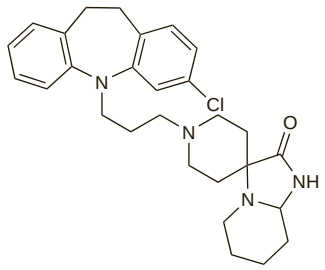
### Mosapramine *(rINN)*

Clospipramine; Mosapramina; Mosapraminum; Y-516. (±)-1′-[3-(3-Chloro-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepin-5-yl)propyl]hexahydrospiro[imidazo[1,2-*a*]pyridine-3(2*H*),4′-piperidin]-2-one.

Мозапрамин

$C_{28}H_{35}ClN_4O$ = 479.1.
*CAS — 89419-40-9.*
*ATC — N05AX10.*
*ATC Vet — QN05AX10.*



#### Profile

Mosapramine is an antipsychotic that has been tried in the treatment of schizophrenia.

◊ References.

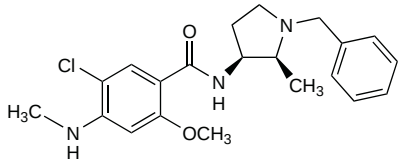

1. Ishigooka J, *et al.* Pilot study of plasma concentrations of mosapramine, a new iminodibenzyl antipsychotic agent, after multiple oral administration in schizophrenic patients. *Curr Ther Res* 1994; **55:** 331–42.
2. Takahashi N, *et al.* Comparison of risperidone and mosapramine addition to neuroleptic treatment in chronic schizophrenia. *Neuropsychobiology* 1999; **39:** 81–5.


### Nemonapride *(rINN)*

Emonapride; Nemonaprida; Némonapride; Nemonapridum; YM-09151-2. (±)-*cis*-*N*-(1-Benzyl-2-methyl-3-pyrrolidinyl)-5-chloro-4-(methylamino)-*o*-anisamide.

Немонаприд

$C_{21}H_{26}ClN_3O_2$ = 387.9.
*CAS — 93664-94-9.*



#### Profile

Nemonapride is a substituted benzamide antipsychotic with general properties similar to those of sulpiride (p.1028). It is given orally in the treatment of schizophrenia in usual doses of 9 to 36 mg daily in divided doses; up to 60 mg daily may be given if necessary.

◊ References.


1. Satoh K, *et al.* Effects of nemonapride on positive and negative symptoms of schizophrenia. *Int Clin Psychopharmacol* 1996; **11:** 279–81.


#### Preparations

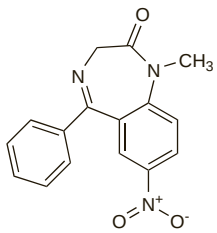
**Proprietary Preparations** (details are given in Part 3)
***Jpn:*** Emilace.

### Nimetazepam *(rINN)*

Menifazepam; Nimétazépam; Nimetazepamum; S-1530. 1,3-Dihydro-1-methyl-7-nitro-5-phenyl-1,4-benzodiazepin-2-one.

Ниметазепам

$C_{16}H_{13}N_3O_3$ = 295.3.
*CAS — 2011-67-8.*



#### Profile

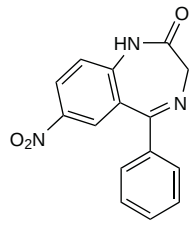
Nimetazepam is a benzodiazepine with the general properties of diazepam (p.986). It has been given orally for the short-term management of insomnia. It appears to have been subject to abuse, especially in South East Asia.

## Nitrazepam *(BAN, USAN, rINN)*

Nitratsepaami; Nitrazépam; Nitrazepám; Nitrazepamas; Nitrazepamum; NSC-58775; Ro-4-5360; Ro-5-3059. 1,3-Dihydro-7-nitro-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

Нитразепам

$C_{15}H_{11}N_3O_3$ = 281.3.
*CAS — 146-22-5.*
*ATC — N05CD02.*
*ATC Vet — QN05CD02.*



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of nitrazepam:
Don; Moggies; Moogles; Nitro's; The Don.

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, and *Jpn.*
**Ph. Eur. 6.2** (Nitrazepam). A yellow, crystalline powder. Practically insoluble in water; slightly soluble in alcohol. Protect from light.

### Dependence and Withdrawal

As for Diazepam, p.987.

◊ For the purpose of withdrawal regimens, 5 mg of nitrazepam may be considered equivalent to about 5 mg of diazepam.

### Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

**Effects on the digestive system.** Two children given nitrazepam as part of their antiepileptic therapy developed drooling, eating difficulty, and aspiration pneumonia; symptoms improved in one patient when the dosage of nitrazepam was reduced.[1] Manometric studies indicated that the onset of normal cricopharyngeal relaxation in swallowing was delayed in these patients until after hypopharyngeal contraction, resulting in impaired swallowing and spillover of material into the trachea. Other workers[2] have found similar effects on swallowing and cricopharyngeal relaxation in children given nitrazepam. The deaths of 6 epileptic children under 5 years of age who were treated with nitrazepam have been reported.[3] Three of the deaths were unexpected, and in view of the previous reports of swallowing difficulties and aspiration, it was recommended that the use of nitrazepam in young children be restricted to those in whom seizure control fails to improve with other antiepileptics. Another study[4] also found an apparently increased risk of death, especially in young patients with intractable epilepsy, associated with nitrazepam therapy.


1. Wyllie E. *et al*. The mechanism of nitrazepam-induced drooling and aspiration. *N Engl J Med* 1986; **314:** 35–8.
2. Lim HCN, *et al.* Nitrazepam-induced cricopharyngeal dysphagia, abnormal esophageal peristalsis and associated bronchospasm: probable cause of nitrazepam-related sudden death. *Brain Dev* 1992; **14:** 309–14.
3. Murphy JV, *et al.* Deaths in young children receiving nitrazepam. *J Pediatr* 1987; **111:** 145–7.
4. Rintahaka PJ, *et al*. Incidence of death in patients with intractable epilepsy during nitrazepam treatment. *Epilepsia* 1999; **40:** 492–6.


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

### Interactions

As for Diazepam, p.989.

### Pharmacokinetics

Nitrazepam is fairly readily absorbed from the gastrointestinal tract, although there is some individual variation. It is about 87% bound to plasma proteins. It crosses the blood-brain and the placental barriers and traces are found in breast milk. Nitrazepam is metabolised in the liver, mainly by nitroreduction followed by acetylation; none of the metabolites possess significant activity. It is excreted in the urine in the form of its metabolites (free or conjugated) with only small amounts of a dose appearing unchanged. Up to about 20% of an oral dose is found in the faeces. Mean elimination half-lives of 24 to 30 hours have been reported.

**Distribution into breast milk.** A mean milk-to-plasma ratio of 0.27 was obtained after giving nitrazepam 5 mg for 5 nights to 9 puerperal women.[1] The accumulation of nitrazepam in milk over the study period was similar to that in plasma.


1. Matheson I, *et al.* Midazolam and nitrazepam in the maternity ward: milk concentrations and clinical effects. *Br J Clin Pharmacol* 1990; **30:** 787–93.


**Hepatic impairment.** The pharmacokinetics of intravenous nitrazepam in 12 patients with cirrhosis of the liver has been compared with 9 healthy subjects aged 22 to 49 years and 8 healthy elderly subjects aged 67 to 76 years.[1] The mean elimination half-life of nitrazepam was 26 hours in young and 38 hours in elderly subjects, the difference, which was not significant, being chiefly due to the greater volume of distribution in elderly subjects. Although there was also no significant difference between young and elderly subjects in percentage of unbound nitrazepam (13.0 and 13.9% respectively) there was a substantially higher unbound fraction in the patients with cirrhosis, the mean value being 18.9%, and clearance of unbound nitrazepam was reduced relative to healthy subjects.


1. Jochemsen R, *et al*. Effect of age and liver cirrhosis on the pharmacokinetics of nitrazepam. *Br J Clin Pharmacol* 1983; **15:** 295–302.


**Metabolism.** Although the acetylation of the reduced metabolite of nitrazepam has been reported to be controlled by acetylator phenotype,[1] no significant differences between either half-life or residual effects of nitrazepam were observed in slow and fast acetylators.[2]


1. Karim AKMB, Price Evans DA. Polymorphic acetylation of nitrazepam. *J Med Genet* 1976; **13:** 17–19.
2. Swift CG, *et al.* Acetylator phenotype, nitrazepam plasma concentrations and residual effects. *Br J Clin Pharmacol* 1980; **9:** 312P–313P.


### Uses and Administration

Nitrazepam is an intermediate-acting benzodiazepine with general properties similar to those of diazepam (p.992). It is used as a hypnotic in the short-term management of insomnia (p.957) and is reported to act in 30 to 60 minutes to produce sleep lasting for 6 to 8 hours. Nitrazepam has also been used in epilepsy, notably for infantile spasms (see below).

The usual oral dose for insomnia is 5 mg at night, although 10 mg may be required in some patients. Elderly or debilitated patients should not be given more than half of the normal adult dose.

**Epilepsy.** Benzodiazepines are sometimes employed in the management of epilepsy (p.465), but their long-term use is limited by problems of sedation, dependence, and tolerance to the antiepileptic effects. Nitrazepam has perhaps been most useful in the treatment of infantile spasms (as for example in West's syndrome) and the so-called infantile myoclonic seizures. The *BNFC* suggests that those aged from 1 month to 2 years may be given initial oral doses of 125 micrograms/kg twice daily, adjusted according to response over 2 to 3 weeks to 250 micrograms/kg twice daily (maximum 500 micrograms/kg, but not exceeding 5 mg, twice daily); the same total daily dose may also be given in 3 divided doses. There has been concern, however, over swallowing difficulties with subsequent aspiration and reports of unexpected death associated with the use of nitrazepam in young children (see Effects on the Digestive System under Adverse Effects, above).

### Preparations

***BP 2008:*** Nitrazepam Oral Suspension; Nitrazepam Tablets.

**Proprietary Preparations** (details are given in Part 3)

***Austral.:*** Alodorm; Mogadon; ***Austria:*** Mogadon; ***Belg.:*** Mogadon; ***Braz.:*** Nitrapan; Nitrazepol; Sonebon; ***Canad.:*** Mogadon; Nitrazadon; ***Denm.:*** Apodorm; Mogadon; Pacisyn; ***Fin.:*** Insomin; ***Fr.:*** Mogadon; ***Ger.:*** Dormalon; Dormo-Puren; Eatan N; Imeson; Mogadan; Novanox; Radedorm; ***Hong Kong:*** Mogadon; ***Hung.:*** Eunoctin; ***India:*** Hypnotex; Nitavan; Nitravet; ***Indon.:*** Dumolid; ***Irl.:*** Mogadon; Somnite†; ***Israel:*** Numbon; ***Ital.:*** Mogadon; ***Malaysia:*** Mogadon†; ***Neth.:*** Mogadon; ***Norw.:*** Apodorm; Mogadon; ***NZ:*** Insoma; Nitrados; ***Rus.:*** Eunoctin (Эуноктин); Nitrosun (Нитросан); Radedorm (Радедорм); ***S.Afr.:*** Arem; Mogadon; Ormodon; Paxadorm; ***Singapore:*** Dima; Nitrados; ***Swed.:*** Apodorm; Mogadon; ***Switz.:*** Mogadon; ***Thai.:*** Alodorm†; Nitrados†; ***UK:*** Mogadon; Remnos; Somnite; ***Venez.:*** Onirema.

**Multi-ingredient:** ***Arg.:*** Cavodan†.