weight heparin, in addition to aspirin, has therefore also been recommended.[3]

1. Royal College of Obstetricians and Gynaecologists. Thromboembolic disease in pregnancy and the puerperium: acute management (February 2007). Available at: http://www.rcog.org.uk/resources/Public/pdf/green_top_28_thromboembolic_minorrevision.pdf (accessed 05/02/08)
2. Royal College of Obstetricians and Gynaecologists. Thromboprophylaxis during pregnancy, labour and after vaginal delivery (January 2004). Available at: http://www.rcog.org.uk/index.asp?PageID=535 (accessed 23/05/05)
3. Bates SM, *et al.* Venous thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008; **133** (suppl): 844S–886S.
4. Rai R, *et al.* Randomised controlled trial of aspirin and aspirin plus heparin in pregnant women with recurrent miscarriage associated with phospholipid antibodies (or antiphospholipid antibodies). *BMJ* 1997; **314:** 253–7.
5. Empson M, *et al.* Recurrent pregnancy loss with antiphospholipid antibody: a systematic review of therapeutic trials. *Obstet Gynecol* 2002; **99:** 135–44.

Reperfusion and revascularisation procedures. Heparin has an established role as an adjunct to percutaneous vascular interventions and bypass surgery, to prevent perioperative thrombosis of the target artery, and is usually given with aspirin or other antiplatelet drugs (see Reperfusion and Revascularisation Procedures, p.1181). High doses are used, particularly in patients undergoing bypass surgery with extracorporeal circulation, and bleeding is a common problem. Although heparin may have an antiproliferative effect, treatment with systemic heparin (unfractionated or low-molecular-weight) appears to have no effect on restenosis;[1] however, a study using local application of enoxaparin suggested that restenosis was reduced.[2] Heparin-coated intracoronary stents have also been used; they improve outcomes compared with balloon angioplasty,[3] but have not been shown to be superior to bare-metal stents[4] or to have any additional effect on restenosis.[5,6] Heparin-coated stents have also been used successfully in cerebrovascular interventions.[7]

1. Grassman ED, *et al.* A randomized trial of the low-molecular-weight heparin certoparin to prevent restenosis following coronary angioplasty. *J Invasive Cardiol* 2001; **13:** 723–8.
2. Kiesz RS, *et al.* Local delivery of enoxaparin to decrease restenosis after stenting: results of initial multicenter trial: Polish-American Local Lovenox NIR Assessment study (The POLONIA study). *Circulation* 2001; **103:** 26–31.
3. Serruys PW, *et al.* Randomised comparison of implantation of heparin-coated stents with balloon angioplasty in selected patients with coronary artery disease (Benestent II). *Lancet* 1998; **352:** 673–81. Correction. *ibid.*; 1478.
4. Mehran R, *et al.* An Internet-based registry examining the efficacy of heparin coating in patients undergoing coronary stent implantation. *Am Heart J* 2005; **150:** 1171–6.
5. Wöhrle J, *et al.* Comparison of the heparin coated vs the uncoated Jostent —no influence on restenosis or clinical outcome. *Eur Heart J* 2001; **22:** 1808–16.
6. Semiz E, *et al.* Comparison of initial efficacy and long-term follow-up of heparin-coated Jostent with conventional NIR stent. *Jpn Heart J* 2003; **44:** 889–98.
7. Parkinson RJ, *et al.* Use of heparin-coated stents in neurovascular interventional procedures: preliminary experience with 10 patients. *Neurosurgery* 2006; **59:** 812–21.

Preparations

BP 2008: Heparin Injection;
USP 31: Anticoagulant Heparin Solution; Heparin Calcium Injection; Heparin Lock Flush Solution; Heparin Sodium Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Calciparine; Cervep; Croneparina; Parinix†; Riveparin; Serianon; Sobrius; Sodiparin; ***Austral.:*** Calcihep†; Calciparine†; Uniparin†; ***Austria:*** Lipohep; Liquemin; Thrombophob; Thrombophob-S; Venoruton Heparin; Viatromb; ***Belg.:*** Calparine; Liquemine†; ***Braz.:*** Actparin; Alimax; Disotron; Heptar; Liquemine; Parinorth†; Trombofob; ***Canad.:*** Hepalean; Hepalean-Lok; ***Cz.:*** Hepa-Gel†; Hepa-Salbe†; Lioton; Lipohep†; Trombex†; Viatromb; ***Fin.:*** Hepaflex; ***Fr.:*** Calciparine; ***Ger.:*** Calciparin; Essaven 60 000; Exhirud Heparin; Hepa-Gel; Hepa-Salbe; Hepaplus†; Hepathromb; Hepathrombin; Liquemin N; Perivar Venensalbe†; Sportino; Thrombareduct; Thrombophob; Traumalitan†; Venalitan; Venoruton Emulgel; Vetren; ***Gr.:*** Calciparine; Croneparina†; Hep Lok†; Hepsal; Monoparin; Multiparin; Pump-Hep†; ***Hong Kong:*** Lioton; ***Hung.:*** Heparibene; Lioton; ***India:*** Beparine; Thrombophob; ***Indon.:*** Inviclot; Thrombophob; ***Irl.:*** Calciparine†; Hep-Rinse†; Heplok†; Hepsal; Minihep†; Monoparin; Multiparin; Unihep†; ***Israel:*** Calciparin; ***Ital.:*** Ateroclar; Bioclarit†; Calciparina; Clarisco; Croneparina; Disebrin; Ecabil; Ecafast; Ecasolv; Emoklar; Epacalcica; Eparical†; Eparinlider; Eparinovis; Eparven; Epsoclar; Epsodil†; Epsodilave; Eudipar†; Flusolv; Hemofluss†; Isoclar; Lioton; Liquemin†; Mica; Normoparin; Pharepa; Reoflus; Sosefluss; Trombolisin; Zepac; ***Mex.:*** Hep-Tec; Inhepar†; Proparin; ***NZ:*** Monoparin†; Multiparin; ***Pol.:*** Coaparin; Heparizen; Lioton; Lipohep; ***Port.:*** Calciparina†; ***Rus.:*** Lioton (Лиотон); Trombless (Тромблесс); ***S.Afr.:*** Calciparine; Thrombophob; ***Spain:*** Calciparina†; Menaven; ***Switz.:*** Calciparine; Demovarin; Gelparine; HepaGel; Hepasol Lipogel; HepaSpray†; Lioton; Liquemine; ***Turk.:*** Calciparine; Liquemine; Nevparin; ***UK:*** Calciparine†; Canusal; Hepsal; Monoparin; Multiparin; ***USA:*** Hep-Lock; Hepflush; ***Venez.:*** Hirox; Liquemine†; Riveparin.

Multi-ingredient: ***Arg.:*** Contractubex; Venostasin; ***Austria:*** Ambenat; Contractubex; Derivon; Dolo-Menthoneurin; Dolobene; Etrat; Heparin Comp; Ichthalgan forte; Lipactin; Pasta Cool; Pertrombon; Sensicutan; Thrombophob; Venobene; Venostasin compositum; Vetren; ***Belg.:*** Lipactin; ***Braz.:*** Contractubex; Dolobene; Trombofob; Venalot H; Venostasin†; ***Canad.:*** Lipactin; ***Cz.:*** Contractubex; Dolo-Rubriment†; Dolobene; Heparin-Gel†; Sensicutan; ***Fin.:*** Lipactin; Trombosol; ***Fr.:*** Cirkan a la Prednacinolone; Esberiven; ***Ger.:*** Contractubex; Dolo-Menthoneurin†; Dolobene; Enelbin-Salbe N†; Essaven Tri-Complex†; Essaven†; Etrat Sportgel†; Heparin Comp†; Heparin Kombi-Gel†; Heparin Plus†; Ichthalgan†; Kelofibrase†; Lipactin; Ostochont†; Sensicutan; Trauma-Puren†; Venengel†; Venoplant AHS†; ***Hong Kong:*** Contractubex; Dolobene; ***Hung.:*** Contractubex; Dolobene; ***India:*** Beparine; Contractubex; Proctosedyl; Thrombophob; ***Indon.:*** Thrombophob; ***Ital.:*** Edeven; Essaven; Flebs; Idracemi Eparina; Luxazone Eparina; Proctosoll; Reparil; Venotrauma†; Via Mal Traumagel; Vit Eparin; Xantervit Eparina; ***Philipp.:*** Contractubex; ***Pol.:*** Alcepalan; Biherpan; Cepan; Contractubex; Dolobene; Savarix; Tointex; ***Port.:*** DM Gel; ***Rus.:*** Contractubex (Контрактубекс); Dolobene (Долобене); Heparin Ointment (Гепариновая Мазь); Hepatrombin (Гепатромбин); Hepatrombin H (Гепатромбин Г); Nigepan (Нигепан); Venolife (Веналайф); ***S.Afr.:*** Essaven†; ***Spain:*** Essavenon; Venacol; ***Switz.:*** Assan; Assan thermo; Butaparin; Contractubex; Dolo-Arthrosenex; Dolobene; Gorgonium; Hepabuzone; Heparinol; Hepathrombine†; Keli-med; Keppur; Lipactin; Lyman; Phlebostasin compositum†; Ralur†; Sportium; Sportusal; Venoplant comp; Venoplant-N†; Venucreme; Venugel.

Heparinoids

Heparinoides.

Profile

The term heparinoid includes heparin derivatives and has also been used more loosely to include naturally occurring and synthetic highly-sulfated polysaccharides of similar structure. Such compounds have been described in many ways; some of the terms used include sulfated glucosaminoglycans; glycosaminoglycan polysulfate compounds; or sulfated mucopolysaccharides.

The following anticoagulants may be described as heparinoids:

- Danaparoid Sodium, p.1255
- Dermatan Sulfate, p.1256
- Pentosan Polysulfate Sodium, p.1367
- Sodium Apolate, p.1397
- Suleparoid, p.1406
- Sulodexide, p.1406

Heparinoid preparations are available with uses ranging from anticoagulation to the alleviation of inflammation (applied topically); some are claimed to have hypolipidaemic properties.

The proprietary names listed in this monograph refer to preparations containing undefined or less readily defined heparinoids that are used in a range of conditions including musculoskeletal and joint disorders, haemorrhoids, lipid disorders, and thromboembolic disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Fleboderma; Hemeran†; Hirudoid; ***Austral.:*** Hirudoid; Lasonil; ***Austria:*** Hemeran; Hirudoid; Lasonil; ***Belg.:*** Hemeran; Hirudoid; Lasonil; ***Braz.:*** Hirudoid; Topcoid; ***Chile:*** Hirudoid; ***Cz.:*** Heparoid; Hirudoid; ***Denm.:*** Hirudoid; ***Fin.:*** Hirudoid; ***Ger.:*** Etrat Sportsalbe MPS†; Hirudoid; Lasonil N†; Sanaven MPS; ***Gr.:*** Hemeran; Lasonil N; ***Hong Kong:*** Bruise Cream†; Hepacare; Hirudoid; ***Hung.:*** Hirudoid; ***India:*** Hirudoid; ***Indon.:*** Hirudoid; ***Ital.:*** Angioflux; Ateran†; Ateroid; Ateroxide; Condral; Erevan†; Glicamin†; Hirudoid; Lasonil†; Lasoven†; Matrix; ***Neth.:*** Hirudoid; Lasonil; ***Norw.:*** Hirudoid; ***NZ:*** Hirudoid; Lasonil; ***Philipp.:*** Hirudoid; ***Pol.:*** Hirudoid; ***Port.:*** Hemeran; Hirudoid; Lasonil; ***Rus.:*** Heparoid (Гепароид); ***Singapore:*** Hirudoid; ***Spain:*** Dinoven; Hirudoid; ***Swed.:*** Hirudoid; ***Switz.:*** Hemeran; Hirudoid; ***Thai.:*** Hirudoid; Varidoid; ***Turk.:*** Hirudoid; Lasonil; ***UK:*** Bruiseze; Hirudoid; Lasonil†; ***Venez.:*** Hirudoid.

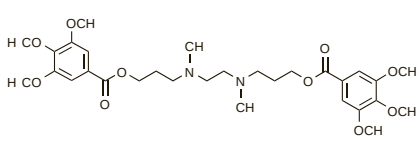
Multi-ingredient: ***Arg.:*** Mantus; ***Austral.:*** Movelat†; ***Austria:*** Lemuval; Mobilat; Mobilisin; Mobilisin plus; Moviflex; ***Belg.:*** Mobilat; Mobilisin; ***Braz.:*** Etrat†; Mobilat; Mobilisin Composto; ***Chile:*** Mobilat; Reparíven; ***Cz.:*** Ibu-Hepa; Ketazon Compositum†; Mobilat; ***Fin.:*** Mobilat; Moviflex†; ***Ger.:*** Dolo Mobilat†; Mobilat Aktiv; Mobilat†; Sanaven†; ***Gr.:*** Bayolin; ***Hong Kong:*** Mobilat†; Prelloran†; ***Hung.:*** Bayolin†; Mobilat N; Mobilisin†; ***Ital.:*** Flebs; Mobilat; Mobilisin; Momendol; Traumal†; ***Mex.:*** Mobilat; ***Neth.:*** Mobilat; ***NZ:*** Movelat†; ***Philipp.:*** Mobilat; ***Pol.:*** Helason; Ibalgin Sport; Lumbolin; Mobilat; ***Port.:*** Anacal; Mobilat; Mobilisin; Rimanal; ***Singapore:*** Mobilat†; ***Spain:*** Lasonil†; Movilat; Movilisin; ***Switz.:*** Dolo-Veniten†; Mobilat N; Mobilisin; Prelloran†; ***Thai.:*** Mobilat; Movelat†; ***UK:*** Anacal; Movelat; ***Venez.:*** Bargonil; Permucal.

Hexobendine *(BAN, USAN, rINN)*

Hexobendina; Hexobendinum.

Гексобендин

$C_{30}H_{44}N_2O_{10}$ = 592.7.
CAS — 54-03-5.
ATC — C01DX06.
ATC Vet — QC01DX06.



Hexobendine Hydrochloride *(BANM, rINNM)*

Hexobendine, Chlorhydrate d'; Hexobendini Hydrochloridum; Hidrocloruro de hexobendina; ST-7090. *NN*′-Ethylenebis(3-methylaminopropyl 3,4,5-trimethoxybenzoate) dihydrochloride.

Гексобендина Гидрохлорид

$C_{30}H_{44}N_2O_{10}$,2HCl = 665.6.
CAS — 50-62-4.
ATC — C01DX06.
ATC Vet — QC01DX06.

Profile

Hexobendine hydrochloride is a vasodilator that has been used in ischaemic heart disease. It is also included in multi-ingredient preparations used in cerebrovascular disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Ustimon.

Multi-ingredient: ***Austria:*** Instenon; ***Hong Kong:*** Instenon; ***Rus.:*** Instenon (Инстенон); ***Thai.:*** Instenon†.

Hirudin

Hirudina; Hirudine.

Profile

Hirudin is a 65-amino-acid protein that is a direct inhibitor of thrombin (see Lepirudin, p.1323). It has been extracted from leeches (p.1323) and this form is used in various topical preparations for peripheral vascular disorders. Recombinant hirudins, such as desirudin (p.1257) and lepirudin (p.1323) and analogues of hirudin, such as bivalirudin (p.1234), are used as anticoagulants.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Exhirud; ***Fr.:*** Hirucreme; ***Ger.:*** Exhirud†.

Multi-ingredient: ***Ger.:*** Haemo-Exhirud†; ***Ital.:*** Hirudex†.

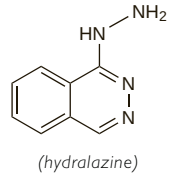
Hydralazine Hydrochloride

(BANM, rINNM)

Apressinum; Hidralazin-hidroklorid; Hidralazino hidrochloridas; Hidrocloruro de hidralazina; Hydralatsiinihydrokloridi; Hydralazin hydrochlorid; Hydralazin Hydrochloridum; Hydralazine, chlorhydrate d'; Hydralazinhydroklorid; Hydralazini hydrochloridum; Hydrallazine Hydrochloride; Idralazina. 1-Hydrazinophthalazine hydrochloride.

Гидралазина Гидрохлорид

$C_8H_8N_4$,HCl = 196.6.
CAS — 86-54-4 (hydralazine); 304-20-1 (hydralazine hydrochloride).
ATC — C02DB02.
ATC Vet — QC02DB02.



(hydralazine)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Hydralazine Hydrochloride). A white or almost white, crystalline powder. Soluble in water; slightly soluble in alcohol; very slightly soluble in dichloromethane. A 2% solution in water has a pH of 3.5 to 4.2. Protect from light.
USP 31 (Hydralazine Hydrochloride). A white to off-white, odourless, crystalline powder. Soluble 1 in 25 of water and 1 in 500 of alcohol; very slightly soluble in ether. A 2% solution in water has a pH of 3.5 to 4.2. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Stability. Discoloration of hydralazine injection was observed on several occasions after storage in a syringe for up to 12 hours.[1] Hydralazine reacts with metals and therefore the injection should be prepared using a nonmetallic filter and should be used as quickly as possible after being drawn through a needle into a syringe.

A study of the rate of degradation of hydralazine hydrochloride, 1 mg/mL in sweetened, aqueous oral liquids showed that glucose, fructose, lactose, and maltose reduced the stability of the drug.[2] In solutions containing mannitol or sorbitol, there was less than 10% degradation of hydralazine after 3 weeks. UK licensed product information states that contact with glucose causes hydralazine to be rapidly broken down and that hydralazine injection is therefore not compatible with glucose solutions.

1. Enderlin G. Discoloration of hydralazine injection. *Am J Hosp Pharm* 1984; **41:** 634.
2. Das Gupta V, *et al.* Stability of hydralazine hydrochloride in aqueous vehicles. *J Clin Hosp Pharm* 1986; **11:** 215–23.

Adverse Effects

Adverse effects are common with hydralazine, particularly tachycardia, palpitations, angina pectoris, severe headache, and gastrointestinal disturbances such as anorexia, nausea, vomiting, and diarrhoea. These adverse effects, and flushing, dizziness, and nasal congestion, which occur less often, may be seen at the start of treatment, especially if the dose is increased quickly. They generally subside with continued treatment. Other less common adverse effects include orthostatic hypoten-