ments such as prostaglandins (see Termination of Pregnancy p.2004). Isosorbide dinitrate has been used similarly after missed abortion.[16]

1. DeSimone CA, *et al.* Intravenous nitro-glycerin aids manual extraction of a retained placenta. *Anesthesiology* 1990; **73:** 787.
2. Lowenwirt IP, *et al.* Safety of intravenous glyceryl trinitrate in management of retained placenta. *Aust N Z J Obstet Gynaecol* 1997; **37:** 20–4.
3. Greenspoon JS, Kovacic A. Breech extraction facilitated by glyceryl trinitrate sublingual spray. *Lancet* 1991; **338:** 124–5.
4. Yadava RP. Sublingual glyceryl trinitrate spray facilitates IUD insertion. *Br J Sex Med* 1990; **17:** 217.
5. Lees C, *et al.* Arrest of preterm labour and prolongation of gestation with glyceryl trinitrate, a nitric oxide donor. *Lancet* 1994; **343:** 1325–6.
6. Smith GN, *et al.* Randomised, double-blind, placebo controlled pilot study assessing nitroglycerin as a tocolytic. *Br J Obstet Gynaecol* 1999; **106:** 736–9.
7. Lees CC, *et al.* Glyceryl trinitrate and ritodrine in tocolysis: an international multicenter randomized study. *Obstet Gynecol* 1999; **94:** 403–8.
8. Bisits A, *et al.* The Randomized Nitric Oxide Tocolysis Trial (RNOTT) for the treatment of preterm labor. *Am J Obstet Gynecol* 2004; **191:** 683–90.
9. El-Sayed YY, *et al.* Randomized comparison of intravenous nitroglycerin and magnesium sulfate for treatment of preterm labor. *Obstet Gynecol* 1999; **93:** 79–83.
10. Duckitt K, Thornton S. Nitric oxide donors for the treatment of preterm labour. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2002 (accessed 28/11/07).
11. Pittrof R, *et al.* Crossover study of glyceryl trinitrate patches for controlling pain in women with severe dysmenorrhoea. *BMJ* 1996; **312:** 884.
12. The Transdermal Nitroglycerine/Dysmenorrhoea Study Group. Transdermal nitroglycerine in the management of pain associated with primary dysmenorrhoea: a multinational pilot study. *J Int Med Res* 1997; **25:** 41–4.
13. Grunewald C, *et al.* Effects of nitroglycerin on the uterine and umbilical circulation in severe preeclampsia. *Obstet Gynecol* 1995; **86:** 600–4.
14. Thomson AJ, *et al.* Randomised trial of nitric oxide donor versus prostaglandin for cervical ripening before first-trimester termination of pregnancy. *Lancet* 1998; **352:** 1093–6.
15. Chen FC-K, *et al.* Isosorbide mononitrate vaginal gel versus misoprostol vaginal gel versus Dilapan-S for cervical ripening before first trimester curettage. *Eur J Obstet Gynecol Reprod Biol* 2008; **138:** 176–9.
16. Arteaga-Troncoso G, *et al.* Intracervical application of the nitric oxide donor isosorbide dinitrate for induction of cervical ripening: a randomised controlled trial to determine clinical efficacy and safety prior to first trimester surgical evacuation of retained products of conception. *BJOG* 2005; **112:** 1615–19.

Oesophageal motility disorders. Achalasia is obstruction caused by failure of the lower oesophageal sphincter to relax and permit passage of food into the stomach. Nitrates such as isosorbide dinitrate have been reported to produce effective relaxation and to reduce symptoms when given sublingually. They have a role when mechanical dilatation of the sphincter or surgery are not feasible (see Oesophageal Motility Disorders, p.1702).

Nitrates may also be employed in oesophageal disorders such as variceal haemorrhage (see below).

Pain. Nitrates have been tried topically in the management of pain. Beneficial results have been reported with glyceryl trinitrate, applied as patches[1] or as a spray,[2] and isosorbide dinitrate spray,[3] in patients with painful diabetic neuropathy. Glyceryl trinitrate has also been used topically in musculoskeletal disorders[4] (see also Soft-tissue Rheumatism, below), and in surgical pain,[5] and intravenously as an adjunct to regional anaesthesia.[6]

Glyceryl trinitrate is also used topically to relieve pain in patients with anal fissure (above). For reference to its use in biliary colic, see Gallstones, above.

1. Rayman G, *et al.* Glyceryl trinitrate patches as an alternative to isosorbide dinitrate spray in the treatment of chronic painful diabetic neuropathy. *Diabetes Care* 2003; **26:** 2697–8.
2. Agrawal RP, *et al.* Glyceryl trinitrate spray in the management of painful diabetic neuropathy: a randomized double blind placebo controlled cross-over study. *Diabetes Res Clin Pract* 2007; **77:** 161–7.
3. Yuen KCJ, *et al.* Treatment of chronic painful diabetic neuropathy with isosorbide dinitrate spray: a double-blind placebo-controlled cross-over study. *Diabetes Care* 2002; **25:** 1699–1703.
4. Paoloni JA, *et al.* Topical nitric oxide application in the treatment of chronic extensor tendinosis at the elbow: a randomized, double-blinded, placebo-controlled clinical trial. *Am J Sports Med* 2003; **31:** 915–20.
5. McCabe JE, *et al.* A randomized controlled trial of topical glyceryl trinitrate before transrectal ultrasonography-guided biopsy of the prostate. *BJU Int* 2007; **100:** 536–8.
6. Sen S, *et al.* The analgesic effect of nitroglycerin added to lidocaine on intravenous regional anesthesia. *Anesth Analg* 2006; **102:** 916–20.

Peripheral vascular disease. In peripheral vascular disease (p.1178) nitrates have been tried as vasodilators and smooth muscle relaxants in order to improve resting blood flow. Glyceryl trinitrate has been applied topically in patients with Raynaud's syndrome[1-3] and in distal limb ischaemia[4] resulting in some benefit but this form of therapy is not widely used in these disorders.

1. Franks AG. Topical glyceryl trinitrate as adjunctive treatment in Raynaud's disease. *Lancet* 1982; **i:** 76–7.
2. Coppock JS, *et al.* Objective relief of vasospasm by glyceryl trinitrate in secondary Raynaud's phenomenon. *Postgrad Med J* 1986; **62:** 15–18.
3. Teh LS, *et al.* Sustained-release transdermal glyceryl trinitrate patches as a treatment for primary and secondary Raynaud's phenomenon. *Br J Rheumatol* 1995; **34:** 636–41.
4. Fletcher S, *et al.* Locally applied transdermal nitrate patches for the treatment of ischaemic rest pain. *Int J Clin Pract* 1997; **51:** 324–5.

Pulmonary hypertension. Glyceryl trinitrate reduces total pulmonary resistance in most patients with pulmonary arterial hypertension (p.1179),[1,2] including when given by inhalation.[3] However, other vasodilators such as calcium-channel blockers, epoprostenol, or bosentan are generally preferred for long-term treatment.

1. Pearl RG, *et al.* Acute hemodynamic effects of nitroglycerin in pulmonary hypertension. *Ann Intern Med* 1983; **99:** 9–13.
2. Weir EK, *et al.* The acute administration of vasodilators in primary pulmonary hypertension. *Am Rev Respir Dis* 1989; **140:** 1623–30.
3. Goyal P, *et al.* Efficacy of nitroglycerin inhalation in reducing pulmonary arterial hypertension in children with congenital heart disease. *Br J Anaesth* 2006; **97:** 208–14.

Quinine oculotoxicity. Intravenous nitrate has been suggested for the management of quinine oculotoxicity (p.613) and its benefit may be due to an increase in retinal vascular bed flow.[1]

1. Moore D, *et al.* Research into quinine ocular toxicity. *Br J Ophthalmol* 1992; **76:** 703.

Soft-tissue rheumatism. There is evidence from animal studies that nitric oxide plays an important role in tendon healing, and randomised studies in patients with tennis elbow (epicondylitis), Achilles tendinosis (tendinitis), and supraspinatus tendinosis showed enhanced subjective and objective recovery when a glyceryl trinitrate patch (releasing 1.25 mg over 24 hours) was applied over the area of tenderness once daily.[1] Glyceryl trinitrate has also been tried in musculoskeletal pain (see Pain, above). For the general management of soft-tissue rheumatism see p.13.

1. Murrell GAC. Using nitric oxide to treat tendinopathy. *Br J Sports Med* 2007; **41:** 227–31.

Variceal haemorrhage. The usual treatment in variceal haemorrhage (p.2346) is injection sclerotherapy or banding ligation which may be performed during the emergency endoscopy procedure. Where endoscopy is unavailable drug therapy may be used; it may also have a role when sclerotherapy fails and some have suggested that initial drug therapy may be preferable to sclerotherapy. Vasoconstrictors that are used include vasopressin and its analogue terlipressin, given with glyceryl trinitrate which counteracts the adverse cardiac effects of vasopressin while potentiating its beneficial effects on portal pressure; somatostatin is also used.

Prophylaxis of a first bleed in patients with portal hypertension is controversial since about 70% of patients who have varices will never bleed. It is postulated that a reduction in portal pressure to below 12 mmHg is necessary to reduce the incidence of variceal bleeding and that treatment with beta blockers alone does not achieve this. More effective drugs are being sought and isosorbide mononitrate (as adjunctive therapy with a beta blocker) is under investigation, both for prophylaxis of a first bleed[1,2] and in the prevention of rebleeding.[3] Early emergency treatment (before endoscopy) with terlipressin given intravenously and glyceryl trinitrate transdermally controlled bleeding and lowered mortality rates in patients with gastrointestinal bleeding and a history or clinical signs of cirrhosis.[4] However, use of oral isosorbide mononitrate with somatostatin infusion for acute variceal bleeding was less effective than somatostatin alone and induced more adverse effects.[5]

1. Angelico M, *et al.* Isosorbide-5-mononitrate versus propranolol in the prevention of first bleeding in cirrhosis. *Gastroenterology* 1993; **104:** 1460–5.
2. Merkel C, *et al.* Randomised trial of nadolol alone or with isosorbide mononitrate for primary prophylaxis of variceal bleeding in cirrhosis. *Lancet* 1996; **348:** 1677–81.
3. Villanueva C, *et al.* Nadolol plus isosorbide mononitrate compared with sclerotherapy for the prevention of variceal rebleeding. *N Engl J Med* 1996; **334:** 1624–9.
4. Levacher S, *et al.* Early administration of terlipressin plus glyceryl trinitrate to control active upper gastrointestinal bleeding in cirrhotic patients. *Lancet* 1995; **346:** 865–8.
5. Junquera F, *et al.* Somatostatin plus isosorbide 5-mononitrate versus somatostatin in the control of acute gastro-oesophageal variceal bleeding: a double blind, randomised, placebo controlled clinical trial. *Gut* 2000; **46:** 127–32.

Venepuncture. Glyceryl trinitrate patches applied to skin adjacent to intravenous infusion sites are used in the prophylactic treatment of phlebitis and extravasation.[1]

Local application of glyceryl trinitrate 1 to 2 mg as ointment was found to be a useful aid to venepuncture in a study of 50 patients undergoing surgery,[2] but conflicting results have been reported in children and neonates.[3,4]

1. Tjon JA, Ansani NT. Transdermal nitroglycerin for the prevention of intravenous infusion failure due to phlebitis and extravasation. *Ann Pharmacother* 2000; **34:** 1189–92.
2. Hecker JF, *et al.* Nitroglycerine ointment as an aid to venepuncture. *Lancet* 1983; **i:** 332–3.
3. Vaksmann G, *et al.* Nitroglycerine ointment as aid to venous cannulation in children. *J Pediatr* 1987; **111:** 89–91.
4. Maynard EC, Oh W. Topical nitroglycerin ointment as an aid to insertion of peripheral venous catheters in neonates. *J Pediatr* 1989; **114:** 474–6.

Preparations

BP 2008: Glyceryl Trinitrate Sublingual Spray; Glyceryl Trinitrate Tablets; Glyceryl Trinitrate Transdermal Patches; ***USP 31:*** Nitroglycerin Injection; Nitroglycerin Ointment; Nitroglycerin Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Dauxona; Enetege; Minitran†; Niglinar; Nitradisc†; Nitro-Dur; Nitroderm TTS; Nitrodom; Nitrogray; ***Austral.:*** Anginine; Lycinate; Minitran; Nitro-Dur; Nitrolingual; Rectogesic; Transiderm-Nitro; ***Austria:*** Cordiplast; Deponit; Minitran; Nitro; Nitro Mack; Nitro Pohl; Nitro-Dur; Nitroderm; Nitrolingual; Perlinganit; ***Belg.:*** Deponit; Diafusor; Minitran; Nitro-Dyl†; Nitroderm; Nitrolingual; Nysconitrine; Trinipatch; Willlong; ***Braz.:*** Nitradisc; Nitroderm TTS; Nitronal†; Tridil; ***Canad.:*** Gen-Nitro; Minitran; Nitro-Dur; Nitroject; Nitrol; Nitrolingual; Nitrong†; Nitrostat; Rho-Nitro; Transderm-Nitro; ***Chile:*** Angiolingual; Nitrocor; Nitroderm; Nitronal†; ***Cz.:*** Deponit†; Maycor Nitrospray†; Minitran†; Nit-Ret; Nitrangin†; Nitrilex†; Nitro Mack†; Nitro Pohl; Nitrolingual†; Nitromint; Perlinganit; Rectogesic; ***Denm.:*** Buccard; Discotrine; Glytrin; Nitrolingual; Nitromex; ***Fin.:*** Deponit; Minitran; Nitro; Nitromex; Perlinganit; Transiderm-Nitro; ***Fr.:*** Cordipatch; Diafusor; Discotrine; Epinitril; Lenitral†; Natispray; Nitriderm TTS; Rectogesic; Trinipatch; ***Ger.:*** Aquo-Trinitrosan; Corangin Nitrospray; Coro-Nitro†; Deponit; Gepan†; MinitranS; neos nitro OPT†; Nitrangin; Nitro Mack†; Nitro Solvay; Nitro-Pflaster-ratiopharm TL†; Nitroderm TTS; Nitrokor†; Nitrolingual; Perlinganit; Trinitrosan; ***Gr.:*** Cardiplast; Epinitril; Nitro Mack†; Nitrodyl; Nitrolingual; Nitrong; Nitroretard; Nitrosylon; Pancoran; Rectogesic; Sodemethin†; Supranitrin; Trinipatch; Trinitrine Simple Laleuf†; ***Hong Kong:*** Angised; Deponit; Lenitral†; Nitro Mack; Nitro Pohl†; Nitro-Dur; Nitrocine; Nitroderm TTS; Nitrolingual; Tridil†; ***Hung.:*** Nitro Pohl; Nitro-Dur; Nitroderm TTS; Nitrolingual; Nitromint; Perlinganit†; Sustac; ***India:*** Angised; Millisrol; Myonit; Myovin; Nitrocontin; Nitroderm TTS; Nitrogesic; Nitrolingual; ***Indon.:*** Nitrocine; Nitrokaf; ***Irl.:*** Deponit; Epinitril†; Glytrin; Nitro-Dur; Nitrocine; Nitrolingual; Nitromin; Nitronal; Suscard; Sustac; Transiderm-Nitro; ***Israel:*** Angised†; Deponit; Nitrocine; Nitroderm TTS; Nitrolingual; Nitronal; Trinipatch†; ***Ital.:*** Adesitrin; Deponit; Dermatrans; Epinitril; Keritrina; Minitran; Natispray; Nitraket; Nitro-Dur; Nitrocor; Nitroderm TTS; Nitrosylon; Perganit; Top-Nitro; Triniplas; Trinitrina; Venitrin; ***Jpn:*** Millisrol; ***Malaysia:*** Deponit; Glytrin†; Nitrocine; Nitroderm; ***Mex.:*** Anglix; Cardinit; Minitran; Nitradisc; Nitro-Dur; Nitroder; Nitroderm TTS; ***Neth.:*** Deponit; Glytrin; Lenitral; Minitran; Nitro Pohl; Nitro-Dur; Nitrolingual; Transiderm-Nitro; Trinipatch; ***Norw.:*** Minitran; Nitro-Dur; Nitrolingual; Nitromex; Nitroven; Transiderm-Nitro; ***NZ:*** Anginine†; Glytrin; Lycinate; Minitran; Nitroderm; Nitrolingual; Nitronal; ***Philipp.:*** Deponit; Minitran; Nitrolingual; Nitronal; Nitrostat; Perlinganit; Transderm-Nitro; ***Pol.:*** Nitracor; Nitrocard; Nitroderm; Nitromint; Perlinganit; Sustonit; Trimonit; ***Port.:*** Dermatrans; Diafusor; Discotrine; Epinitril; Glytrin; Nitradisc; Nitro-Dur; Nitroderm TTS; Nitromint; Plastranit; Rectogesic; Trinipatch†; ***Rus.:*** Deponit (Депонит); Nirmin (Нирмин); Nitro (Нитро); Nitrocor (Нитрокор); Nitroject (Нитроджект); Nitromint (Нитроминт); Nitrong (Нитронг); Nitrospray (Нитроспрей); Perlinganit (Перлинганит); Sustac (Сустак); Sustonit (Сустонит); ***S.Afr.:*** Angised; Nitrocine; Nitrolingual; Tridil; ***Singapore:*** Angised; Deponit; Glytrin†; Nitro Mack†; Nitrocine; Rectogesic; ***Spain:*** Cordiplast; Dermatrans; Diafusor; Epinitril; Minitran; Nitradisc; Nitro-Dur; Nitroderm; Nitroplast; Solinitrina; Trinipatch; Trinispray; Vernies; ***Swed.:*** Glytrin; Minitran; Nitrolingual; Nitromex; Perlinganit†; Suscard; Transiderm-Nitro; ***Switz.:*** Deponit; Minitran; Nitro Mack; Nitro-Dur; Nitroderm TTS; Nitrolingual; Nitronal; Perlinganit; Trinitrine; ***Thai.:*** Amitacon†; Angised†; Glytrin; Nitro Mack†; Nitrocine; Nitroderm; Nitroject; ***Turk.:*** Deponit; Nitroderm TTS; Nitrolingual; Perlinganit; ***UAE:*** Cardispray†; ***UK:*** Coro-Nitro; Deponit; Glytrin; Minitran; Nitro-Dur; Nitrocine; Nitrolingual; Nitromin; Nitronal; Percutol; Rectogesic; Suscard; Sustac†; Transiderm-Nitro; Trintek; ***USA:*** Minitran; Nitrek; Nitro-Bid; Nitro-Derm; Nitro-Dur; Nitro-Time; Nitrodisc; Nitrogard; Nitroglyn†; Nitrolingual; NitroMist; Nitrong†; NitroQuick; Nitrostat; NitroTab†; Transderm-Nitro; Transdermal-NTG; Tridil†; ***Venez.:*** Minitran†; Nitro Mack; Nitrocor; Nitroderm; Tridil†.

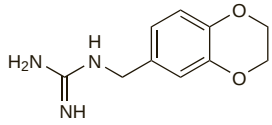
Multi-ingredient: ***Arg.:*** Trinitron; ***Austria:*** Myocardon; Percucor†; Spasmocor; ***Ger.:*** Nitrangin compositum†; ***Pol.:*** Pentaerythritol Compositum; ***Spain:*** Cafinitrina; ***USA:*** Emergent-Ez.

Guabenxan *(rINN)*

Guabenxán; Guabenxane; Guabenxanum. (1,4-Benzodioxan-6-ylmethyl)guanidine.

Гуабенксан

$C_{10}H_{13}N_3O_2$ = 207.2.
CAS — 19889-45-3.



Profile
Guabenxan is an antihypertensive with properties similar to guanethidine (below). It has been given orally as the sulfate.

Guanabenz Acetate *(USAN, rINNM)*

Acetato de guanabenzo; Guanabenz, Acétate de; Guanabenzi Acetas; NSC-68982 (guanabenz); Wy-8678 (guanabenz). (2,6-Dichlorobenzylideneamino)guanidine acetate.

Гуанабенза Ацетат

$C_8H_8Cl_2N_4,C_2H_4O_2$ = 291.1.
CAS — 5051-62-7 (guanabenz); 23256-50-0 (guanabenz acetate).