It is probably not necessary to stop reserpine during anaesthesia, although the effects of CNS depressants may be enhanced by reserpine.

Interactions
Patients taking reserpine may be hypersensitive to adrenaline and other direct-acting sympathomimetics, which should not be given except to antagonise reserpine. The effects of indirect-acting sympathomimetics such as ephedrine may be decreased by reserpine. The hypotensive effects of reserpine are enhanced by thiazide diuretics and other antihypertensives. Reserpine may cause excitation and hypertension in patients receiving MAOIs. Use of digitalis or quinidine with reserpine may cause cardiac arrhythmias. Reserpine may enhance the effects of CNS depressants.

Antiparkinsonian drugs. For the inhibitory effect of reserpine on the antiparkinsonian actions of *levodopa*, see Antihypertensives, p.807.

Pharmacokinetics
Reserpine is absorbed from the gastrointestinal tract with a bioavailability of 50%. It is extensively metabolised and is excreted slowly in the urine and faeces. In the first 4 days, about 8% is excreted in the urine, mainly as metabolites, and about 60% in the faeces, mainly unchanged. Reserpine crosses the placenta and the blood-brain barrier and also appears in breast milk.

Uses and Administration
Reserpine is an alkaloid obtained from the roots of certain species of *Rauwolfia* (Apocynaceae), mainly *Rauwolfia serpentina* and *R. vomitoria*, or by synthesis. The material obtained from natural sources may contain closely related alkaloids.

Reserpine is an antihypertensive drug that causes depletion of noradrenaline stores in peripheral sympathetic nerve terminals and depletion of catecholamine and serotonin stores in the brain, heart, and many other organs resulting in a reduction in blood pressure, bradycardia, and CNS depression. The hypotensive effect is mainly due to a reduction in cardiac output and a reduction in peripheral resistance. Cardiovascular reflexes are partially inhibited, but orthostatic hypotension is rarely a problem at the doses used in hypertension. When given orally the full effect is only reached after several weeks of treatment and persists for up to 6 weeks after treatment is stopped.

Reserpine has been used in the management of hypertension (p.1171) and in chronic psychoses (p.954) such as schizophrenia. It has also been used in the treatment of Raynaud's syndrome (see Vasospastic Arterial Disorders, p.1188).

In **hypertension**, reserpine may be given orally in an initial dose of up to 500 micrograms daily for about 2 weeks, subsequently reduced to the lowest dose necessary to maintain the response; some sources recommend an initial dose of 50 to 100 micrograms. A maintenance dose of about 100 to 250 micrograms daily may be adequate and 500 micrograms should not normally be exceeded. To reduce adverse effects and tolerance smaller doses of reserpine may be used with a thiazide diuretic.

Reserpine has been used in chronic **psychoses** in daily doses of up to 1 mg.

Preparations
USP 31: Reserpine and Chlorothiazide Tablets; Reserpine and Hydrochlorothiazide Tablets; Reserpine Elixir; Reserpine Injection; Reserpine Tablets; Reserpine, Hydralazine Hydrochloride, and Hydrochlorothiazide Tablets.

Proprietary Preparations (details are given in Part 3)
Braz.: Ortoserpina†; ***Indon.:*** Resapin; Serpasil; ***Port.:*** Serfinato†.

Multi-ingredient: ***Arg.:*** Hygroton-Reserpina†; Normatensil†; ***Austria:*** Brinerdin; Darebon; ***Braz.:*** Adelfan-Esidrex†; Higroton Reserpina; Id Sedin†; Vagoplex†; ***Cz.:*** Crystepin; Neocrystepin; ***Fr.:*** Tensionorme; ***Ger.:*** Adelphan-Esidrix†; Barotonal†; Bendigon N†; Briserin N; Darebon†; Dislapin†; Durotan†; Modenol†; Tri-Thiazid Reserpin†; Triniton; ***Gr.:*** Hygroton-Reserpine; Neourizine; ***Hong Kong:*** Adelphane-Esidrex; ***India:*** Adelphane; Adelphane-Esidrex; ***Indon.:*** Dellasidrex; Ser-Ap-Es; ***Ital.:*** Brinerdina; Igroton-Reserpina; ***Mex.:*** Higroton-Res; ***Pol.:*** Normatens; ***Port.:*** Brinerdine†; ***Rus.:*** Adelphane-Esidrex (Адельфан-эзидрекс); Crystepin (Кристепин); Triresid K (Тирезид К); ***S.Afr.:*** Brinerdin; Hygroton-Reserpine†; Protensin-M; ***Spain:*** Adelfan-Esidrex†; Brinerdina†; Higrotona Reserpina†; Tensiocomplet; ***Switz.:*** Adelphan-Esidrex; Brinerdine; Hygroton-Reserpine; ***Thai.:*** Bedin; Brinerdin; Hydrares; Hyperdine†; Hypery†; Iso-Triraupin†; Mano-Ap-Es; Medeserpine Co†; Reser; Ser-Ap-Es; ***Turk.:*** Adelphan; Adelphan-Esidrex; Regroton; ***USA:*** Demi-Regroton; Diupres; Diutensen-R†; Hydrap-ES†; Hydro-Serp†; Hydropres; Hydroserpine†; Marpres; Metatensin†; Regroton; Renese R†; Salutensin†; Ser-Ap-Es†; Tri-Hydroserpine†.

Reteplase *(BAN, USAN, rINN)*

BM-06.022; Reteplaasi; Reteplas; Reteplasa; Rétéplase; Reteplasum; rPA. 173-L-Serine-174-L-tyrosine-175-L-glutamine-173–527-plasminogen activator (human tissue-type).

Ретеплаза

$C_{1736}H_{2653}N_{499}O_{522}S_{22}$ = 39571.1.

CAS — 133652-38-7.

ATC — B01AD07.

ATC Vet — QB01AD07.

Description. Reteplase is a nonglycosylated protein produced by recombinant DNA technology. It consists of selected domains of human tissue plasminogen activator.

Incompatibility. Reteplase may precipitate out of solution if it is given with heparin in the same intravenous line.[1] Reteplase and heparin must therefore be given separately; if a single intravenous line is used it must be flushed thoroughly with sodium chloride 0.9% or with glucose 5% before, and after, reteplase injection.

1. Committee on Safety of Medicines/Medicines Control Agency. Reteplase (Rapilysin): incompatibility with heparin. *Current Problems* 2000; **26:** 5. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007462&RevisionSelectionMethod=LatestReleased (accessed 20/06/06)

Adverse Effects, Treatment, and Precautions
As for Streptokinase, p.1402. Allergic reactions may be less likely to occur with reteplase than with streptokinase.

Interactions
As for Streptokinase, p.1404.

Pharmacokinetics
Based on fibrinolytic activity, reteplase is reported to have an initial half-life of about 14 minutes and a terminal half-life of 1.6 hours in patients with myocardial infarction.

Uses and Administration
Reteplase is a thrombolytic drug. It converts plasminogen to plasmin, a proteolytic enzyme which has fibrinolytic effects. The mechanisms of fibrinolysis are discussed further under Haemostasis and Fibrinolysis on p.1045. Reteplase has some fibrin specificity (see Thrombolytics, p.1156).

Reteplase is used similarly to streptokinase (p.1404) in acute myocardial infarction (p.1175). It is given intravenously as soon as possible after the onset of symptoms. The dose is 10 units given by slow intravenous injection (but over not more than 2 minutes), and this dose of 10 units is repeated once, 30 minutes after the start of the first injection.

◊ General references.

1. Noble S, McTavish D. Reteplase: a review of its pharmacological properties and clinical efficacy in the management of acute myocardial infarction. *Drugs* 1996; **52:** 589–605.
2. Wooster MB, Luzier AB. Reteplase: a new thrombolytic for the treatment of acute myocardial infarction. *Ann Pharmacother* 1999; **33:** 318–24.
3. Llevadot J, *et al.* Bolus fibrinolytic therapy in acute myocardial infarction. *JAMA* 2001; **286:** 442–9.
4. Simpson D, *et al.* Reteplase: a review of its use in the management of thrombotic occlusive disorders. *Am J Cardiovasc Drugs* 2006; **6:** 265–85.

Catheters and cannulas. Reteplase has been used[1] successfully to clear thrombi in central venous catheters. A single dose of 0.4 units of reteplase was given as a 1 unit/mL solution, further diluted to the volume required to fill the catheter. The minimum dwell time was 30 minutes and the solution was aspirated after treatment. A second dose of 0.4 units was given if necessary.

1. Owens L. Reteplase for clearance of occluded venous catheters. *Am J Health-Syst Pharm* 2002; **59:** 1638–40.

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Rapilysin; ***Austria:*** Rapilysin; ***Belg.:*** Rapilysin; ***Canad.:*** Retavase; ***Cz.:*** Rapilysin; ***Denm.:*** Rapilysin; ***Fin.:*** Rapilysin; ***Fr.:*** Rapilysin; ***Ger.:*** Rapilysin; ***Gr.:*** Rapilysin; Repilysin†; ***Irl.:*** Rapilysin; ***Ital.:*** Rapilysin; ***Neth.:*** Rapilysin; ***Norw.:*** Rapilysin; ***NZ:*** Rapilysin; ***Port.:*** Rapilysin; ***Spain:*** Rapilysin; ***Swed.:*** Rapilysin; ***Switz.:*** Rapilysin; ***UK:*** Rapilysin; ***USA:*** Retavase.

Reviparin Sodium *(BAN, rINN)*

Revipariininatrium; Reviparina sódica; Réviparine Sodique; Reviparinnatrium; Reviparinum Natricum.

Ревипарин Натрий

CAS — 9041-08-1.

ATC — B01AB08.

ATC Vet — QB01AB08.

Description. Reviparin sodium 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 3150 and 5150 with a characteristic value of about 4150. The degree of sulfation is about 2.1 per disaccharide unit.

Units
As for Low-molecular-weight Heparins, p.1329.

Adverse Effects, Treatment, and Precautions
As for Low-molecular-weight Heparins, p.1329.

Severe bleeding with reviparin sodium may be reduced by the slow intravenous injection of protamine sulfate; about 1.2 mg of protamine sulfate is stated to inhibit the effect of 100 units of reviparin sodium.

Interactions
As for Low-molecular-weight Heparins, p.1329.

Pharmacokinetics
Reviparin sodium is absorbed after subcutaneous administration with a bioavailability of about 95%. Peak plasma concentrations are reached after about 3 hours. Reviparin sodium is excreted mainly in the urine; the elimination half-life is about 3 hours.

Uses and Administration
Reviparin sodium is a low-molecular-weight heparin (p.1329) with anticoagulant activity. It is used in the prevention and treatment of venous thromboembolism (p.1189) and has been used to prevent coagulation during haemodialysis.

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.

In the prophylaxis of venous thromboembolism during surgery, reviparin sodium is given subcutaneously in a dose of 1432 units once daily, with the first dose given 2 hours before surgery.

◊ References.

1. Wellington K, *et al.* Reviparin: a review of its efficacy in the prevention and treatment of venous thromboembolism. *Drugs* 2001; **61:** 1185–209.
2. Yusuf S, *et al.* CREATE Trial Group Investigators. Effects of reviparin, a low-molecular-weight heparin, on mortality, reinfarction, and strokes in patients with acute myocardial infarction presenting with ST-segment elevation. *JAMA* 2005; **293:** 427–35.

Preparations
Proprietary Preparations (details are given in Part 3)
Austria: Clivarin; ***Cz.:*** Clivarin; ***Denm.:*** Clivarin†; ***Fr.:*** Clivarine†; ***Ger.:*** Clivarin; ***Gr.:*** Clivarin; ***Hong Kong:*** Clivarine; ***Hung.:*** Clivarin; ***India:*** Clivarine; ***Ital.:*** Clivarina; ***Pol.:*** Clivarin; ***Port.:*** Clivarin; ***UK:*** Clivarine†.

Rilmenidine Phosphate *(rINNM)*

Fosfato de rilmenidina; Oxaminozoline Phosphate; Rilmenidiinidivetyfosfaatti; Rilmenidin Dihdrojen Fosfat; Rilmenidin fosfát; Rilmenidin-dihidrogén-foszfát; Rilmenidindivätefosfat; Rilmenidine Acid Phosphate; Rilmenidine Dihydrogen Phosphate; Rilménidine, dihydrogénophosphate de; Rilmenidine Hydrogen Phosphate; Rilménidine, Phosphate de; Rilmenidini dihydrogenophosphas; Rilmenidini Phosphas; Rilmenidino divandenilio fosfatas; S-3341-3. 2-[(Dicyclopropylmethyl)amino]-2-oxazoline phosphate.

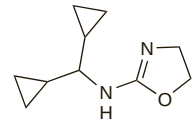
Рильменидина Фосфат

$C_{10}H_{16}N_2O,H_3PO_4$ = 278.2.

CAS — 54187-04-1 (rilmenidine); 85409-38-7 (rilmenidine phosphate).

ATC — C02AC06.

ATC Vet — QC02AC06.



(rilmenidine)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Rilmenidine Dihydrogen Phosphate). A white or almost white powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane.

Profile
Rilmenidine is a centrally acting antihypertensive that appears to act through stimulation of central imidazoline receptors and also has alpha$_2$-adrenoceptor agonist activity. It has general properties similar to those of clonidine (p.1247), but is reported to cause less sedation and central adverse effects. In the management of hypertension (p.1171) it has been given as the phosphate, but doses are expressed in terms of the base. Rilmenidine phosphate 1.5 mg is equivalent to about 1 mg of rilmenidine. The dose is 1 mg daily, as a single oral dose; this may be increased if necessary, after 1 month, to 2 mg daily in divided doses.

◊ References.

1. Bousquet P, Feldman J. Drugs acting on imidazoline receptors: a review of their pharmacology, their use in blood pressure control and their potential interest in cardioprotection. *Drugs* 1999; **58:** 799–812.