inappropriate activation of complement. Hereditary or acquired abnormalities of the complement system are associated with a variety of disorders depending on which part of the system is affected, and include recurrent infections, partial lipodystrophy, hereditary angioedema, paroxysmal nocturnal haemoglobinuria, non-specific vasculitis, glomerulonephritis, cardiovascular disease, rheumatoid arthritis, sepsis, asthma, acute respiratory distress syndrome, psoriasis, SLE, bullous pemphigoid, discoid lupus, and graft survival after solid organ transplantation.

A number of substances are used or are under investigation for their ability to block activation of the complement system:

- complement C1 esterase inhibitor (p.2287) is given as replacement therapy in the treatment of hereditary angioedema
- eculizumab (p.2299) is a monoclonal antibody that targets the terminal C5 protein of complement and is given in the treatment of paroxysmal nocturnal haemoglobinuria
- pexelizumab (p.2366) is a similar substance under investigation in patients undergoing coronary artery revascularisation procedures
- mirococept (APT-070, SCR1-3) is a derivative of soluble complement receptor type 1 (SCR1) under investigation for the prevention of post transplantation graft dysfunction
- TP-10, a form of SCR1 has also been investigated for respiratory disorders
- myristoylated-peptidyl-recombinant human CD59 is under investigation for paroxysmal nocturnal haemoglobinuria

◊ References.

1. Bhole D, Stahl GL. Therapeutic potential of targeting the complement cascade in critical care medicine. *Crit Care Med* 2003; **31** (suppl): S97–S104.
2. Brook E, *et al*. Opportunities for new therapies based on the natural regulators of complement activation. *Ann N Y Acad Sci* 2005; **1056:** 176–88.

Complement C1 Esterase Inhibitor

Inhibidor de la C1 esterasa.

C1-Ингибитор Комплемента

ATC — B02AB03.

ATC Vet — QB02AB03.

Profile

Complement C1 esterase inhibitor is an endogenous complement blocker (p.2286) that plays a role in regulation of the complement system. It is prepared from human plasma and given as replacement therapy in hereditary angioedema (p.1081), in which there is a deficiency of natural complement C1-esterase inhibitor. It is given for both short-term prophylaxis and treatment of acute life-threatening attacks by slow intravenous injection or infusion in typical doses of 500 units or, in severe cases, 1000 units. The dose may be repeated if necessary after a few hours.

A recombinant human complement C1 esterase inhibitor (rh C1INH) is under investigation.

◊ Complement C1 esterase inhibitor may be effective in both the prevention and treatment of acute hereditary angioedema.[1] It has also been tried in the management of other conditions including sepsis (see Septicaemia, p.190) and capillary leak syndrome.[2] It is under investigation for the treatment of pancreatitis and for use in allogeneic lung transplantation, thermal injury, and shock.[2] It is also being studied as a means of limiting reperfusion injury in patients with acute myocardial infarction.[3]

1. Waytes AT, *et al*. Treatment of hereditary angioedema with a vapor-heated C1 inhibitor concentrate. *N Engl J Med* 1996; **334:** 1630–4.
2. Caliezi C, *et al*. C1-esterase inhibitor: an anti-inflammatory agent and its potential use in the treatment of diseases other than hereditary angioedema. *Pharmacol Rev* 2000; **52:** 91–112.
3. de Zwaan C, *et al*. Continuous 48-h C1-inhibitor treatment, following reperfusion therapy, in patients with acute myocardial infarction. *Eur Heart J* 2002; **23:** 1670–7.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Angioneurina†; Berinert P; ***Austria:*** Berinert; ***Cz.:*** Berinert; ***Fr.:*** Esterasine†; ***Ger.:*** Berinert; ***Hung.:*** Berinert P; ***Ital.:*** C1 Inattivatore Umano†; ***Neth.:*** Cetor; ***Switz.:*** Berinert.

Condurango

Condurango Bark; Condurango cortex; Condurango, écorce de; Eagle-vine Bark.

Pharmacopoeias. In *Jpn* and *Swiss*.

Profile

Condurango, the dried stem bark of *Marsdenia condurango* (*Gonolobus condurango*) (Asclepiadaceae), has been used as a bitter.

Homoeopathy. Condurango has been used in homoeopathic medicines under the following names: Marsdenia cundurango; Cond.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Sigman-Haustropfen; ***Braz.:*** Camomila; Estomafitino†; ***Ger.:*** Majocarmin forte†; Nervogastrol N†; Pankreaplex Neu†; Pascopankreat; Pascopankreat novo†; ***Pol.:*** Herbaton; ***Switz.:*** Elixir tonique N; Padma-Lax; Padmed Laxan; Stomacine.

Congo Red

CI Direct Red 28; Colour Index No. 22120; Czerwień Kongo; Rojo Congo; Rubrum Congoensis. Disodium 3,3′-[biphenyl-4,4′-diylbis(azo)]bis[4-aminonaphthalene-1-sulphonate].

$C_{32}H_{22}N_6Na_2O_6S_2$ = 696.7.

CAS — 573-58-0.

Profile

Congo red is used as a stain in the diagnosis of amyloidosis. It causes amyloid in tissue samples to fluoresce under polarised light.

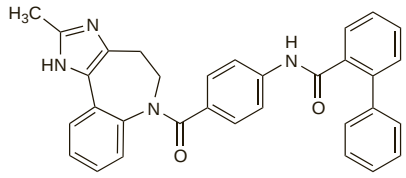
Conivaptan Hydrochloride *(rINNM)* ⊗

CI-1025; Conivaptan, Chlorhydrate de; Conivaptán, hidrocloruro de; Conivaptani Hydrochloridum; YM-087 (conivaptan or conivaptan hydrochloride). 4″-[(4,5-Dihydro-2-methylimidazo[4,5-*d*][1]benzazepin-6(1*H*)-yl)carbonyl]-2-biphenylcarboxanilide hydrochloride.

Кониваптана Гидрохлорид

$C_{32}H_{26}N_4O_2$,HCl = 535.0.

CAS — 210101-16-9 (conivaptan); 168626-94-6 (conivaptan hydrochloride).



(conivaptan)

Adverse Effects and Precautions

The most common adverse effects of conivaptan are infusion site reactions such as erythema, pain, phlebitis, and swelling, which are usually mild but can be severe enough in some patients that infusion must be stopped. Other adverse effects include atrial fibrillation, gastrointestinal disturbances, pyrexia, thirst, electrolyte disturbances, headache, and hypertension or hypotension.

Conivaptan is contra-indicated in hypovolaemic hyponatraemia, and is not indicated for the treatment of patients with congestive heart failure. Rapid correction of serum-sodium concentrations with conivaptan could increase the risk of osmotic demyelination syndrome. Conivaptan should be used with caution in hepatic or renal impairment because systemic exposure can be increased.

Interactions

As a substrate of the cytochrome P450 isoenzyme CYP3A4, concentrations of conivaptan can be increased by CYP3A4 inhibitors. The use of conivaptan with potent CYP3A4 inhibitors such as ketoconazole, itraconazole, clarithromycin, ritonavir, and indinavir is contra-indicated. Conivaptan itself is also a potent inhibitor of CYP3A4 and may increase the concentrations of other substrates of this isoenzyme, including amlodipine, midazolam, and simvastatin.

Conivaptan can reduce the clearance, and subsequently increase concentrations, of digoxin.

Pharmacokinetics

Conivaptan is metabolised by the cytochrome P450 isoenzyme CYP3A4, but inhibits its own metabolism. Using a regimen of intravenous loading dose followed by continuous infusion, concentrations of conivaptan initially decrease from the loading dose peak over about 12 hours, then gradually increase. After stopping the infusion, conivaptan has an elimination half-life of about 5 hours. Conivaptan is highly bound to plasma proteins.

Uses and Administration

Conivaptan hydrochloride is a vasopressin V_{1a} and V_2 receptor antagonist. In the management of hyponatraemia it acts mainly at V_2 receptors in the renal collecting ducts to increase the excretion of free water. It is used to treat euvolaemic and hypervolaemic hyponatraemia (p.1670), and is not indicated for congestive heart failure.

Conivaptan hydrochloride is given by intravenous infusion. To minimise infusion site irritation, it should be diluted in glucose 5% infusion (loading doses are given in 100 mL of fluid, the subsequent infusions in 250 mL) and given through a large vein; the infusion site should be changed every 24 hours. A loading dose of 20 mg is given over 30 minutes, followed by a continuous infusion of 20 mg over 24 hours. Treatment may be continued at a dose of 20 mg daily titrated to a maximum of 40 mg daily if required. The maximum duration of the infusion is 4 days. If a rapid rise in serum-sodium occurs (more than 12 mmol/litre in 24 hours) conivaptan should be stopped, and serum-sodium and neurological status should be carefully monitored because of the risk of osmotic demyelination syndrome. If hypovolaemia or hypotension develop, conivaptan should be stopped and volume status and vital signs should be monitored. Conivaptan may be resumed at a lower dose, if still indicated, when the rise in serum-sodium has stopped, if there is no evidence of adverse neurological effects and the patient is euvolaemic and no longer hypotensive.

◊ References.

1. Walter KA. Conivaptan: new treatment for hyponatremia. *Am J Health-Syst Pharm* 2007; **64:** 1385–95.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Vaprisol.

Convallaria

Convalaria; Convallariae Herba; Lily of the Valley; Maiblume; Maiglöckchenkraut; May Lily; Muguet; Ziele konwalii.

CAS — 3253-62-1 (convallatoxol); 13473-51-3 (convalloside); 13289-19-5 (convallatoxoloside); 508-75-8 (convallatoxin).

Pharmacopoeias. In *Ger.* and *Pol.* (from *C. majalis* or closely related species).

Profile

Convallaria consists of the dried flowers, herb, or the rhizomes and roots of lily of the valley, *Convallaria majalis* (Liliaceae). Several crystalline glycosides have been obtained from the plant including convallarin, convalloside, convallatoxoloside, and convallatoxin.

Convallaria contains cardiac glycosides and has actions on the heart similar to those of digoxin (p.1259). Convallaria is used in herbal medicine.

Homoeopathy. Convallaria has been used in homoeopathic medicines under the following names: Convallaria majalis; Conval. m.

◊ *Convallaria majalis* has been designated unsafe for inclusion in foods, beverages, or drugs by the FDA in the USA.[1]

1. Larkin T. *FDA Consumer* 1983; **17** (Oct.): 5.

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Convacard†; Valdig-N Burger†; ***Pol.:*** Convafort.

Multi-ingredient: ***Arg.:*** Passacanthine†; ***Austria:*** Omega; ***Ger.:*** Cardibisana†; Convallocor-SL; Convastabil; Miroton; Miroton N†; Oxacant N†; Oxacant-forte N†; Oxacant-Khella N†; Viscorapas duo†; ***Pol.:*** Cardiol C; Kelicardina; Neocardina.

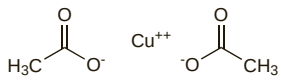
Copper Acetate

Cuivre, acétate de; Cupri acetas; Cupric Acetate; Kopparacetat; Kuparisetaatti; Miedzi(II) octan; Vario acetatas.

Ацетат Меди; Уксуснокислая Медь

$(C_2H_3O_2)_2Cu,H_2O$ = 199.6.

CAS — 142-71-2 (anhydrous).



Pharmacopoeias. *Eur.* (see p.vii) includes a form for homoeopathic preparations.

Ph. Eur. 6.2 (Copper Acetate Monohydrate for Homoeopathic Preparations; Cupri Acetas Monohydricus ad Praeparationes Homoeopathicas). Greenish-blue crystals or green powder. Soluble in water; slightly soluble or very slightly soluble in alcohol.

Profile

Copper acetate has been used in a variety of dermatological preparations. It is now more usually used complexed with a tripeptide in the form of prezatide copper acetate (p.1611). This acts as a source of ionic copper, which is needed by lysyl oxidase, a copper-dependent enzyme that has a crucial role in the crosslinking of collagen and elastin. For the nutritional and other uses of copper and its salts, see p.1936.

Homoeopathy. Copper acetate has been used in homoeopathic medicines under the following names: Cuprum aceticum; Cup. acet.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ital.:*** Verel; ***Mex.:*** Emplasto Monopolis.