Epilepsy. Pregabalin is one of the newer drugs used as adjunctive therapy in patients with partial seizures with or without secondary generalisation (p.465). It appears to be reasonably well tolerated.

References.

1. Miller R, *et al.* Exposure-response analysis of pregabalin add-on treatment of patients with refractory partial seizures. *Clin Pharmacol Ther* 2003; **73:** 491–505.
2. Arroyo S, *et al.* Pregabalin add-on treatment: a randomized, double-blind, placebo-controlled, dose-response study in adults with partial seizures. *Epilepsia* 2004; **45:** 20–7.
3. Elger CE, *et al.* Pregabalin add-on treatment in patients with partial seizures: a novel evaluation of flexible-dose and fixed-dose treatment in a double-blind, placebo-controlled study. *Epilepsia* 2005; **46:** 1926–36.
4. Hamandi K, Sander JW. Pregabalin: a new antiepileptic drug for refractory epilepsy. *Seizure* 2006; **15:** 73–8.
5. Lozsadi D, *et al.* Pregabalin add-on for drug-resistant partial epilepsy. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 09/06/08).

Neuropathic pain. Antiepileptics are among the drugs used to manage neuropathic pain, which is often insensitive to opioid analgesics (see Choice of Analgesic, p.2). Although carbamazepine appears to be the antiepileptic most frequently used, pregabalin is also given in the treatment of peripheral neuropathic pain[1] including postherpetic neuralgia[2,3] (p.9) and painful diabetic neuropathy[4,5] (p.6). Pregabalin may also be used in central neuropathic pain[6,7] (p.6).

1. Blommel ML, Blommel AL. Pregabalin: an antiepileptic agent useful for neuropathic pain. *Am J Health-Syst Pharm* 2007; **64:** 1475–82.
2. Sabatowski R, *et al.* Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomised, placebo-controlled clinical trial. *Pain* 2004; **109:** 26–35.
3. Frampton JE, Foster RH. Pregabalin: in the treatment of postherpetic neuralgia. *Drugs* 2005; **65:** 111–18.
4. Rosenstock J, *et al.* Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain* 2004; **110:** 628–38.
5. Frampton JE, Scott LJ. Pregabalin: in the treatment of painful diabetic peripheral neuropathy. *Drugs* 2004; **64:** 2813–20.
6. Siddall PJ, *et al.* Pregabalin in central neuropathic pain associated with spinal cord injury: a placebo-controlled trial. *Neurology* 2006; **67:** 1792–800.
7. Vranken JH, *et al.* Pregabalin in patients with central neuropathic pain: a randomized, double-blind, placebo-controlled trial of a flexible-dose regimen. *Pain* 2008; **136:** 150–7.

Postoperative pain. There is growing interest in the use of analgesic adjuvants including antiepileptics such as pregabalin to modulate opioid dosage and efficacy for postoperative pain (see p.4).

References.

1. Dahl JB, *et al.* 'Protective premedication': an option with gabapentin and related drugs? A review of gabapentin and pregabalin in the treatment of post-operative pain. *Acta Anaesthesiol Scand* 2004; **48:** 1130–6.
2. Tiippana EM, *et al.* Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. *Anesth Analg* 2007; **104:** 1545–56.

Soft-tissue rheumatism. Three large, multicentre controlled studies[1-3] have shown that pregabalin in oral doses of between 300 and 600 mg daily is effective in reducing pain and other core symptoms of fibromyalgia (see Soft-tissue Rheumatism, p.13) such as sleep disturbance and fatigue. The drug was reported to be generally well tolerated, dizziness and somnolence being the most common adverse effects. Pain relief appears to be largely independent of reduction in anxiety or depression scores.[4]

1. Crofford LJ, *et al.* Pregabalin 1008-105 Study Group. Pregabalin for the treatment of fibromyalgia syndrome: results of a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2005; **52:** 1264–73.
2. Mease PJ, *et al.* A randomized, double-blind, placebo-controlled, phase III trial of pregabalin in the treatment of patients with fibromyalgia. *J Rheumatol* 2008; **35:** 502–14.
3. Crofford LJ, *et al.* Fibromyalgia relapse evaluation and efficacy for durability of meaningful relief (FREEDOM): a 6-month, double-blind, placebo-controlled trial with pregabalin. *Pain* 2008; **136:** 419–31.
4. Arnold LM, *et al.* The effect of anxiety and depression on improvements in pain in a randomized, controlled trial of pregabalin for treatment of fibromyalgia. *Pain Med* 2007; **8:** 633–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Lyrica; ***Austral.:*** Lyrica; ***Belg.:*** Lyrica; ***Canad.:*** Lyrica; ***Chile:*** Lyrica; Pregobin; ***Cz.:*** Lyrica; ***Denm.:*** Lyrica; ***Fin.:*** Lyrica; ***Fr.:*** Lyrica; ***Ger.:*** Lyrica; ***Gr.:*** Lyrica; ***Hong Kong:*** Lyrica; ***Hung.:*** Lyrica; ***India:*** Pregab; ***Indon.:*** Lyrica; ***Irl.:*** Lyrica; ***Ital.:*** Lyrica; ***Mex.:*** Lyrica; ***Neth.:*** Lyrica; ***Norw.:*** Lyrica; ***NZ:*** Lyrica; ***Philipp.:*** Lyrica; ***Pol.:*** Lyrica; ***Port.:*** Lyrica; ***Rus.:*** Lyrica (Лирика); ***Singapore:*** Lyrica; ***Spain:*** Lyrica; ***Swed.:*** Lyrica; ***Switz.:*** Lyrica; ***UK:*** Lyrica; ***USA:*** Lyrica; ***Venez.:*** Lyrica.

Primidone *(BAN, rINN)*

Desoxifenobarbitona; Hexamidinum; Primaclona; Primaclone; Primidon; Primidona; Primidonas; Primidoni; Primidonum; Prymidon. 5-Ethyl-5-phenylperhydropyrimidine-4,6-dione.

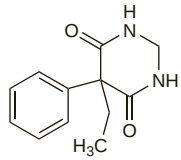
Примидон

$C_{12}H_{14}N_2O_2$ = 218.3.

CAS — 125-33-7.

ATC — N03AA03.

ATC Vet — QN03AA03.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.

Ph. Eur. 6.2 (Primidone). A white or almost white, crystalline powder. Very slightly soluble in water; slightly soluble in alcohol. It dissolves in alkaline solutions.

USP 31 (Primidone). A white, odourless, crystalline powder. Soluble 1 in 2000 of water and 1 in 200 of alcohol; very slightly soluble in most organic solvents.

Adverse Effects, Treatment, and Precautions

As for Phenobarbital, p.492.

Adverse effects may be more frequent than with phenobarbital. Most patients rapidly develop tolerance to the adverse effects of primidone, including ataxia, dizziness, drowsiness, headache, nausea and vomiting, nystagmus, skin rashes, and visual disturbances.

Care is required when withdrawing primidone therapy—see also Uses and Administration, below.

Effects on the blood. For a report of delayed agranulocytosis in a patient treated with phenytoin and primidone, see p.495.

Effects on the endocrine system. For mention of the effects of antiepileptics on *sexual function* in male epileptic patients, see under Phenytoin, p.496.

Overdosage. Crystalluria has been reported[1] after acute overdosage of primidone and 7 other reported cases were also reviewed. Based on these few reports, crystalluria appears to be associated with serum-primidone concentrations in excess of 80 micrograms/mL. There is evidence from 2 reports of renal damage associated with crystal formation *in vivo*. Vigorous hydration is recommended in patients at risk, in order to lessen the potential for renal toxicity and improve elimination.

1. Lehmann DF. Primidone crystalluria following overdose: a report of a case and an analysis of the literature. *Med Toxicol* 1987; **2:** 383–7.

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

Tremor. It was noted that patients receiving primidone for essential tremor have a high incidence of acute adverse reactions after small initial doses.[1] This could be due to the absence of induced hepatic enzymes in these patients previously not exposed to antiepileptics.

1. Findley LJ, *et al.* Primidone in essential tremor of the hands and head: a double blind controlled clinical study. *J Neurol Neurosurg Psychiatry* 1985; **48:** 911–15.

Interactions

Primidone is metabolised in the body in part to phenobarbital, and interactions recorded for phenobarbital (p.493) might potentially occur in patients receiving primidone. In addition, enzyme-inducing drugs enhance this metabolism and have the potential to produce elevated phenobarbital concentrations.

Antiepileptics. Both *phenytoin*[1] and *carbamazepine*[2] have been reported to enhance the metabolism of primidone to phenobarbital and when primidone was combined with phenytoin there have been instances of phenobarbital toxicity.[3] *Vigabatrin* has been reported[4] to lower plasma concentrations of primidone in some patients, although it is unlikely that dosage changes would be necessary. *Valproate* may increase plasma concentrations of primidone and phenobarbital, but patient response seems to be inconsistent.[5-7]

1. Reynolds EH, *et al.* Interaction of phenytoin and primidone. *BMJ* 1975; **2:** 594–5.
2. Baciewicz AM. Carbamazepine drug interactions. *Ther Drug Monit* 1986; **8:** 305–17.
3. Galdames D, *et al.* Interacción fenitoína-primidona: intoxicación por fenobarbital, en un adulto tratado con ambas drogas. *Rev Med Chil* 1980; **108:** 716–20.
4. Browne TR, *et al.* A multicentre study of vigabatrin for drug-resistant epilepsy. *Br J Clin Pharmacol* 1989; **27** (suppl 1): 95S–100S.
5. Windorfer A, *et al.* Elevation of diphenylhydantoin and primidone serum concentration by addition of dipropylacetate, a new anticonvulsant drug. *Acta Paediatr Scand* 1975; **64:** 271–2.
6. Bruni J. Valproic acid and plasma levels of primidone and derived phenobarbital. *Can J Neurol Sci* 1981; **8:** 91–2.
7. Yukawa E, *et al.* The effect of concurrent administration of sodium valproate on serum levels of primidone and its metabolite phenobarbital. *J Clin Pharm Ther* 1989; **14:** 387–92.

Pharmacokinetics

Primidone is readily absorbed from the gastrointestinal tract and is reported to have a plasma half-life ranging from 10 to 15 hours, which is shorter than those of its principal metabolites phenylethylmalonamide and phenobarbital, both of which are active. Therapeutic plasma concentrations of primidone have been suggested to be between 5 and 12 micrograms/mL. It is excreted in urine as unchanged drug (40%) and metabolites.

Primidone is widely distributed but is only partially bound to plasma proteins; it has been suggested that it exhibits variable binding of up to about 20%. It crosses the placenta and is distributed into breast milk.

The pharmacokinetics of primidone may be affected by use with other antiepileptics (see under Interactions, above).

Uses and Administration

Primidone is an antiepileptic that is partially metabolised to phenobarbital (p.494), but is also considered to have some antiepileptic activity in its own right. It may be given to control partial and generalised tonic-clonic seizures. Primidone is also used in the management of essential tremor.

In the treatment of **epilepsy** the dose of primidone should be adjusted according to response; a limited correlation with plasma concentrations has suggested that concentrations of 5 to 12 micrograms/mL (23 to 55 micromoles/litre) are usually necessary, but the *BNF* recommends monitoring of phenobarbital concentrations instead.

Recommended initial oral doses in the UK are 125 mg at bedtime increased, if necessary, by 125 mg every 3 days to a total of 500 mg daily given in 2 divided doses. If necessary, the daily dose may be increased further every 3 days by 250 mg up to a maximum of 1.5 g daily given in divided doses. Usual maintenance doses are 0.75 to 1.5 g daily; maintenance doses are usually given as 2 divided doses. Dosage recommendations in the USA are generally similar although a maximum daily dose of 2 g is permitted.

For doses in children, see below.

As with other antiepileptics, withdrawal of primidone or transition to or from another type of antiepileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures. For a discussion on whether or not to withdraw antiepileptic therapy in seizure-free patients, see p.465.

For **essential tremor** primidone is usually started at daily oral doses of 50 mg as the syrup or 62.5 mg as the tablet, increased gradually over 2 to 3 weeks if necessary, to a maximum of 750 mg daily.

Administration in children. Children may be given primidone to control partial and generalised tonic-clonic seizures. Recommended initial oral doses in the UK are 125 mg at bedtime, increased if necessary, by 125 mg every 3 days to the following usual maintenance daily doses (given in 2 divided doses) according to age:

- up to 2 years: 250 to 500 mg
- 2 to 5 years: 500 to 750 mg
- 6 to 9 years: 750 to 1000 mg

Children aged over 9 years may be given the usual adult dose (see above).

In the USA, a lower initial oral dose of 50 mg daily is recommended. This is doubled every 3 days, to reach a usual maintenance dose of 125 to 250 mg 3 times daily (10 to 25 mg/kg daily in divided doses) after 10 or more days. Children over 8 years of age may be given the usual adult dose as above.

Epilepsy. Primidone, like its metabolite phenobarbital, is used in the treatment of epilepsy (p.465) for partial seizures with or

without secondary generalisation and for primary generalised tonic-clonic seizures. However, because of problems of sedation, it is usually reserved for use in cases unresponsive to other antiepileptics. It has been suggested that it may be suitable for use in patients with QT-interval prolongation.[1]

1. Christidis D, *et al.* Is primidone the drug of choice for epileptic patients with QT-prolongation? A comprehensive analysis of literature. *Seizure* 2006; **15:** 64–6.

Neonatal apnoea. Results from a preliminary study suggested that adjunctive treatment with primidone[1] might be of value in neonatal apnoea resistant to first-line therapy with xanthines alone, but subsequent confirmatory studies seem to be lacking.

1. Miller CA, *et al.* The use of primidone in neonates with theophylline-resistant apnea. *Am J Dis Child* 1993; **147:** 183–6.

Neonatal seizures. Primidone has been tried in the management of neonatal seizures (p.471).

Tremor. A beta blocker is often the first drug used in patients with essential tremor who require regular treatment (p.1231) but primidone[1] may also be tried. A high incidence of acute adverse reactions has been reported after initial doses (see Tremor, under Adverse Effects, above). There has been concern that long-term use may produce tolerance to primidone's effects, although a small study has found a reduced response in only a few patients.[2] A later study[3] found a dose of 250 mg daily to be as or more effective than 750 mg daily without there being evidence of loss of efficacy during a 12-month follow-up.

1. Koller WC, Royse VL. Efficacy of primidone in essential tremor. *Neurology* 1986; **36:** 121–4.
2. Sasso E, *et al.* Primidone in the long-term treatment of essential tremor: a prospective study with computerized quantitative analysis. *Clin Neuropharmacol* 1990; **13:** 67–76.
3. Serrano-Dueñas M. Use of primidone in low doses (250 mg/day) versus high doses (750 mg/day) in the management of essential tremor: double-blind comparative study with one-year follow-up. *Parkinsonism Relat Disord* 2003; **10:** 29–33.

Preparations

BP 2008: Primidone Oral Suspension; Primidone Tablets;
USP 31: Primidone Oral Suspension; Primidone Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Mysoline; ***Austral.:*** Mysoline; ***Austria:*** Cyral; Mysoline; ***Belg.:*** Mysoline†; ***Braz.:*** Epidona†; Mysoline; ***Canad.:*** Mysoline†; ***Chile:*** Mysoline†; ***Cz.:*** Liskantin; ***Denm.:*** Mysoline†; ***Fin.:*** Mysoline†; ***Fr.:*** Mysoline†; ***Ger.:*** Liskantin; Mylepsinum; Resimatil; ***Gr.:*** Mysoline; ***Hung.:*** Sertan; ***India:*** Mysoline†; ***Irl.:*** Mysoline; ***Israel:*** Prysoline; ***Ital.:*** Mysoline; ***Mex.:*** Mysoline; ***Neth.:*** Mysoline; ***Norw.:*** Mysoline†; ***Pol.:*** Mizodin; ***Port.:*** Mysoline; ***Rus.:*** Hexamidin (Гексамидин); ***S.Afr.:*** Mysoline; ***Spain:*** Mysoline; ***Swed.:*** Mysoline†; ***Switz.:*** Mysoline; ***Turk.:*** Mysoline; ***UK:*** Mysoline; ***USA:*** Mysoline; ***Venez.:*** Mutigan†.

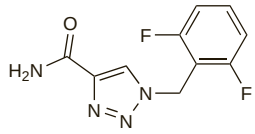
Multi-ingredient: ***Cz.:*** Mysoline†.

Rufinamide *(BAN, USAN, rINN)*

60231/4; CGP-33101; E-2080; RUF-331; Rufinamida; Rufinamidum. 1-(2,6-Difluorobenzyl)-1*H*-1,2,3-triazole-4-carboxamide.

Руфинамид

$C_{10}H_8F_2N_4O$ = 238.2.
CAS — 106308-44-5.
ATC — N03AF03.
ATC Vet — QN03AF03.



Adverse Effects and Precautions

The most common adverse effects with rufinamide include headache, dizziness, fatigue, somnolence, nausea, and vomiting. Other reported adverse effects include anorexia, weight loss, anxiety, insomnia, vertigo, nystagmus, tremor, dyspepsia, constipation, and diarrhoea. Convulsions, including status epilepticus, have occurred. Lymphadenopathy, abnormal liver function tests, and haematuria, as well as fever and rash, have been reported as part of a hypersensitivity syndrome.

Rufinamide can reduce the QT interval and should be used with caution in those with a shortening of their QT interval or with a family history of congenital short QT syndrome.

Care is required when withdrawing rufinamide therapy—see Uses and Administration, below.

Breast feeding. For comment on antiepileptic therapy and breast feeding, see p.467.

Driving. For a comment on antiepileptic drugs and driving, see p.468.

Pregnancy. For comments on the management of epilepsy during pregnancy, see p.468.

Interactions

There are complex interactions between antiepileptics, and toxicity may be enhanced without a corresponding increase in antiepileptic activity. Such interactions are very variable and unpredictable and plasma monitoring is often advisable with combination therapy. Rufinamide plasma concentrations are reportedly decreased by carbamazepine, phenobarbital, phenytoin, vigabatrin, or primidone. In contrast, significant increases in rufinamide plasma concentrations can occur with valproate and dosage adjustments may be necessary (see Uses and Administration, below).

Rufinamide induces the cytochrome P450 isoenzyme CYP3A4 and may be expected to decrease plasma concentrations of drugs metabolised by this route, such as oral contraceptives. Rufinamide reportedly increases steady-state plasma concentrations of phenytoin.

Pharmacokinetics

Rufinamide is well absorbed after oral doses; peak plasma concentrations are reached after about 6 hours. Food increases the bioavailability of rufinamide by about 34 to 40%. It is 34% bound to serum proteins, mainly to albumin.

Rufinamide is hydrolysed to an inactive metabolite and has a plasma elimination half-life of about 6 to 10 hours, although clearance in children is reported to be slower. It is mainly excreted in urine as the inactive metabolite.

◊ References

1. Cardot JM, *et al.* The influence of food on the disposition of the antiepileptic rufinamide in healthy volunteers. *Biopharm Drug Dispos* 1998; **19:** 259–62.

Uses and Administration

Rufinamide is an antiepileptic used as an adjunct in the treatment of seizures associated with the Lennox-Gastaut syndrome (p.465) in patients aged 4 years and over. Rufinamide is given orally in 2 divided doses daily with food. The initial daily dose in patients weighing less than 30 kg is 200 mg, increased according to response in increments of 200 mg every 2 days to a usual maximum of 1 g daily; the recommended maximum dose in those taking *valproate* is 600 mg daily. In patients weighing more than 30 kg, the initial daily dose is 400 mg, increased according to response in increments of 400 mg every 2 days to a maximum daily dose of 1.8 g in those weighing up to 50 kg, 2.4 g in those weighing up to 70 kg, and 3.2 g in those over 70 kg.

As with other antiepileptics, withdrawal of rufinamide therapy or transition to or from another type of antiepileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures. UK licensed product information recommends reducing the daily dose by about 25% every 2 days. For a discussion on whether or not to withdraw antiepileptic therapy in seizure-free patients, see p.465.

Rufinamide has also been investigated as adjunctive therapy in the treatment of partial and primary generalised tonic-clonic seizures.

◊ References.

1. Jain KK. An assessment of rufinamide as an anti-epileptic in comparison with other drugs in clinical development. *Expert Opin Invest Drugs* 2000; **9:** 829–40.
2. Pålhagen S, *et al.* Rufinamide: a double-blind, placebo-controlled proof of principle trial in patients with epilepsy. *Epilepsy Res* 2001: **43:** 115–24.
3. Deeks ED, *et al.* Rufinamide. *CNS Drugs* 2006; **20:** 751–60.
4. Cheng-Hakimian A, *et al.* Rufinamide: pharmacology, clinical trials, and role in clinical practice. *Int J Clin Pract* 2006; **60:** 1497–501.
5. Glauser T, *et al.* Rufinamide for generalized seizures associated with Lennox-Gastaut syndrome. *Neurology* 2008; **70:** 1950–8.

Preparations

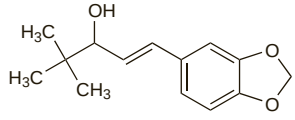
Proprietary Preparations (details are given in Part 3)
Cz.: Inovelon; ***Port.:*** Inovelon; ***UK:*** Inovelon.

Stiripentol *(USAN, rINN)*

BCX-2600; Estiripentol; Stiripentolum. 4,4-Dimethyl-1-[(3,4-methylenedioxy)phenyl]-1-penten-3-ol.

Стирипентол

$C_{14}H_{18}O_3$ = 234.3.
CAS — 49763-96-4.
ATC — N03AX17.
ATC Vet — QN03AX17.



Adverse Effects and Precautions

The most common adverse effects of stiripentol include anorexia, weight loss, insomnia, drowsiness, ataxia, hypotonia, and dystonia. Other common adverse effects include nausea, vomiting, and aggressiveness, and other mood or behavioural disorders. Neutropenia is also reported to be common; persistent severe neutropenia usually resolves spontaneously when stiripentol is stopped. Photosensitivity, rash, and urticaria have occurred. Patients may exhibit altered liver enzyme values.

Growth rates, blood counts, and hepatic function should be monitored periodically in patients given stiripentol.

Interactions

Stiripentol is a potent inhibitor of several cytochrome P450 isoenzymes, including CYP1A2, CYP2C19, and CYP3A4, and may markedly reduce clearance of drugs metabolised by these enzymes. The possibility of an effect on stiripentol metabolism by other inhibitors or inducers of these enzymes should also be borne in mind.

For interactions of stiripentol with other antiepileptics, see under Carbamazepine, p.474, Diazepam, p.990, and Phenytoin, p.498.

Uses and Administration

Stiripentol is used with clobazam and valproate as adjunctive therapy in the treatment of refractory generalised tonic-clonic seizures in severe myoclonic epilepsy in infancy. It is thought to be less potent than some conventional antiepileptics, but may reduce their adverse effects when used adjunctively.

Stiripentol is given orally and should be started at a low dose, gradually increased over 3 days, to the recommended dose of 50 mg/kg daily given in 2 or 3 divided doses with food (but not with dairy products, carbonated drinks, fruit juice, or food and drinks that contain caffeine or theophylline). After starting adjunctive stiripentol therapy, the daily dose of clobazam may be reduced by 25% every week if there are signs of adverse effects or overdosage with clobazam. The daily dose of valproate is not usually adjusted, however, it may be reduced by 30% every week if there are signs of gastrointestinal adverse effects.

Epilepsy. A 24-week study[1] in 10 children found that stiripentol might be effective as adjunctive therapy for the treatment of atypical absence seizures (p.465). Further studies suggested benefit from adjunctive use in children with partial epilepsy[2] and severe myoclonic epilepsy.[2-4]

1. Farwell JR, *et al.* Stiripentol in atypical absence seizures in children: an open trial. *Epilepsia* 1993; **34:** 305–11.
2. Perez J, *et al.* Stiripentol: efficacy and tolerability in children with epilepsy. *Epilepsia* 1999; **40:** 1618–26.
3. Chiron C, *et al.* Stiripentol in severe myoclonic epilepsy in infancy: a randomised placebo-controlled syndrome-dedicated trial. *Lancet* 2000; **356:** 1638–42.
4. Chiron C. Stiripentol. *Expert Opin Invest Drugs* 2005; **14:** 905–11.

Preparations

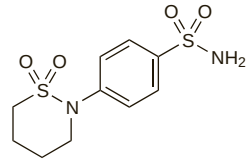
Proprietary Preparations (details are given in Part 3)
Cz.: Diacomit; ***Fr.:*** Diacomit; ***Port.:*** Diacomit.

Sultiame *(BAN, rINN)*

Riker-594; Sulthiame *(USAN)*; Sultiaami; Sultiam; Sultiamo; Sultiamum. 4-(Tetrahydro-2*H*-1,2-thiazin-2-yl)benzenesulphonamide *S,S*-dioxide.

Сультиам

$C_{10}H_{14}N_2O_4S_2$ = 290.4.
CAS — 61-56-3.
ATC — N03AX03.
ATC Vet — QN03AX03.



Pharmacopoeias. In *Jpn.*

Profile

Sultiame is a carbonic anhydrase inhibitor that has been used as an antiepileptic in most forms of epilepsy (p.465) except absence seizures. It has usually been given with other antiepileptics and it is believed that much of its activity is due to the inhibition of metabolism of the other drugs.

Sultiame has been given orally in initial doses of 100 mg twice daily or 50 mg three times daily gradually increased according to response to 200 mg three times daily. A dose of 5 to 10 mg/kg daily, adjusted according to response, has been recommended in Rolandic epilepsy.

Interactions. For the effect of sultiame on *phenytoin*, see p.498.

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

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ospolot; ***Austral.:*** Ospolot; ***Austria:*** Ospolot; ***Cz.:*** Ospolot; ***Ger.:*** Ospolot; ***Gr.:*** Ospolot; ***Hung.:*** Ospolot; ***Israel:*** Ospolot; ***Switz.:*** Ospolot.