the inward sodium current in cardiac cells. Flecainide, because of its sodium-channel blocking action, exaggerates this deficiency and the resulting ST-segment elevation, and aids in diagnosis; however, it may precipitate serious ventricular arrhythmias[10] and must not be used for treatment.

1. Simpson JM, Sharland GK. Fetal tachycardias: management and outcome of 127 consecutive cases. *Heart* 1998; **79:** 576–81.
2. Krapp M, *et al*. Flecainide in the intrauterine treatment of fetal supraventricular tachycardia. *Ultrasound Obstet Gynecol* 2002; **19:** 158–64.
3. Rasheed A, *et al*. Neonatal ECG changes caused by supratherapeutic flecainide following treatment for fetal supraventricular tachycardia. *Heart* 2003; **89:** 470.
4. Hall CM, Ward Platt MP. Neonatal flecainide toxicity following supraventricular tachycardia treatment. *Ann Pharmacother* 2003; **37:** 1343–4.
5. Task Force of the Working Group on Arrhythmias of the European Society of Cardiology. CAST and beyond: implications of the cardiac arrhythmias suppression trial. *Circulation* 1990; **81:** 1123–7. [Simultaneous publication occurred in *Eur Heart J* 1990; **11:** 194–9].
6. The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989; **321:** 406–12.
7. Echt DS, *et al*. Mortality and morbidity in patients receiving encainide, flecainide, or placebo: The Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991; **324:** 781–8.
8. The Cardiac Arrhythmia Suppression Trial II Investigators. Effect of the antiarrhythmic agent moricizine on survival after myocardial infarction. *N Engl J Med* 1992; **327:** 227–33.
9. Singleton CB, McGuire MA. The Brugada syndrome: a recently recognised genetic disease causing sudden cardiac death. *Med J Aust* 2000; **173:** 415–8.
10. Gasparini M, *et al*. Flecainide test in Brugada syndrome: a reproducible but risky tool. *Pacing Clin Electrophysiol* 2003; **26:** 338–41.

Pain. Class Ic antiarrhythmics such as flecainide are among the drugs that have been used as analgesic adjuvants in neuropathic pain (p.8), although the evidence for benefit with flecainide is limited. A positive response has been reported[1,2] in patients with severe pain due to nerve infiltration, but a controlled trial had to be stopped[3] when supplies of the drug were withdrawn after the finding of increased mortality in a study in post-infarction patients (CAST; see Cardiac Arrhythmias, above), and a later study[4] found that flecainide was effective in only a minority of patients with cancer pain. A small study[5] has suggested that flecainide may be effective in postherpetic neuralgia.

1. Dunlop R, *et al*. Analgesic effects of oral flecainide. *Lancet* 1988; **i:** 420–1.
2. Sinnott C, *et al*. Flecainide in cancer nerve pain. *Lancet* 1991; **337:** 1347.
3. Dunlop RJ, *et al*. Flecainide in cancer nerve pain. *Lancet* 1991; **337:** 1347.
4. Chong SF, *et al*. Pilot study evaluating local anesthetics administered systemically for treatment of pain in patients with advanced cancer. *J Pain Symptom Manage* 1997; **13:** 112–17.
5. Ichimata M, *et al*. Analgesic effects of flecainide on postherpetic neuralgia. *Int J Clin Pharmacol Res* 2001; **21:** 15–19.

Preparations

BP 2008: Flecainide Injection; Flecainide Tablets;
USP 31: Flecainide Acetate Tablets.

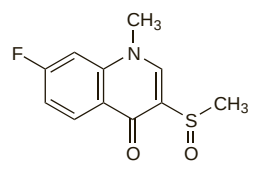
Proprietary Preparations (details are given in Part 3)
Arg.: Diondel; Tambocor†; ***Austral.:*** Flecatab; Tambocor; ***Austria:*** Aristocor; ***Belg.:*** Apocard; Tambocor; ***Canad.:*** Tambocor; ***Chile:*** Tambocor; ***Cz.:*** Tambocor; ***Denm.:*** Tambocor; ***Fin.:*** Tambocor; ***Fr.:*** Flecaine; ***Ger.:*** flecadura; Tambocor; ***Gr.:*** Tambocor; ***Hong Kong:*** Tambocor; ***Irl.:*** Tambocor; ***Israel:*** Tambocor; ***Ital.:*** Almarytm; ***Malaysia:*** Tambocor; ***Mex.:*** Tambocor; ***Neth.:*** Tambocor; ***Norw.:*** Tambocor; ***NZ:*** Tambocor; ***Philipp.:*** Tambocor; ***Port.:*** Apocard; ***S.Afr.:*** Tambocor; ***Singapore:*** Tambocor; ***Spain:*** Apocard; ***Swed.:*** Tambocor; ***Switz.:*** Tambocor; ***Thai.:*** Tambocor; ***UK:*** Tambocor; ***USA:*** Tambocor.

Flosequinan *(BAN, USAN, rINN)*

BTS-49465; Floséquinan; Flosequinán; Flosequinanum. 7-Fluoro-1-methyl-3-methylsulphinyl-4-quinolone.

Флозехинан

$C_{11}H_{10}FNO_2S$ = 239.3.
CAS — 76568-02-0.
ATC — C01DB01.
ATC Vet — QC01DB01.



Profile

Flosequinan is a direct-acting arteriovenous vasodilator that was used as an adjunct to the conventional treatment of heart failure, but was withdrawn from the market after findings of excess mortality.

◊ References.

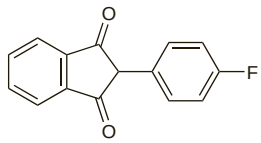
1. Kamali F, Edwards C. Possible role of metabolite in flosequinan-related mortality. *Clin Pharmacokinet* 1995; **29:** 396–403.

Fluindione *(rINN)*

Fluindiona; Fluindionum; Fluorindione; LM-123. 2-(4-Fluorophenyl)indan-1,3-dione.

Флуиндион

$C_{15}H_9FO_2$ = 240.2.
CAS — 957-56-2.



Profile

Fluindione is an oral indanedione anticoagulant with actions similar to those of warfarin (p.1425). It is used in the management of thromboembolic disorders (p.1187) but, as the indanediones are generally more toxic than warfarin (see Phenindione, p.1369), its use is limited.

The usual initial dose is 20 mg daily; the dose is then adjusted according to coagulation tests.

Preparations

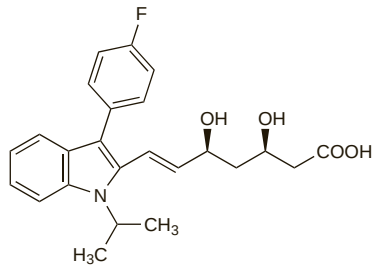
Proprietary Preparations (details are given in Part 3)
Fr.: Previscan.

Fluvastatin Sodium *(BANM, USAN, rINNM)*

Fluvastatina sódica; Fluvastatine sodique; Fluvastatinum natricum; Natrii Fluvastatinum; XU-62-320. Sodium (±)-(3*R**,5*S**,6*E*)-7-[3-(*p*-Fluorophenyl)-1-isopropylindol-2-yl]-3,5-dihydroxy-6-heptenoate.

Натрий Флувастатин

$C_{24}H_{25}FNNaO_4$ = 433.4.
CAS — 93957-54-1 (fluvastatin); 93957-55-2 (fluvastatin sodium).
ATC — C10AA04.
ATC Vet — QC10AA04.



(fluvastatin)

Pharmacopoeias. In *US.*
USP 31 (Fluvastatin Sodium). A white to pale yellow, brownish-pale yellow, or reddish-pale yellow, hygroscopic powder. Soluble in water, in alcohol, and in methyl alcohol. A 1% solution in water has a pH of 8.0 to 10.0. Store in airtight containers at a temperature not exceeding 40°. Protect from light and moisture.

Adverse Effects and Precautions

As for Simvastatin, p.1390.

Interactions

The interactions of statins with other drugs are described under simvastatin (p.1392). Fluvastatin is metabolised mainly by the cytochrome P450 isoenzyme CYP2C9 and does not have the same interactions with CYP3A4 inhibitors as simvastatin, although caution has been advised when such combinations are used. However, interactions may occur with inhibitors of CYP2C9, such as fluconazole; use with rifampicin, a CYP2C9 inducer, may reduce the bioavailability of fluvastatin by about 50%.

Pharmacokinetics

Fluvastatin is rapidly and completely absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism in the liver, its primary site of action. Metabolism is mainly by the cytochrome P450 isoenzyme CYP2C9, with only a small amount metabolised by CYP3A4. An absolute bioavailability of about 24% has been reported. It is more than 98% bound to plasma proteins. About 90% is excreted in the faeces, mainly as metabolites, with only about 6% being excreted in the urine.

◊ General reviews.

1. Scripture CD, Pieper JA. Clinical pharmacokinetics of fluvastatin. *Clin Pharmacokinet* 2001; **40:** 263–81.

Uses and Administration

Fluvastatin, a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (or statin), is a lipid regulating drug with actions on plasma lipids similar to those of simvastatin (p.1394). It is used to reduce total cholesterol, LDL-cholesterol, apolipoprotein B, and triglycerides, and to increase HDL-cholesterol, in the treatment of hyperlipidaemias (p.1169), including hypercholesterolaemias and combined (mixed) hyperlipidaemia (type IIa or IIb hyperlipoproteinaemias). It is also given as secondary prophylaxis for cardiovascular risk reduction (p.1164) in patients with ischaemic heart disease, including patients who have had a percutaneous coronary intervention.

Fluvastatin is given orally as the sodium salt, but doses are expressed in terms of the base; 21.06 mg of fluvastatin sodium is equivalent to about 20 mg of base. The usual initial dose is 20 to 40 mg of fluvastatin once daily in the evening. This may be increased, if necessary, at intervals of 4 weeks or more, up to 80 mg daily, in two divided doses or as a once-daily modified-release preparation; patients requiring a large reduction in LDL-cholesterol may be started on the 80 mg daily dose. A dose of 80 mg daily may also be used in patients who have had a percutaneous coronary intervention.

For the use of fluvastatin in children, see below.

◊ References.

1. Langtry HD, Markham A. Fluvastatin: a review of its use in lipid disorders. *Drugs* 1999; **57:** 583–606.
2. Corsini A, *et al*. Fluvastatin: clinical and safety profile. *Drugs* 2004; **64:** 1305–23.
3. Winkler K, *et al*. Risk reduction and tolerability of fluvastatin in patients with the metabolic syndrome: a pooled analysis of thirty clinical trials. *Clin Ther* 2007; **29:** 1987–2000.
4. McDonald KJ, Jardine AG. The use of fluvastatin in cardiovascular risk management. *Expert Opin Pharmacother* 2008; **9:** 1407–14.

Administration in children. Fluvastatin may be used in the management of children aged 10 to 16 years with heterozygous familial hypercholesterolaemia.[1] US licensed product information recommends an initial oral dose of 20 mg once daily, increased as required, at intervals of 6 weeks, to a maximum dose of 80 mg daily in 2 divided doses or as a once-daily modified-release preparation.

1. van der Graaf A, *et al*. Efficacy and safety of fluvastatin in children and adolescents with heterozygous familial hypercholesterolaemia. *Acta Paediatr* 2006; **95:** 1461–6.

Preparations

USP 31: Fluvastatin Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Lescol; ***Austral.:*** Lescol; Vastin; ***Austria:*** Lescol; ***Belg.:*** Lescol; ***Braz.:*** Lescol; ***Canad.:*** Lescol; ***Cz.:*** Lescol; ***Denm.:*** Canef; Lescol; ***Fin.:*** Canef; Lescol; ***Fr.:*** Fractal; Lescol; ***Ger.:*** Cranoc; LOCOL; ***Gr.:*** Hovalin; Lescol; ***Hong Kong:*** Lescol; ***Hung.:*** Lescol; Lochol; ***Indon.:*** Lescol; ***Irl.:*** Lescol; ***Israel:*** Lescol; ***Ital.:*** Lescol; Lipaxan; Primesin; ***Jpn:*** Lochol; ***Malaysia:*** Lescol; ***Mex.:*** Canef†; Lescol; ***Neth.:*** Canef; Lescol; Vaditon; ***Norw.:*** Lescol; ***NZ:*** Lescol†; ***Philipp.:*** Lescol; ***Pol.:*** Lescol; ***Port.:*** Canef; Cardiol; Lescol; ***Rus.:*** Lescol (Лескол); ***S.Afr.:*** Lescol; ***Singapore:*** Lescol; ***Spain:*** Digaril; Lescol; Liposit; Lymetel; Princess Prolib†; Vaditon; ***Swed.:*** Canef; Lescol; ***Switz.:*** Lescol; Primesin; ***Thai.:*** Lescol; ***Turk.:*** Lescol; ***UK:*** Lescol; ***USA:*** Lescol; ***Venez.:*** Lescol†.