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

◊ References

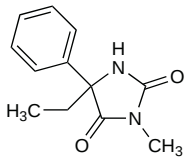
1. Bauer J, *et al*. Losigamone add-on therapy in partial epilepsy: a placebo-controlled study. *Acta Neurol Scand* 2001; **103:** 226–30.
2. Baulac M, Klement S. Losigamone Study Group. Efficacy and safety of losigamone in partial seizures: a randomized double-blind study. *Epilepsy Res* 2003; **55:**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

Mephenytoin *(BAN, USAN, rINN)*

Mefenitoína; Mefenytoiini; Mefenytoin; Mephenetoin; Méphénytoïne; Mephenytoinum; Methantoin; Methoin; NSC-34652; Phenantoin. 5-Ethyl-3-methyl-5-phenylhydantoin.

Мефенитоин

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

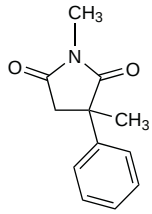
Proprietary Preparations (details are given in Part 3)
Austria: Epilan; ***Cz.:*** Epilan†.

Mesuximide *(BAN, rINN)*

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

Мезуксимид

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

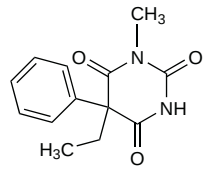
Proprietary Preparations (details are given in Part 3)
Austria: Petinutin; ***Canad.:*** Celontin; ***Ger.:*** Petinutin; ***Israel:*** Celontin†; ***Neth.:*** Celontin; ***Switz.:*** Petinutin; ***USA:*** Celontin.

Methylphenobarbital *(BAN, rINN)*

Enphenemalum; Mephobarbital; Methylfenobarbital; Méthylphénobarbital; Methylphenobarbitalum; Methylphenobarbitone; Metilfenobarbitál; Metilfenobarbital; Metilfenobarbitalis; Metylfenobarbital; Metyylifenobarbitaali; 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)
Austral.: Prominal†; ***USA:*** Mebaral.

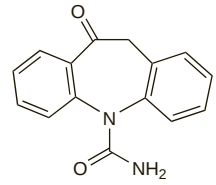
Multi-ingredient: ***Arg.:*** Cumatil L; ***Ital.:*** Dintoinale; Metinal-Idantoina; Metinal-Idantoina L.

Oxcarbazepine *(BAN, USAN, rINN)*

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

Окскарбазепин

$C_{15}H_{12}N_2O_2$ = 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 pancytopenia[2] in a 40-year-old woman, and reversible thrombocytopenia[3] 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 reported[1] 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 report[2] 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 study[4] 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