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.

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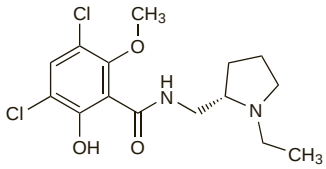
### Raclopride *(BAN, rINN)*

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.

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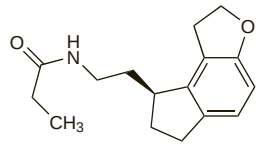
### Ramelteon *(BAN, USAN, rINN)*

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.

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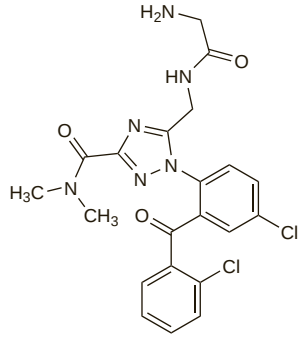
### Rilmazafone Hydrochloride *(rINNM)*

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,2$H_2O$ = 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.

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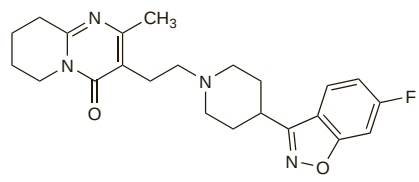
# Risperidone *(BAN, USAN, rINN)*

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