

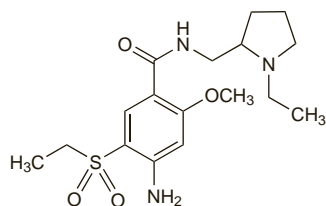
traxaf; Pharnax; Siampraxol; Xanaxine; Xanax; Xiemed; **Turk.:** Xanax; **UK:** Xanax; **USA:** Niravam; Xanax; **Venez.:** Abaxon; Alprami; Ansilan; Dan-ox†; Tafil.

**Multi-ingredient Arg.:** Alplax Digest; Alplax Net; Ansielx Digest; Euciton Stress; Novo Vegetabil†; Sidoma; Tensium Gastric; Tranquinal Soma; **India:** Fludep Plus; Restyl Forte; Restyl Plus; Stresnil; Zopax Plus.

## Amisulpride (BAN, rINN)

Amisulprid; Amisulprid; Amisulprida; Amisulpridas; Amisulpridi; Amisulpridum; Amisulprid; DAN-216. 4-Amino-N-[(1-ethyl-2-pyrrolidinyl)methyl]-5-(ethylsulphonyl)-2-methoxybenzamide; (RS)-4-Amino-N-[(1-ethylpyrrolidin-2-yl)methyl]-5-(ethylsulfonyl)-o-anisamide.

Амисулприд  
C<sub>17</sub>H<sub>27</sub>N<sub>3</sub>O<sub>4</sub>S = 369.5.  
CAS — 71675-85-9.  
ATC — N05AL05.  
ATC Vet — QN05AL05.



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

**Ph. Eur. 6.2** (Amisulpride). A white or almost white crystalline powder. Practically insoluble in water; sparingly soluble in dehydrated alcohol; freely soluble in dichloromethane.

## Adverse Effects, Treatment, and Precautions

Although amisulpride may share some of the adverse effects seen with the classical antipsychotics (see Chlorpromazine, p.969), the incidence and severity of such effects may vary. Insomnia, anxiety, and agitation are common adverse effects with amisulpride. Other less common effects include drowsiness and gastrointestinal disorders such as constipation, nausea, vomiting, and dry mouth. Allergic reactions, abnormal liver function tests, and seizures have been reported rarely.

Hyperprolactinaemia, which may result in galactorrhoea, amenorrhoea, impaired fertility, gynaecomastia, breast pain, and sexual dysfunction, has occurred with amisulpride use. Weight gain has also been noted. Dose-related extrapyramidal dysfunction may occur, but symptoms such as acute dystonia, parkinsonism, and akathisia are generally mild at licensed doses. Tardive dyskinesia has been reported after long-term use and there have been rare cases of neuroleptic malignant syndrome. Hypotension and bradycardia have been reported occasionally; QT prolongation, in rare cases leading to torsade de pointes, has also been noted. The risk of QT prolongation is increased by pre-existing conditions such as bradycardia, hypokalaemia, and congenital or acquired QT prolongation; patients should be reviewed for these conditions before starting amisulpride treatment. Certain medications may also increase the risk (see Interactions, below).

Amisulpride should not be given to patients with pheochromocytoma or prolactin-dependent tumours. It should be used with caution in patients with severe renal impairment, or a history of epilepsy or Parkinson's disease. The risk of hypotension and sedation is increased in elderly patients.

Amisulpride may affect the performance of skilled tasks including driving.

Withdrawal symptoms have occurred rarely when amisulpride has been stopped abruptly; a gradual dose reduction may be appropriate when stopping amisulpride.

**Dementia.** The FDA has issued advice against the use of atypical antipsychotics in the treatment of behavioural problems in elderly patients with dementia after analysis of placebo-controlled studies showed an increased risk of mortality with certain drugs of this class. See under Risperidone, p.1024.

**Effects on body-weight.** A review<sup>1</sup> has suggested that the risk of weight gain with amisulpride treatment is less than with olanzapine or risperidone, although cases have been reported.<sup>2</sup> The increased risk of weight gain with some atypical antipsychotics is also discussed under Adverse Effects of Clozapine, p.981.

1. McKeage K, Plosker GL. Amisulpride: a review of its use in the management of schizophrenia. *CNS Drugs* 2004; **18**: 933–56.
2. Papadimitriou GN, *et al.* Acute weight gain induced by amisulpride monotherapy in a first-episode schizophrenic patient. *Int Clin Psychopharmacol* 2006; **21**: 181–4.

**Effects on carbohydrate metabolism.** The increased risk of glucose intolerance and diabetes mellitus with some atypical antipsychotics, and recommendations on monitoring, are discussed under Adverse Effects of Clozapine, p.981.

**Effects on lipid metabolism.** The increased risk of hyperlipidaemia with some atypical antipsychotics is discussed under Adverse Effects of Chlorpromazine, p.970. See also Effects on Carbohydrate Metabolism under Adverse Effects of Clozapine, p.981.

**Overdosage.** The effects of overdosage of amisulpride in 2 patients have been reported.<sup>1</sup> The first patient had taken about 3 g of amisulpride and an unknown amount of dosulepin and was found to have had a blood-amisulpride concentration of 9.63 micrograms/mL. Generalised convulsions, which resolved spontaneously, were followed by coma, motor restlessness, tachycardia, and slight prolongation of the QT interval. The patient was treated with gastric lavage and had recovered within 48 hours. The second patient, who had been found dead, had a blood-amisulpride concentration of 41.7 micrograms/mL. Severe cardiotoxicity occurred in 4 further cases of amisulpride overdoses of between about 4 and 32 g reported to Australian poisons information centres;<sup>2</sup> all 4 had marked QT prolongation, with bundle branch block or torsade de pointes, and one, who was thought to have ingested between 16 and 24 g, died after cardiac arrest.

1. Tracqui A, *et al.* Amisulpride poisoning: a report on two cases. *Hum Exp Toxicol* 1995; **14**: 294–8.
2. Isbister GK, *et al.* Amisulpride deliberate self-poisoning causing severe cardiac toxicity including QT prolongation and torsades de pointes. *Med J Aust* 2006; **184**: 354–6.

**Pregnancy.** For comments on the use of some atypical antipsychotics during pregnancy, see under Precautions of Clozapine, p.983.

## Interactions

Amisulpride should not be given with drugs that may induce arrhythmias (including torsade de pointes); such drugs include some antiarrhythmics, cisapride, thioridazine, erythromycin, and halofantrine. The risk of arrhythmias is also increased with drugs that prolong the QT interval, such as pimozide, haloperidol, and tricyclic antidepressants, and with drugs that produce bradycardia or hypokalaemia, including beta blockers, some calcium-channel blockers, clonidine, digoxin, guanfacine, potassium-depleting diuretics, and lithium; use of these drugs with amisulpride requires caution.

The central effects of other CNS depressants including alcohol may be enhanced by amisulpride. Amisulpride may also enhance the effects of antihypertensive drugs. The dopamine-blocking activity of amisulpride may antagonise the actions of dopaminergics such as levodopa and they should not be given together.

◇ In 7 patients receiving amisulpride, introduction of lithium resulted in an average increase of 32% of the dose-corrected plasma concentration of amisulpride.<sup>1</sup> An earlier study had noted that plasma concentrations of amisulpride were raised in patients also taking clozapine.<sup>2</sup>

1. Bergemann N, *et al.* Increase in plasma concentrations of amisulpride after receiving co-medication with lithium. *Pharmacopsychiatry* 2005; **38**: 44.
2. Bergemann N, *et al.* Plasma amisulpride levels in schizophrenia or schizoaffective disorder. *Eur Neuropsychopharmacol* 2004; **14**: 245–50.

## Pharmacokinetics

Amisulpride is absorbed from the gastrointestinal tract but bioavailability is reported to be only about 48%. An initial peak in plasma concentration has been reported to occur 1 hour after oral doses and a second higher peak after 3 to 4 hours. Plasma protein binding is reported to be only about 16%. Metabolism is limited, with most of a dose appearing in the urine as unchanged drug. The terminal elimination half-life is about 12 hours.

## References

1. Rosenzweig P, *et al.* A review of the pharmacokinetics, tolerability and pharmacodynamics of amisulpride in healthy volunteers. *Hum Psychopharmacol* 2002; **17**: 1–13.

## Uses and Administration

Amisulpride is a substituted benzamide atypical antipsychotic. It is reported to have a high affinity for dopamine D<sub>2</sub> and D<sub>3</sub> receptors. Amisulpride is used mainly in the management of psychoses such as schizophrenia but in some countries it has also been tried in depression (p.373).

For acute psychotic episodes in adults and adolescents aged 15 years and over a daily dosage of between 400 and 800 mg may be given orally in 2 divided doses, increased if necessary to 1200 mg daily. For patients with mainly negative symptoms, daily doses between 50 and 300 mg are recommended. Daily doses of up to 300 mg may be given as a single dose. Amisulpride has also been given by intramuscular injection in doses of 400 mg daily.

**Administration in renal impairment.** For patients with renal impairment, the oral dose of amisulpride should be reduced according to creatinine clearance (CC):

- CC between 30 and 60 mL/minute, half the usual dose
- CC between 10 and 30 mL/minute, one-third the usual dose

Similar reductions are also recommended when amisulpride is given intramuscularly.

**Schizophrenia.** Reviews<sup>1,2</sup> of amisulpride indicate that it may be more effective than classical antipsychotics against general and negative symptoms of schizophrenia (p.955), and has fewer extrapyramidal adverse effects.

1. Leucht S, *et al.* Amisulpride, an unusual "atypical" antipsychotic: a meta-analysis of randomized controlled trials. *Am J Psychiatry* 2002; **159**: 180–90.
2. Mota Neto JIS, *et al.* Amisulpride for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2002 (accessed 24/05/05).

## Preparations

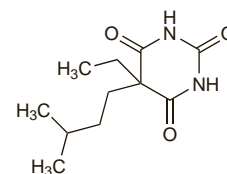
**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Enorden; **Austral.:** Solian; **Austria:** Majorem; **Belg.:** Solian; **Braz.:** Socian; **Chile:** Socian; **Cz.:** Deniban; **Solian; Denm.:** Solian; **Fr.:** Solian; **Ger.:** Amisulid; **Solian; Gr.:** Solian; **Hong Kong:** Solian; **Hung.:** Amiprid; **Amitrex; Ir.:** Solian; **Israel:** Solian; **Ital.:** Deniban; **Solian; Sulamid; Mex.:** Solian; **Norw.:** Solian; **NZ:** Solian; **Philipp.:** Solian; **Pol.:** Solian; **Port.:** Amitrex; **Socian; Rus.:** Solian (Солман); **S.Afr.:** Solian; **Singapore:** Solian; **Spain:** Amilandej; **Solian; Switz.:** Solian; **Turk.:** Solian; **UK:** Solian.

## Amobarbital (BAN, rINN)

Amobarbitala; Amobarbital; Amobarbitalis; Amobarbitalum; Amylobarbitone; Pentymalum. 5-Ethyl-5-isopentylbarbituric acid.

Амобарбитал  
C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub> = 226.3.  
CAS — 57-43-2.  
ATC — N05CA02.  
ATC Vet — QN05CA02.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of amobarbital: Amys; Birds; Blue; Blue angels; Blue birds; Blue bullets; Blue clouds; Blue devils; Blue dolls; Blue heaven; Blue heavens; Blues.

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), and *Jpn.*

**Ph. Eur. 6.2** (Amobarbital). A white or almost white, crystalline powder. Very slightly soluble in water; freely soluble in alcohol; soluble in dichloromethane. Forms water-soluble compounds with alkali hydroxides and carbonates and with ammonia.

## Amobarbital Sodium (BANM, rINNM)

Amobarbitalnatrium; Amobarbital sódico; Amobarbital sodique; Amobarbital sodná sůl; Amobarbitalio natrio druska; Amobarbitalnatrium; Amobarbital-nátrium; Amobarbitalum natrium; Amylobarbitone Sodium; Barbamylum; Natrii Amobarbitalum; Pentymalnatium; Sodium Amobarbital; Soluble Amylobarbitone. Sodium 5-ethyl-5-isopentylbarbiturate.

Натрий Амобарбитал  
C<sub>11</sub>H<sub>17</sub>N<sub>2</sub>NaO<sub>3</sub> = 248.3.  
CAS — 64-43-7.  
ATC — N05CA02.  
ATC Vet — QN05CA02.