excreted mainly in the urine as unchanged polythiazide and metabolites.

◊ References.

1. Hobbs DC, Twomey TM. Kinetics of polythiazide. *Clin Pharmacol Ther* 1978; **23:** 241–6.

Uses and Administration

Polythiazide is a thiazide diuretic with actions and uses similar to those of hydrochlorothiazide (p.1310). It is given orally for hypertension (p.1171), and for oedema, including that associated with heart failure (p.1165).

Diuresis begins within about 2 hours of an oral dose, and lasts for 24 to 48 hours.

In the treatment of **hypertension** the usual dose is stated to be 2 to 4 mg daily, either alone or with other antihypertensives although doses of only 0.5 to 1 mg may be adequate. In the treatment of **oedema** the usual dose is 1 to 4 mg daily.

Preparations

BP 2008: Polythiazide Tablets.

Proprietary Preparations (details are given in Part 3)
Belg.: Renese†; ***USA:*** Renese†.

Multi-ingredient: ***Ger.:*** Polypress†; ***USA:*** Minizide†; Renese R†.

Potassium Canrenoate *(BANM, rINN)* ⊗

Aldadiene Potassium; Canrénoate de Potassium; Canrenoate Potassium *(USAN)*; Canrenoato de potasio; Kalii Canrenoas; Kaliumkanrenoaatti; Kaliumkanrenoat; MF-465a; SC-14266. Potassium 17-hydroxy-3-oxo-17α-pregna-4,6-diene-21-carboxylate.

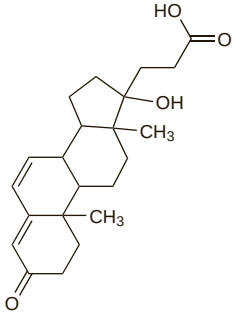
Калия Канреноат

$C_{22}H_{29}KO_4$ = 396.6.

CAS — 4138-96-9 (canrenoic acid); 2181-04-6 (potassium canrenoate).

ATC — C03DA02.

ATC Vet — QC03DA02.



(canrenoic acid)

Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions

As for Spironolactone, p.1400. Irritation or pain may occur at the site of injection.

Effects on endocrine function. A lower incidence of gynaecomastia has been reported in patients with hepatic cirrhosis and ascites during use of potassium canrenoate than with equivalent doses of spironolactone,[1] and spironolactone-induced gynaecomastia disappeared when spironolactone was replaced by potassium canrenoate in a patient with hyperaldosteronism.[2] This suggests that metabolites other than canrenone (a common metabolite of both canrenoate and spironolactone thought to be responsible for their activity) or possibly spironolactone itself may be responsible for the anti-androgenic effects of spironolactone.[3,4]

1. Bellati G, Idéo G. Gynaecomastia after spironolactone and potassium canrenoate. *Lancet* 1986; **i:** 626.
2. Dupont A. Disappearance of spironolactone-induced gynaecomastia during treatment with potassium canrenoate. *Lancet* 1985; **ii:** 731.
3. Gardiner P. Spironolactone and potassium canrenoate metabolism. *Lancet* 1985; **ii:** 1432.
4. Overdiek JWPM, Merkus FWHM. Spironolactone metabolism and gynaecomastia. *Lancet* 1986; **i:** 1103.

Interactions

As for Spironolactone, p.1401.

Uses and Administration

Potassium canrenoate is a potassium-sparing diuretic with actions and uses similar to those of spironolactone (p.1401). Canrenone (p.1239) is a metabolite common to both drugs, but its contribution to the pharmacological action is unclear. Potassium canrenoate is used in the treatment of refractory oedema associated with heart failure (p.1165) or hepatic disease when an injectable aldosterone antagonist is required. It may be given in doses of 200 to 400 mg daily, increasing to 800 mg daily in exceptional cases; it is given by slow intravenous injection over a period of 2 to 3 minutes for each 200 mg or by intravenous infusion in glucose 5% or sodium chloride 0.9%.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Aldactone; ***Belg.:*** Canrenol; Soldactone; ***Cz.:*** Aldactone; Canrenol†; ***Fr.:*** Soludactone; ***Ger.:*** Aldactone; Kalium-Can; ***Hung.:*** Aldactone†; ***Ital.:*** Dikantal; Diurek; Kanrenol; Luvion; Venactone†; ***Neth.:*** Soldactone; ***Norw.:*** Soldactone†; ***Pol.:*** Aldactone; ***Switz.:*** Soldactone.

Multi-ingredient: ***Ital.:*** Kadiur.

Prajmalium Bitartrate *(BAN, rINN)*

Bitartrato de prajmalio; GT-1012; NPAB; Prajmalii Bitartras; Prajmaline Bitartrate; Prajmalium, Bitartrate de. *N*-Propylajmalinium hydrogen tartrate.

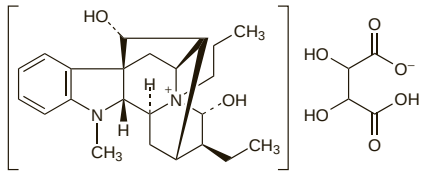
Праймалия Битартрат

$C_{23}H_{33}N_2O_2,C_4H_5O_6$ = 518.6.

CAS — 35080-11-6 (prajmalium); 2589-47-1 (prajmalium bitartrate).

ATC — C01BA08.

ATC Vet — QC01BA08.



Adverse Effects and Precautions

As for Ajmaline, p.1206.

Effects on the liver. Cholestatic jaundice associated with pruritus, chills, and eosinophilia[1] was attributed to an allergic reaction to prajmalium bitartrate in a patient 20 days after the start of treatment.

1. Rotmensch HH, *et al.* Cholestatic jaundice: an immune response to prajmalium bitartrate. *Postgrad Med J* 1980; **56:** 738–41.

Effects on mental state. Confusion and disorientation in time and place[1] occurred on 2 occasions in a 67-year-old man given prajmalium bitartrate 100 mg daily for the control of tachycardia; the confusion rapidly disappeared when prajmalium was withdrawn.

1. Lessing JB, Copperman IJ. Severe cerebral confusion produced by prajmalium bitartrate. *BMJ* 1977; **2:** 675.

Uses and Administration

Prajmalium is a class I antiarrhythmic (p.1153) and is the *N*-propyl derivative of ajmaline (p.1206). It is given orally as the bitartrate in the management of supraventricular and ventricular arrhythmias (p.1160) in initial doses of 60 to 80 mg daily. Maintenance doses of 20 to 40 mg daily in divided doses are used.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Neo-Gilurytmal; ***Cz.:*** Neo-Gilurytmal; ***Ger.:*** Neo-Gilurytmal; ***Hung.:*** Neo-Gilurytmal; ***Indon.:*** Neo-Gilurytmal; ***Israel:*** Neo-Gilurythmal†.

Multi-ingredient: ***Spain:*** Cresophene.

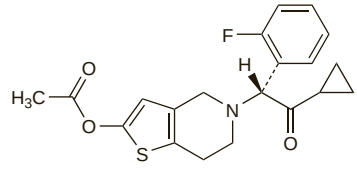
Prasugrel Hydrochloride *(USAN, rINNM)*

LY-640315; Prasugrel, Chlorhydrate de; Prasugrel, hidrocloruro de; Prasugreli Hydrochloridum. 5-[(1*RS*)-2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate hydrochloride.

Празугрела Гидрохлорид

$C_{20}H_{20}FNO_3S,HCl$ = 409.9.

CAS — 389574-19-0.



(prasugrel)

Profile

Prasugrel hydrochloride is a thienopyridine antiplatelet drug with similar properties to clopidogrel (p.1250). It is under development for cardiovascular disorders.

◊ References.

1. Wiviott SD, *et al.* Randomized comparison of prasugrel (CS-747, LY640315), a novel thienopyridine P2Y antagonist, with clopidogrel in percutaneous coronary intervention: results of the Joint Utilization of Medications to Block Platelets Optimally (JUMBO)-TIMI 26 trial. *Circulation* 2005; **111:** 3366–73.
2. Jakubowski JA, *et al.* A multiple dose study of prasugrel (CS-747), a novel thienopyridine P2Y inhibitor, compared with clopidogrel in healthy humans. *Br J Clin Pharmacol* 2006; **63:** 421–30.
3. Brandt JT, *et al.* A comparison of prasugrel and clopidogrel loading doses on platelet function: magnitude of platelet inhibition is related to active metabolite formation. *Am Heart J* 2007; **153:** 66.
4. Wiviott SD, *et al.* TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2007; **357:** 2001–15.
5. Wiviott SD, *et al.* PRINCIPLE-TIMI 44 Investigators. Prasugrel compared with high loading- and maintenance-dose clopidogrel in patients with planned percutaneous coronary intervention: the Prasugrel in Comparison to Clopidogrel for Inhibition of Platelet Activation and Aggregation-Thrombolysis in Myocardial Infarction 44 trial. *Circulation* 2007; **116:** 2923–32.
6. Antman EM, *et al.* Early and late benefits of prasugrel in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a TRITON-TIMI 38 (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel-Thrombolysis In Myocardial Infarction) analysis. *J Am Coll Cardiol* 2008; **51:** 2028–33.

Pravastatin Sodium *(BANM, USAN, rINNM)*

CS-514; Eptastatin Sodium; 3β-Hydroxycompactin Sodium; Natrii Pravastatinum; Pravastatiininatrium; Pravastatin sodná sůl; Pravastatina sódica; Pravastatine sodique; Pravastatinnatrium; Pravastatino natrio druska; Pravastatinum natricum; Pravasztatinnátrium; SQ-31000. Sodium (3*R*,5*R*)-7-{(1*S*,2*S*,6*S*,8*S*,8a*R*)-1,2,6,7,8,8a-hexahydro-6-hydroxy-2-methyl-8-[(*S*)-2-methylbutyryloxy]-1-naphthyl}-3,5-dihydroxyheptanoate.

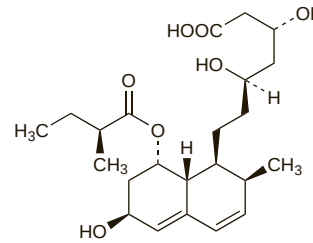
Натрий Правастатин

$C_{23}H_{35}O_7Na$ = 446.5.

CAS — 81093-37-0 (pravastatin); 81131-70-6 (pravastatin sodium).

ATC — C10AA03.

ATC Vet — QC10AA03.



(pravastatin)

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

Ph. Eur. 6.2 (Pravastatin Sodium). A white to yellowish-white, hygroscopic, powder or crystalline powder. Freely soluble in water and in methyl alcohol; soluble in dehydrated alcohol. A 5% solution in water has a pH of 7.2 to 9.0. Store in airtight containers.

USP 31 (Pravastatin Sodium). A white to yellowish white hygroscopic powder. Freely soluble in water and in methyl alcohol; soluble in alcohol; practically insoluble in chloroform, in ether, and in ethyl acetate; very slightly soluble in acetonitrile. Store in airtight containers.

Adverse Effects and Precautions

As for Simvastatin, p.1390.

Interactions

The interactions of statins with other drugs are described under simvastatin (p.1392). Pravastatin is not significantly metabolised by the cytochrome P450 enzyme system and does not have the same interactions with enzyme inhibitors as simvastatin, although caution has been advised when such combinations are used. Increased plasma-pravastatin concentrations have been reported in some patients receiving ciclosporin and low doses should be used (see Uses and Administration, below).

Pharmacokinetics

Pravastatin is rapidly but incompletely absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism in the liver, its primary site of action. The absolute bioavailability of pravastatin is 17%. About 50% of the circulating drug is bound to plasma proteins. The plasma elimination half-life of pravastatin is 1.5 to 2 hours. About 70% of an oral dose of prav-