The incidence of extrapyramidal effects was lower with quetiapine therapy but the risk of dry mouth and somnolence was higher. Quetiapine was not found to benefit negative symptoms.

1. Srisurapanont M, *et al.* Quetiapine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2004 (accessed 30/05/05).

Tourette's syndrome. When drug treatment is required for tics and behavioural disturbances in Tourette's syndrome (see Tics, p.954) haloperidol or pimozide are commonly used but atypical antipsychotics, including quetiapine, are increasingly being tried.[1-3]

1. Mukaddes NM, Abali O. Quetiapine treatment of children and adolescents with Tourette's disorder. *J Child Adolesc Psychopharmacol* 2003; **13:** 295–9.
2. Little AE, *et al.* Quetiapine in the treatment of tic disorder. *Ann Pharmacother* 2006; **40:** 1472.
3. de Jonge JL, *et al.* Quetiapine in patients with Tourette's disorder: an open-label, flexible-dose study. *J Clin Psychiatry* 2007; **68:** 1148–50.

Preparations

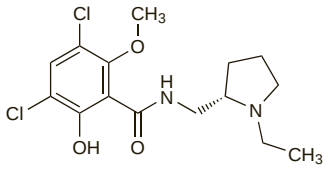
Proprietary Preparations (details are given in Part 3)
Arg.: Quetiazic; Seroquel; Vesparax; ***Austral.:*** Seroquel; ***Austria:*** Seroquel; ***Belg.:*** Seroquel; ***Braz.:*** Seroquel; ***Canad.:*** Seroquel; ***Chile:*** Norsic; Quetidin; Seroquel; ***Cz.:*** Ketilept; Kventiax; Nantarid; Quepita; Questax; Quetin; Seroquel; Stadaquel; ***Denm.:*** Seroquel; ***Fin.:*** Seroquel; ***Ger.:*** Seroquel; ***Gr.:*** Seroquel; ***Hong Kong:*** Seroquel; ***Hung.:*** Ketilept; Seroquel; ***India:*** Quel; Seroquin; Socalm; ***Indon.:*** Seroquel; ***Irl.:*** Seroquel; ***Israel:*** Seroquel; ***Ital.:*** Seroquel; ***Jpn:*** Seroquel; ***Malaysia:*** Seroquel; ***Mex.:*** Seroquel; ***Neth.:*** Seroquel; ***Norw.:*** Seroquel; ***NZ:*** Quetapel; Seroquel; ***Philipp.:*** Seroquel; ***Pol.:*** Ketrel; Seroquel; ***Port.:*** Alzen; Seroquel; ***Rus.:*** Seroquel (Сероквель); ***S.Afr.:*** Seroquel; ***Singapore:*** Seroquel; ***Spain:*** Seroquel; ***Swed.:*** Seroquel; ***Switz.:*** Seroquel; ***Thai.:*** Seroquel; ***Turk.:*** Seroquel; ***UK:*** Seroquel; ***USA:*** Seroquel; ***Venez.:*** Seroquel.

Raclopride *(BAN, rINN)*

A-40664 (raclopride tartrate); FLA-870; Racloprida; Racloprid-ium; Raclopridum; Rakloprid; Rakloprid. (*S*)-3,5-Dichloro-*N*-(1-ethylpyrrolidin-2-ylmethyl)-2-hydroxy-6-methoxybenzamide.

Раклоприд

$C_{15}H_{20}Cl_2N_2O_3$ = 347.2.
CAS — 84225-95-6 (raclopride); 98185-20-7 (raclopride tartrate).



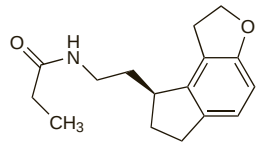
Profile
Raclopride is a substituted benzamide related to sulpiride (p.1028). It has been investigated for the treatment of psychoses. Since it binds selectively and with high affinity to D_2 dopaminergic receptors, raclopride labelled with carbon-11 has been tried as a tracer in computerised tomographic studies of neurological disorders associated with dysfunction of brain D_2 dopaminergic receptors.

Ramelteon *(BAN, USAN, rINN)*

Rameltéon; Ramelteón; Ramelteonum; TAK-375. (-)-*N*-{2-[(8*S*)-1,6,7,8-Tetrahydro-2*H*-indeno[5,4-*b*]furan-8-yl]ethyl}propanamide.

Рамельтеон

$C_{16}H_{21}NO_2$ = 259.3.
CAS — 196597-26-9.
ATC — N05CH02.
ATC Vet — QN05CH02.



Profile
Ramelteon is a melatonin receptor agonist used as a hypnotic in the management of insomnia (p.957), particularly in patients who have difficulty falling asleep. The usual oral dose is 8 mg taken within 30 minutes of bedtime; it should not be taken with or immediately after a high-fat meal. Ramelteon is not recommended for patients with severe hepatic impairment; it should be used with caution in those with moderate impairment.

Ramelteon is metabolised mainly via the cytochrome P450 isoenzyme CYP1A2 and consequently, it should not be used with fluvoxamine, a potent inhibitor of this isoenzyme; it should also be used with caution in patients taking other drugs that inhibit this isoenzyme.

◊ References.

1. Karim A, *et al.* Disposition kinetics and tolerance of escalating single doses of ramelteon, a high-affinity MT and MT melatonin receptor agonist indicated for treatment of insomnia. *J Clin Pharmacol* 2006; **46:** 140–8.
2. Greenblatt DJ, *et al.* Age and gender effects on the pharmacokinetics and pharmacodynamics of ramelteon, a hypnotic agent acting via melatonin receptors MT and MT . *J Clin Pharmacol* 2007; **47:** 485–96.

Preparations

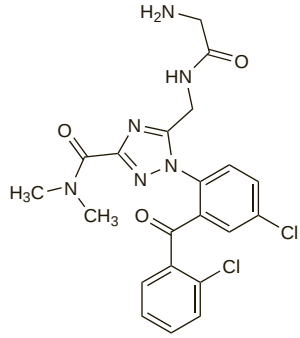
Proprietary Preparations (details are given in Part 3)
Fr.: Rozerem; ***Jpn:*** Rozerem; ***USA:*** Rozerem.

Rilmazafone Hydrochloride *(rINNM)*

Hidrocloruro de rilmazafona; Rilmazafone, Chlorhydrate de; Rilmazafoni Hydrochloridum; 450191-S. 5-[(2-Aminoacetamido)methyl]-1-[4-chloro-2-(*o*-chlorobenzoyl)phenyl]-*N*,*N*-dimethyl-1*H*-1,2,4-triazole-3-carboxamide hydrochloride dihydrate.

Рильмазафона Гидрохлорид

$C_{21}H_{20}Cl_2N_6O_3$,HCl,2H_2O = 547.8.
CAS — 99593-25-6 (rilmazafone); 85815-37-8 (anhydrous rilmazafone hydrochloride).



(rilmazafone)

Profile
Rilmazafone hydrochloride is a hypnotic and sedative used in the short-term treatment of insomnia in usual oral doses of 1 to 2 mg at bedtime; it is also used in similar doses as a premedicant.

Preparations

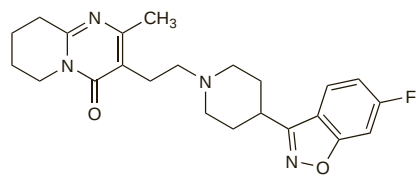
Proprietary Preparations (details are given in Part 3)
Jpn: Rhythmy.

Risperidone *(BAN, USAN, rINN)*

R-64766; Risperidon; Risperidona; Risperidonas; Rispéridone; Risperidoni; Risperidonum; Riszperidon; Rysperydon. 3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidino]ethyl}-6,7,8,9-tetrahydro-2-methylpyrido[1,2-*a*]pyrimidin-4-one.

Рисперидон

$C_{23}H_{27}FN_4O_2$ = 410.5.
CAS — 106266-06-2.
ATC — N05AX08.
ATC Vet — QN05AX08.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Risperidone). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in dichloromethane; dissolves in dilute acid solutions. Protect from light.
USP 31 (Risperidone). A white or almost white powder. Practically insoluble in water; sparingly soluble in alcohol; soluble in dichloromethane.

Adverse Effects, Treatment, and Precautions

Although risperidone 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. Risperidone is reported to be less likely to cause sedation or extrapyramidal effects (see also Uses and Administration, below) but agitation may occur more frequently. Other common adverse effects include insomnia, anxiety, and headache. Dyspepsia, nausea and vomiting, abdominal pain, constipation, blurred vision, sexual dysfunction including priapism, urinary incontinence, rash and other allergic reactions, drowsiness, concentration difficulties, dizziness, fatigue, and rhinitis have been reported less commonly. In addition to orthostatic hypotension, hypertension has been reported infrequently. Other adverse effects with risperidone include cerebrovascular accidents, tachycardia, weight gain, oedema, increased liver enzyme values, and decreases in neutrophil or thrombocyte counts. Risperidone may cause dose-dependent increases in prolactin levels. In rare cases, hyperglycaemia and exacerbation of pre-existing diabetes mellitus have also been reported. Clinical monitoring for hyperglycaemia has been recommended, especially in patients with or at risk of developing diabetes. Other rare effects include seizures, body temperature dysregulation, hyponatraemia, neuroleptic malignant syndrome, and tardive dyskinesia.

Risperidone should be used with caution in patients with cardiovascular disease, including conditions associated with QT prolongation, or conditions predisposing to hypotension. Caution is also recommended in patients with a history of or at risk of developing cerebrovascular disease, in patients with Parkinson's disease or epilepsy, and in patients with hepatic or renal impairment.

Risperidone may affect the performance of skilled tasks such as driving.

Gradual withdrawal of risperidone is recommended because of the risk of withdrawal symptoms, including sweating, nausea and vomiting, and rebound psychosis, with abrupt cessation.

Breast feeding. From the study of concentrations of risperidone and its active metabolite, 9-hydroxyrisperidone, in the breast milk of a mother receiving 6 mg daily by mouth, it was estimated that a breast-fed infant would ingest the daily equivalent of 4.3% (as risperidone equivalents) of the weight-adjusted maternal dose.[1] Later case reports[2] of 3 women receiving risperidone 3 mg daily, 4 mg daily, and 1.5 mg daily, by mouth, estimated that a breast-fed infant would receive the daily equivalent of 2.3%, 2.8%, and 4.7%, respectively, of the weight-adjusted maternal dose. Where breast feeding occurred, in the latter 2 cases, no adverse effects were reported in the breast-fed infants; risperidone and 9-hydroxyrisperidone were not detected in the plasma of either infant.

Licensed product information states that patients receiving risperidone should not breast feed; the US information also recommends that patients should not breast feed for at least 12 weeks after intramuscular injection.

1. Hill RC, *et al.* Risperidone distribution and excretion into human milk: case report and estimated infant exposure during breast-feeding. *J Clin Psychopharmacol* 2000; **20:** 285–6.
2. Ilett KF, *et al.* Transfer of risperidone and 9-hydroxyrisperidone into human milk. *Ann Pharmacother* 2004; **38:** 273–6.

Dementia. After analysis of data from controlled studies there was evidence that the use of risperidone in elderly patients with dementia appeared to be associated with an increased risk of cerebrovascular adverse effects such as stroke and transient ischaemic attacks. In 4 studies, involving 764 such patients treated with risperidone, there were 29 cases of cerebrovascular adverse events (4 fatal) versus 7 cases (1 fatal) in 466 patients given placebo. Postmarketing data for elderly dementia patients, representing over 2.4 million patient-years of exposure, included 37 cases, of which 16 were fatal.[1]

The UK CSM[2] have therefore recommended that risperidone should not be used to treat behavioural problems in elderly patients with dementia. Similarly, the CSM[2] and the EMEA[3] have recommended that olanzapine should not be used to treat behavioural problems or dementia-related psychosis in elderly patients with dementia after analysis of placebo-controlled studies revealed a threefold increase in cerebrovascular adverse effects including stroke and a twofold increase in all-cause mortality. It was considered[2] that the risk may not be confined to use in dementia and should be considered relevant to any patient with a

history of stroke or transient ischaemic attack or other risk factors for cerebrovascular disease, including hypertension, diabetes, current smoking, or atrial fibrillation. The FDA[4] has also issued advice against the use of all atypical antipsychotics in the treatment of behavioural problems in elderly patients with dementia. Their advice was based on an unpublished analysis of 17 placebo-controlled studies involving aripiprazole, olanzapine, quetiapine, or risperidone use in elderly demented patients with behavioral disorders: the analysis found that 15 studies showed an increase in the mortality rate in the drug-treated group compared to the placebo-treated patients. A total of 5106 patients were included in these studies, and a 1.6- to 1.7-fold increase in mortality was seen; most of the deaths appeared due to cardiovascular events or infection. Another published meta-analysis[5] of placebo-controlled studies also had similar findings.

However, 2 large retrospective population-based studies in the elderly (1 involving 10 385 patients given atypicals and 1015 given classical antipsychotics,[6] the other involving 17 845 given atypicals and 14 865 given classical antipsychotics[7]), suggested that use of atypical antipsychotics was not associated with a statistically significant increased risk of stroke compared with the classical drugs.

For further discussion of the problems associated with the use of antipsychotics in disturbed behaviour in the elderly, see p.954.

1. Janssen-Ortho Inc./Health Canada. Important drug safety information: Risperdal (risperidone) and cerebrovascular adverse events in placebo-controlled dementia trials (issued 11/10/02). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/risperdal_hpc-cps-eng.pdf (accessed 21/08/08)
2. Duff G. Atypical antipsychotic drugs and stroke: message from Professor G Duff, Chairman of Committee on Safety of Medicines (issued 09/03/04). Available at: http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con019488.pdf (accessed 21/08/08)
3. EMEA. EMEA public statement on the safety of olanzapine (Zyprexa, Zyprexa Velotab): cerebrovascular adverse events and increased mortality in elderly patients with dementia (issued 09/03/04). Available at: http://www.emea.europa.eu/pdfs/human/press/pus/085604en.pdf (accessed 21/08/08)
4. FDA. FDA issues public health advisory for antipsychotic drugs used for treatment of behavioral disorders in elderly patients (issued 11th April, 2005). Available at: http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01350.html (accessed 30/05/05)
5. Schneider LS, *et al.* Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA* 2005; **294:** 1934–43.
6. Herrmann N, *et al.* Atypical antipsychotics and risk of cerebrovascular accidents. *Am J Psychiatry* 2004; **161:** 1113–15.
7. Gill SS, *et al.* Atypical antipsychotic drugs and risk of ischaemic stroke: population based retrospective cohort study. *BMJ* 2005; **330:** 445–8.

Effects on body-weight. The increased risk of weight gain with some atypical antipsychotics is discussed under Adverse Effects of Clozapine, p.981.

Further references.

1. Safer DJ. A comparison of risperidone-induced weight gain across the age span. *J Clin Psychopharmacol* 2004; **24:** 429–36.

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

Further references.

1. Koller EA, *et al.* Risperidone-associated diabetes mellitus: a pharmacovigilance study. *Pharmacotherapy* 2003; **23:** 735–44.
2. Ramaswamy K, *et al.* Risk of diabetic ketoacidosis after exposure to risperidone or olanzapine. *Drug Safety* 2007; **30:** 589–99.

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.

Effects on the liver. There has been a report of 2 cases of hepatotoxicity associated with risperidone.[1] An idiosyncratic reaction to risperidone was suspected in another patient who developed hepatotoxicity after receiving only 2 doses of risperidone.[2]

1. Fuller MA, *et al.* Risperidone-associated hepatotoxicity. *J Clin Psychopharmacol* 1996; **16:** 84–5.
2. Phillips EJ, *et al.* Rapid onset of risperidone-induced hepatotoxicity. *Ann Pharmacother* 1998; **32:** 843.

Effects on the skin. A patient developed facial and periorbital oedema 2 weeks after her dose of risperidone reached 6 mg daily.[1] The oedema subsided when the dose was halved but recurred shortly after it was again increased to 6 mg. She had previously had a similar reaction to lithium and there was also a family history of angioedema.

1. Cooney C, Nagy A. Angio-oedema associated with risperidone. *BMJ* 1995; **311:** 1204.

Extrapyramidal disorders. In reports of 3 cases of tardive dystonia associated with oral risperidone therapy,[1,2] onset ranged from 3 to 8 months after starting the drug. Dyskinesia has also been reported 5 days after the withdrawal of oral risperidone and citalopram therapy.[3] In another report,[4] three patients receiving risperidone orally developed early-onset tardive dyskinesia despite the addition of antimuscarinic therapy with biperiden or trihexyphenidyl. Extrapyramidal adverse effects have also been reported within 24 hours of intramuscular risperidone injection.[5] However, the incidence of extrapyramidal effects (p.971) is generally lower with atypical than classical antipsychotics.

1. Vercueil L, Foucher J. Risperidone-induced tardive dystonia and psychosis. *Lancet* 1999; **353:** 981.
2. Krebs MO, Olie JP. Tardive dystonia induced by risperidone. *Can J Psychiatry* 1999; **44:** 507–508.
3. Miller LJ. Withdrawal-emergent dyskinesia in a patient taking risperidone/citalopram. *Ann Pharmacother* 2000; **34:** 269.
4. Suzuki E, *et al.* Tardive dyskinesia with risperidone and anticholinergics. *Am J Psychiatry* 2002; **159:** 1948.
5. Adamou M, Hale AS. Extrapyramidal syndrome and long-acting injectable risperidone. *Am J Psychiatry* 2004; **161:** 756–7.

Mania. Although it is used in the treatment of bipolar disorder, risperidone has been associated with reports of mania in both schizophrenic and bipolar patients.[1-3]

1. Dwight MM, *et al.* Antidepressant activity and mania associated with risperidone treatment of schizoaffective disorder. *Lancet* 1994; **344:** 554–5.
2. Zolezzi M, Badr MG. Risperidone-induced mania. *Ann Pharmacother* 1999; **33:** 380–1.
3. Aubry J-M, *et al.* Possible induction of mania and hypomania by olanzapine or risperidone: a critical review of reported cases. *J Clin Psychiatry* 2000; **61:** 649–55.

Neuroleptic malignant syndrome. Neuroleptic malignant syndrome (p.972) has occasionally been associated with risperidone.[1-5]

1. Sharma R, *et al.* Risperidone-induced neuroleptic malignant syndrome. *Ann Pharmacother* 1996; **30:** 775–8.
2. Tarsy D. Risperidone and neuroleptic malignant syndrome. *JAMA* 1996; **275:** 446.
3. Reeves RR, *et al.* Neuroleptic malignant syndrome during a change from haloperidol to risperidone. *Ann Pharmacother* 2001; **35:** 698–701.
4. Gerritsen AA, *et al.* Het maligne neurolepticasyndroom bij gebruik van risperidon. *Ned Tijdschr Geneeskd* 2004; **148:** 1801–4.
5. Norris B, *et al.* Neuroleptic malignant syndrome with delayed onset of fever following risperidone administration. *Ann Pharmacother* 2006; **40:** 2260–4.

Overdosage. A 3½-year-old child developed extrapyramidal symptoms after accidental ingestion of a single 4-mg tablet of risperidone.[1] The child was initially treated with gastric lavage, activated charcoal, and sorbitol; extrapyramidal symptoms responded to treatment with diphenhydramine and the child recovered completely. The need to monitor for and treat hypotension after overdosage with risperidone was highlighted in a report[2] of a 15-year-old girl who took 40 mg of risperidone. A 72-year-old woman receiving risperidone 6 mg daily was found unconscious, hypotensive, and hypothermic.[3] Other reported symptoms include first-degree heart block, prolonged QT interval, and respiratory arrest; she recovered after supportive treatment.

1. Cheslik TA, Erramouspe J. Extrapyramidal symptoms following accidental ingestion of risperidone in a child. *Ann Pharmacother* 1996; **30:** 360–3.
2. Himstreet JE, Daya M. Hypotension and orthostasis following a risperidone overdose. *Ann Pharmacother* 1998; **32:** 267.
3. Rassam S, Srinivasa R. Respiratory depression after accidental risperidone overdose. *Am J Emerg Med* 2002; **20:** 570.

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

Further references.

1. Coppola D, *et al.* Evaluating the postmarketing experience of risperidone use during pregnancy: pregnancy and neonatal outcomes. *Drug Safety* 2007; **30:** 247–64.

Interactions

The central effects of other CNS depressants, including alcohol, may be enhanced by risperidone. Risperidone may also enhance the effects of antihypertensives. There may be an increased risk of QT prolongation when risperidone is given with other drugs that are known to cause this effect. Risperidone may antagonise the actions of levodopa and other dopaminergics.

Carbamazepine has been shown to decrease the antipsychotic fraction (risperidone plus 9-hydroxyrisperidone) of risperidone and a similar effect may be seen with other enzyme inducers. Fluoxetine may increase the plasma concentrations of the antipsychotic fraction by raising the concentration of risperidone. Dose adjustment of risperidone may be necessary in such situations.

Antiepileptics. For the effect of risperidone on *valproate*, see p.511.

Antipsychotics. For a report suggesting that risperidone might increase plasma concentrations of *clozapine*, see p.984. For a report of asymptomatic QT prolongation associated with *quetiapine* in a patient also receiving risperidone, see under Overdosage of Quetiapine, p.1023.

Antivirals. Dystonia and worsening of tremors were reported 1 week after adding *indinavir* and *ritonavir* to treatment with risperidone in a patient with AIDS;[1] he recovered once all 3 drugs were withdrawn and following treatment with clonazepam. An early exposure to risperidone, indinavir, and ritonavir had not resulted in any extrapyramidal adverse effects. The authors considered this to reflect the patient's relatively short exposure to risperidone at the time.

1. Kelly DV, *et al.* Extrapyramidal symptoms with ritonavir/indinavir plus risperidone. *Ann Pharmacother* 2002; **36:** 827–30.

Pharmacokinetics

Risperidone is readily absorbed after oral doses, peak plasma concentrations being reached within 1 to 2 hours. It is extensively metabolised in the liver by hydroxylation to its main active metabolite, 9-hydroxyrisperidone (paliperidone, p.1015); oxidative *N*-dealkylation is a minor metabolic pathway. Hydroxylation is mediated by the cytochrome P450 isoenzyme CYP2D6 and is the subject of genetic polymorphism. Excretion is mainly in the urine and, to a lesser extent, in the faeces. Risperidone and 9-hydroxyrisperidone are about 90% and 77% bound to plasma proteins, respectively. Both are distributed into breast milk.

Metabolism. Although the hydroxylation of risperidone is subject to genetic polymorphism, the pharmacokinetics and effects of the active antipsychotic fraction (risperidone plus 9-hydroxyrisperidone) have been reported to vary little between extensive and poor metabolisers.[1] A mean value of 19.5 hours has been reported for the terminal elimination half-life of the active fraction following oral doses of risperidone.[1]

1. Huang M-L, *et al.* Pharmacokinetics of the novel antipsychotic agent risperidone and the prolactin response in healthy subjects. *Clin Pharmacol Ther* 1993; **54:** 257–68.

Uses and Administration

Risperidone is a benzisoxazole atypical antipsychotic, reported to be an antagonist at dopamine D_2, serotonin ($5\text{-}HT_2$), adrenergic (α_1 and α_2), and histamine (H_1) receptors. It is given orally for the treatment of schizophrenia and other psychoses and in the short-term treatment of acute manic or mixed episodes associated with bipolar disorder. In the USA, risperidone is used similarly in children and also for the treatment of irritability associated with autistic disorder; for further details see Administration in Children and Disturbed Behaviour, below. Risperidone may also be given by deep intramuscular injection for maintenance therapy in patients with schizophrenia or other psychoses tolerant to oral antipsychotics.

For **schizophrenia**, the usual initial oral dose of risperidone is 2 mg daily; this may be increased to 4 mg daily on the second day, and subsequently adjusted as required in steps of 1 or 2 mg according to tolerance, at intervals of not less than 24 hours. Most patients benefit from doses of 4 to 6 mg daily. Risperidone may be given once daily or in 2 divided doses. Extrapyramidal symptoms may be more likely with doses above 10 mg daily; US licensed product information does not recommend daily doses above 6 mg if divided into 2 doses, although higher doses are permitted if given as a single dose. The maximum recommended dose is 16 mg daily.

An initial oral dose of 500 micrograms twice daily slowly increased in steps of 500 micrograms twice daily, if necessary, to a dose of 1 to 2 mg twice daily is recommended for elderly or debilitated patients. Above doses of 1.5 mg twice daily, increases should be made at intervals of at least 1 week.

The long-acting formulation of risperidone should be given by deep intramuscular injection every 2 weeks. Patients with no history of risperidone use should be given risperidone orally for several days to assess tolerability. Treatment may then be started as follows:

- patients not stabilised on oral risperidone: 25 mg every 2 weeks
- patients stabilised on oral risperidone for at least 2 weeks in doses of 4 mg daily or less: 25 mg every 2 weeks
- patients stabilised on oral risperidone for at least 2 weeks in doses above 4 mg daily: 37.5 mg every 2 weeks
- elderly patients should be given a maximum of 25 mg every 2 weeks

Oral risperidone should be continued for the first 3 weeks after the first injection.

Dose increases of 12.5 mg may be considered at least 4 weeks after the previous adjustment up to a maximum of 50 mg every 2 weeks; the clinical effects of a dose adjustment may not be seen for at least 3 weeks after the change.

For the treatment of **mania** in bipolar disorder, a recommended initial oral dose is 2 to 3 mg once daily. Dosage adjustments of 1 mg daily may be made at intervals of not less than 24 hours up to a total of 6 mg daily. The initial dosage regimen in elderly or debilitated patients should be reduced as for schizophrenia (see above).

Reduced doses are recommended in patients with hepatic or renal impairment, see below.

Action. Risperidone is described as an atypical antipsychotic; although it has a lower propensity to produce parkinsonism, dystonias and akathisias have been reported.[1] (See also Extrapyramidal Disorders, above.) The traditional hypothesis is that antipsychotics work through inhibition of dopamine D_2 receptors and that extrapyramidal adverse effects result from blockade of D_2 receptors in the striatum (see p.975). Like clozapine, risperidone has a high affinity for 5-HT_2 receptors and, like haloperidol, it has a high affinity for dopamine D_2 receptors. Risperidone also binds to alpha-adrenergic and histamine H_1 sites. It is unclear whether risperidone's antipsychotic effect is due to activity at dopamine D_2 receptors or at another site. It has been suggested[1] that other potent effects of risperidone may be counterbalancing the D_2 activity to produce its atypicality.

1. Kerwin RW. The new atypical antipsychotics: a lack of extrapyramidal side-effects and new routes in schizophrenia research. *Br J Psychiatry* 1994; **164:** 141–8.

Administration in children. In the USA, risperidone is licensed for the treatment of schizophrenia in adolescents aged 13 to 17 years, for the short-term treatment of acute manic or mixed episodes associated with bipolar disorder in children and adolescents aged 10 to 17 years, and for the treatment of irritability associated with autistic disorder in those aged 5 to 16 years.

For **schizophrenia** or **mania**, an initial oral dose of 500 micrograms is given once daily in the morning or in the evening. This may be increased in steps of 0.5 or 1 mg according to tolerance, at intervals of not less than 24 hours, to a dose of 3 mg daily for schizophrenia or 2.5 mg daily for mania. The maximum recommended dose for both indications is 6 mg daily. The total daily dose may be given in 2 divided doses to those who experience persistent somnolence.

For the treatment of **irritability associated with autistic disorder**, the following oral doses are given once daily or in 2 divided doses according to body-weight:

- under 20 kg: the usual initial daily dose is 250 micrograms; this may be increased to 500 micrograms daily after at least 4 days and subsequently adjusted as required in steps of 250 micrograms, generally at intervals of no less than 2 weeks. The maximum recommended dose is 1 mg daily. Caution should be exercised with dosage for children who weigh less than 15 kg
- 20 kg and over: the usual initial daily dose is 500 micrograms; this may be increased to 1 mg daily after at least 4 days and subsequently adjusted as required in steps of 500 micrograms, generally at intervals of no less than 2 weeks. The maximum recommended dose is 2.5 mg daily in those weighing over 20 kg and 3 mg daily in those over 45 kg
- For those who experience persistent somnolence, the total daily dose may be given as a single dose at bedtime, or in 2 divided doses, or in a reduced dose

For further details on the use of risperidone in children with autism see Disturbed Behaviour, below.

Risperidone is not licensed in the UK for use in children aged under 15 years; however, the *BNFC* suggests that it may be used in those aged 12 years and over for the oral treatment of acute and chronic psychoses. Doses are similar to those used in the treatment of schizophrenia in adults (see above). The *BNFC* also suggests that risperidone may be used, under specialist supervision, in children over 5 years of age for the short-term treatment of severe aggression in autism; doses are similar to those licensed for autistic disorders in the USA.

Administration in hepatic or renal impairment. The recommended initial oral dose of risperidone in patients with renal or hepatic impairment is 500 micrograms twice daily; this may be slowly increased in steps of 500 micrograms twice daily, if necessary, to a dose of 1 to 2 mg twice daily. Above doses of 1.5 mg twice daily, increases should be made at intervals of at least 1 week.

Patients with schizophrenia who tolerate an oral dose of risperidone of at least 2 mg daily may be switched to the long-acting formulation of risperidone; a dose of 25 mg by deep intramuscular injection every 2 weeks is recommended. Alternatively, an initial dose of 12.5 mg by deep intramuscular injection may be given.

AIDS. Risperidone was used successfully to control HIV- or AIDS-related psychosis in 21 patients, some of whom also had manic symptoms.[1] No extrapyramidal symptoms were reported during treatment. However, for reports suggesting that risperidone can induce or exacerbate manic symptoms in patients with schizoaffective disorders, see under Mania in Adverse Effects, above. For an interaction between risperidone and antiretroviral therapy in a patient with AIDS, see under Interactions, above.

1. Singh AN, *et al.* Treatment of HIV-related psychotic disorders with risperidone: a series of 21 cases. *J Psychosom Res* 1997; **42:** 489–93.

Anxiety disorders. Although there have been anecdotal reports[1,2] of improvement after the addition of risperidone to treatment in patients with obsessive-compulsive disorder refractory to conventional treatment, there has also been a report[3] of a patient whose obsessive-compulsive behaviour recurred when he was treated with risperidone for tardive dyskinesia.

1. Jacobsen FM. Risperidone in the treatment of affective illness and obsessive-compulsive disorder. *J Clin Psychiatry* 1995; **56:** 423–9.
2. McDougle CJ, *et al.* Risperidone addition in fluvoxamine-refractory obsessive-compulsive disorder: three cases. *J Clin Psychiatry* 1995; **56:** 526–8.
3. Remington G, Adams M. Risperidone and obsessive-compulsive symptoms. *J Clin Psychopharmacol* 1994; **14:** 358–9.

Bipolar disorder. Risperidone is of benefit for the treatment of mania, including in patients with bipolar disorder (p.372), and the use of atypical antipsychotics in the management of such patients is increasing. However, there have been individual case reports of risperidone-induced mania (see above).

References.

1. Segal J, *et al.* Risperidone compared with both lithium and haloperidol in mania: a double-blind randomized controlled trial. *Clin Neuropharmacol* 1998; **21:** 176–80.
2. Sachs GS, *et al.* Combination of a mood stabilizer with risperidone or haloperidol for treatment of acute mania: a double-blind, placebo-controlled comparison of efficacy and safety. *Am J Psychiatry* 2002; **159:** 1146–54.
3. Yatham LN, *et al.* Mood stabilisers plus risperidone or placebo in the treatment of acute mania: international, double-blind, randomised controlled trial. *Br J Psychiatry* 2003; **182:** 141–7. Correction. *ibid.*; 369.
4. Hirschfeld RM, *et al.* Rapid antimanic effect of risperidone monotherapy: a 3-week multicenter, double-blind, placebo-controlled trial. *Am J Psychiatry* 2004; **161:** 1057–65.
5. Nguyen LN, Guthrie SK. Risperidone treatment of bipolar mania. *Ann Pharmacother* 2006; **40:** 674–82.
6. Rendell JM, *et al.* Risperidone alone or in combination for acute mania. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2006 (accessed 16/05/06).
7. Nguyen LN, Guthrie SK. Risperidone treatment of bipolar mania. *Ann Pharmacother* 2006; **40:** 674–82.

Disturbed behaviour. Although risperidone has been used for the management of behavioural disturbances[1,2] in **elderly patients with dementia** (p.954), such use is no longer recommended, see Dementia, under Adverse Effects, above. Furthermore, despite anecdotal reports[3] of efficacy in patients with Lewy-body dementia, other reports[4] suggest that these patients are likely to be just as sensitive to risperidone as to classical antipsychotics (see the Elderly in Precautions for Chlorpromazine, p.973).

There is evidence[5-10] that risperidone may be effective in reducing behavioural disturbances in **children with autism** (see Disturbed Behaviour, p.954), but it appears to have little effect on core symptoms, and it has been pointed out that the marked hyperprolactinaemia induced by risperidone could lead to hypogonadism, and deleterious effects on adolescent bones.[11] A systematic review[12] concluded that risperidone may be of some benefit for symptoms such as hyperactivity, irritability, repetition, and social withdrawal although this must be weighed against the risk of adverse effects, notably weight gain. The authors noted that only 3 studies were analysed, including 1 that was carried out in adults, and the data available were limited; further studies were considered warranted. Nonetheless, in some countries, including the USA, risperidone is licensed for the treatment of irritability associated with autistic disorder in children and adolescents aged 5 to 16 years; for details of doses see Administration in Children, above.

1. De Deyn PP, *et al.* A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. *Neurology* 1999; **53:** 946–55.
2. Falsetti AE. Risperidone for control of agitation in dementia patients. *Am J Health-Syst Pharm* 2000; **57:** 862–70.
3. Allen RL, *et al.* Risperidone for psychotic and behavioural symptoms in Lewy body dementia. *Lancet* 1995; **346:** 185.
4. McKeith IG, *et al.* Neuroleptic sensitivity to risperidone in Lewy body dementia. *Lancet* 1995; **346:** 699.
5. Research Units on Pediatric Psychopharmacology Autism Network. Risperidone in children with autism and serious behavioral problems. *N Engl J Med* 2002; **347:** 314–21.
6. Shea S, *et al.* Risperidone in the treatment of disruptive behavioral symptoms in children with autistic and other pervasive developmental disorders. Abstract: *Pediatrics* 2004; **114:** 1329. Full version: http://pediatrics.aappublications.org/cgi/reprint/114/5/e634 (accessed 15/01/07)
7. Reyes M, *et al.* A randomized, double-blind, placebo-controlled study of risperidone maintenance treatment in children and adolescents with disruptive behavior disorders. *Am J Psychiatry* 2006; **163:** 402–10.
8. Reyes M, *et al.* Long-term safety and efficacy of risperidone in children with disruptive behaviour disorders: results of a 2-year extension study. *Eur Child Adolesc Psychiatry* 2006; **15:** 97–104.
9. Chavez B, *et al.* Role of risperidone in children with autism spectrum disorder. *Ann Pharmacother* 2006; **40:** 909–16.
10. Scott LJ, Dhillon S. Risperidone: a review of its use in the treatment of irritability associated with autistic disorder in children and adolescents. *Pediatr Drugs* 2007; **9:** 343–54.
11. Valiquette G. Risperidone in children with autism and serious behavioral problems. *N Engl J Med* 2002; **347:** 1890–1.
12. Jesner OS, *et al.* Risperidone for autism spectrum disorder. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 10/04/08).

Dystonias. Antipsychotics are sometimes useful in the treatment of idiopathic dystonia (p.809) in patients who have failed to respond to treatment with levodopa or antimuscarinics, but, as with classical antipsychotics, there is the risk of adding drug-induced extrapyramidal effects to the dystonia. Risperidone has been reported to be of benefit in a few patients with idiopathic segmental dystonia partly insensitive to haloperidol.[1]

1. Zuddas A, Cianchetti C. Efficacy of risperidone in idiopathic segmental dystonia. *Lancet* 1996; **347:** 127–8.

Parkinsonism. There have been conflicting reports of the use of risperidone as an antipsychotic in a small number of patients with Parkinson's disease (see also Disturbed Behaviour, p.954). While some patients found that risperidone ameliorated levodopa-induced hallucinations without worsening extrapyramidal symptoms,[1,2] others reported that risperidone produced a substantial worsening of symptoms.[2,3]

1. Meco G, *et al.* Risperidone for hallucinations in levodopa-treated Parkinson's disease patients. *Lancet* 1994; **343:** 1370–1.
2. Leopold NA. Risperidone treatment of drug-related psychosis in patients with parkinsonism. *Mov Disord* 2000; **15:** 301–4.
3. Ford B, *et al.* Risperidone in Parkinson's disease. *Lancet* 1994; **344:** 681.

Schizophrenia. Risperidone is claimed to produce a relatively low incidence of extrapyramidal effects and to have efficacy against both positive and negative symptoms of schizophrenia. Most of the earlier studies compared risperidone with haloperidol but, of these, some of the major studies[1-3] were criticised for potential methodological flaws[4,5] and it was difficult to determine any difference in efficacy including effect on negative symptoms. A later systematic review[6] suggested that risperidone's benefits over haloperidol or other classical antipsychotics were marginal; although it did appear to reduce the risk of extrapyramidal effects compared with haloperidol, the latter produces a relatively high incidence of such effects. Furthermore, the risk of extrapyramidal effects with risperidone appears to be dose-dependent:[7] although similar to that for placebo overall, at doses of more than 10 mg the risk appears to approach that associated with haloperidol. In a more recent double-blind randomised study[8] the relapse rate after at least 2 years of treatment in patients with first-episode psychosis, who had initially responded to relatively small daily doses of risperidone (mean modal 3.3 mg) or haloperidol (2.9 mg), was 42% (82 of 197 patients) and 55% (111 of 203), respectively. The median time to relapse was also longer for risperidone (466 days) when compared with haloperidol (205 days). In the few comparative studies with other atypical antipsychotics, risperidone has appeared to be of similar efficacy to clozapine.[9] However, another systematic review[10] concluded that such equivalence with clozapine cannot be assumed. For a systematic review of studies comparing risperidone with olanzapine, see p.1013. There is insufficient evidence to indicate whether risperidone is effective for treatment-resistant or poorly responsive patients but there is some evidence that patients stabilised on risperidone may be less likely to relapse.[11] A systematic review[12] of the use of the long-acting injectable formulation of risperidone in schizophrenia considered that, although it might offer the advantage of better compliance, there was little evidence of benefit over oral use.

1. Chouinard G, *et al.* A Canadian multicenter placebo-controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenic patients. *J Clin Psychopharmacol* 1993; **13:** 25–40.
2. Marder SR, Meibach RC. Risperidone in the treatment of schizophrenia. *Am J Psychiatry* 1994; **151:** 825–35.
3. Peuskens J, *et al.* Risperidone Study Group. Risperidone in the treatment of patients with chronic schizophrenia: a multi-national, multi-centre, double-blind, parallel-group study versus haloperidol. *Br J Psychiatry* 1995; **166:** 712–26.
4. Livingston MG. Risperidone. *Lancet* 1994; **343:** 457–60.
5. Musser WS, Kirisci L. Critique of the Canadian multicenter placebo-controlled study of risperidone and haloperidol. *J Clin Psychopharmacol* 1995; **15:** 226–8.
6. Hunter RH, *et al.* Risperidone versus typical antipsychotic medication for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2003 (accessed 30/05/05).
7. Owens DGC. Extrapyramidal side effects and tolerability of risperidone: a review. *J Clin Psychiatry* 1994; **55** (suppl 5): 29–35.
8. Schooler N, *et al.* Risperidone and haloperidol in first-episode psychosis: a long-term randomized trial. *Am J Psychiatry* 2005; **162:** 947–53.

9. Klieser E, *et al.* Randomized, double-blind, controlled trial of risperidone versus clozapine in patients with chronic schizophrenia. *J Clin Psychopharmacol* 1995; **15** (suppl 1): 45S–51S.
10. Gilbody SM, *et al.* Risperidone versus other atypical antipsychotic medication for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2000 (accessed 30/05/05).
11. Csernansky JG, *et al.* A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. *N Engl J Med* 2002; **346:** 16–22.
12. Hosalli P, Davis JM. Depot risperidone for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2003 (accessed 30/05/05).

Stuttering. Risperidone 0.5 to 2 mg daily was found to be of benefit in the management of stuttering in a placebo-controlled study[1] involving 16 patients but there has also been a case report[2] of a patient whose stuttering returned during treatment with risperidone.

1. Maguire GA, *et al.* Risperidone for the treatment of stuttering. *J Clin Psychopharmacol* 2000; **20:** 479–82.
2. Lee H-J, *et al.* A case of risperidone-induced stuttering. *J Clin Psychopharmacol* 2001; **21:** 115–16.

Tourette's syndrome. When drug treatment is required for tics and behavioural disturbances in Tourette's syndrome (see Tics, p.954) haloperidol or pimozide are commonly used but atypical antipsychotics, especially risperidone, are being increasingly tried.[1-3]

1. Bruun RD, Budman CL. Risperidone as a treatment for Tourette's syndrome. *J Clin Psychiatry* 1996; **57:** 29–31.
2. Bruggeman R, *et al.* Risperidone versus pimozide in Tourette's disorder: a comparative double-blind parallel-group study. *J Clin Psychiatry* 2001; **62:** 50–6.
3. Scahill L, *et al.* A placebo-controlled trial of risperidone in Tourette syndrome. *Neurology* 2003; **60:** 1130–5.

Preparations

USP 31: Risperidone Tablets.

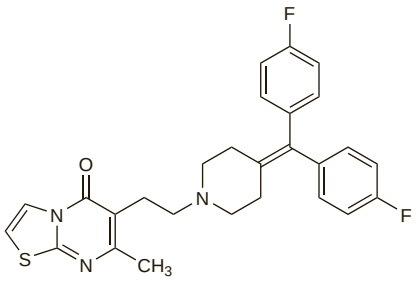
Proprietary Preparations (details are given in Part 3)
Arg.: Dozic; Dropicine; Edalen; Restelea; Riatul; Risper; Risperdal; Risperin; Rispex; Sequinan; ***Austral.:*** Risperdal; ***Austria:*** Belivon†; Risperdal; Rispolin; ***Belg.:*** Risperdal; ***Braz.:*** Respidon; Risperdal; Viverdal; Zargus; ***Canad.:*** Risperdal; ***Chile:*** Dagotil; Goval; Radigen; Risperdal; Spiron; ***Cz.:*** Apo-Risper; Medorisper; Ridoner; Rigenin; Rileptid; Ripetomar; Risepro; Rispadim; Rispedep; Rispedolet; Rispedospes; Rispemar; Rispen; Rispera; Risperdal; Risperinin; Risperit; Rispimed; Rispolux; Risset; Rorendo; ***Denm.:*** Risperdal; ***Fin.:*** Risperdal; ***Fr.:*** Risperdal; ***Ger.:*** Risperdal; ***Gr.:*** Adovia; Axelabron; Depolan; Depredon; Dixine; Helposper; Isipredon; Lassen; Lucipral; Nerve; Novoris; Preridon; Rifocus; Ripepral; Risenar; Risgal; Risidral; Rispalm; Rispefar; Risperascol; Risperdal; Risperom; Risperoprol; Rispogen; Wisperdon; Zafitral; ***Hong Kong:*** Risperdal; ***Hung.:*** Hunperdal; Perdox; Ripedon; Risperdal; Rispolux; Rispons; Ronkal; Rosipin; Torendo; Ziperid; ***India:*** Respidon; Risnia; Risperdal; Rispid†; Rozidal; Sizorisp†; ***Indon.:*** Neripros; Persidal; Risperdal; Rizodal; Zofredal; ***Irl.:*** Risperdal; ***Israel:*** Risperdal; ***Ital.:*** Belivon; Risperdal; ***Jpn:*** Risperdal; ***Malaysia:*** Risperdal; ***Mex.:*** Risperdal; ***Neth.:*** Belivon; Risperdal; Rispimed; Rispimedica; ***Norw.:*** Risperdal; ***NZ:*** Ridal; Risperdal; ***Philipp.:*** Risperdal; ***Pol.:*** Lioxam; Mepharis; Rispen; Risperatio; Risperiwin; Risperon; Rispolept; Rispolux; Risset; Ryspolit; Speridan; Ziperid; ***Port.:*** Belivon†; Perdin; Risperdal; ***Rus.:*** Rileptid (Рилептид); Risdonal (Рисдонал); Rispolept (Рисполепт); Risset (Риссет); Speridan (Сперидан); ***S.Afr.:*** Risperdal; ***Singapore:*** Risperdal; ***Spain:*** Arketin; Diaforin; Risfarmal; Risperdal; ***Swed.:*** Risperdal; ***Switz.:*** Risperdal; ***Thai.:*** Risperdal; ***Turk.:*** Risperdal; ***UK:*** Risperdal; ***USA:*** Risperdal; ***Venez.:*** Ridal; Risperdal; Risperid.

Ritanserin *(BAN, USAN, rINN)*

R-55667; Ritanserina; Ritansérine; Ritanserinum. 6-{2-[4-(4,4′-Difluorobenzhydrylidene)piperidino]ethyl}-7-methyl[1,3]thiazolo[3,2-*a*]pyrimidin-5-one.

Ритансерин

$C_{27}H_{25}F_2N_3OS$ = 477.6.
CAS — 87051-43-2.



Profile

Ritanserin is a serotonin antagonist that has been studied in a variety of disorders including anxiety disorders, depression, and schizophrenia. It is reported to have little sedative action.

Action. Ritanserin is a relatively selective antagonist at serotonin (5-hydroxytryptamine, 5-HT) receptors of the 5-HT_2 subtype, although it also has appreciable affinity for 5-HT_{1C} receptors.[1] Unlike ketanserin (p.1320), it does not block α_1-adrenergic receptors. Ritanserin has anxiolytic activity; it also hastens the onset of slow-wave sleep although sleep may be impaired on withdrawal.

Ritanserin may interfere with platelet function[2,3] but has been reported to have no significant effect on blood pressure, blood flow, or heart rate in patients with hypertension.[2,4] Features characteristic of class III antiarrhythmic activity have also been noted.[2]

1. Marsden CA. The pharmacology of new anxiolytics acting on 5-HT neurones. *Postgrad Med J* 1990; **66** (suppl 2): S2–S6.
2. Stott DJ, *et al.* The effects of the 5HT antagonist ritanserin on blood pressure and serotonin-induced platelet aggregation in patients with untreated essential hypertension. *Eur J Clin Pharmacol* 1988; **35:** 123–9.
3. Wagner B, *et al.* Effect of ritanserin, a 5-hydroxytryptamine - receptor antagonist, on platelet function and thrombin generation at the site of plug formation in vivo. *Clin Pharmacol Ther* 1990; **48:** 419–23.
4. Chau NP, *et al.* Comparative haemodynamic effects of ketanserin and ritanserin in the proximal and distal upper limb circulations of hypertensive patients. *Eur J Clin Pharmacol* 1989; **37:** 215–20.

Substance dependence. Despite some encouraging preliminary data[1] suggesting that ritanserin might influence the desire to drink alcohol, subsequent studies[2,3] have failed to support a role for ritanserin in patients with *alcohol* dependence (p.1626).

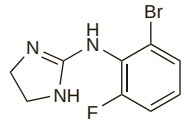
1. Meert TF. Ritanserin and alcohol abuse and dependence. *Alcohol Alcohol* 1994; **2** (suppl): 523–30.
2. Johnson BA, *et al.* Ritanserin Study Group. Ritanserin in the treatment of alcohol dependence—a multi-center clinical trial. *Psychopharmacology (Berl)* 1996; **128:** 206–15.
3. Wiesbeck GA, *et al.* The effects of ritanserin on mood, sleep, vigilance, clinical impression, and social functioning in alcohol-dependent individuals. *Alcohol Alcohol* 2000; **35:** 384–9.

Romifidine *(BAN, rINN)*

Romifidiini; Romifidin; Romifidina; Romifidinum; STH-2130. 2-Bromo-6-fluoro-*N*-(1-imidazolin-2-yl)aniline.

Ромифидин

$C_9H_9BrFN_3$ = 258.1.
CAS — 65896-16-4.
ATC Vet — QN05CM93.



Profile

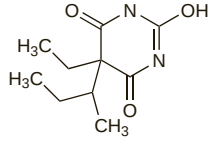
Romifidine is an α_2-adrenoceptor agonist with sedative, muscle relaxant, and analgesic properties and is used in veterinary medicine.

Secbutabarbital *(rINN)*

Butabarbital; Butabarbitone; Secbutabarbitalum; Secbutobarbital *(BAN)*; Secbutobarbitone. 5-sec-Butyl-5-ethylbarbituric acid.

Секбутабарбитал

$C_{10}H_{16}N_2O_3$ = 212.2.
CAS — 125-40-6.



NOTE. Butabarbital should be distinguished from Butobarbital (p.967).

Pharmacopoeias. In *US*.
USP 31 (Butabarbital). A white, odourless, crystalline powder. Very slightly soluble in water; soluble in alcohol, in chloroform, in ether, and in aqueous solutions of alkali hydroxides and carbonates. Store in airtight containers.

Secbutabarbital Sodium *(rINNM)*

Butabarbital Sodium; Natrii Secbutabarbitalum; Secbutabarbital sódico; Secbutabarbital Sodique; Secbutobarbital Sodium *(BANM)*; Secbutobarbitone Sodium; Secumalnatrium; Sodium Butabarbital. Sodium 5-sec-butyl-5-ethylbarbiturate.

Натрий Секбутабарбитал

$C_{10}H_{15}N_2NaO_3$ = 234.2.
CAS — 143-81-7.

Pharmacopoeias. In *US*.
USP 31 (Butabarbital Sodium). A white powder. Soluble 1 in 2 of water, 1 in 7 of alcohol, and 1 in 7000 of chloroform; practically insoluble in absolute ether. pH of a 10% solution in water is between 10.0 and 11.2. Store in airtight containers.

Profile

Secbutabarbital is a barbiturate with general properties similar to those of amobarbital (p.961). It was used as a hypnotic and sedative although barbiturates are no longer considered appropriate for such purposes. For the short-term management of insomnia (p.957) it was usually given as the sodium salt in oral doses of 50 to 100 mg at night; as a sedative 15 to 30 mg has been given 3 or 4 times daily. Secbutabarbital base has also been given.

Preparations

USP 31: Butabarbital Sodium Elixir; Butabarbital Sodium Tablets.

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

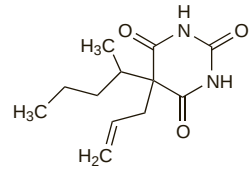
Multi-ingredient: ***USA:*** Butibel; Phenazopyridine Plus; Urelief Plus; ***Venez.:*** Butropina; Eumidral.

Secobarbital *(rINN)*

Meballymal; Quinalbarbitone; Sécobarbital; Secobarbitalum; Secobarbitone; Sekobarbitaali. 5-Allyl-5-(1-methylbutyl)barbituric acid.

Секобарбитал

$C_{12}H_{18}N_2O_3$ = 238.3.
CAS — 76-73-3.
ATC — N05CA06.
ATC Vet — QN05CA06; QN51AA02.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of secobarbital: F-40s; Marshmallow reds; M&Ms; Mexican reds; Pink ladies; Pink lady; Pinks; RDs; Red birds; Red bullets; Red devil; Red devils; Red dolls; Red lillies; Reds; Seccies; Seccy; Seco; Seggy.

Pharmacopoeias. In *US*.
USP 31 (Secobarbital). A white amorphous or crystalline odourless powder. Very slightly soluble in water; freely soluble in alcohol, in ether, and in solutions of fixed alkali hydroxides and carbonates; soluble in chloroform; soluble 1 in 8.5 of 0.5N sodium hydroxide. A saturated solution in water has a pH of about 5.6. Store in airtight containers.

Secobarbital Sodium *(BAN, rINNM)*

Meballymalnatrium; Natrii Secobarbitalum; Quinalbarbitone Sodium; Secobarbital sódico; Sécobarbital Sodique; Secobarbitalum Natricum; Secobarbitone Sodium. Sodium 5-allyl-5-(1-methylbutyl)barbiturate.

Натрий Секобарбитал

$C_{12}H_{17}N_2NaO_3$ = 260.3.
CAS — 309-43-3.
ATC — N05CA06.
ATC Vet — QN05CA06.

Pharmacopoeias. In *Chin.* and *US*.
USP 31 (Secobarbital Sodium). A white odourless hygroscopic powder. Very soluble in water; soluble in alcohol; practically insoluble in ether. pH of a 10% solution in water is between 9.7 and 10.5. Solutions decompose on standing, heat accelerating the decomposition. Store in airtight containers.

Incompatibility. Secobarbital may be precipitated from preparations containing secobarbital sodium depending on the concentration and pH. Secobarbital sodium has, therefore, been reported to be incompatible with many other drugs, particularly acids and acidic salts.

Dependence and Withdrawal

As for Amobarbital, p.962.

Adverse Effects, Treatment, and Precautions

As for Amobarbital, p.962.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving secobarbital, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding. However, for the view that barbiturates should not be used in women who are breast feeding, see under Amobarbital, p.962.

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 28/04/04)

Industrial exposure. Exposure to secobarbital sodium among 6 workers in the pharmaceutical industry resulted in absorption of substantial amounts of the drug, with blood concentrations approaching those expected after a therapeutic dose.[1] There continued to be evidence of absorption, despite protective masks to reduce inhalation, and it appeared that substantial absorption was taking place through the skin.

1. Baxter PJ, *et al.* Exposure to quinalbarbitone sodium in pharmaceutical workers. *BMJ* 1986; **292:** 660–1.