intrarenal obstruction by crystalline deposits, and an interaction with NSAIDs (see under Interactions, below).[13] Elderly patients may be particularly at risk.[12]

1. Ettinger B, *et al.* Triamterene-induced nephrolithiasis. *Ann Intern Med* 1979; **91:** 745–6.
2. Socolow EL. Triamterene-induced nephrolithiasis. *Ann Intern Med* 1980; **92:** 437.
3. Gault MH, *et al.* Triamterene urolithiasis. *Can Med Assoc J* 1981; **124:** 1556–7.
4. Grunberg RW, Silberg SJ. Triamterene-induced nephrolithiasis. *JAMA* 1981; **245:** 2494–5.
5. Fairley KF, *et al.* Abnormal urinary sediment in patients on triamterene. *Lancet* 1983; **i:** 421–2.
6. Spence JD, *et al.* Effects of triamterene and amiloride on urinary sediment in hypertensive patients taking hydrochlorothiazide. *Lancet* 1985; **ii:** 73–5.
7. Ettinger B, *et al.* Triamterene nephrolithiasis. *JAMA* 1980; **244:** 2443–5.
8. White DJ, Nancollas GH. Triamterene and renal stone formation. *J Urol (Baltimore)* 1982; **127:** 593–7.
9. Werness PG, *et al.* Triamterene urolithiasis: solubility, pK, effect on crystal formation, and matrix binding of triamterene and its metabolites. *J Lab Clin Med* 1982; **99:** 254–62.
10. Jick H, *et al.* Triamterene and renal stones. *J Urol (Baltimore)* 1982; **127:** 224–5.
11. Woolfson RG, Mansell MA. Does triamterene cause renal calculi? *BMJ* 1991; **303:** 1217–18.
12. Lynn KL, *et al.* Renal failure with potassium-sparing diuretics. *N Z Med J* 1985; **98:** 629–33.
13. Sica DA, Gehr TWB. Triamterene and the kidney. *Nephron* 1989; **51:** 454–61.

Effects on the skin. Photodermatitis has been reported in a patient taking triamterene.[1] Pseudoporphyria, possibly associated with exposure to sunlight, occurred in a patient with vitiligo during treatment with triamterene and hydrochlorothiazide.[2]

1. Fernández de Corres L, *et al.* Photodermatitis from triamterene. *Contact Dermatitis* 1987; **17:** 114–15.
2. Motley RJ. Pseudoporphyria due to Dyazide in a patient with vitiligo. *BMJ* 1990; **300:** 1468.

Precautions

As for Amiloride Hydrochloride, p.1209. Triamterene should also be given with caution to patients with hyperuricaemia or gout, or a history of renal calculi. Patients with depleted folic acid stores such as those with hepatic cirrhosis may be at increased risk of megaloblastic anaemia.

Triamterene may interfere with the fluorescent measurement of quinidine. It may slightly colour the urine blue.

Interactions

As for Amiloride Hydrochloride, p.1209.

Digoxin. For a report of the effect of triamterene on digoxin, see p.1262.

Dopaminergics. For a report of increased *amantadine* toxicity associated with hydrochlorothiazide and triamterene, see p.793.

NSAIDs. There have been several reports of renal failure in patients taking triamterene and NSAIDs.[1,2] Both types of drug are nephrotoxic and in combination the effect appears to be additive.[3-5] It has been suggested that the suppression of urinary prostaglandins by NSAIDs could potentiate the nephrotoxic effects of triamterene.[1]

NSAIDs may also antagonise the diuretic action of triamterene.[6]

1. Favre L, *et al.* Reversible acute renal failure from combined triamterene and indomethacin: a study in healthy subjects. *Ann Intern Med* 1982; **96:** 317–20.
2. Härkönen M, Ekblom-Kullberg S. Reversible deterioration of renal function after diclofenac in patient receiving triamterene. *BMJ* 1986; **293:** 698–9.
3. Bailey RR. Adverse renal reactions to non-steroidal anti-inflammatory drugs and potassium-sparing diuretics. *Adverse Drug React Bull* 1988; (Aug.): 492–5.
4. Lynn KL, *et al.* Renal failure with potassium-sparing diuretics. *N Z Med J* 1985; **98:** 629–33.
5. Sica DA, Gehr TWB. Triamterene and the kidney. *Nephron* 1989; **51:** 454–61.
6. Webster J. Interactions of NSAIDs with diuretics and β-blockers: mechanisms and clinical implications. *Drugs* 1985; **30:** 32–41.

Pharmacokinetics

Triamterene is variably but fairly rapidly absorbed from the gastrointestinal tract. The bioavailability has been reported to be about 50%. The plasma half-life has been reported to be about 2 hours. It is estimated to be about 60% bound to plasma proteins. It is extensively metabolised and is mainly excreted in the urine in the form of metabolites with some unchanged triamterene. Triamterene crosses the placenta and may be distributed into breast milk.

◊ References.

1. Pruitt AW, *et al.* Variations in the fate of triamterene. *Clin Pharmacol Ther* 1977; **21:** 610–19.
2. Gundert-Remy U, *et al.* Plasma and urinary levels of triamterene and certain metabolites after oral administration to man. *Eur J Clin Pharmacol* 1979; **16:** 39–44.
3. Gilfrich HJ, *et al.* Pharmacokinetics of triamterene after iv administration to man: determination of bioavailability. *Eur J Clin Pharmacol* 1983; **25:** 237–41.
4. Sörgel F, *et al.* Oral triamterene disposition. *Clin Pharmacol Ther* 1985; **38:** 306–12.

Hepatic impairment. Triamterene clearance was markedly decreased in 7 patients with alcoholic cirrhosis and ascites.[1] The diuretic effect lasted for up to 48 hours in cirrhotic patients compared with 8 hours in healthy controls.

1. Villeneuve JP, *et al.* Triamterene kinetics and dynamics in cirrhosis. *Clin Pharmacol Ther* 1984; **35:** 831–7.

Renal impairment. Urinary excretion of triamterene and its metabolite, hydroxytriamterene sulfate, was significantly reduced in patients with renal impairment[1] and in the elderly whose renal function was reduced.[2] Accumulation of the active metabolite was possible in patients with renal impairment.[1]

1. Knauf H, *et al.* Delayed elimination of triamterene and its active metabolite in chronic renal failure. *Eur J Clin Pharmacol* 1983; **24:** 453–6.
2. Williams RL, *et al.* Absorption and disposition of two combination formulations of hydrochlorothiazide and triamterene: influence of age and renal function. *Clin Pharmacol Ther* 1986; **40:** 226–32.

Uses and Administration

Triamterene is a weak diuretic with potassium-sparing properties which has actions and uses similar to those of amiloride (p.1210). It produces a diuresis in about 2 to 4 hours, with a duration of 7 to 9 hours. The full therapeutic effect may be delayed until after several days of treatment.

Triamterene adds to the natriuretic but diminishes the kaliuretic effects of other diuretics. It is mainly used, as an adjunct to thiazide diuretics such as hydrochlorothiazide and loop diuretics such as furosemide, to conserve potassium in those at risk from hypokalaemia during the treatment of refractory oedema associated with hepatic cirrhosis, heart failure (p.1165), and the nephrotic syndrome. It is also used with other diuretics in the treatment of hypertension (p.1171).

When triamterene is given alone in the treatment of **oedema**, the oral dosage range is 150 to 250 mg daily, given in 2 divided doses, after breakfast and lunch. Doses may be given on alternate days for maintenance therapy. More than 300 mg daily should not be given.

Smaller doses are used initially when other diuretics are also given. When used with hydrochlorothiazide, for example, in the treatment of **hypertension**, an initial dose of 50 mg of triamterene daily may be used.

Potassium supplements should not be given.

Preparations

BP 2008: Co-triamterzide Tablets; Triamterene Capsules;
USP 31: Triamterene and Hydrochlorothiazide Capsules; Triamterene and Hydrochlorothiazide Tablets; Triamterene Capsules.

Proprietary Preparations (details are given in Part 3)
Belg.: Dytac; ***Canad.:*** Dyrenium†; ***Neth.:*** Dytac†; ***UK:*** Dytac; ***USA:*** Dyrenium.

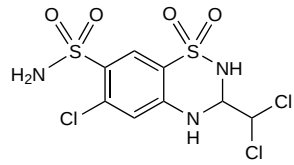
Multi-ingredient: ***Austral.:*** Hydrene; ***Austria:*** Confit; Dytide H; Hydrotrix; Salodiur; Triamteren comp; Triastad HCT; Trioral/HCT; ***Belg.:*** Diucomb†; Dyta-Urese; Dytenzide; ***Braz.:*** Diurana; Iguassina; ***Canad.:*** Apo-Triazide; Novo-Triamzide; Nu-Triazide; ***Chile:*** Drinamil; Hidroronol T; Uren; ***Fin.:*** Furesis comp; Uretren Comp; ***Fr.:*** Isobar; Prestole; ***Ger.:*** Beta-Turfa; dehydro sanol tri; Diu Venostasin; Diucomb; Diuretikum Verla; Diutensat comp†; Diutensat†; Dociteren; duradiuret†; Dytide H; Haemiton compositum†; Hydrotrix; Jenateren comp†; Neotri; Nephral; Propra comp; Sali-Puren†; Thiazid-comp; Tri-Thiazid; Tri-Thiazid Reserpin†; Triampur Compositum; Triamteren comp; Triamteren HCT; Triamteren tri-comp; Triamteren-H†; Triarese; triazid†; Turfa; Veratide; ***Hong Kong:*** Apo-Triazide; Dyazide; Triam-Co†; ***India:*** Ditide; ***Irl.:*** Dyazide; ***Ital.:*** Fluss 40; ***Malaysia:*** Apo-Triazide†; ***Mex.:*** Dyazide; ***Neth.:*** Dyta-Urese; Dytenzide; ***NZ:*** Triamizide; ***Port.:*** Dyazide; Triam Tiazida R; ***Rus.:*** Apo-Triazide (Апотриазид); Triam-Co (Триам-ко); Triampur Compositum (Триампур Композитум); ***S.Afr.:*** Dyazide; Renezide; ***Singapore:*** Apo-Triazide; ***Spain:*** Salidur; ***Switz.:*** Dyazide; Dyrenium compositum; t/h-basan; ***Thai.:*** Dazid†; Dinazide; Dyazide; Dyterene†; ***Turk.:*** Triamteril; ***UK:*** Dyazide; Dytide; Frusene; Kalspare; Triamaxco†; Triamco; ***USA:*** Dyazide; Maxzide.

Trichlormethiazide *(rINN)* ⊗

Trichlorméthiazide; Trichlormethiazidum; Triclormetiazida; Triklorimetiatsidi; Triklormetiazid. 6-Chloro-3-dichloromethyl-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Трихлорметиазид

$C_8H_8Cl_3N_3O_4S_2$ = 380.7.
CAS — 133-67-5.
ATC — C03AA06.
ATC Vet — QC03AA06.



Pharmacopoeias. In *Jpn* and *US*.
USP 31 (Trichlormethiazide). A white or practically white, crystalline powder, odourless or with a slight characteristic odour. Soluble 1 in 1100 of water, 1 in 48 of alcohol, 1 in 5000 of chloroform, 1 in about 4 of dimethylformamide, 1 in about 9 of dioxan, and 1 in 1400 of ether; freely soluble in acetone; soluble in methyl alcohol.

Profile

Trichlormethiazide is a thiazide diuretic with properties similar to those of hydrochlorothiazide (p.1307). It is given orally for oedema, including that associated with heart failure (p.1165), and for hypertension (p.1171).

Diuresis begins about 2 hours after an oral dose, and lasts about 24 hours.

In the treatment of oedema the usual dose is 1 to 4 mg daily or intermittently. In the treatment of hypertension the usual dose is 2 to 4 mg daily, either alone, or with other antihypertensives. In some patients 1 mg daily may be adequate. In children over 6 months of age a dose of 70 micrograms/kg daily in one or two doses has been used.

Preparations

USP 31: Trichlormethiazide Tablets.

Proprietary Preparations (details are given in Part 3)
USA: Diurese†; Metahydrin†; Naqua†.

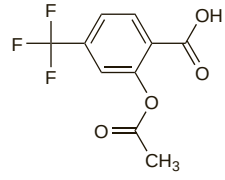
Multi-ingredient: ***Fin.:*** Uretren Comp; ***Ger.:*** Esmalorid†; ***Spain:*** Rulun; ***USA:*** Metatensin†.

Triflusal *(BAN, rINN)*

Triflusaali; Triflusalis; Triflusalum; Trifluzál; UR-1501. 2-Acetoxy-4-trifluoromethylbenzoic acid; *O*-Acetyl-4-(trifluoromethyl)salicylic acid.

Трифлусал

$C_{10}H_7F_3O_4$ = 248.2.
CAS — 322-79-2.
ATC — B01AC18.
ATC Vet — QB01AC18.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Triflusal). A white or almost white crystalline powder. Practically insoluble in water; very soluble in dehydrated alcohol; freely soluble in dichloromethane. Store in airtight containers at a temperature not exceeding 25°.

Profile

Triflusal is an inhibitor of platelet aggregation used in the management of thromboembolic disorders (p.1187) in usual oral doses of 300 to 900 mg daily.

◊ References.

1. Murdoch D, Plosker GL. Triflusal: a review of its use in cerebral infarction and myocardial infarction, and as thromboprophylaxis in atrial fibrillation. *Drugs* 2006; **66:** 671–92.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Disgren; ***Braz.:*** Disgren; ***Chile:*** Logrosal†; ***Gr.:*** Aflen; Reoflen; ***Hung.:*** Disgren; ***Ital.:*** Triflux; ***Mex.:*** Disgren; ***Port.:*** Tecnosal; ***Spain:*** Anpeval; Disgren; ***Venez.:*** Disgren.