

6. Glauser TA, *et al.* Pharmacokinetics of levetiracetam in infants and young children with epilepsy. *Epilepsia* 2007; **48**: 1117–22.
7. Tomson T, *et al.* Pharmacokinetics of levetiracetam during pregnancy, delivery, in the neonatal period, and lactation. *Epilepsia* 2007; **48**: 1111–16.
8. Hirsch LJ, *et al.* Effect of age and comedication on levetiracetam pharmacokinetics and tolerability. *Epilepsia* 2007; **48**: 1351–9.

Uses and Administration

Levetiracetam is an analogue of piracetam (p.368). It is used as an adjunct in the treatment of partial seizures with or without secondary generalisations in adults and children aged 4 years and over; in the UK, adults and adolescents aged 16 years and over may also be given levetiracetam as monotherapy for this indication. In addition, levetiracetam is licensed for adjunctive use in the treatment of myoclonic seizures in adults and children aged 12 years and over with juvenile myoclonic epilepsy. It is also licensed for use as an adjunct in the treatment of primary generalised tonic-clonic seizures in adults and children with idiopathic generalised epilepsy; for this indication, in the UK, licensed use is restricted to children aged 12 years and over, whereas in the USA, it is licensed from 6 years of age.

The daily oral dose of levetiracetam is given in two divided doses.

- The initial adult dose when used as an adjunct is 1 g on the first day of treatment; thereafter, the daily dose may be increased in steps of 1 g every 2 to 4 weeks until effective antiepileptic control is achieved, up to a maximum dose of 3 g daily.

The initial dose in children weighing less than 50 kg is 20 mg/kg daily which may be increased in steps of 20 mg/kg every 2 weeks to a maximum of 60 mg/kg daily.

Children and adolescents weighing 50 kg or more should be given the usual adult dose (see above).

When used as monotherapy, the initial dose of levetiracetam is 500 mg daily, increased after 2 weeks to 1 g daily. Further increases may be made in steps of 500 mg every 2 weeks up to a maximum of 3 g daily.

When oral use is not feasible, levetiracetam may be given by intravenous infusion over 15 minutes in doses similar to those used orally; as with the oral formulation, details of licensed uses and ages may vary from country to country. UK licensed product information states that there has been no experience with the use of intravenous levetiracetam for more than 4 days.

Reduced doses are recommended in renal and severe hepatic impairment (see below).

As with other antiepileptics, withdrawal of levetiracetam 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 in adults by 1 g every 2 to 4 weeks; in children, the dose reduction should not exceed 20 mg/kg every 2 weeks. For a discussion on whether or not to withdraw antiepileptic therapy in seizure-free patients, see p.465.

References

1. De Smedt T, *et al.* Levetiracetam: the profile of a novel anticonvulsant drug—part I: preclinical data. *CNS Drug Rev* 2007; **13**: 43–56.
2. De Smedt T, *et al.* Levetiracetam: part II, the clinical profile of a novel anticonvulsant drug. *CNS Drug Rev* 2007; **13**: 57–78.

Administration in children. Licensed indications and doses of levetiracetam in children vary from country to country, see Uses and Administration, above. It is mainly used for partial and myoclonic seizures, and in idiopathic generalised epilepsy, often as an adjunct. A retrospective review¹ of 122 children aged from 1 month to 2 years given levetiracetam either as monotherapy (48 patients) or adjunctive therapy (74 patients) found that 70 achieved seizure remission. Of these, a longer duration of remission was seen in those receiving less than 30 mg/kg daily of levetiracetam. A case series² of 3 infants aged from 2 days to 3 months reported that levetiracetam 30 mg/kg daily was effective in the treatment of refractory neonatal seizures.

1. Perry MS, Benatar M. Efficacy and tolerability of levetiracetam in children younger than 4 years: a retrospective review. *Epilepsia* 2007; **48**: 1123–7.
2. Shoemaker MT, Rotenberg JS. Levetiracetam for the treatment of neonatal seizures. *J Child Neurol* 2007; **22**: 95–8.

The symbol † denotes a preparation no longer actively marketed

Administration in hepatic impairment. No dose adjustment is needed in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, creatinine clearance (CC) may underestimate concomitant renal impairment, and UK licensed product information recommends that the usual adult maintenance dose (see above) should be reduced by 50% in those with a CC of less than 70 mL/minute.

Administration in renal impairment. Reduced doses of levetiracetam are recommended for patients with renal impairment. Suitable daily doses according to UK and US licensed product information, based on creatinine clearance (CC) and given in 2 divided doses, are:

- CC 50 to 79 mL/minute: 1 to 2 g
- CC 30 to 49 mL/minute: 500 mg to 1.5 g
- CC less than 30 mL/minute: 500 mg to 1 g

Patients receiving dialysis may be given a loading dose of 750 mg when starting levetiracetam followed by doses of 500 mg to 1 g once daily; a supplemental dose of 250 to 500 mg is recommended after dialysis.

Doses may be given orally or intravenously, as necessary.

See also above for dosage recommendations in those patients with severe hepatic impairment and concomitant renal impairment.

Epilepsy. Levetiracetam is used in epilepsy (p.465) as an adjunct or monotherapy in the management of partial seizures with or without secondary generalisation.^{1–6} It is also used as an adjunct in myoclonic seizures^{7–9} and for generalised tonic-clonic seizures,¹⁰ although valproate is the drug of choice in the latter where these are associated with the syndrome of primary generalised epilepsy. Levetiracetam may be considered as second-line drug for atonic or tonic seizures, and has been tried in Lennox-Gastaut syndrome and in juvenile absence epilepsy.¹¹ In children, levetiracetam has also been tried as adjunctive therapy for nonconvulsive status epilepticus,¹² in infantile spasms,¹³ and in severe myoclonic epilepsy of infancy,¹⁴ and as monotherapy in partial and generalised epilepsy.¹⁵

1. Dooley M, Plosker GL. Levetiracetam: a review of its adjunctive use in the management of partial onset seizures. *Drugs* 2000; **60**: 871–93.
2. Chaisewikul R, *et al.* Levetiracetam add-on for drug-resistant localization related (partial) epilepsy. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2001 (accessed 09/06/08).
3. Welty TE, *et al.* Levetiracetam: a different approach to the pharmacotherapy of epilepsy. *Ann Pharmacother* 2002; **36**: 296–304.
4. Leach JP. Levetiracetam in the management of epilepsy. *Hosp Med* 2004; **65**: 740–4.
5. Abou-Khalil B. Benefit-risk assessment of levetiracetam in the treatment of partial seizures. *Drug Safety* 2005; **28**: 871–90.
6. Steinhoff BJ, *et al.* The SKATE study: an open-label community-based study of levetiracetam as add-on therapy for adults with uncontrolled partial epilepsy. *Epilepsia* 2007; **48**: 6–14.
7. Crest C, *et al.* Levetiracetam in progressive myoclonic epilepsy: an exploratory study in 9 patients. *Neurology* 2004; **62**: 640–3.
8. Specchio LM, *et al.* Open label, long-term, pragmatic study on levetiracetam in the treatment of juvenile myoclonic epilepsy. *Epilepsia* 2006; **47**: 32–9.
9. Noachtar S, *et al.* Levetiracetam for the treatment of idiopathic generalized epilepsy with myoclonic seizures. *Neurology* 2008; **70**: 607–16.
10. Berkovic SF, *et al.* Placebo-controlled study of levetiracetam in idiopathic generalized epilepsy. *Neurology* 2007; **69**: 1751–60.
11. NICE. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care (issued October 2004). Available at: <http://www.nice.org.uk/nicemedia/pdf/CG020fullguideline.pdf> (accessed 09/06/08)
12. Trabacca A, *et al.* Levetiracetam in nonconvulsive status epilepticus in childhood: a case report. *J Child Neurol* 2007; **22**: 639–41.
13. Mikati MA, *et al.* Response of infantile spasms to levetiracetam. *Neurology* 2008; **70**: 574–5.
14. Striano P, *et al.* An open-label trial of levetiracetam in severe myoclonic epilepsy of infancy. *Neurology* 2007; **69**: 250–4.
15. Khurana DS, *et al.* Levetiracetam monotherapy in children with epilepsy. *Pediatr Neurol* 2007; **36**: 227–30.

Movement disorders. Levetiracetam may be of benefit in some movement disorders. It has been tried in antipsychotic-induced tardive dyskinesia^{1–3} and with equivocal benefit in levodopa-induced tardive dyskinesia^{4,5} (see under Extrapyramidal Disorders on p.971). There is also limited evidence of benefit with levetiracetam for the treatment of chorea (p.953) in Huntington's disease^{6,7} and in paroxysmal kinesigenic choreoathetosis.⁸

1. Konitsiotis S, *et al.* Levetiracetam in tardive dyskinesia: an open label study. *Mov Disord* 2006; **21**: 1219–21.
2. Meco G, *et al.* Levetiracetam in tardive dyskinesia. *Clin Neuropharmacol* 2006; **29**: 265–8.
3. Woods SW, *et al.* Effects of levetiracetam on tardive dyskinesia: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry* 2008; **69**: 546–54.
4. Zesiewicz TA, *et al.* Open-label pilot study of levetiracetam (Keppra) for the treatment of levodopa-induced dyskinesias in Parkinson's disease. *Mov Disord* 2005; **20**: 1205–9.
5. Lyons KE, Pahwa R. Efficacy and tolerability of levetiracetam in Parkinson disease patients with levodopa-induced dyskinesia. *Clin Neuropharmacol* 2006; **29**: 148–53.

6. Zesiewicz TA, *et al.* Open-label pilot study of levetiracetam (Keppra) for the treatment of chorea in Huntington's disease. *Mov Disord* 2006; **21**: 1998–2001.
7. de Tommaso M, *et al.* Efficacy of levetiracetam in Huntington disease. *Clin Neuropharmacol* 2005; **28**: 280–4.
8. Chatterjee A, *et al.* Levetiracetam in the treatment of paroxysmal kinesigenic choreoathetosis. *Mov Disord* 2002; **17**: 614–15.

Muscle spasm. Levetiracetam has been tried with some success in Meige's syndrome,¹ and hemifacial spasm.² For use in stiff-man syndrome see below.

1. Yardimci N, *et al.* Levetiracetam in Meige's syndrome. *Acta Neurol Scand* 2006; **114**: 63–6.
2. Deleu D. Levetiracetam in the treatment of idiopathic hemifacial spasm. *Neurology* 2004; **62**: 2134–5.

Psychiatric disorders. Levetiracetam has psychotropic properties and has been tried in the management of anxiety disorders¹ (p.952) including social anxiety disorder² (see Phobic Disorders, p.953), post-traumatic stress disorder³ (p.953), and panic disorder⁴ (p.952). There is also limited evidence⁵ from case reports and small open-label studies that levetiracetam may be of benefit in the treatment of bipolar disorder (p.372).

1. Kinrys G, *et al.* Levetiracetam as adjunctive therapy for refractory anxiety disorders. *J Clin Psychiatry* 2007; **68**: 1010–13.
2. Simon NM, *et al.* An open-label study of levetiracetam for the treatment of social anxiety disorder. *J Clin Psychiatry* 2004; **65**: 1219–22.
3. Kinrys G, *et al.* Levetiracetam for treatment-refractory posttraumatic stress disorder. *J Clin Psychiatry* 2006; **67**: 211–14.
4. Papp LA. Safety and efficacy of levetiracetam for patients with panic disorder: results of an open-label, fixed-flexible dose study. *J Clin Psychiatry* 2006; **67**: 1573–6.
5. Muralidharan A, Bhagwagar Z. Potential of levetiracetam in mood disorders: a preliminary review. *CNS Drugs* 2006; **20**: 969–79.

Restless legs syndrome. Levetiracetam has been reported to be of benefit in the treatment of refractory restless legs syndrome (see Sleep-associated Movement Disorders, p.958).¹

1. Della Marca G, *et al.* Levetiracetam can be effective in the treatment of restless legs syndrome with periodic limb movements in sleep: report of two cases. *J Neurol Neurosurg Psychiatry* 2006; **77**: 566–7.

Status epilepticus. Levetiracetam has been tried, with some success, in the management of nonconvulsive status epilepticus¹ and refractory status epilepticus.² For the conventional management of status epilepticus see p.469.

1. Rupprecht S, *et al.* Levetiracetam as a treatment option in nonconvulsive status epilepticus. *Epilepsia* 2007; **48**: 238–44.
2. Patel NC, *et al.* The use of levetiracetam in refractory status epilepticus. *Seizure* 2006; **15**: 137–41.

Stiff-man syndrome. In a report¹ of a patient with stiff-man syndrome, substitution of levetiracetam for previous valproate therapy (because of suspected valproate-induced parkinsonism) resulted in complete suppression of paroxysmal spasms; benefit was sustained with continued therapy over 2 years of follow-up.

1. Rüegg SJ, *et al.* Levetiracetam improves paroxysmal symptoms in a patient with stiff-person syndrome. *Neurology* 2004; **62**: 338.

Tremor. A beta blocker is often the first drug used in patients with essential tremor who require regular treatment (p.1231); however, levetiracetam has also been tried with some success.¹ Benefit was also reported² with levetiracetam in the treatment of tremor secondary to multiple sclerosis.

1. Bushara KO, *et al.* The effect of levetiracetam on essential tremor. *Neurology* 2005; **64**: 1078–80.
2. Striano P, *et al.* Levetiracetam for cerebellar tremor in multiple sclerosis: an open-label pilot tolerability and efficacy study. *J Neurol* 2006; **253**: 762–6.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Keppra; **Levon:** Keppra; **Belg.:** Keppra; **Canad.:** Keppra; **Chile:** Kopodex; **Cz.:** Keppra; **Denm.:** Keppra; **Fin.:** Keppra; **Fr.:** Keppra; **Ger.:** Keppra; **Gr.:** Keppra; **Hong Kong:** Keppra; **Hung.:** Keppra; **India:** Levroxa; **Indon.:** Keppra; **Irl.:** Keppra; **Israel:** Keppra; **Ital.:** Keppra; **Malaysia:** Keppra; **Mex.:** Keppra; **Neth.:** Keppra; **Norw.:** Keppra; **NZ:** Keppra; **Philipp.:** Keppra; **Pol.:** Keppra; **Port.:** Keppra; **Rus.:** Keppra (Kenpa); **S.Afr.:** Keppra; **Singapore:** Keppra; **Spain:** Keppra; **Swed.:** Keppra; **Switz.:** Keppra; **Thai:** Keppra; **Turk.:** Keppra; **UK:** Keppra; **USA:** Keppra.

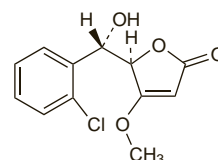
Losigamone (rINN)

AO-33; Losigamona; Losigamonom. (5R)-5-[(α 5)-o-Chloro- α -hydroxybenzyl]-4-methoxy-2(5H)-furanone.

ЛОЗИГАМОН

C₁₂H₁₁ClO₄ = 254.7.

CAS — 112856-44-7.



Profile

Losigamone is an antiepileptic that has been investigated as adjunctive therapy in the treatment of partial seizures.

References

1. Bauer J, *et al.* Losigamone add-on therapy in partial epilepsy: a placebo-controlled study. *Acta Neurol Scand* 2001; **103**: 226–30.
2. Baulac M, Klement S. Losigamone Study Group. Efficacy and safety of losigamone in partial seizures: a randomized double-blind study. *Epilepsy Res* 2003; **55**: 177–89.

Mephenytoin (BAN, USAN, rINN)

Mefenitoína; Mefenytol; Mefenytol; Mephentoin; Méphénytoïne; Mephénytoinum; Methantoin; Methoin; NSC-34652; Phenantoin. 5-Ethyl-3-methyl-5-phenylhydantoin.

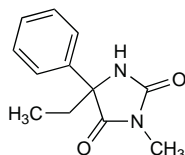
Мепенитоин

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

CAS — 50-12-4.

ATC — N03AB04.

ATC Vet — QN03AB04.

**Pharmacopoeias.** In *US*.

USP 31 (Mephenytoin). Store in airtight containers.

Profile

Mephenytoin is a hydantoin antiepileptic with actions similar to those of phenytoin (p.495), but it is more toxic. Because of its potential toxicity it is not one of the main drugs used in the treatment of epilepsy (p.465) and is given only to patients unresponsive to other treatment. Some of the adverse effects of mephenytoin may be due to the metabolite, 5-ethyl-5-phenylhydantoin (also termed nirvanol). Like phenytoin the rate of metabolism of mephenytoin is subject to genetic polymorphism.

Mephenytoin is given in an initial oral daily dose of 50 to 100 mg for 1 week; thereafter the daily dose is increased by 50 to 100 mg at weekly intervals until the optimum dose is reached, which is usually between 200 and 600 mg daily for an adult and 100 and 400 mg daily for a child; daily maintenance doses are usually taken in 3 divided doses.

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

Preparations

USP 31: Mephenytoin Tablets.

Proprietary Preparations (details are given in Part 3)

Austria: Epilan; **Cz:** Epilant.

Mesuximide (BAN, rINN)

Mesuximidi; Mesuximid; Mesuximida; Mésuximide; Mesuximidum; Methsuximide; PM-396. N,2-Dimethyl-2-phenylsuccinimide.

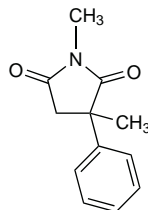
Мезуксимида

$C_{12}H_{13}NO_2 = 203.2$.

CAS — 77-41-8.

ATC — N03AD03.

ATC Vet — QN03AD03.

**Pharmacopoeias.** In *US*.

USP 31 (Methsuximide). A white to greyish-white crystalline powder. Is odourless or has a slight odour. Soluble 1 in 350 of water, 1 in 3 of alcohol, 1 in less than 1 of chloroform, and 1 in 2 of ether. Store in airtight containers.

Profile

Mesuximide is a succinimide antiepileptic with actions similar to those of ethosuximide (p.479) that is used in the treatment of absence seizures; although it also has some activity in complex partial seizures it is reported to be less well tolerated than ethosuximide, and is usually only given to patients unresponsive to other antiepileptic treatment. It is thought to owe its activity to its major metabolite *N*-desmethylmesuximide.

The usual initial oral dosage is a single dose of 300 mg daily for the first week, and this is increased by 300 mg at weekly intervals to an optimum dosage, according to response. The suggested maximum daily dose is 1.2 g in divided doses.

Epilepsy. Mesuximide is used for absence seizures that are refractory to less toxic antiepileptics such as ethosuximide or valproate, which are the usual first-line drugs (see p.465). Mesuximide has also been tried in complex partial seizures and myoclonic seizures.

References

1. Tennison MB, *et al.* Methsuximide for intractable childhood seizures. *Pediatrics* 1991; **87**: 186–9.
2. Sigler M, *et al.* Effective and safe but forgotten: methsuximide in intractable epilepsies in childhood. *Seizure* 2001; **10**: 120–4.

Interactions. For the effect of mesuximide on lamotrigine and valproate, see p.486 and p.511 respectively.

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

Preparations

USP 31: Methsuximide Capsules.

Proprietary Preparations (details are given in Part 3)

Austria: Petinutin; **Canada:** Celontin; **Ger:** Petinutin; **Israel:** Celontin; **Neth:** Celontin; **Switz:** Petinutin; **USA:** Celontin.

Methylphenobarbital (BAN, rINN)

Enphenemalum; Mephobarbital; Methylfenobarbital; Méthylphénobarbital; Methylphenobarbitalum; Methylphenobarbitone; Metilfenobarbital; Metilfenobarbital; Metilfenobarbitalis; Metylphenobarbital; Metylifenobarbitali; Phemitone. 5-Ethyl-1-methyl-5-phenylbarbituric acid.

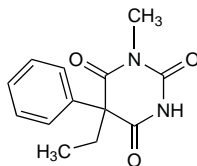
Метилфенобарбитал

$C_{13}H_{14}N_2O_3 = 246.3$.

CAS — 115-38-8.

ATC — N03AA01.

ATC Vet — QN03AA01.

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

Ph. Eur. 6.2 (Methylphenobarbital). A white or almost white, crystalline powder or colourless crystals. Practically insoluble in water; very slightly soluble in dehydrated alcohol. It forms water-soluble compounds with alkali hydroxides and carbonates, and with ammonia.

USP 31 (Mephobarbital). A white, odourless, crystalline powder. Slightly soluble in water, in alcohol, and in ether; soluble in chloroform and in solutions of fixed alkali hydroxides and carbonates. Its saturated solution in water is acid to litmus.

Dependence and Withdrawal, Adverse Effects, Treatment, and Precautions

As for Phenobarbital, p.492.

Interactions

As for Phenobarbital, p.493.

Pharmacokinetics

Methylphenobarbital is incompletely absorbed from the gastrointestinal tract. It is demethylated to phenobarbital (p.494) in the liver.

Uses and Administration

Methylphenobarbital is used similarly to phenobarbital (p.494) in the treatment of epilepsy (p.465). It is given in oral doses of up to 600 mg daily. It has also been used as a sedative in a usual dose of 50 mg 3 or 4 times daily.

Preparations

BP 2008: Methylphenobarbital Tablets;

USP 31: Mephobarbital Tablets.

Proprietary Preparations (details are given in Part 3)

Austrol: Prominalf; **USA:** Mebaral.

Multi-ingredient: **Arg:** Cumati L; **Ital:** Dintoinale; Metinal-Idantoina; Metinal-Idantoina L.

Oxcarbazepine (BAN, USAN, rINN)

GP-47680; KIN-493; Okskarbatsepiini; Okskarbazepin; Oxcarbazepin; Oxcarbazepina; Oxcarbazépine; Oxcarbazepinum. 10,11-Dihydro-10-oxo-5H-dibenz[b,f]azepine-5-carboxamide.

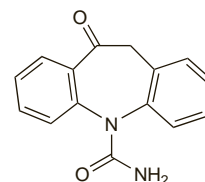
Окскарбаэепин

$C_{15}H_{12}N_2O_2 = 252.3$.

CAS — 28721-07-5.

ATC — N03AF02.

ATC Vet — QN03AF02.

**Adverse Effects, Treatment, and Precautions**

As for Carbamazepine, p.472.

Hypersensitivity reactions such as skin rashes (see also under Carbamazepine, p.473) occur less frequently with oxcarbazepine than with carbamazepine. However, cross-sensitivity does occur and about 25 to 30% of patients hypersensitive to carbamazepine may experience such reactions with oxcarbazepine. Reductions in plasma-sodium levels have also been observed with oxcarbazepine (see Hyponatraemia, below). Patients with cardiac insufficiency and secondary heart failure should be weighed regularly to detect fluid retention. Oxcarbazepine may, very rarely, impair cardiac conduction and patients with pre-existing conduction disorders should be carefully monitored. Very rarely, oxcarbazepine treatment has been associated with pancreatitis.

Dosage reductions are recommended in renal impairment.

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.

Effects on the blood. Although it would appear that oxcarbazepine is less likely than carbamazepine to cause blood dyscrasias such as leucopenia, individual cases have been reported. In one such case leucopenia and hyponatraemia developed in a 57-year-old woman while taking oxcarbazepine;¹ she recovered after treatment with filgrastim. It was noted that the patient had experienced a similar reaction when taking carbamazepine. Oxcarbazepine has also been associated with reversible pancytopenia² in a 40-year-old woman, and reversible thrombocytopenia³ in a 63-year-old woman.

1. Ryan M, *et al.* Hyponatremia and leukopenia associated with oxcarbazepine following carbamazepine therapy. *Am J Health-Syst Pharm* 2001; **58**: 1637–9.
2. Calamaras MR, *et al.* Pancytopenia associated with the introduction of oxcarbazepine. *J Clin Psychopharmacol* 2007; **27**: 217–18.
3. Mahmud J, *et al.* Oxcarbazepine-induced thrombocytopenia. *Psychosomatics* 2006; **47**: 73–4.

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

Effects on sexual function. For mention of the effects of antiepileptics including oxcarbazepine on sexual function in male epileptic patients, see Effects on the Endocrine System, under Phenytoin, p.496.

Hyponatraemia. Hyponatraemia appears to be more pronounced at clinical doses of oxcarbazepine than with carbamazepine. Hyponatraemia was reported¹ in 12 of 15 patients in whom oxcarbazepine was substituted for carbamazepine therapy. The fall in plasma-sodium concentrations appeared to be related to the dose of oxcarbazepine. In another report² hyponatraemia occurred in 23% of 350 patients whose serum-sodium concentrations were monitored. The manufacturers state that in 14 controlled studies sodium levels of less than 125 mmol/litre occurred in 2.5% of 1524 patients treated with oxcarbazepine compared to no such patients in the control groups. Most patients remain asymptomatic but some may experience drowsiness, increase in seizure frequency, and impaired consciousness.³ In a later study⁴ in 97 patients taking oxcarbazepine and 451 taking carbamazepine, hyponatraemia occurred in 29 (12 severe) of the former and in 61 (13 severe) of the latter. The authors failed to