tions of alkali hydroxides and slightly soluble in dilute acids. Protect from light.

USP 31 (Torsemide). A white to off-white, crystalline powder. Practically insoluble in water and in ether; slightly soluble in alcohol, in methyl alcohol, in 0.1N sodium hydroxide, and in 0.1N hydrochloric acid; very slightly soluble in acetone and in chloroform.

Adverse Effects and Precautions

As for Furosemide, p.1292.

Interactions

As for Furosemide, p.1293.

Pharmacokinetics

Torasemide is well absorbed from the gastrointestinal tract. Peak serum concentrations are achieved within 1 hour of oral doses. Torasemide is metabolised by the cytochrome P450 isoenzyme CYP2C9, which shows genetic polymorphism. Metabolism takes place in the liver and inactive metabolites are excreted in the urine. The elimination half-life of torasemide is about 3.5 hours. Torasemide is extensively bound to plasma proteins. In patients with heart failure both hepatic and renal clearance are reduced. In patients with renal impairment, the renal clearance is reduced but total plasma clearance is not significantly altered.

◊ References.

1. Knauf H, Mutschler E. Clinical pharmacokinetics and pharmacodynamics of torasemide. *Clin Pharmacokinet* 1998; **34:** 1–24.
2. Vormfelde SV, *et al.* CYP2C9 polymorphisms and the interindividual variability in pharmacokinetics and pharmacodynamics of the loop diuretic drug torsemide. *Clin Pharmacol Ther* 2004; **76:** 557–66.

Uses and Administration

Torasemide is a loop diuretic with actions similar to those of furosemide (p.1294).

Torasemide is used for oedema associated with heart failure (p.1165), including pulmonary oedema, and with renal and hepatic disorders. It is also used in the treatment of hypertension (p.1171), either alone or with other antihypertensives.

Diuresis after oral use starts within 1 hour, reaches a maximum in about 1 to 2 hours, and lasts for up to 8 hours; after intravenous injection its effects are evident within 10 minutes but like oral use can last up to 8 hours.

In the treatment of **oedema** the usual oral dose is 5 mg once daily increased according to response to 20 mg once daily; doses of up to 40 mg daily have been required in some patients. Torasemide may also be given intravenously in usual initial doses of 10 to 20 mg daily. Higher doses may sometimes be necessary, especially in oedema of renal origin; the dose should be increased stepwise as necessary to a maximum of 200 mg daily, although doses should not exceed 40 mg daily in patients with hepatic cirrhosis.

In the treatment of **hypertension** torasemide is given in initial oral doses of 2.5 to 5 mg daily; US licensed product information allows the dose to be increased to 10 mg daily if required, although UK licensed product information suggests that doses above 5 mg are unlikely to produce additional benefit.

◊ Reviews.

1. Blose JS, *et al.* Torsemide: a pyridine-sulfonylurea loop diuretic. *Ann Pharmacother* 1995; **29:** 396–402.
2. Dunn CJ, *et al.* Torasemide: an update of its pharmacological properties and therapeutic efficacy. *Drugs* 1995; **49:** 121–42.
3. Brater DC. Benefits and risks of torasemide in congestive heart failure and essential hypertension. *Drug Safety* 1996; **14:** 104–120.
4. Ishido H, Senzaki H. Torasemide for the treatment of heart failure. *Cardiovasc Hematol Disord Drug Targets* 2008; **8:** 127–32.

Preparations

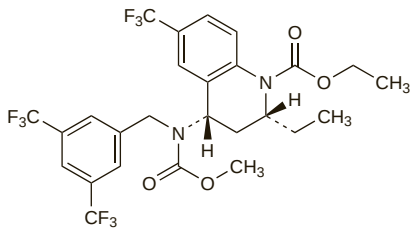
Proprietary Preparations (details are given in Part 3)
Arg.: Torem; ***Austria:*** Unat; ***Belg.:*** Torrem; ***Chile:*** Unat†; ***Cz.:*** Diuver; Trifas†; ***Ger.:*** Toracard; Toragamma; Torasid; Torem; Unat; ***Hong Kong:*** Unat; ***India:*** Dytor; ***Ital.:*** Diuremid; Diuresix; Toradiur; ***Jpn:*** Luprac; ***Pol.:*** Diuver; Trifas; ***Rus.:*** Diuver (Диувер); ***S.Afr.:*** Unat; ***Spain:*** Dilutol; Isodiur; Sutril; Tadegan; ***Swed.:*** Torem; ***Switz.:*** Toramide; Torasem; Torasis; Torem; ***Thai.:*** Unat; ***UK:*** Torem; ***USA:*** Demadex.

Torcetrapib *(USAN, rINN)*

CP-529414; Torcétrapib; Torcetrapibum. Ethyl (2*R*,4*S*)-4-{[3,5-bis(trifluoromethyl)benzyl](methoxycarbonyl)amino}-2-ethyl-6-(trifluoromethyl)-3,4-dihydroquinoline-1(2*H*)-carboxylate.

Торцетрапиб

$C_{26}H_{25}F_9N_2O_4$ = 600.5.
CAS — 262352-17-0.



Profile

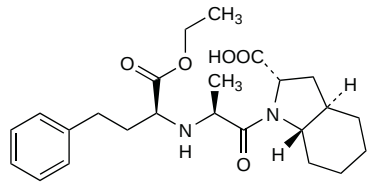
Torcetrapib is a cholesteryl ester transfer protein inhibitor. It increases plasma concentrations of high-density lipoprotein (HDL)-cholesterol and has been investigated in the management of lipid disorders. Development was stopped after the finding of increased mortality associated with torcetrapib in randomised, controlled studies.

Trandolapril *(BAN, rINN)*

RU-44570; Trandolapriili; Trandolaprilum; Trandolapryl. Ethyl (2*S*,3a*R*,7a*S*)-1-{(*S*)-*N*-[(*S*)-1-carboxy-3-phenylpropyl]alanyl}hexahydro-2-indolinecarboxylate; (2*S*,3a*R*,7a*S*)-1-{*N*-[(*S*)-1-Ethoxycarbonyl-3-phenylpropyl]-L-alanyl}perhydroindole-2-carboxylic acid.

Трандолаприл

$C_{24}H_{34}N_2O_5$ = 430.5.
CAS — 87679-37-6.
ATC — C09AA10.
ATC Vet — QC09AA10.



Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Trandolapril). A white or almost white powder. Practically insoluble in water; sparingly soluble in dehydrated alcohol; freely soluble in dichloromethane. Protect from light.

Adverse Effects, Treatment, and Precautions

As for ACE inhibitors, p.1193.

Interactions

As for ACE inhibitors, p.1196.

Pharmacokinetics

Trandolapril acts as a prodrug of the diacid trandolaprilat, its active metabolite. After oral doses of trandolapril the bioavailability of trandolaprilat is 40 to 60%. Trandolapril is metabolised in the liver to trandolaprilat and to some inactive metabolites. Peak plasma concentrations of trandolaprilat are achieved 4 to 6 hours after an oral dose of trandolapril. Trandolaprilat is more than 80% bound to plasma proteins. About 33% of an oral dose of trandolapril is excreted in the urine, mainly as trandolaprilat; the rest is excreted in the faeces. The effective half-life for accumulation of trandolaprilat is 16 to 24 hours after multiple doses of trandolapril.

Impaired renal function decreases the excretion of trandolaprilat. Trandolaprilat is removed by haemodialysis.

◊ References.

1. Bevan EG, *et al.* Effect of renal function on the pharmacokinetics and pharmacodynamics of trandolapril. *Br J Clin Pharmacol* 1993; **35:** 128–35.

Uses and Administration

Trandolapril is an ACE inhibitor (p.1193). It is used in the treatment of hypertension (p.1171) and in left ventricular dysfunction following myocardial infarction (p.1175).

Trandolapril owes its activity to trandolaprilat to which it is converted after oral doses. The haemodynamic effects are seen about 1 hour after an oral dose and the maximum effect occurs after 8 to 12 hours. The haemodynamic action lasts for at least 24 hours, allowing once-daily dosing.

In the treatment of **hypertension** the initial oral dose is 500 micrograms once daily. Since there may be a precipitous fall in blood pressure in some patients when starting therapy with an ACE inhibitor, the first dose should preferably be given at bedtime. In patients already taking a diuretic, the diuretic should be stopped, if possible, 2 to 3 days before starting trandolapril and resumed later if necessary. In patients with co-existing heart failure treatment with trandolapril should begin under close medical supervision. The usual maintenance dose for hypertension is 1 to 2 mg once daily, although up to 4 mg daily may be given, as a single dose or in 2 divided doses.

In **myocardial infarction**, treatment with trandolapril may be started 3 days after the infarction in an initial dose of 500 micrograms once daily, gradually increased to a maximum of 4 mg once daily.

A reduction in dosage may be necessary in patients with renal impairment (see below).

◊ References.

1. Zannad F. Trandolapril: How does it differ from other angiotensin converting enzyme inhibitors? *Drugs* 1993; **46** (suppl 2): 172–82.
2. Wiseman LR, McTavish D. Trandolapril: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in essential hypertension. *Drugs* 1994; **48:** 71–90.
3. Køber L, *et al.* A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 1995; **333:** 1670–6.
4. Peters DC, *et al.* Trandolapril: an update of its pharmacology and therapeutic use in cardiovascular disorders. *Drugs* 1998; **56:** 871–93.

Administration in renal impairment. The initial dose of trandolapril in patients with renal impairment should not exceed 500 micrograms daily. UK licensed product information states that the maximum maintenance dose should be 2 mg daily in patients with a creatinine clearance of less than 10 mL/minute.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Nortensin†; ***Austral.:*** Gopten; Odrik; Tranalpha; ***Austria:*** Gopten; ***Braz.:*** Gopten; Odrik†; ***Canad.:*** Mavik; ***Cz.:*** Gopten; Tanap; ***Denm.:*** Gopten; Odrik; ***Fin.:*** Gopten†; ***Fr.:*** Gopten†; Odrik; ***Ger.:*** Gopten†; Udrik; ***Gr.:*** Afenil; Odrik; ***Hung.:*** Gopten; ***Indon.:*** Gopten; ***Irl.:*** Gopten; Odrik; ***Ital.:*** Gopten; ***Jpn:*** Odric; Preran; ***Mex.:*** Gopten†; ***Neth.:*** Gopten; Odrik; ***Norw.:*** Gopten; ***NZ:*** Gopten; Odrik; ***Pol.:*** Gopten; ***Port.:*** Gopten; Odrik; ***Rus.:*** Gopten (Гоптен); ***S.Afr.:*** Gopten†; Mavik; ***Spain:*** Gopten; Odrik; ***Swed.:*** Gopten; ***Switz.:*** Gopten; ***Turk.:*** Gopten; ***UK:*** Gopten; Odrik†; ***USA:*** Mavik.

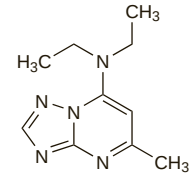
Multi-ingredient: ***Arg.:*** Tarka†; ***Austral.:*** Tarka; ***Austria:*** Tarka; ***Canad.:*** Tarka; ***Cz.:*** Tarka; ***Denm.:*** Tarka; ***Fin.:*** Tarka†; ***Fr.:*** Ocadrik†; Tarka; ***Ger.:*** Tarka; Udramil†; ***Gr.:*** Tarka; Ziaxel; ***Hung.:*** Tarka; ***Indon.:*** Tarka; ***Ital.:*** Tarka; ***Mex.:*** Tarka; ***Neth.:*** Tarka; Ziaxel; ***NZ:*** Ziaxel; ***Philipp.:*** Tarka; ***Pol.:*** Tarka; ***Port.:*** Tarka; Ziaxal; ***Rus.:*** Tarka (Тарка); ***S.Afr.:*** Tarka; ***Spain:*** Tarka; Tricen; ***Swed.:*** Tarka; ***Switz.:*** Tarka; ***Turk.:*** Tarka; ***UK:*** Tarka; ***USA:*** Tarka; ***Venez.:*** Tarka.

Trapidil *(BAN, rINN)*

AR-12008; Tarpidil; Trapidiili; Trapidilis; Trapidilum. 7-Diethylamino-5-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine.

Трапидил

$C_{10}H_{15}N_5$ = 205.3.
CAS — 15421-84-8.
ATC — C01DX11.
ATC Vet — QC01DX11.



Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn.*
Ph. Eur. 6.2 (Trapidil). A white or almost white crystalline powder. Freely soluble in water; soluble in dehydrated alcohol and in dichloromethane. Protect from light.

Profile
Trapidil is a vasodilator and an inhibitor of platelet aggregation. It is also an antagonist of platelet-derived growth factor. It is used orally in the management of ischaemic heart disease in doses of 400 to 600 mg daily, in divided doses; doses of up to 600 mg daily may be used to prevent restenosis after angioplasty (but see below). Ischaemic heart disease is discussed under Atherosclerosis (p.1159) and the treatment of its clinical manifestations is described under Angina Pectoris (p.1157) and Myocardial Infarction (p.1175).

◊ References to anti-platelet activity.

1. Yasue H, *et al.* Effects of aspirin and trapidil on cardiovascular events after acute myocardial infarction: Japanese Antiplatelets Myocardial Infarction Study (JAMIS) Investigators. *Am J Cardiol* 1999; **83:** 1308–13.

◊ References to pharmacokinetics.

1. Harder S, *et al.* Pharmacokinetics of trapidil, an antagonist of platelet derived growth factor, in healthy subjects and in patients with liver cirrhosis. *Br J Clin Pharmacol* 1996; **42:** 443–9.

Angioplasty and stenting. Although angiographic studies[1-3] have found that trapidil reduces the rate of restenosis after balloon angioplasty (see Reperfusion and Revascularisation Procedures, p.1181), no effect on clinical outcomes[3] has been shown. Studies investigating the use of trapidil after coronary stenting[3,4] have shown no benefit in terms of restenosis or clinical events, and it was concluded that trapidil is not indicated for this purpose.

1. Okamoto S, *et al.* Effects of trapidil (triazolopyrimidine), a platelet-derived growth factor antagonist, in preventing restenosis after percutaneous transluminal coronary angioplasty. *Am Heart J* 1992; **123:** 1439–44.
2. Maresta A, *et al.* Trapidil (triazolopyrimidine), a platelet-derived growth factor antagonist, reduces restenosis after percutaneous transluminal coronary angioplasty: results of the randomized, double-blind STARC study. *Circulation* 1994; **90:** 2710–15.
3. Maresta A, *et al.* Starc II, a multicenter randomized placebo-controlled double-blind clinical trial of trapidil for 1-year clinical events and angiographic restenosis reduction after coronary angioplasty and stenting. *Catheter Cardiovasc Interv* 2005; **64:** 375–82.
4. Serruys PW, *et al.* The TRAPIST study: a multicentre randomized placebo controlled clinical trial of trapidil for prevention of restenosis after coronary stenting, measured by 3-D intravascular ultrasound. *Eur Heart J* 2001; **22:** 1938–47.

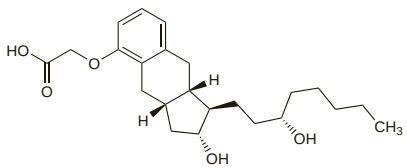
Preparations
Proprietary Preparations (details are given in Part 3)
Austria: Rocornal†; ***Braz.:*** Travisco; ***Cz.:*** Rocornal†; ***Ger.:*** Rocornal; ***Ital.:*** Avantrin†; Travisco; ***Jpn:*** Rocornal.

Treprostinil *(USAN, rINN)*

LRX-15; Tréprostinil; Treprostinilo; Treprostinilum; Treprostinol; 15AU81; U-62840; UT-15. ({(1*R*,2*R*,3a*S*,9a*S*)-2,3,3a,4,9,9a-Hexahydro-2-hydroxy-1-[(3*S*)-3-hydroxyoctyl]-1*H*-benz[*f*]inden-5-yl}oxy)acetic acid.

Трепростинил

$C_{23}H_{34}O_5$ = 390.5.
CAS — 81846-19-7.
ATC — B01AC21.
ATC Vet — QB01AC21.



Treprostinil Sodium *(rINNM)*

Natrii Treprostinilum; Tréprostinil Sodique; Treprostinilo sódico.

Натрий Трепростинил

$C_{23}H_{33}NaO_5$ = 412.5.
CAS — 289480-64-4.
ATC — B01AC21.
ATC Vet — QB01AC21.

Adverse Effects and Precautions
Infusion site pain and reactions, including erythema, induration, and rash, are the most common adverse effects reported during subcutaneous infusion of treprostinil. Other effects include headache, nausea, diarrhoea, jaw pain, oedema, vasodilatation, dizziness, hypotension, and pruritus.

Abrupt cessation of the infusion should be avoided, because symptoms of pulmonary hypertension may worsen. Treprostinil should be used with caution in hepatic impairment.

Interactions
Since treprostinil is a vasodilator and inhibitor of platelet aggregation, care should be taken in patients receiving other vasodilators or anticoagulants.

Pharmacokinetics
Treprostinil sodium is rapidly and completely absorbed after subcutaneous injection. It is metabolised by the liver and eliminated with a terminal half-life of about 4 hours. About 80% of a dose is excreted in the urine, mainly as metabolites.

◊ References.

1. Wade M, *et al.* Absolute bioavailability and pharmacokinetics of treprostinil sodium administered by acute subcutaneous infusion. *J Clin Pharmacol* 2004; **44:** 83–8.
2. Wade M, *et al.* Pharmacokinetics of treprostinil sodium administered by 28-day chronic continuous subcutaneous infusion. *J Clin Pharmacol* 2004; **44:** 503–9.
3. Laliberte K, *et al.* Pharmacokinetics and steady-state bioequivalence of treprostinil sodium (Remodulin) administered by the intravenous and subcutaneous route to normal volunteers. *J Cardiovasc Pharmacol* 2004; **44:** 209–14.
4. McSwain CS, *et al.* Dose proportionality of treprostinil sodium administered by continuous subcutaneous and intravenous infusion. *J Clin Pharmacol* 2008; **48:** 19–25.

Uses and Administration
Treprostinil, a vasodilator and platelet aggregation inhibitor, is an analogue of the prostaglandin epoprostenol (prostacyclin; p.1279). Treprostinil sodium is given by continuous subcutaneous infusion in the treatment of pulmonary hypertension (p.1179); if this route cannot be tolerated, treprostinil sodium may be given by continuous infusion through a central venous catheter. Doses are calculated in terms of treprostinil: treprostinil sodium 1.32 nanograms is equivalent to about 1.25 nanograms of treprostinil. The infusion is started with a dose equivalent to treprostinil 1.25 nanograms/kg per minute; if this is not tolerated the dose should be halved. The infusion rate can be increased according to patient response, by increments of up to 1.25 nanograms/kg per minute each week for the first 4 weeks, followed by increases of up to 2.5 nanograms/kg per minute each week. There is limited experience with doses above 40 nanograms/kg per minute. The dose of treprostinil should be reduced in hepatic impairment, see below.

Inhaled treprostinil is under investigation in pulmonary hypertension, and intravenous use has been investigated for intermittent claudication.

◊ References.

1. Moller ER, *et al.* Trial of a novel prostacyclin analog, UT-15, in patients with severe intermittent claudication. *Vasc Med* 2000; **5:** 231–7.
2. Simonneau G, *et al.* Continuous subcutaneous infusion of treprostinil, a prostacyclin analogue, in patients with pulmonary arterial hypertension: a double-blind, randomized placebo-controlled trial. *Am J Respir Crit Care Med* 2002; **165:** 800–804.
3. Vachiéry J-L, *et al.* Transitioning from IV epoprostenol to subcutaneous treprostinil in pulmonary arterial hypertension. *Chest* 2002; **121:** 1561–5.
4. Vachiéry JL, Naeije R. Treprostinil for pulmonary hypertension. *Expert Rev Cardiovasc Ther* 2004; **2:** 183–91.
5. Oudiz RJ, *et al.* Treprostinil, a prostacyclin analogue, in pulmonary arterial hypertension associated with connective tissue disease. *Chest* 2004; **126:** 420–7.
6. Gomberg-Maitland M, *et al.* Efficacy and safety of sildenafil added to treprostinil in pulmonary hypertension. *Am J Cardiol* 2005; **96:** 1334–6.
7. Fernandez B, Strootman D. The prostacyclin analog, treprostinil sodium, provides symptom relief in severe Buerger's disease—a case report and review of literature. *Angiology* 2006; **57:** 99–102.
8. Voswinckel R, *et al.* Inhaled treprostinil for treatment of chronic pulmonary arterial hypertension. *Ann Intern Med* 2006; **144:** 149–50.
9. Channick RN, *et al.* Safety and efficacy of inhaled treprostinil as add-on therapy to bosentan in pulmonary arterial hypertension. *J Am Coll Cardiol* 2006; **48:** 1433–7.

Administration in hepatic impairment. Clearance of treprostinil is reduced in patients with hepatic impairment. The manufacturers recommend that the initial dose should be 0.625 nanograms/kg per minute, and should be increased cautiously, in mild to moderate impairment. Treprostinil has not been studied in severe hepatic impairment.

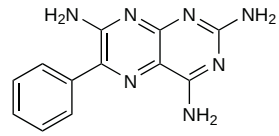
Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Remodulin; ***Chile:*** Remodulin; ***Cz.:*** Remodulin; ***Fr.:*** Remodulin; ***Gr.:*** Remodulin; ***Israel:*** Remodulin; ***Port.:*** Remodulin; ***Switz.:*** Remodulin; ***USA:*** Remodulin.

Triamterene *(BAN, USAN, rINN)* ⊗

NSC-77625; SKF-8542; Triamtereeni; Triamterén; Triamteren; Triamterenas; Triamtérène; Triamtereno; Triamterenum; Triantereno. 6-Phenylpteridine-2,4,7-triamine; 2,4,7-Triamino-6-phenylpteridine.

Триамтерен

$C_{12}H_{11}N_7$ = 253.3.
CAS — 396-01-0.
ATC — C03DB02.
ATC Vet — QC03DB02.



NOTE. Compounded preparations of triamterene may be represented by the following names:

- Co-triamterzide (*BAN*)—triamterene 2 parts and hydrochlorothiazide 1 part (w/w)
- Co-triamterzide (*PEN*)—triamterene and hydrochlorothiazide.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Triamterene). A yellow, crystalline powder. Very slightly soluble in water and in alcohol. Protect from light.
USP 31 (Triamterene). A yellow, odourless, crystalline powder. Practically insoluble in water, in chloroform, in ether, in benzene, and in dilute alkali hydroxides; very slightly soluble in alcohol, in acetic acid, and in dilute mineral acids; soluble 1 in 30 of formic acid and 1 in 85 of 2-methoxyethanol. Store in airtight containers. Protect from light.

Adverse Effects
As for Amiloride Hydrochloride, p.1209. Triamterene has also been reported to cause photosensitivity reactions, increases in uric acid concentrations, and blood dyscrasias. Renal calculi may occur in susceptible patients, and megaloblastic anaemia has been reported in patients with depleted folic acid stores such as those with hepatic cirrhosis. Reversible renal failure, due either to acute interstitial nephritis or to an interaction with NSAIDs (see under Interactions, below) has occurred.

Incidence of adverse effects. In a postmarketing surveillance study of 70 898 patients[1] taking triamterene with hydrochlorothiazide the most common adverse effects were fatigue, dizziness, and nausea. Adverse effects necessitated withdrawal in 8.1% of patients. A subgroup analysis of 21 731 patients[2] indicated that hyperkalaemia was more common in elderly patients and in those with diabetes mellitus.

1. Hollenberg NK, Mickiewicz CW. Postmarketing surveillance in 70,898 patients treated with a triamterene/hydrochlorothiazide combination (Maxzide). *Am J Cardiol* 1989; **63:** 37B–41B.
2. Hollenberg NK, Mickiewicz CW. Hyperkalemia in diabetes mellitus: effect of a triamterene-hydrochlorothiazide combination. *Arch Intern Med* 1989; **149:** 1327–30.

Effects on the blood. There have been case reports of pancytopenia associated with triamterene therapy.[1,2] Some patients had hepatic cirrhosis and the antifolate activity of triamterene was considered responsible.[2]

1. Castellano G, *et al.* Pancitopenia aguda y megaloblastosis medular durante el tratemiento con triamterene de la ascitis causada por cirrosis hepática: aportación de dos casos. *Gastroenterol Hepatol* 1983; **6:** 540–4.
2. Remacha A, *et al.* Triamterene-induced megaloblastosis: report of two new cases, and review of the literature. *Biol Clin Hematol* 1983; **5:** 127–34.

Effects on the kidneys. There have been a number of reports[1-4] of renal calculi containing triamterene or its metabolites, generally in patients also taking hydrochlorothiazide. An abnormal urinary sediment was described which was thought to represent precipitated triamterene.[5] These observations were expanded in a crossover study:[6] abnormal urinary sediment was seen in 14 of 26 patients taking triamterene but in none taking amiloride. Triamterene and its metabolites were identified by others in 181 of 50 000 renal calculi.[7] Triamterene either formed the nucleus of the stone or was deposited with calcium oxalate or uric acid. One-third of the 181 stones were entirely or mainly composed of triamterene and its metabolites and it was suggested that supersaturation of the urine with these substances could provide suitable nuclei for the crystallisation of calcium oxalate.[8] However, other workers were unable to confirm this and suggested that triamterene and its metabolites could become incorporated into the protein matrix of existing stones.[9] In addition, an epidemiological study[10] found no evidence that triamterene use was associated with an increased incidence of renal stones. Some authors[11] have therefore considered that there was not enough evidence to contra-indicate the drug in patients with a history of recurrent renal calculi.

Deposition of triamterene in the urine may also play a part in the development of interstitial nephritis, which was diagnosed in 4 patients also taking hydrochlorothiazide, over a period of 4 years.[6]

Triamterene has also been associated with transient decline in renal function and the development of renal failure.[12,13] Several mechanisms may be responsible including interstitial nephritis,