Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Lamuran.

Multi-ingredient: ***Austria:*** Defluina; ***Fr.:*** Duxil†; Iskedyl; ***Hong Kong:*** Duxaril; ***Philipp.:*** Duxaril; ***Port.:*** Duxil; Transoxyl†; ***Singapore:*** Duxaril; ***Spain:*** Duxor†; ***Thai.:*** Duxaril; Iso-Triraupin†.

Rauwolfia Serpentina

Chotachand; Rauvolfia; Rauwolfia; Rauwolfiae Radix; Rauwolfiawurzel.
CAS — 8063-17-0 (rauwolfia).
ATC — C02AA04.

Pharmacopoeias. In *Ger.* and *US.*
USP 31 (Rauwolfia Serpentina). The dried roots of *Rauwolfia serpentina* (Apocynaceae). It contains not less than 0.15% of reserpine-rescinnamine group alkaloids calculated as reserpine. Store at 15° to 30° in a dry place.

Profile

Rauwolfia serpentina contains numerous alkaloids, the most active as hypotensive agents being the ester alkaloids, reserpine and rescinnamine. Other alkaloids present have structures related to reserpic acid, but are not esterified, and include ajmaline (rauwolfine), ajmalinine, ajmalicine, isoajmaline (isorauwolfine), serpentine, rauwolfinine, and sarpagine. The actions of rauwolfia serpentina are those of its alkaloids and it has been used for the same purposes as reserpine, p.1387. It has been given orally as the powdered whole root.

Rauwolfia vomitoria has also been used.

A crude form of rauwolfia serpentina has been used in India for centuries as preparations such as Sarpagandha, in the treatment of insomnia and certain forms of mental illness.

Preparations

USP 31: Rauwolfia Serpentina Tablets.

Proprietary Preparations (details are given in Part 3)

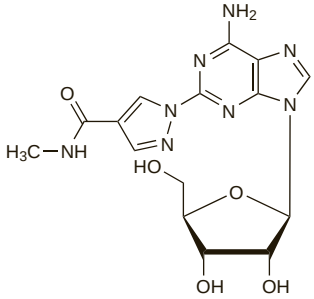
Multi-ingredient: ***Ger.:*** Hyperforat-forte†; ***Rus.:*** Speman Forte (Спеман Форте); ***Spain:*** Rulun; ***USA:*** Rauzide†.

Regadenoson *(BAN, USAN, rINN)*

CVT-3146; Régadénoson; Regadenosón; Regadenosonum. 1-(6-Amino-9-β-D-ribofuranosyl-9*H*-purin-2-yl)-*N*-methyl-1*H*-pyrazole-4-carboxamide monohydrate.

Регаденозон

$C_{15}H_{18}N_8O_5$, H_2O = 408.4.
CAS — 313348-27-5 (regadenoson); 875148-45-1 (regadenoson monohydrate).



Adverse Effects, Treatment, and Precautions

As for Adenosine, p.1202. Regadenoson may be used with caution in patients with asthma or chronic obstructive pulmonary disease.

Interactions

As for Adenosine, p.1202.

Pharmacokinetics

After intravenous injection of regadenoson, peak plasma concentrations are reached within 1 to 4 minutes and decline in a multi-exponential fashion. The initial half-life is about 2 to 4 minutes, followed by an intermediate stage with a half-life of about 30 minutes, during which the pharmacodynamic effect is lost; the half-life during the terminal phase is about 2 hours. Regadenoson does not appear to be metabolised; about 57% of a dose is excreted unchanged in the urine.

◊ References.

1. Gordi T, *et al.* A population pharmacokinetic/pharmacodynamic analysis of regadenoson, an adenosine A -receptor agonist, in healthy male volunteers. *Clin Pharmacokinet* 2006; **45:** 1201–12.
2. Gordi T, *et al.* Regadenoson pharmacokinetics and tolerability in subjects with impaired renal function. *J Clin Pharmacol* 2007; **47:** 825–33.

Uses and Administration

Regadenoson has similar properties to adenosine (p.1202) but has a greater selectivity for the adenosine A_{2A}-receptor. It is a coronary vasodilator and increases coronary blood flow and is used to provide a pharmacological stress as an adjunct to radionuclide myocardial perfusion imaging. It is given intravenously in a single dose of 400 micrograms by rapid injection over about 10 seconds, followed by 5 mL of sodium chloride 0.9%; the radionuclide should be given 10 to 20 seconds after the sodium chloride.

◊ References.

1. Hendel RC, *et al.* Initial clinical experience with regadenoson, a novel selective A agonist for pharmacologic stress single-photon emission computed tomography myocardial perfusion imaging. *J Am Coll Cardiol* 2005; **46:** 2069–75.
2. Iskandrian AE, *et al.* Adenosine versus regadenoson comparative evaluation in myocardial perfusion imaging: results of the ADVANCE phase 3 multicenter international trial. *J Nucl Cardiol* 2007; **14:** 645–58.

Preparations

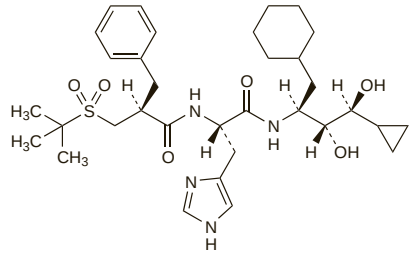
Proprietary Preparations (details are given in Part 3)
USA: Lexiscan.

Remikiren *(rINN)*

Rémikirène; Remikireno; Remikirenum; Ro-42-5892. (α*S*)-α-[(α*S*)-α-[(*tert*-Butylsulfonyl)methyl]hydrocinnamamido]-*N*-[(1*S*,2*R*,3*S*)-1-(cyclohexylmethyl)-3-cyclopropyl-2,3-dihydroxypropyl]imidazole-4-propionamide.

Ремикирен

$C_{33}H_{50}N_4O_6S$ = 630.8.
CAS — 126222-34-2.
ATC — C09XA01.
ATC Vet — QC09XA01.



Profile

Remikiren inhibits the actions of renin and thus prevents the conversion of angiotensinogen into angiotensin I. It is orally active and has been investigated in the management of hypertension and heart failure.

◊ A number of renin antagonists have been investigated as specific inhibitors of the renin-angiotensin system.[1,2] Remikiren is a nonpeptide that is active intravenously and orally, but it is reported to have a very low oral bioavailability.

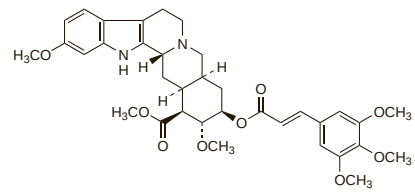
1. Frishman WH, *et al.* Renin inhibition: a new approach to cardiovascular therapy. *J Clin Pharmacol* 1994; **34:** 873–80.
2. Rongen GA, *et al.* Clinical pharmacokinetics and efficacy of renin inhibitors. *Clin Pharmacokinet* 1995; **29:** 6–14.

Rescinnamine *(BAN, rINN)*

Rescinamina; Rescinnamin; Rescinnaminum; Resinnamiini. Methyl-*O*-(3,4,5-trimethoxycinnamoyl)reserpate.

Ресциннамин

$C_{35}H_{42}N_2O_9$ = 634.7.
CAS — 24815-24-5.
ATC — C02AA01.
ATC Vet — QC02AA01.



Profile

Rescinnamine is an ester alkaloid isolated from the root of *Rauwolfia serpentina* or *R. vomitoria*. It has properties similar to those described under reserpine (below) and has been used in the treatment of hypertension.

Preparations

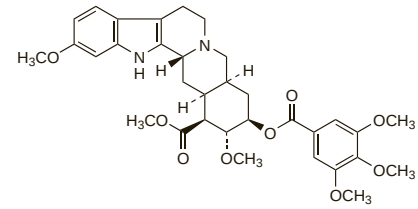
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Thai.:*** Iso-Triraupin†.

Reserpine *(BAN, rINN)*

Reserpiini; Reserpin; Reserpina; Réserpine; Reserpinum; Reszerpin; Rezerpin; Rezerpina; Rezerpinas. Methyl 11,17α-dimethoxy-18β-(3,4,5-trimethoxybenzoyloxy)-3β,20α-yohimbane-16β-carboxylate; Methyl *O*-(3,4,5-trimethoxybenzoyl)reserpate.

Резерпин

$C_{33}H_{40}N_2O_9$ = 608.7.
CAS — 50-55-5.
ATC — C02AA02.
ATC Vet — QC02AA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*
Ph. Eur. 6.2 (Reserpine). It occurs as small, white to slightly yellow crystals or a crystalline powder. It darkens slowly on exposure to light. Practically insoluble in water; very slightly soluble in alcohol. Protect from light.
USP 31 (Reserpine). A white or pale buff to slightly yellowish, odourless, crystalline powder. It darkens slowly on exposure to light, but more rapidly when in solution. Insoluble in water; soluble 1 in 1800 of alcohol and 1 in 6 of chloroform; freely soluble in acetic acid; very slightly soluble in ether; slightly soluble in benzene. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Stability. Reserpine is unstable in the presence of alkalis, particularly when the drug is in solution.

Adverse Effects

Adverse effects commonly include nasal congestion, headache and CNS symptoms including depression, drowsiness, dizziness, lethargy, nightmares, and symptoms of increased gastrointestinal tract motility including diarrhoea, abdominal cramps, and, at higher doses, increased gastric acid secretion. Respiratory distress, cyanosis, anorexia, and lethargy may occur in infants whose mothers have taken reserpine before delivery.

Higher doses may cause flushing, bradycardia, severe depression which may lead to suicide, and extrapyramidal effects. Hypotension, coma, convulsions, respiratory depression, and hypothermia also occur in overdosage. Hypotension is also more common in patients after a cerebrovascular accident.

Breast engorgement and galactorrhoea, gynaecomastia, increased prolactin concentrations, decreased libido, impotence, sodium retention, oedema, decreased or increased appetite, weight gain, miosis, dry mouth, sialorrhoea, dysuria, rashes, pruritus, and thrombocytopenic purpura have also been reported.

Large doses of reserpine have been shown to be tumorigenic in *rodents*. Several reports have suggested an association between reserpine and the development of neoplasms of the breast (see below) but other surveys have failed to confirm this.

Neoplasms of the breast. Although early studies suggested that the incidence of breast cancer was up to 3 to 4 times greater in hypertensive women treated with rauwolfia preparations than in control groups, analysis[1] of both prospective trials and case-control studies found only a low-grade association between use of rauwolfia preparations and risk of malignancy.

1. Grossman E, *et al.* Antihypertensive therapy and the risk of malignancies. *Eur Heart J* 2001; **22:** 1343–52.

Treatment of Adverse Effects

Withdrawal of reserpine or reduction of the dosage causes the reversal of many adverse effects although mental disorders may persist for months and hypotensive effects may persist for weeks after the cessation of treatment. If overdosage occurs activated charcoal may be considered within 1 hour of ingestion. Treatment is generally supportive and symptomatic. Severe hypotension may respond to placing the patient in the supine position with the feet raised. Direct-acting sympathomimetics may be effective for treatment of severe hypotension, but should be given with caution. The patient must be observed for at least 72 hours.

Precautions

Reserpine should not be used in patients with depression or a history of depression, with active peptic ulcer disease or ulcerative colitis, or in patients with Parkinson's disease. It should also be avoided in phaeochromocytoma.

It should be used with caution in debilitated or elderly patients, and in the presence of cardiac arrhythmias, myocardial infarction, renal insufficiency, gallstones, epilepsy, or allergic conditions such as bronchial asthma.

Reserpine is contra-indicated in patients having ECT and an interval of at least 7 to 14 days should be allowed between the last dose of reserpine and the start of any ECT.