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†.

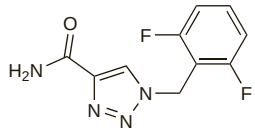
Multi-ingredient: ***Cz.:*** Mysoline†.

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

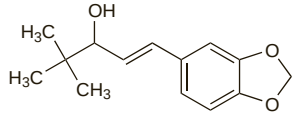
Proprietary Preparations (details are given in Part 3)
Cz.: Inovelon; ***Port.:*** Inovelon; ***UK:*** Inovelon.

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

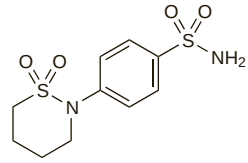
Proprietary Preparations (details are given in Part 3)
Cz.: Diacomit; ***Fr.:*** Diacomit; ***Port.:*** Diacomit.

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.

Tiagabine Hydrochloride

(BANM, USAN, rINNM)

Abbott-70569.1; ABT-569; Hidrocloruro de tiagabina; NNC-05-0328; NO-05-0328; Tiagabine, Chlorhydrate de; Tiagabini Hydrochloridum. (–)-(*R*)-1-[4,4-Bis(3-methyl-2-thienyl)-3-butenyl]-nipecotic acid hydrochloride.

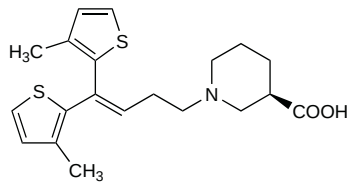
Тиагабина Гидрохлорид

$C_{20}H_{25}NO_2S_2,HCl$ = 412.0.

CAS — 115103-54-3 (tiagabine); 145821-59-6 (tiagabine hydrochloride).

ATC — N03AG06.

ATC Vet — QN03AG06.



(tiagabine)

Pharmacopoeias. In *US.*

USP 31 (Tiagabine Hydrochloride). A white to off-white powder. Sparingly soluble in water; freely soluble in alcohol and methyl alcohol; soluble in isopropyl alcohol; very slightly soluble in chloroform; practically insoluble in *n*-heptane. Store in airtight containers at a temperature not exceeding 30°. Protect from light.

Stability. An extemporaneously prepared suspension containing tiagabine hydrochloride 1 mg/mL in a mixture of simple syrup and 1% methylcellulose was found,[1] when stored in plastic amber bottles, to be stable for 6 weeks at 25° or 13 weeks at 4°. When prepared in a 1:1 mixture of *Ora-Plus* and *Ora-Sweet* (*Paddock, USA*), the suspension was stable for 10 weeks at 25° or 13 weeks at 4°.

1. Nahata MC, Morosco RS. Stability of tiagabine in two oral liquid vehicles. *Am J Health-Syst Pharm* 2003; **60:** 75–7.

Adverse Effects

The most common adverse effects include dizziness, nervousness, tiredness, somnolence, and tremor. Other reported adverse effects include irritability, confusion, depression, psychosis, difficulties in concentration, diarrhoea, abdominal pain, nausea, ataxia, emotional lability, and nystagmus. Bruising, rashes, speech difficulties, and a flu-like syndrome of chills, fever, myalgia, and headache have also been reported. Visual field defects have been reported rarely and decreased white blood cell counts have been noted at routine screenings.

Incidence of adverse effects. A systematic review[1] considered 5 double-blind studies involving about 1000 patients of whom 675 were receiving tiagabine as adjunctive therapy for refractory partial seizures. Withdrawal due to adverse effects was infrequent and occurred in 15% of patients receiving tiagabine compared with 5% receiving placebo. Adverse effects were usually associated with dose titration, and were generally mild to moderate in severity, and transient. Another review[2] by the same author on data from all clinical studies (52 studies involving nearly 3100 patients) reported that in 21% of patients receiving tiagabine had the drug stopped for adverse effects, mostly during the first 6 months of therapy. Sub-analysis showed that figures for placebo-controlled, adjunctive studies were similar to those of the earlier review.

1. Leppik IE. Tiagabine: the safety landscape. *Epilepsia* 1995; **36** (suppl 6): S10–S13.
2. Leppik IE, *et al.* Safety of tiagabine: summary of 53 trials. *Epilepsy Res* 1999; **33:** 235–46.

Effects on the eyes. Unlike vigabatrin, which is associated with visual field defects (see p.513), studies of visual function in patients taking tiagabine, another GABAergic antiepileptic, have been generally reassuring. However, in a case report[1] a 39-year-old patient was noted to have visual field defects while receiving long-term tiagabine therapy for bipolar disorder. The defects reversed after tiagabine was withdrawn.

1. Kaufman KR, *et al.* Visual fields and tiagabine: a quandary. *Seizure* 2001; **10:** 525–9.

Effects on mental function. For a review of the effects of antiepileptic therapy on *cognition*, and the effects of tiagabine on *mood* (including the risk of suicidal ideation) see p.468.

Effects on the nervous system. Acute dystonic reactions occurred in 3 patients when tiagabine was added to their existing carbamazepine treatment;[1] the reactions were associated with an increase in the dose of tiagabine to 20 mg or more. In all cases the dystonias disappeared despite continuing tiagabine therapy at the same dose, although in one patient carbamazepine was withdrawn.

There have been case reports of nonconvulsive status epilepticus,[2-4] associated with tiagabine. The authors of one such report[2] noted that, in placebo-controlled studies, the incidence of such an event was no higher in the tiagabine group than in the placebo group. However, a retrospective analysis[5] of inpatients with refractory localised epilepsy found that non convulsive status epilepticus occurred more frequently in patients treated with tiagabine (6.7%) than in those who were not (1.1%).

The FDA has warned of the risk of seizures with tiagabine when used in *non-epileptic patients* for unlicensed indications;[6] it had received over 30 reports of new-onset seizures or status epilepticus in such patients. Predisposing factors may include the use of other drugs known to lower the seizure threshold, and probably the dose. Although some cases were noted after doses as low as 4 mg daily, licensed doses in patients with epilepsy take into account the customary use of other enzyme-inducing antiepileptics which can roughly halve the plasma levels of tiagabine by inducing its metabolism. For reports of status epilepticus occurring in non-epileptic patients after tiagabine overdosage, see below.

1. Wolańczyk T, Grabowska-Grzyb A. Transient dystonias in three patients treated with tiagabine. *Epilepsia* 2001; **42:** 944–6.
2. Fitzek S, *et al.* Drug-induced nonconvulsive status epilepticus with low dose of tiagabine. *Epileptic Disord* 2001; **3:** 147–50.
3. Skardoutsou A, *et al.* Non-convulsive status epilepticus associated with tiagabine therapy in children. *Seizure* 2003; **12:** 599–601.
4. Vinton A, *et al.* Tiagabine-induced generalised non convulsive status epilepticus in patients with lesional focal epilepsy. *J Clin Neurosci* 2005; **12:** 128–33.
5. Koepp MJ, *et al.* Status epilepticus and tiagabine therapy revisited. *Epilepsia* 2005; **46:** 1625–32.
6. Food and Drug Administration. Tiagabine hydrochloride (marketed as Gabitril): seizures in patients without epilepsy (issued 18/02/05). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/TiagabineHCP.pdf (accessed 09/06/08)

Overdosage. A 30-year-old man who took 320 mg of tiagabine in overdose together with 400 mg of phenytoin showed no serious signs of toxicity other than significantly depressed levels of consciousness from which he quickly recovered.[1] Plasma concentrations of tiagabine measured 4 hours after ingestion were 30 times higher than those seen with therapeutic doses; phenytoin concentrations just exceeded the therapeutic range. A 46-year-old woman[2] who ingested about 72 mg of tiagabine exhibited facial grimacing, rigid flexure posturing of the upper extremities, and dilated pupils. She was uncommunicative and unresponsive to commands. Treatment with benzodiazepines was given, and symptoms resolved within 12 hours of admission.

Seizures, including status epilepticus, are a recognised adverse effect of tiagabine (see above); there have been reports of status epilepticus occurring in non-epileptic patients after overdosage, including non convulsive status epilepticus[3] in a 14-year-old girl who took about 180 mg of tiagabine, and myoclonic status epilepticus[4] in an 18-year-old man who took 120 mg of tiagabine with 400 mg of lamotrigine.

A retrospective review[5] of 57 overdoses with tiagabine reported to several poison centres in the USA found that the most common adverse effects were lethargy (in 56%), seizures (37%, including status epilepticus in 5%), agitation (32%), confusion (30%), and coma (28%). Other adverse effects included tachycardia, respiratory depression, tremor, and hallucinations; no deaths were reported. The mean onset and duration of symptoms were 1.3 and 9.1 hours, respectively. The lowest dose associated with seizures was 96 mg.

1. Leach JP, *et al.* Deliberate overdose with the novel anticonvulsant tiagabine. *Seizure* 1995; **4:** 155–7.
2. Cantrell FL, *et al.* Intentional overdose with tiagabine: an unusual clinical presentation. *J Emerg Med* 2004; **27:** 271–2.
3. Jette N, *et al.* Tiagabine-induced nonconvulsive status epilepticus in an adolescent without epilepsy. *Neurology* 2006; **67:** 1514–15.
4. Vollmar C, Noachtar S. Tiagabine-induced myoclonic status epilepticus in a nonepileptic patient. *Neurology* 2007; **68:** 310.
5. Spiller HA, *et al.* Retrospective evaluation of tiagabine overdose. *Clin Toxicol* 2005; **43:** 855–9.

Precautions

Hepatic metabolism of tiagabine is reduced in patients with hepatic impairment, and dosage should therefore be reduced and/or the intervals between doses increased. It should not be used in patients with severely impaired hepatic function.

Use of tiagabine in non-epileptic patients may be associated with an increased risk of seizures— see Effects on the Nervous System, above.

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

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

Driving. For 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. The hepatic metabolism of tiagabine is accelerated by antiepileptics that induce enzymes of the cytochrome P450 system such as carbamazepine, phenobarbital, phenytoin, or primidone. Plasma concentrations of tiagabine may be reduced up to threefold by use with these drugs.

Pharmacokinetics

Tiagabine is readily absorbed after oral doses, with a bioavailability of 89%. Food reduces the rate but not the extent of absorption. The absorption and elimination pharmacokinetics of tiagabine are linear within the therapeutic dosage range.

Tiagabine is widely distributed throughout the body and plasma protein binding is 96%.

Tiagabine is extensively metabolised in the liver and excreted as metabolites in the faeces or, to a lesser extent, in the urine; less than 2% of a dose is eliminated as unchanged drug. The plasma-elimination half-life is 7 to 9 hours, although this may be reduced to 2 to 3 hours by liver enzyme-inducing drugs (see also Interactions, above).

◊ References.

1. Gustavson LE, Mengel HB. Pharmacokinetics of tiagabine, a γ-aminobutyric acid-uptake inhibitor, in healthy subjects after single and multiples doses. *Epilepsia* 1995; **36:** 605–11.
2. So EL, *et al.* Pharmacokinetics of tiagabine as add-on therapy in patients taking enzyme-inducing antiepilepsy drugs. *Epilepsy Res* 1995; **22:** 221–6.
3. Snel S, *et al.* The pharmacokinetics of tiagabine in healthy elderly volunteers and elderly patients with epilepsy. *J Clin Pharmacol* 1997; **37:** 1015–20.
4. Cato A, *et al.* Effect of renal impairment on the pharmacokinetics and tolerability of tiagabine. *Epilepsia* 1998; **39:** 43–7.
5. Samara EE, *et al.* Population analysis of the pharmacokinetics of tiagabine in patients with epilepsy. *Epilepsia* 1998; **39:** 868–73.

Uses and Administration

Tiagabine is a nipecotic acid derivative used in the treatment of epilepsy (p.465) as adjunctive therapy for refractory partial seizures with or without secondary generalisation. It inhibits the uptake of GABA into neuronal and glial cells, and therefore increases the availability of GABA at receptor sites.

UK licensing information states that tiagabine hydrochloride is given as the monohydrate, but doses are described in terms of tiagabine; dose forms providing the equivalent of 5, 10, and 15 mg of tiagabine are available. In the USA, however, the licensed product is stated to contain anhydrous tiagabine hydrochloride, and doses are described in terms of this substance; dose forms providing 2, 4, 12, and 16 mg are available. As a result, the doses in the UK and US literature may not be directly comparable.

In the UK, the initial oral daily dose as adjunctive therapy in adults and children over 12 years of age is the equivalent of tiagabine 5 to 10 mg as a single dose or in 2 divided doses, increased weekly as necessary by increments of 5 to 10 mg. The usual maintenance dose is 30 to 45 mg daily, in 2 or 3 divided doses, in patients receiving enzyme-inducing antiepileptics; in patients *not* taking enzyme-inducing drugs an initial maintenance dosage of 15 to 30 mg daily is suggested. Lower initial doses of the hydrochloride are recommended in the USA. Doses should be taken with food to avoid rapid rises in plasma concentrations, thereby reducing the incidence of adverse effects. Reduced doses should be given in hepatic impairment—see below.

As with other antiepileptics, withdrawal of tiagabine 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 gradual