Uses and Administration

Thiamazole is a thiourea antithyroid drug that acts by blocking the production of thyroid hormones (see p.2165). It is used in the management of hyperthyroidism (p.2165), including the treatment of Graves' disease, the preparation of hyperthyroid patients for thyroidectomy, use as an adjunct to radio-iodine therapy, and the treatment of thyroid storm.

Thiamazole is given orally usually in an initial dosage of 15 to 60 mg daily. It is usually given in three divided doses but a single daily dose is also possible. Improvement is usually seen in 1 to 3 weeks and control of symptoms in 1 to 2 months. When the patient is euthyroid the dose is gradually reduced to a maintenance dose, usually 5 to 15 mg daily. Alternatively, the dose may be continued at the initial level with supplemental levothyroxine as a *blocking-replacement regimen*. Either form of maintenance treatment is usually continued for 1 to 2 years. The initial dose for children is 400 micrograms/kg daily in 3 divided doses; for maintenance this dose may be halved.

Thiamazole doses of 80 to 240 mg daily, usually in 3 or 4 divided doses, have been given intravenously in the management of thyroid storm.

Preparations

USP 31: Methimazole Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Danantizol; ***Austria:*** Favistan†; ***Belg.:*** Strumazol; ***Braz.:*** Tapazol; ***Canad.:*** Tapazole; ***Chile:*** Thyrozol; Tirozol 5/10†; ***Cz.:*** Favistan†; Thyrozol; ***Denm.:*** Thycapzol; ***Ger.:*** Favistan; Thyrozol; ***Gr.:*** Unimazole; ***Hung.:*** Metothyrin; ***Indon.:*** Thyrozol; ***Israel:*** Mercaptizol; ***Ital.:*** Tapazole; ***Mex.:*** Tapazol; Tizorol; ***Neth.:*** Strumazol; ***Philipp.:*** Strumazol; Tapazole; ***Pol.:*** Metizol; Thyrozol; ***Port.:*** Metibasol; ***Rus.:*** Mercazolil (Мерказолил); Thyrozol (Тирозол); ***Singapore:*** Thyrozol; ***Spain:*** Tirodril; ***Swed.:*** Thacapzol; ***Switz.:*** Tapazole†; ***Thai.:*** Tapazole; Timazol; ***Turk.:*** Thyromazol; ***USA:*** Northyx; Tapazole; ***Venez.:*** Tapazol.

Multi-ingredient: ***Ital.:*** Bromazolo.

Thyroglobulin *(USAN, rINN)*

Thyroglobuline; Thyroglobulinum; Tiroglobulina.

Тироглобулин

CAS — 9010-34-8.

Profile

Thyroglobulin is an extract obtained by the fractionation of porcine thyroid glands, that yields levothyroxine and liothyronine on hydrolysis. It has been used in the treatment of hypothyroidism, but such treatment with mixtures of thyroid hormones or preparations of animal extracts is not recommended.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Tiroide Vister.

Thyroid

Dry Thyroid; Getrocknete Schilddrüse; Glándula tiroides, extracto de; NSC-26492; Thyreoidin; Thyroid Extract; Thyroid Gland; Thyroidea; Thyroideum Siccum; Tiroide Secca.

ATC — H03AA05.
ATC Vet — QH03AA05.

Pharmacopoeias. In *Chin.*, *Jpn*, and *US*.

USP 31 (Thyroid). It is the cleaned, dried, and powdered thyroid gland, previously deprived of connective tissue and fat, obtained from domesticated animals used for food by humans. On hydrolysis it yields not less than 90% and not more than 110% each of the labelled amounts of levothyroxine and liothyronine calculated on the dried basis. It is free from iodine in inorganic or any form of combination other than that peculiar to the thyroid gland. It may contain a suitable diluent such as glucose, lactose, sodium chloride, starch, or sucrose. A yellowish to buff-coloured amorphous powder, having a slight, characteristic, meat-like odour. Store in airtight containers.

Profile

Thyroid has been used in the treatment of hypothyroidism, but treatment with mixtures of thyroid hormones or preparations of animal extracts is not recommended.

Preparations

USP 31: Thyroid Tablets.

Proprietary Preparations (details are given in Part 3)
Ital.: Cinetic; ***Mex.:*** Amet; ***Thai.:*** Thiroyd; ***USA:*** Nature Throid.

Multi-ingredient: ***Braz.:*** Emagrex†; Obesidex†; Obesifran†; ***India:*** Ebexid; ***Thai.:*** Metharmon-F.

Thyrotrophin *(BAN, rINN)*

Thyroid-stimulating Hormone; Thyrotrophic Hormone; Thyrotrophine; Thyrotrophinum; Thyrotropin; Thyrotropinum; Tirotrofina; TSH; Tyrotropiini; Tyrotropin.

Тиротропин

CAS — 9002-71-5.
ATC — H01AB01; V04CJ01.
ATC Vet — QH01AB01; QV04CJ01.

Description. Thyrotrophin is a glycoprotein from the anterior pituitary with a molecular weight in man of about 30 000.

Thyrotropin Alfa *(BAN, USAN, rINN)*

rhTSH; Thyrotropine Alfa; Thyrotropinum Alfa; Tirotropina alfa.

Тиротропин Альфа

CAS — 194100-83-9.
ATC — V04CJ01.
ATC Vet — QV04CJ01.

Units

0.037 units of human pituitary thyrotrophin for immunoassay and bioassay are contained in about 7.5 micrograms of thyrotrophin, with albumin 1 mg and lactose 5 mg, in one ampoule of the second International Reference Preparation (1983).

Adverse Effects

Infrequent adverse effects of thyrotrophin include nausea, vomiting, headache, a desire to micturate, and flushing. High doses may produce excessive thyroid stimulation, with angina, tachycardia or arrhythmias, dyspnoea, sweating, nervousness and irritability. Hypersensitivity reactions, including skin rash and urticaria, erythema and swelling at the injection site, and anaphylaxis have occurred, particularly on repeated use.

Precautions

Thyrotrophin should not be given to patients with recent myocardial infarction or uncorrected adrenocortical insufficiency, including adrenocortical insufficiency secondary to hypopituitarism. Care is also required in patients with cardiovascular disease.

Uses and Administration

Thyrotrophin is a glycoprotein that is secreted by the anterior lobe of the pituitary and has an alpha subunit essentially the same as that of the gonadotrophins. Its main actions are to increase iodine uptake by the thyroid and the formation and secretion of the thyroid hormones. It may produce hyperplasia of thyroid tissue. Thyrotrophin secretion is controlled by a hypothalamic releasing hormone (Protirelin, p.2175) and by circulating thyroid hormones; somatostatin (p.1809) inhibits the release of thyrotrophin.

Thyrotrophin has been used with radio-iodine in the diagnosis of hypothyroidism (p.2167) and to differentiate between primary and secondary hypothyroidism, but direct radio-immunoassay of circulating endogenous thyroid-stimulating hormone may be preferred. Thyrotrophin increases the uptake of radio-iodine by the thyroid and has been used as a diagnostic tool and as an adjunct in the treatment of certain types of thyroid cancer.

Thyrotropin alfa is a recombinant form of thyrotrophin used as an adjunctive diagnostic tool for serum-thyroglobulin testing, with or without radio-iodine imaging, in the follow-up of patients with thyroid cancer. It is also used to increase radio-iodine uptake for ablation of thyroid remnant tissue after thyroidectomy. The usual thyrotropin alfa regimen consists of 2 intramuscular doses of 900 micrograms given 24 hours apart. Radio-iodine is given 24 hours after the second dose of thyrotropin alfa for radio-iodine imaging or remnant ablation. Diagnostic scanning is performed 48 to 72 hours after the radio-iodine has been given, but post-therapy scanning may be delayed by additional days to allow background activity to decline. Samples for serum-thyroglobulin testing should be taken 72 hours after the second thyrotropin alfa dose.

Goitre and thyroid nodules. Thyrotropin alfa is under investigation[1-4] as an adjunct to increase thyroid uptake of radio-iodine (^{131}I) in the treatment of selected patients with nodular goitre (p.2165).

1. Nielsen VE, *et al.* The effects of recombinant human thyrotropin, in normal subjects and patients with goitre. *Clin Endocrinol (Oxf)* 2004; **61:** 655–63.
2. Duick DS, Baskin HJ. Significance of radioiodine uptake at 72 hours versus 24 hours after pretreatment with recombinant human thyrotropin for enhancement of radioiodine therapy in patients with symptomatic nontoxic or toxic multinodular goiter. *Endocr Pract* 2004; **10:** 253–60.
3. Nielsen VE, *et al.* Recombinant human thyrotropin markedly changes the I kinetics during I therapy of patients with nodular goiter: an evaluation by a randomized double-blinded trial. *J Clin Endocrinol Metab* 2005; **90:** 79–83.
4. Albino CC, *et al.* Recombinant human thyrotropin as adjuvant in the treatment of multinodular goiters with radioiodine. *J Clin Endocrinol Metab* 2005; **90:** 2775–80.

Malignant neoplasms of the thyroid. Patients with well-differentiated thyroid carcinoma (p.674) undergo surgery, with or without iodine-131 treatment. They then receive thyroid hormone therapy to suppress thyrotrophin (TSH), because most differentiated thyroid cancers express TSH receptors and grow in response to thyrotrophin stimulation. Monitoring for tumour recurrence in subsequent years requires interruption of thyroid hormone treatment so that thyrotrophin levels rise, and stimulate the uptake of a subsequent dose of iodine-131 by any residual or recurrent tumour. However, this results in hypothyroidism, with associated symptoms that may be severe in some patients.[1]

Studies[2,3] have examined the use of thyrotropin alfa as an alternative prelude to radio-iodine scanning, and found that it did stimulate radio-iodine uptake, although the sensitivity of scanning may depend on the technique used; thyrotropin alfa might be considered a suitable alternative to thyroid hormone withdrawal. In patients with CNS or spinal metastases, or who have substantial disease in the thyroid bed, thyrotropin alfa may cause tumour expansion with acute complications; it has been recommended[1] that prophylactic corticosteroid therapy should be considered in these cases.

Thyroid hormone withdrawal is also used in the treatment of differentiated thyroid cancer, to increase uptake of radio-iodine for thyroid remnant ablation and treatment of metastatic disease. The use of thyrotropin alfa as an alternative adjunct is under investigation.[4]

1. Basaria M, *et al.* The use of recombinant thyrotropin in the follow-up of patients with differentiated thyroid cancer. *Am J Med* 2002; **112:** 721–5.
2. Ladenson PW, *et al.* Comparison of administration of recombinant human thyrotropin with withdrawal of thyroid hormone for radioactive iodine scanning in patients with thyroid carcinoma. *N Engl J Med* 1997; **337:** 888–96.
3. Haugen BR, *et al.* A comparison of recombinant human thyrotropin and thyroid hormone withdrawal for the detection of thyroid remnant or cancer. *J Clin Endocrinol Metab* 1999: **84:** 3877–85.
4. Robbins RJ, Robbins AK. Recombinant human thyrotropin and thyroid cancer management. *J Clin Endocrinol Metab* 2003; **88:** 1993–8.

Preparations

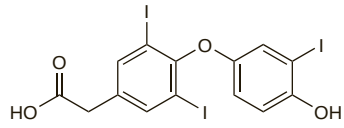
Proprietary Preparations (details are given in Part 3)
Austria: Thyrogen; ***Belg.:*** Thyrogen; ***Braz.:*** Thyrogen†; ***Canad.:*** Thyrogen; ***Cz.:*** Thyrogen; ***Denm.:*** Thyrogen; ***Fin.:*** Thyrogen; ***Fr.:*** Thyrogen; ***Ger.:*** Thyrogen; ***Gr.:*** Thyrogen; ***Hung.:*** Thyrogen; ***Israel:*** Thyrogen; Thytropar†; ***Ital.:*** Thyrogen; ***Neth.:*** Thyrogen; ***Norw.:*** Thyrogen; ***Pol.:*** Thyrogen; ***Port.:*** Thyrogen; ***Singapore:*** Thyrogen; ***Spain:*** Thyrogen; ***Swed.:*** Thyrogen; ***UK:*** Thyrogen; ***USA:*** Thyrogen.

Tiratricol *(rINN)*

Tiratricolum; Tiratrikol; Tiratrikoli; Triac; Triiodothyroacetic Acid. [4-(4-Hydroxy-3-iodophenoxy)-3,5-di-iodophenyl]acetic acid.

Тиратрикол

$C_{14}H_9I_3O_4$ = 621.9.
CAS — 51-24-1.
ATC — D11AX08; H03AA04.
ATC Vet — QD11AX08; QH03AA04.



NOTE. Tri-ac has also been used as a name for proprietary preparations containing other drugs.

Profile

Tiratricol, a metabolite of tri-iodothyronine, is reported to be less active than the thyroid hormones but is given orally to suppress the secretion of thyroid-stimulating hormone.

Obesity. Abnormal thyroid function tests, severe diarrhoea, fatigue, lethargy, and profound weight loss have occurred in patients taking dietary supplements containing tiratricol.[1,2] The FDA has warned that tiratricol may cause heart attacks and strokes, and has advised consumers not to take these products.[3]

1. Anonymous. Triax : a harmful product sold on the internet. *WHO Drug Inf* 2000; **14:** 30.
2. Bauer BA, *et al.* Symptomatic hyperthyroidism in a patient taking the dietary supplement tiratricol. *Mayo Clin Proc* 2002; **77:** 587–90.
3. FDA. FDA warns against consuming dietary supplements containing tiratricol. FDA Talk Paper T00-64, 21 Nov 2000. Available at: http://www.fda.gov/bbs/topics/ANSWERS/ANS01057.html (accessed 18/05/05)

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Dimagrir Triac†; Nulobes; Triacana; ***Braz.:*** Redulip†; Triac†; Trimag†; ***Chile:*** Triacana†; ***Fr.:*** Teatrois; Triacana†.

The incidence and prevalence of renal calculi is increasing.[1,2] The lifetime risk of stone development varies between populations but is about 15% for white men and 6% for white women, with a lifetime recurrence rate of up to 50%.[3] Risk factors include obesity, low fluid intake, and a diet high in protein, refined carbohydrates, and salt.[1] Some conditions can promote calculi formation, including renal tubular acidosis, primary hyperparathyroidism, sarcoidosis, primary hyperoxaluria, inflammatory bowel disease, hyperuricaemic conditions, and cystic fibrosis.[4] Drug-induced calculi can be formed by crystallisation of poorly soluble drugs with a high urinary excretion, or by an effect on calcium oxalate or purine metabolism.[5]

Treatment. Most renal calculi are small, and stones that are less than 5 mm in diameter will usually pass spontaneously.[6-9] Patients may be asymptomatic or may pass small stones with relatively little discomfort, but passage of a larger stone down the ureter can be accompanied by excruciating pain (renal or ureteral colic) requiring analgesia (see Biliary and Renal Colic, p.5). If there is no obstruction, infection, or other complication, conservative treatment is favoured, with the patient being monitored radiographically over several weeks to see if the stone will pass of its own accord.[10] There is some interest in the possible use of drug treatment to ease the spontaneous passage of the stone. Small studies using a calcium-channel blocker (usually nifedipine) or an alpha$_1$-adrenoceptor blocker such as tamsulosin, sometimes with a corticosteroid such as deflazacort, have reported improvements in the rate of stone expulsion and expulsion time, and reductions in analgesic requirements, in patients with uncomplicated lower ureteral stones. A meta-analysis[11] of 9 such studies confirmed the apparent benefit of such treatment; patients had a 65% greater likelihood of spontaneous stone passage than those not given these drugs. Although a suitable randomised controlled study is required to confirm efficacy, such treatment may offer a viable alternative to lithotripsy or uteroscopy.[11] A literature review[12] suggested that daily doses of nifedipine 30 mg, doxazosin 4 mg, tamsulosin 400 micrograms, or terazosin 5 mg given for 28 to 45 days are effective in enhancing expulsion of ureteral stones that are less than 15 mm in diameter.

Where intervention is considered necessary for stone removal the choice of technique depends on the size, composition, and location of the stone. Extracorporeal shock wave lithotripsy is generally favoured, but other procedures such as ureteroscopy or percutaneous nephrolithotomy are used for more complex cases.[7,8,13] Antibacterials may be needed for infection (see Urinary-tract Infections, p.199).

Prevention. In the prevention of recurrence it is important to identify, and where possible correct, any underlying disease process or biochemical or anatomical abnormality. Certain general measures are also appropriate. Patients should drink at least 2 to 3 litres of fluid daily in order to maintain an adequate volume of urine.[1,3,7,14] In hot climates or working environments a higher volume of fluid should be taken.

In preventing the recurrence of *calcium stones*, a balanced diet that is low in protein and salt[1,3,10,15] and high in fibre[1,7] is generally advocated. In the past patients were advised to decrease their calcium intake, but studies have found an inverse relationship between dietary calcium intake and stone formation.[3,7,14,15] Also, because oxalate is bound by calcium in the gut, preventing its absorption, a low calcium intake can increase oxalate absorption and the risk of stone formation. Therefore, a normal level of dietary intake of calcium is now advised[1,3,7,15,16] (an exception to this is in patients with absorptive hypercalciuria type I, a rare condition of intestinal calcium hyperabsorption).[1] However, calcium supplements appear to increase the risk of stone formation and are generally avoided.[3,7,15] If they are used, they should be taken with meals to avoid hypercalciuria.[1,16] Excessive dietary oxalate intake should also be avoided;[3,7,10,15] foods containing large quantities of bioavailable oxalate include spinach, rhubarb, nuts, and cocoa.[15]

Where pharmacological therapy is indicated, choice of treatment depends on the underlying metabolic abnormality and stone composition. Alkaline citrate, usually given as potassium citrate, is commonly used to prevent the recurrence of calcium stones. It acts as a urinary alkaliniser and increases citrate excretion; citrate forms complexes with calcium to reduce urinary saturation of calcium salts and inhibits crystallisation.[2,7,14,16] Potassium citrate is the main treatment option in patients with hypocitraturia and renal tubular acidosis.[1,3,7] In hypercalciuria, a thiazide diuretic or indapamide can also be used to increase distal tubular calcium reabsorption;[1-3,6,7,10,14,17] potassium citrate can also prevent diuretic-induced hypokalaemia in these patients. In the prevention of calcium stones with hyperoxaluria, a restriction of oxalate-rich food and an adequate dietary calcium intake (or calcium supplements taken with meals) are advocated.[6,10,15,16] The use of magnesium has also been suggested[1] although it may be no better than placebo.[3,7] Some patients with primary hyperoxaluria may respond to high doses of pyridoxine.[1,3,7,10,16] In hyperuricosuria, reduced purine intake and allopurinol may be effective.[1,3,7,10]

Prevention of *uric acid stones* is based on adequate fluid intake, a low purine diet, and urinary alkalinisation with potassium citrate. Allopurinol may be used if there are high levels of urate.[1-3,6,7] Acetazolamide has been used short term.[6]

Struvite stones are caused by urease-producing bacteria. Antibacterials are used, and may be required long term, with urinary acidification using ammonium chloride[7] or methionine.[1,7] Dietary phosphate restriction may also be appropriate for patients with phosphate excretion of more than 35 mmol/day.[1] Acetohydroxamic acid, an inhibitor of bacterial urease, may be used as an adjunct in selected cases of severe infection,[7] but its use has been limited by adverse effects.[3,10]

Cystine stones are associated with cystinuria (p.1459) and are prevented by alkalinisation of the urine and a high fluid intake (3 to 4 litres daily).[2,3,6,7] Penicillamine may be used as a chelating agent.[3,6,10] Ascorbic acid, tiopronin,[1,7] and captopril[7] have also been suggested.

1. Straub M, Hautmann RE. Developments in stone prevention. *Curr Opin Urol* 2005; **15:** 119–26.
2. Moe OW. Kidney stones: pathophysiology and medical management. *Lancet* 2006; **367:** 333–44.
3. Reynolds TM. Chemical pathology clinical investigation and management of nephrolithiasis. *J Clin Pathol* 2005; **58:** 134–40.
4. Matlaga BR, Assimos DG. Urologic manifestations of nonurologic disease: urolithiasis. *Urol Clin North Am* 2003; **30:** 91–9.
5. Daudon M, Jungers P. Drug-induced renal calculi: epidemiology, prevention and management. *Drugs* 2004; **64:** 245–75.
6. Bihl G, Meyers A. Recurrent renal stone disease—advances in pathogenesis and clinical management. *Lancet* 2001; **358:** 651–6.
7. Tiselius H-G, *et al.* European Association of Urology guidelines on urolithiasis (update March 2008). Available at: http://www.uroweb.org/fileadmin/tx_eauguidelines/Urolithiasis.pdf (accessed 02/09/08)
8. Anagnostou T, Tolley D. Management of ureteric stones. *Eur Urol* 2004; **45:** 714–21.
9. Miller NL, Lingeman JE. Management of kidney stones. *BMJ* 2007; **334:** 468–72.
10. Parmar MS. Kidney stones. *BMJ* 2004; **328:** 1420–4.
11. Hollingsworth JM, *et al.* Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet* 2006; **368:** 1171–9.
12. Beach MA, Mauro LS. Pharmacologic expulsive treatment of ureteral calculi. *Ann Pharmacother* 2006; **40:** 1361–8.
13. Preminger GM, *et al.* American Urological Association. AUA guideline on management of staghorn calculi: diagnosis and treatment recommendations. *J Urol (Baltimore)* 2005; **173:** 1991–2000. Also available at: http://www.auanet.org/guidelines/staghorncalculi05.cfm (accessed 29/11/05)
14. Pearle MS. Prevention of nephrolithiasis. *Curr Opin Nephrol Hypertens* 2001; **10:** 203–9.
15. Baker MJ, Longyhore DS. Dietary calcium, calcium supplements, and the risk of calcium oxalate kidney stones. *Am J Health-Syst Pharm* 2006; **63:** 772–5.
16. Tiselius H-G. Epidemiology and medical management of stone disease. *BJU Int* 2003; **91:** 758–67.
17. Pearle MS, *et al.* Meta-analysis of randomized trials for medical prevention of calcium oxalate nephrolithiasis. *J Endourol* 1999; **13:** 679–85.

Renal colic

For the treatment of urological pain see Biliary and Renal Colic, p.5.

Renal failure

For discussions of acute and chronic renal failure and their management, see p.1672.

Sexually transmitted diseases

For discussion of sexually transmitted diseases and their treatment see p.191.

Syndrome of inappropriate ADH secretion

In some patients secretion of antidiuretic hormone (ADH; vasopressin) occurs despite hypotonicity of the extracellular fluid and normal or raised fluid volume, and such patients are said to have the syndrome of inappropriate ADH secretion (SIADH). With severe water excess, the resultant hyponatraemia may result in symptoms ranging from lassitude or headache to profound neurological symptoms such as confusion, convulsions, or coma. Some patients may experience inappropriate thirst as well as ADH secretion, thus exacerbating their condition. For a discussion of sodium homoeostasis and dilutional hyponatraemia, see p.1670.

Conditions that can precipitate SIADH include CNS disorders, infections such as encephalitis and meningitis, head trauma, porphyria, or pulmonary diseases such as tuberculosis and pneumonia. ADH may also be secreted ectopically from malignancies, most commonly from small-cell bronchial carcinoma. SIADH may also be drug-induced; drugs associated with the condition include carbamazepine, chlorpropamide, cytotoxic drugs such as cyclophosphamide and the vinca alkaloids, oxytocin, some antipsychotics, tricyclic antidepressants, and SSRIs.

Diagnosis of SIADH is initially prompted by the presence of hyponatraemia and corresponding plasma hypo-osmolality with or without neurological symptoms. Hypervolaemia, persistent excess sodium excretion, lack of oedema, and normality of both renal and adrenal function are confirmatory.

Mild water excess is frequently asymptomatic and may not require specific therapy, but patients with SIADH often have a more severe disorder and treatment is best aimed at the underlying cause. If such treatment is not possible or if symptoms persist, water restriction may be considered. However, fluid restriction is unpleasant, particularly for patients who retain inappropriate thirst, and may not be tolerable. In these patients demeclocycline may be given to antagonise the effect of ADH on the renal tubules. Lithium has been given as an alternative but has a high frequency of adverse effects, and phenytoin has been used occasionally to inhibit pituitary ADH secretion. Diuretics such as furosemide (used with oral sodium chloride) have also been tried in an attempt to optimise diuresis while retaining sodium. In patients with life-threatening severe acute water intoxication (see Hyponatraemia, p.1670), treatment initially involves cautious improvement of the profound hyponatraemia by intravenous infusion of hypertonic (usually 3%) or isotonic sodium chloride, often with furosemide or another loop diuretic to avoid volume expansion. Drugs that act directly in the renal tubules as vasopressin V_2 receptor antagonists are under investigation.

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2. Kovacs L, Robertson GL. Syndrome of inappropriate antidiuresis. *Endocrinol Metab Clin North Am* 1992; **21:** 859–75.
3. Miller M. Syndromes of excess antidiuretic hormone release. *Crit Care Clin* 2001; **17:** 11–23.
4. Verbalis JG. Vasopressin V receptor antagonists. *J Mol Endocrinol* 2002; **29:** 1–9.
5. Rabinstein AA. Vasopressin antagonism: potential impact on neurologic disease. *Clin Neuropharmacol* 2006; **29:** 87–93.
6. Ellison DH, Berl T. The syndrome of inappropriate antidiuresis. *N Engl J Med* 2007; **356:** 2064–72.

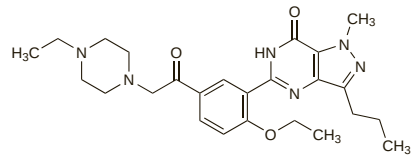
Urinary-tract infections

The treatment of urinary-tract infections is discussed on p.199.

Acetildenafil

Hongdenafil. 5-{2-Ethoxy-5-[2-(4-ethylpiperazine-1-yl)-acetyl]-phenyl}-1-methyl-3-*n*-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]-pyrimidin-7-one.

$C_{25}H_{34}N_6O_3$ = 466.6.



Profile

Acetildenafil is an analogue of sildenafil (p.2193) that has been used in various preparations or dietary supplements and illegally promoted in some countries for the management of erectile dysfunction. Other analogues of sildenafil detected in similar products include homosildenafil and hydroxyhomosildenafil.