abnormal movements, and for the treatment of panic disorder (see Psychiatric Disorders, below).

For **epilepsy** and **myoclonus** treatment is started with small doses that are progressively increased to an optimum dose according to response. Total daily doses may initially be taken in 3 or 4 divided doses; however, once the maintenance dose has been reached, the daily amount may be given as a single dose at night. In the UK the initial oral dose is 1 mg (500 micrograms in the elderly) at night for 4 nights gradually increased over 2 to 4 weeks to a usual maintenance dose of 4 to 8 mg daily; it is recommended that the total dose should not exceed 20 mg daily. Dosage recommendations in the USA are generally similar although initial doses of up to 1.5 mg daily are permitted and dosage increments of 0.5 to 1 mg every 3 days are recommended. There is little value in routinely monitoring plasma-clonazepam concentrations.

Clonazepam may be an alternative to other benzodiazepines in the emergency management of **status epilepticus**. The usual dose is 1 mg given by slow intravenous injection over at least 2 minutes or by intravenous infusion, repeated if necessary to a maximum total dose of 20 mg.

For doses in children, see below.

As with other antiepileptics, withdrawal of clonazepam 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. For a discussion on whether or not to withdraw antiepileptic therapy in seizure-free patients, see p.465 and above.

In the treatment of **panic disorder**, clonazepam is given in an initial oral dose of 250 micrograms twice daily. This may be increased after 3 days to a total of 1 mg daily; a few patients may benefit from further increases, up to a maximum of 4 mg daily. In order to minimise drowsiness, clonazepam may be taken as a single dose at bedtime. Withdrawal should again be gradual.

Administration. Serum concentrations of clonazepam after buccal, intranasal, or intravenous dosage were measured in a crossover study[1] in 7 healthy males. The results showed that intranasal clonazepam may offer an alternative to buccal use in patients with serial seizures but the initial concentrations were too low to recommend its use as an alternative to intravenous clonazepam in the management of status epilepticus. The nasal formulation used in this study contained dimethyl-β-cyclodextrin as a solubiliser and absorption enhancer.

1. Schols-Hendriks MWG, *et al.* Absorption of clonazepam after intranasal and buccal administration. *Br J Clin Pharmacol* 1995; **39:** 449–51.

Administration in children. For **epilepsy** and **myoclonus** treatment with clonazepam is started with small doses that are progressively increased to an optimum dose according to response. Total daily doses are taken in 3 divided doses; however, once the maintenance dose has been reached, the daily amount may be given as a single dose at night. Alternatively, the *BNFC* suggests giving the initial dose at night for 4 nights and gradually increasing it over 2 to 4 weeks. In the UK, the recommended initial oral daily dose is up to 250 micrograms for infants and children aged up to 5 years, or up to 500 micrograms for older children. The following usual maintenance doses are given according to age:

- neonate to 1 year (although the BNFC recommends a minimum age of 1 month): 0.5 to 1 mg daily
- 1 to 5 years: 1 to 3 mg daily
- 5 to 12 years: 3 to 6 mg daily

Older children may be given the usual adult dose (see above).

If control of childhood epilepsy ceases to be adequate with clonazepam, the dose may be increased, or treatment interrupted for 2 or 3 weeks. The *BNFC* states that the UK injection formulation (*Rivotril; Roche, UK*) can be given orally if necessary; this may not apply to other injection formulations available elsewhere.

In the USA, doses may be given according to body weight. Infants and children aged up to 10 years or weighing up to 30 kg may be given an initial daily dose of 10 to 30 micrograms/kg (maximum 50 micrograms/kg) in 2 or 3 divided doses. This may be increased by a total of 250 to 500 micrograms every 3 days to a maintenance dose of 100 to 200 micrograms/kg daily given in 3 divided doses.

In the emergency management of **status epilepticus**, clonazepam is used as an alternative to other benzodiazepines. The usual dose in children is 500 micrograms given by slow intravenous injection or by intravenous infusion. Alternatively, the *BNFC* suggests giving the following doses by slow intravenous injection over at least 2 minutes according to age:

- neonates: 100 micrograms/kg, repeated if necessary after 24 hours
- 1 month to 12 years: 50 micrograms/kg (maximum 1 mg), repeated if necessary

Older children may be given the usual adult dose.

In children aged over 1 month, these doses by injection may be followed by an intravenous infusion of 10 micrograms/kg per hour, adjusted according to response to a maximum of 60 micrograms/kg per hour.

Extrapyramidal disorders. Clonazepam may be of benefit in some extrapyramidal disorders. It has been tried in the management of patients with *tic disorders* such as *Tourette's syndrome* (p.954) but evidence of efficacy from controlled studies is limited.[1] Some use clonazepam in preference to haloperidol[2] since it does not carry the risk of tardive dyskinesia associated with such antipsychotics and a case report[3] described the successful use of clonazepam for haloperidol-induced tardive Tourette's syndrome in an adult patient. There is also limited evidence of benefit with clonazepam in antipsychotic-induced *akathisia*[4,5] and *tardive dyskinesia*[6,7] (see under Extrapyramidal Disorders, p.971), and of improvement in *dysarthria* in a study in patients with parkinsonism.[8]

1. Goetz CG. Clonidine and clonazepam in Tourette syndrome. *Adv Neurol* 1992; **58:** 245–51.
2. Truong DD, *et al.* Clonazepam, haloperidol, and clonidine in tic disorders. *South Med J* 1988; **81:** 1103–5.
3. Reid SD. Neuroleptic-induced tardive Tourette treated with clonazepam: a case report and literature review. *Clin Neuropharmacol* 2004; **27:** 101–4.
4. Kutcher S, *et al.* Successful clonazepam treatment of neuroleptic-induced akathisia in older adolescents and young adults: a double-blind, placebo-controlled study. *J Clin Psychopharmacol* 1989; **9:** 403–6.
5. Pujalte D, *et al.* A double-blind comparison of clonazepam and placebo in the treatment of neuroleptic-induced akathisia. *Clin Neuropharmacol* 1994; **17:** 236–42.
6. Thaker GK, *et al.* Clonazepam treatment of tardive dyskinesia: a practical GABAmimetic strategy. *Am J Psychiatry* 1990: **147:** 445–51.
7. Shapleske J, *et al.* Successful treatment of tardive dystonia with clozapine and clonazepam. *Br J Psychiatry* 1996; **168:** 516–18.
8. Biary N, *et al.* A double-blind trial of clonazepam in the treatment of parkinsonian dysarthria. *Neurology* 1988; **38:** 255–8.

Hiccup. For the management of intractable hiccups see under Chlorpromazine, p.976. Clonazepam may also be of value, especially in neurogenic hiccups.

Neuropathic pain. The management of *phantom limb pain* (p.9) can be difficult, and tricyclic antidepressants and antiepileptics are used for the neuropathic components of the pain. Rapid and marked pain relief was achieved in 2 patients with lancinating phantom limb pain after treatment with clonazepam with or without amitriptyline.[1]

Although carbamazepine is the drug of choice in the treatment of *trigeminal neuralgia* (p.9), clonazepam may be used in carbamazepine-intolerant patients.

1. Bartusch SL, *et al.* Clonazepam for the treatment of lancinating phantom limb pain. *Clin J Pain* 1996; **12:** 59–62.

Psychiatric disorders. Although the risk of dependence with benzodiazepines may outweigh their benefits in panic disorder (p.952), clonazepam has been used for the treatment of panic disorder with or without agoraphobia, and reported benefit in such patients[1] suggests a similar action to alprazolam. A literature review[2] evaluated the use of clonazepam in a range of psychiatric disorders and found that it may also be effective in the treatment of social anxiety disorder (see Phobic Disorders, p.953) although further studies are warranted. There was evidence to suggest that clonazepam may be useful in acute mania (p.372) and for the augmentation of antidepressant therapy with SSRIs in depression (p.373). A study[3] found that augmentation was significantly more effective with a daily dose of 3 mg of clonazepam than with lower doses.

1. Davidson JRT, Moroz G. Pivotal studies of clonazepam in panic disorder. *Psychopharmacol Bull* 1998; **34:** 169–74.
2. Nardi AE, Perna G. Clonazepam in the treatment of psychiatric disorders: an update. *Int Clin Psychopharmacol* 2006; **21:** 131–42.
3. Morishita S, Aoki S. Clonazepam in the treatment of prolonged depression. *J Affect Disord* 1999; **53:** 275–8.

Sleep-associated movement disorders. Treatment of sleep-associated movement disorders (p.958) including sleep behaviour disorder, restless legs syndrome, and periodic limb movements in sleep is largely empirical, but benzodiazepines such as clonazepam are often used.[1] Small studies have provided some evidence for benefit with clonazepam therapy in these disorders,[2-4] including bruxism.[5]

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.
2. Montagna P, *et al.* Clonazepam and vibration in restless legs syndrome. *Acta Neurol Scand* 1984; **69:** 428–30.
3. Peled R, Lavie P. Double-blind evaluation of clonazepam on periodic leg movements in sleep. *J Neurol Neurosurg Psychiatry* 1987; **50:** 1679–81.
4. Saletu M, *et al.* Restless legs syndrome (RLS) and periodic limb movement disorder (PLMD): acute placebo-controlled sleep laboratory studies with clonazepam. *Eur Neuropsychopharmacol* 2001; **11:** 153–61.
5. Saletu A, *et al.* On the pharmacotherapy of sleep bruxism: placebo-controlled polysomnographic and psychometric studies with clonazepam. *Neuropsychobiology* 2005; **51:** 214–25.

Stiff-man syndrome. Clonazepam has been used as an alternative to diazepam in the management of stiff-man syndrome (see under Muscle Spasm, p.993) and is reported[1] to be effective for familial startle disease, a rare congenital form of stiff-man syndrome.

1. Ryan SG, *et al.* Startle disease, or hyperekplexia: response to clonazepam and assignment of the gene (STHE) to chromosome 5q by linkage analysis. *Ann Neurol* 1992; **31:** 663–8.

Tinnitus. Clonazepam is one of many drugs that have been tried in tinnitus (p.1866), but although it has been reported to be effective in some patients it is rarely used because of problems with adverse effects.

References.

1. Ganança MM, *et al.* Clonazepam in the pharmacological treatment of vertigo and tinnitus. *Int Tinnitus J* 2002; **8:** 50–3.
2. Albertino S, *et al.* Pulsatile tinnitus: treatment with clonazepam and propranolol. *Rev Bras Otorrinolaringol (Engl Ed)* 2005; **71:** 111–13.

Preparations

BP 2008: Clonazepam Injection;
USP 31: Clonazepam Oral Suspension; Clonazepam Tablets.

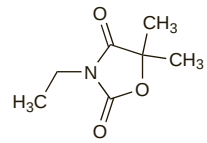
Proprietary Preparations (details are given in Part 3)
Arg.: Alerion; Ciclox; Clonabay; Clonagin; Clonax; Clonazen 2; Cloner; Diocam; Edictum; Felanor; Flozepan; Induzepam; Leptic; Miozepam; Neuryl; Olimer; Placidiax; Riuclonaz; Rivotril; Sedovanon; Sensaton; Solfidin; ***Austral.:*** Paxam; Rivotril; ***Austria:*** Rivotril; ***Belg.:*** Rivotril; ***Braz.:*** Clonotril; Clopan; Epileptil; Navotrax; Rivotril; Uni Clonazepax; ***Canad.:*** Clonapam†; Rivotril; ***Chile:*** Acepran; Clonapam; Clonex; Clozanil; Crismol; Neuryl; Ravotril; Ropsil; Valpax; ***Cz.:*** Antelepsin†; Rivotril; ***Denm.:*** Rivotril: ***Fin.:*** Rivatril; ***Fr.:*** Rivotril; ***Ger.:*** Antelepsin; Rivotril; ***Gr.:*** Rivotril; ***Hong Kong:*** Rivotril; ***Hung.:*** Clonapam; Clonogal†; Rivotril; ***India:*** Epitril; Epizam; Ozepam; ***Indon.:*** Rivotril; ***Irl.:*** Rivotril; ***Israel:*** Clonex; Rivotril; ***Ital.:*** Rivotril; ***Malaysia:*** Rivotril; ***Mex.:*** Kenoket; Kriadex; Rivotril; Zymanta; ***Neth.:*** Rivotril; ***Norw.:*** Rivotril; ***NZ:*** Paxam; Rivotril; ***Philipp.:*** Rivotril; ***Pol.:*** Rivotril; ***Port.:*** Rivotril; ***S.Afr.:*** Rivotril; ***Spain:*** Rivotril; ***Swed.:*** Iktorivil; ***Switz.:*** Rivotril; ***Thai.:*** Povanil; Rivotril; ***Turk.:*** Rivotril; ***UK:*** Rivotril; ***USA:*** Klonopin; ***Venez.:*** Rivotril.

Ethadione

Etadiona. 3-Ethyl-5,5-dimethyl-2,4-oxazolidinedione.

Этадион

$C_7H_{11}NO_3$ = 157.2.
CAS — 520-77-4.
ATC — N03AC03.
ATC Vet — QN03AC03.



Profile

Ethadione is an oxazolidinedione antiepileptic that has been given orally to treat epilepsy in patients with absence seizures resistant to other therapy.

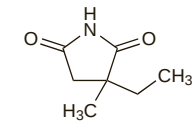
Preparations

Ethosuximide *(BAN, USAN, rINN)*

CI-366; CN-10395; Ethosuximid; Éthosuximide; Ethosuximidum; Etosüksimid; Etosuksimidas; Etosuksimidi; Etosuksymid; Etosuximid; Etosuximida; Etoszuximid; NSC-64013; PM-671. 2-Ethyl-2-methylsuccinimide.

Этосуксимид

$C_7H_{11}NO_2$ = 141.2.
CAS — 77-67-8.
ATC — N03AD01.
ATC Vet — QN03AD01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Ethosuximide). A white or almost white powder or waxy solid. It exhibits polymorphism. Freely soluble in water;

very soluble in alcohol and in dichloromethane. Protect from light.

USP 31 (Ethosuximide). A white to off-white crystalline powder or waxy solid, having a characteristic odour. Freely soluble in water and in chloroform; very soluble in alcohol and in ether; very slightly soluble in petroleum spirit. Store in airtight containers.

Adverse Effects and Treatment

Gastrointestinal adverse effects including nausea, vomiting, diarrhoea, anorexia, gastric upset, and abdominal pain occur quite often with ethosuximide. Other effects that may occur include headache, fatigue, lethargy, drowsiness, dizziness, ataxia, hiccup, and mild euphoria.

More rarely dyskinesias, personality changes, depression, psychosis, sleep disturbances including night terrors, skin rashes, erythema multiforme or Stevens-Johnson syndrome, SLE, photophobia, gum hypertrophy, tongue swelling, myopia, increased libido, and vaginal bleeding have been reported. There are a few reports of blood disorders including eosinophilia, leucopenia, agranulocytosis, thrombocytopenia, pancytopenia, and aplastic anaemia; fatalities have occurred.

Abnormal renal and liver function values have been recorded.

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

Precautions

Ethosuximide should be used with caution in patients with impaired hepatic or renal function. Licensed product information recommends regular hepatic and renal-function tests (and some suggest blood counts) during treatment with ethosuximide, although the practical value of such monitoring has been questioned. Patients or their carers should be told how to recognise signs of blood toxicity and they should be advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising, or bleeding develop.

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

Breast feeding. Ethosuximide is distributed in significant amounts into breast milk; hyperexcitability and poor suckling have been reported in the infant. Although licensed product information recommends that breast feeding should be avoided, the American Academy of Pediatrics[1] considers that ethosuximide is usually compatible with breast feeding.

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

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 09/06/08)

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

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

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.

Antibacterials. *Isoniazid* raises the plasma concentration of ethosuximide and increases the risk of toxicity. Psychotic behaviour has been reported[1] in a patient stabilised on ethosuximide and sodium valproate, after the introduction of isoniazid. Serum-ethosuximide concentrations rose substantially until both ethosuximide and isoniazid were stopped.

1. van Wieringen A, Vrijlandt CM. Ethosuximide intoxication caused by interaction with isoniazid. *Neurology* 1983; **33:** 1227–8.

Antidepressants. As with all antiepileptics, antidepressants may antagonise the antiepileptic activity of ethosuximide by lowering the convulsive threshold.

Antiepileptics. Since ethosuximide has a limited spectrum of antiepileptic action, patients with mixed seizure syndromes may require addition of other antiepileptics. *Carbamazepine*, *phenobarbital*, and *phenytoin* have all been shown[1] to increase the clearance of ethosuximide and thus reduce plasma concentrations. This interaction is likely to be clinically relevant and higher ethosuximide dosages may be necessary to achieve therapeutic drug levels. The effect of *valproic acid* on ethosuximide concentrations is unclear. One study[2] showed a marked increase in serum ethosuximide concentrations once valproate was added to combination therapies; increases in ethosuximide concentrations have also been noted in healthy subjects when taken with valproic acid.[3] Conversely, other studies have reported reductions[4] or no significant changes in serum ethosuximide concentrations[5,6] with valproic acid. For the effect of ethosuximide on valproic acid, see p.511.

1. Giaccone M, *et al.* Effect of enzyme inducing anticonvulsants on ethosuximide pharmacokinetics in epileptic patients. *Br J Clin Pharmacol* 1996; **41:** 575–9.
2. Mattson RH, Cramer JA. Valproic acid and ethosuximide interaction. *Ann Neurol* 1980; **7:** 583–4.
3. Pisani F, *et al.* Valproic acid-ethosuximide interaction: a pharmacokinetic study. *Epilepsia* 1984; **25:** 229–33.
4. Battino D, *et al.* Ethosuximide plasma concentrations: influence of age and associated concomitant therapy. *Clin Pharmacokinet* 1982; **7:** 176–80.
5. Fowler GW. Effect of dipropylacetate on serum levels of anticonvulsants in children. *Proc West Pharmacol Soc* 1978; **21:** 37–40.
6. Bauer LA, *et al.* Ethosuximide kinetics: possible interaction with valproic acid. *Clin Pharmacol Ther* 1982; **31:** 741–5.

Antipsychotics. As with all antiepileptics, antipsychotics may antagonise the antiepileptic activity of ethosuximide by lowering the convulsive threshold.

Pharmacokinetics

Ethosuximide is readily absorbed from the gastrointestinal tract and extensively hydroxylated in the liver to its principal metabolite which is reported to be inactive. Ethosuximide is excreted in the urine mainly in the form of its metabolites, either free or conjugated, but about 12 to 20% is also excreted unchanged.

Ethosuximide is widely distributed throughout the body, but is not significantly bound to plasma proteins. A half-life of about 40 to 60 hours has been reported for adults with a shorter half-life of about 30 hours in children.

Monitoring of plasma concentrations has been suggested as an aid in assessing control and the therapeutic range of ethosuximide is usually quoted as being 40 to 100 micrograms/mL (about 300 to 700 micromoles/litre); concentrations in saliva and tears have also been measured.

Ethosuximide crosses the placental barrier, and is distributed into breast milk.

The pharmacokinetics of ethosuximide are affected by use with other antiepileptics (see under Interactions, above).

Uses and Administration

Ethosuximide is a succinimide antiepileptic used in the treatment of absence seizures (below). It may also be used for myoclonic seizures. Ethosuximide is ineffective against tonic-clonic seizures and may unmask them if given alone in mixed seizure types.

A plasma-ethosuximide concentration of 40 to 100 micrograms/mL (about 300 to 700 micromoles/litre) appears to be generally necessary. The initial dose is 500 mg daily by mouth. The dosage is then adjusted in steps of 250 mg every 4 to 7 days, according to response. Control of seizures is usually produced with a daily dose of 1 to 1.5 g, although some patients may require doses of up to 2 g; strict supervision is necessary when the dose exceeds 1.5 g. Daily doses at the higher end of the range should be given in 2 divided doses.

For doses in children, see below.

As with other antiepileptics, withdrawal of ethosuximide 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. For a discussion on whether or not to withdraw antiepileptic therapy in seizure-free patients, see p.465.

Administration in children. Ethosuximide may be used in the treatment of absence (petit mal) seizures and for myoclonic seizures in infants and children. In the UK, the following recommended oral doses are given according to age:

- up to 6 years of age: an initial dose of 250 mg daily, increased gradually in small steps every few days to a usual dose of 20 mg/kg daily; licensed information for one product (*Emeside; Chemidex, UK*) recommends that the dose should not exceed 1 g. (Similar dosages are recommended in the USA for children aged between 3 to 6 years). The *BNFC* suggests giving the daily dose as 2, or if necessary 3, divided doses
- aged 6 years and above: usual adult doses (see above)

Epilepsy. Ethosuximide is a drug of choice in the treatment of absence seizures; it may also be used for myoclonic, atonic, and tonic seizures but is ineffective in other forms of epilepsy (p.465). Ethosuximide may be given with other antiepileptics in the treatment of mixed-seizure syndromes that include absences. It has been suggested that ethosuximide may provoke tonic-clonic seizures, but there is not a great deal of evidence for this. One early report indicated that 22 of 85 patients receiving a regimen of ethosuximide, mesuximide, and trimethadione for absence seizures developed tonic-clonic seizures[1] and another of similar vintage reported exacerbation of mixed-seizure types in 7 patients receiving ethosuximide.[2] However, it is recognised that patients with absence seizures have a high incidence of generalised tonic-clonic seizures[3] and it would presumably be difficult to distinguish such attacks from any putative effect of ethosuximide. Furthermore, ethosuximide is not effective against tonic-clonic seizures, and in patients with mixed-seizure types it might be expected to unmask the non-absence components of the disease.

Ethosuximide has also been tried in the management of absence status epilepticus (p.469).

1. Friedel B, Lempp R. Grand-mal-Provokation bei der Behandlung kindlicher petit-mal mit Oxazolidinen oder Succinimiden und ihre therapeutischen Konsequenzen. *Z Kinderheilk* 1962; **87:** 42–51.
2. de Haas AML, Kuilman M. Ethosuximide (α-ethyl-α-methylsuccinimide) and grand mal. *Epilepsia* 1964; **5:** 90–6.
3. Glauser TA. Succinimides: Adverse Effects. In: Levy RG, *et al.*, eds. *Antiepileptic drugs* 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002; 658–64.

Preparations

BP 2008: Ethosuximide Capsules; Ethosuximide Oral Solution;
USP 31: Ethosuximide Capsules; Ethosuximide Oral Solution.

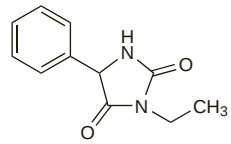
Proprietary Preparations (details are given in Part 3)
Arg.: Zarontin; ***Austral.:*** Zarontin; ***Austria:*** Petinimid; Suxinutin; ***Belg.:*** Zarontin; ***Canad.:*** Zarontin; ***Chile:*** Suxinutin; ***Cz.:*** Petinimid; Suxilep†; ***Denm.:*** Zarondan; ***Fin.:*** Suxinutin; ***Fr.:*** Zarontin; ***Ger.:*** Petnidan; Suxilep; Suxinutin†; ***Gr.:*** Zarontin; ***Hung.:*** Petnidan; Suxinutin†; ***Irl.:*** Zarontin; ***Israel:*** Zarontin†; ***Ital.:*** Zarontin; ***Mex.:*** Fluozoid; ***Neth.:*** Ethymal; Zarontin†; ***NZ:*** Zarontin; ***Pol.:*** Petinimid; ***Rus.:*** Suxilep (Суксилеп); ***S.Afr.:*** Zarontin; ***Spain:*** Zarontin†; ***Swed.:*** Suxinutin; ***Switz.:*** Petinimid; Suxinutin†; ***UK:*** Emeside; Zarontin; ***USA:*** Zarontin.

Ethotoin *(BAN, rINN)*

Éthotoïne; Ethotoinum; Etotoiini; Etotoin; Etotoína. 3-Ethyl-5-phenylhydantoin.

Этотоин

$C_{11}H_{12}N_2O_2$ = 204.2.
CAS — 86-35-1.
ATC — N03AB01.
ATC Vet — QN03AB01.



Pharmacopoeias. In *US.*

USP 31 (Ethotoin). A white crystalline powder. Insoluble in water; freely soluble in dehydrated alcohol and in chloroform; soluble in ether. Store in airtight containers.

Profile

Ethotoin is a hydantoin antiepileptic with actions similar to those of phenytoin (p.495), but it is reported to be both less toxic and less effective and is not commonly used in epilepsy (p.465).

Ethotoin is given orally for tonic-clonic and complex partial seizures in initial doses of up to 1 g daily, increased gradually at intervals of several days to 2 to 3 g daily, given in 4 to 6 divided doses after meals.

Administration. A study[1] of the pharmacokinetics of ethotoin given at more convenient intervals of every 8 hours.

1. Browne TR, Szabo GK. A pharmacokinetic rationale for three times daily administration of ethotoin (Peganone). *J Clin Pharmacol* 1989; **29:** 270–1.

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

Preparations

USP 31: Ethotoin Tablets.

Proprietary Preparations (details are given in Part 3)
USA: Peganone.