membrane-stabilising activity. Nadolol is given orally in the management of hypertension (p.1171), angina pectoris (p.1157), and cardiac arrhythmias (p.1160). It is also used in the management of hyperthyroidism (p.2165) and in the prophylactic treatment of migraine (p.616).

In the treatment of **hypertension**, nadolol is usually given in an initial dose of 40 to 80 mg once daily, increased weekly according to response to 240 mg or more daily.

In **angina pectoris**, the usual initial dose is 40 mg once daily, increased weekly according to response to usual doses of up to 160 mg daily; some patients may require up to 240 mg daily. Doses of 40 to 160 mg once daily have also been given for **cardiac arrhythmias**.

Doses of 40 to 160 mg once daily are used in **migraine** prophylaxis.

As an adjunct in the treatment of **hyperthyroidism**, doses of 80 to 160 mg once daily have been given; most patients are reported to require the higher dose.

Patients with renal impairment may require a reduction in dose (see below).

Administration in renal impairment. Nadolol is excreted mainly in the urine and doses should be reduced in patients with renal impairment, usually by increasing the dosage interval. For patients with hypertension or angina pectoris, US licensed product information recommends the following dosage intervals, based on creatinine clearance (CC):

- CC between 31 and 50 mL/minute per 1.73 m^2: give every 24 to 36 hours
- CC between 10 and 30 mL/minute per 1.73 m^2: give every 24 to 48 hours
- CC less than 10 mL/minute per 1.73 m^2: give every 40 to 60 hours.

Preparations

USP 31: Nadolol and Bendroflumethiazide Tablets; Nadolol Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Corgard; ***Belg.:*** Corgard; ***Braz.:*** Corgard; ***Canad.:*** Apo-Nadol; Corgard; ***Chile:*** Corgard; ***Fr.:*** Corgard; ***Ger.:*** Solgol; ***Hong Kong:*** Apo-Nadol; Corgard†; ***Ital.:*** Corgard; ***Malaysia:*** Corgard†; ***Mex.:*** Corgard; ***NZ:*** Corgard; ***Port.:*** Anabet; ***S.Afr.:*** Corgard; ***Spain:*** Corgard; Solgol; ***Switz.:*** Corgard; ***UK:*** Corgard; ***USA:*** Corgard; ***Venez.:*** Corgard.

Multi-ingredient: ***Ger.:*** Sotaziden N; ***Mex.:*** Corgaretic; ***S.Afr.:*** Corgaretic; ***UK:*** Corgaretic†; ***USA:*** Corzide.

Nadroparin Calcium *(BAN, rINN)*

CY-216; Nadropariinikalsium; Nadroparin Kalsiyum; Nadroparin vápenatá sůl; Nadroparina cálcica; Nadroparine calcique; Nadroparinkalcium; Nadroparin-kalcium; Nadroparino kalcio druska; Nadroparinum calcicum.

Надропарин Кальций

ATC — B01AB06.
ATC Vet — QB01AB06.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Nadroparin Calcium). It is prepared by nitrous acid depolymerisation of heparin obtained from the intestinal mucosa of pigs. The majority of the components have a 2-*O*-sulfo-α-L-idopyranosuronic acid structure at the non-reducing end and a 6-*O*-sulfo-2,5-anhydro-D-mannitol structure at the reducing end of their chain. The mass-average molecular mass ranges between 3600 and 5000, with a characteristic value of 4300. The mass percentage of chains lower than 2000 is not more than 15%. The degree of sulfation is about 2 per disaccharide unit.
The potency is not less than 95 units and not more than 130 units of anti-factor Xa activity per mg with reference to the dried substance, and the ratio of anti-factor Xa activity to anti-factor IIa (antithrombin) activity is between 2.5 and 4.0.

Profile

Nadroparin calcium is a low-molecular-weight heparin (p.1329) with anticoagulant properties. It is used in the treatment and prophylaxis of venous thromboembolism (p.1189) and to prevent clotting during extracorporeal circulation. It is also used in the management of unstable angina (p.1157).

Doses are expressed in terms of anti-factor Xa activity (anti-Xa units) although different values may be encountered in the literature depending upon the reference preparation used. For *prophylaxis* of **venous thromboembolism** during surgery, patients at moderate risk of thrombosis are given 2850 units of nadroparin calcium by subcutaneous injection daily for at least 7 days or until the patient is ambulant; the first dose is given 2 to 4 hours before the procedure. For patients at high risk of thrombosis the dose is adjusted according to body-weight. Usual doses are 38 units/kg 12 hours before surgery, 12 hours postoperatively and then daily until 3 days after the procedure; the dose is then increased by 50% to 57 units/kg daily. The total duration of treatment should be at least 10 days.

For the *treatment* of thromboembolism, nadroparin calcium is given in a dose of 85 units/kg by subcutaneous injection every 12 hours for up to 10 days. Alternatively, a dose of 171 units/kg is given once daily.

For prevention of clotting in the extracorporeal circulation during **haemodialysis** sessions lasting less than 4 hours, nadroparin calcium is given into the arterial line of the circuit at the beginning of the dialysis session. The usual dose is 2850 units for patients weighing less than 50 kg, 3800 units for patients weighing 50 to 69 kg, and 5700 units for patients weighing 70 kg or more. Doses should be reduced in patients at high risk of haemorrhage.

In the management of unstable **angina**, nadroparin calcium is given subcutaneously in a dose of 86 units/kg every 12 hours, for about 6 days. An initial dose of 86 units/kg may be given intravenously. Low-dose aspirin should also be given.

Elimination of nadroparin is prolonged in renal impairment, and doses may need to be reduced in moderate or severe impairment.

◊ References.

1. Barradell LB, Buckley MM. Nadroparin calcium: a review of its pharmacology and clinical applications in the prevention and treatment of thromboembolic disorders. *Drugs* 1992; **44:** 858–88.

Preparations

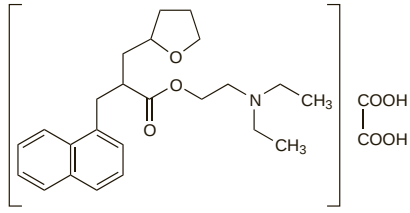
Proprietary Preparations (details are given in Part 3)
Arg.: Fraxiparine; ***Austria:*** Fraxiparin; ***Belg.:*** Fraxiparine; Fraxodi; ***Braz.:*** Fraxiparina; ***Canad.:*** Fraxiparine; ***Chile:*** Fraxiparine; ***Cz.:*** Fraxiparine; ***Fr.:*** Fraxiparine; Fraxodi; ***Ger.:*** Fraxiparin; Fraxodi; ***Gr.:*** Fraxiparine; ***Hong Kong:*** Fraxiparine; ***Hung.:*** Fraxiparine; Fraxodi; ***Indon.:*** Fraxiparine; ***Israel:*** Fraxiparine; ***Ital.:*** Fraxiparina; Fraxodi; Seledie; Seleparina; ***Malaysia:*** Fraxiparine; ***Mex.:*** Fraxiparine; Fraxodi; ***Neth.:*** Fraxiparine; Fraxodi; ***Norw.:*** Fraxiparine†; ***NZ:*** Fraxiparine†; ***Philipp.:*** Fraxiparine; ***Pol.:*** Fraxiparine; Fraxodi; ***Port.:*** Fraxiparina; Fraxodi; ***Rus.:*** Fraxiparine (Фраксипарин); ***S.Afr.:*** Fraxiparine; ***Singapore:*** Fraxiparine; ***Spain:*** Fraxiparina; ***Swed.:*** Fraxiparine†; ***Switz.:*** Fraxiforte; Fraxiparine; ***Thai.:*** Fraxiparine; ***Turk.:*** Fraxiparine; Fraxodi; ***Venez.:*** Fraxiparina.

Naftidrofuryl Oxalate *(BANM, rINNM)*

EU-1806; LS-121; Nafronyl Oxalate *(USAN)*; Naftidrofuril-hidrogén-oxalát; Naftidrofurilio-vandenilio oksalatas; Naftidrofuryl Hydrogen Oxalate; Naftidrofuryl, hydrogénooxalate de; Naftidrofuryl, Oxalate de; Naftidrofuryli hydrogenooxalas; Naftidrofuryli Oxalas; Naftidrofuryl-oxalát; Naftidrofurylväteoxalat; Naftidrofuryylivetyoksalaatti; Oxalato de naftidrofurilo. 2-Diethylaminoethyl 3-(1-naphthyl)-2-tetrahydrofurfurylpropionate hydrogen oxalate.

Нафтидрофурила Оксалат

$C_{24}H_{33}NO_3.C_2H_2O_4$ = 473.6.
CAS — 31329-57-4 (naftidrofuryl); 3200-06-4 (naftidrofuryl oxalate).
ATC — C04AX21.
ATC Vet — QC04AX21.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Naftidrofuryl Hydrogen Oxalate; Naftidrofuryl Oxalate BP 2008). A white or almost white powder. Freely soluble in water; freely soluble or soluble in alcohol; slightly or sparingly soluble in acetone.

Adverse Effects

Naftidrofuryl oxalate given orally may cause nausea and epigastric pain. Rash has been reported occasionally. Hepatitis or hepatic failure has occurred rarely. Convulsions and depression of cardiac conduction may occur after overdosage. After intravenous use cardiac arrhythmias, hypotension, and convulsions have been reported and intravenous preparations have been withdrawn from the market (see below).

◊ In early 1995 the UK CSM published details of adverse reactions to naftidrofuryl.[1] After parenteral doses of naftidrofuryl 47 reports of 79 reactions had been received, the most serious consequences being 9 cases of cardiac arrhythmias, 3 of convulsions, and 2 of hypotension. It was also noted that 2 fatal cases of cardiac arrest had occurred in Germany after bolus intravenous doses and it was stressed that the drug must not be given as a bolus but as a slow intravenous infusion. Additionally, 16 reports, including one fatality, of hepatitis or hepatic failure associated with oral naftidrofuryl had been received although this appeared to be a rare reaction.

Later in 1995, after a review conducted in the UK and Europe, it was announced by the CSM that intravenous naftidrofuryl was to be withdrawn.[2] It was considered that the risks of cardiac and neurological toxicity outweighed the benefits of intravenous dosage in peripheral vascular disease. The oral form of naftidrofuryl would remain available.

1. Committee on Safety of Medicines/Medicines Control Agency. Adverse reactions with naftidrofuryl (Praxilene). *Current Problems* 1995; **21:** 2. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015618&RevisionSelectionMethod=LatestReleased (accessed 08/05/08)
2. Committee on Safety of Medicines/Medicines Control Agency. Withdrawal of naftidrofuryl infusion (Praxilene Forte). *Current Problems* 1995; **21:** 7. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015619&RevisionSelectionMethod=LatestReleased (accessed 08/05/08)

Effects on the kidneys. Calcium oxalate crystals in the renal tubules of 2 patients with acute renal failure[1] were associated with the high amounts of oxalate they had received when naftidrofuryl oxalate was given intravenously.

1. Moesch C, *et al.* Renal intratubular crystallisation of calcium oxalate and naftidrofuryl oxalate. *Lancet* 1991; **338:** 1219–20.

Uses and Administration

Naftidrofuryl oxalate is used as a vasodilator in the treatment of peripheral (p.1178) and cerebral vascular disorders (p.1165). It is also claimed to enhance cellular oxidative capacity thereby protecting cells against the results of ischaemia.

Naftidrofuryl oxalate is given orally in usual doses of 100 to 200 mg three times daily for peripheral vascular disorders and 100 mg three times daily for cerebrovascular disorders.

Naftidrofuryl oxalate has also been given parenterally. However, intravenous use has been associated with serious adverse effects (see above) and intravenous preparations have been withdrawn.

◊ References.

1. De Backer TLM, *et al.* Naftidrofuryl for intermittent claudication. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 08/05/08).

Preparations

BP 2008: Naftidrofuryl Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Iridus†; ***Austria:*** Dusodril; Naftodril; ***Belg.:*** Praxilene; ***Braz.:*** Iridux; ***Cz.:*** Enelbin; ***Fr.:*** Di-Actane; Gevatran; Naftilux; Praxilene; ***Ger.:*** Artocoron†; Azunaftil†; Dusodril; Nafti; Naftilong; ***Gr.:*** Praxilene; ***Hong Kong:*** Praxilene; ***Hung.:*** Naftilong; ***Indon.:*** Frilix; Nafoxal; Praxilene; Vascuprax; ***Irl.:*** Praxilene; ***Ital.:*** Praxilene; ***Mex.:*** Iridus; ***Philipp.:*** Praxilene; ***Port.:*** Praxilene; ***Singapore:*** Praxilene; ***Spain:*** Praxilene; ***Switz.:*** Praxilene; Sodipryl retard; ***Thai.:*** Praxilene; ***UK:*** Praxilene; ***Venez.:*** Fuxaten†; Iridus.

Nasaruplase *(rINN)*

Nasaruplasa; Nasaruplasum; Prourokinase, Glycosylated. Prourokinase (enzyme-activating) (human clone pA3/pD2/pF1 protein moiety), glycosylated.

Назаруплаза

CAS — 99821-44-0.

NOTE. The term prourokinase has been used for both nasaruplase and saruplase (p.1390).

Nasaruplase Beta *(USAN, rINN)*

Abbott-74187; ABT-187; Nasaruplasa beta; Nasaruplase Bêta; Nasaruplasum Beta. Prourokinase (enzyme-activating) human (clone pUK4/pUK18 protein moiety), glycosylated (murine cell line SP2/0).

Назаруплаза Бета

CAS — 136653-69-5.

Profile

Nasaruplase is a thrombolytic under investigation in acute ischaemic stroke.

◊ References.

1. Furlan A, *et al.* Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. *JAMA* 1999; **282:** 2003–11.

Nateplase *(rINN)*

Nateplasa; Natéplase; Nateplasum. A mixture of *N*-[N^2-(*N*-glycyl-L-alanyl)-L-arginyl]plasminogen activator (human tissue-type 1-chain form, protein moiety), glycoform β (major component) and plasminogen activator (human tissue-type 1-chain form, protein moiety), glycoform β.

Натеплаза

CAS — 159445-63-3.

Profile

Nateplase is a thrombolytic related to alteplase (p.1207) that has been used in acute myocardial infarction (p.1175).

Preparations

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