08.
ATC Vet — QN01AX01; QN05AD08.



Pharmacopoeias. In *Eur.* (see p.vii), *Jpn,* and *US.*
Ph. Eur. 6.2 (Droperidol). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in dichloromethane and in dimethylformamide. Protect from light.
USP 31 (Droperidol). A white to light tan amorphous or microcrystalline powder. Practically insoluble in water; soluble 1 in 140 of alcohol, 1 in 4 of chloroform, and 1 in 500 of ether. Store under nitrogen in airtight containers at a temperature of 8° to 15°. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969. There is an increased risk of cardiotoxicity and prolongation of the QT interval (see p.970) with droperidol. Droperidol should not be used in patients with known or suspected QT prolongation; it should also be used with extreme caution in patients at risk of arrhythmias, including those