a higher incidence of stroke in a group of patients given doses of 500 micrograms compared with a group receiving 300 micrograms. Patients with a history of stroke appeared to be at greater risk.

Uses and Administration

Ranibizumab is a recombinant humanised monoclonal antibody used in the treatment of neovascular (wet) age-related macular degeneration. It is given by intravitreal injection into the affected eye in doses of 500 micrograms once a month initially for 3 to 4 months. In the UK, after the first 3 months, maintenance treatment is based on regular assessment of visual acuity, with ranibizumab being given if the patient had a loss of greater than 5 letters in visual acuity; the interval between consecutive doses should be at least one month. In the USA, if monthly administration is not feasible after the first four injections, treatment may be given once every 3 months, although this is not as effective as monthly doses.

Age-related macular degeneration. Ranibizumab is a recombinant humanised monoclonal antibody fragment related to bevacizumab (p.684) used in the treatment of (wet) age-related macular degeneration (AMD) (p.785). It binds to and inhibits vascular endothelial growth factor A (VEGF-A), which is a stimulant of angiogenesis thought to play a role in the neovascularisation and retinal changes associated with AMD. Ranibizumab inhibits all active forms of VEGF-A.[1]

Positive outcomes have been reported from two international multicentre randomised controlled phase III studies.[2,3] Vision loss was prevented and mean visual acuity improved in patients given either monthly injections of 300 micrograms or 500 micrograms for 2 years compared with patients receiving sham injections.[2] Ranibizumab given in the same doses was also shown to be superior to photodynamic therapy with verteporfin at 1 year in the second study.[3]

A review[4] of interim results of other ongoing phase III studies of ranibizumab for AMD suggests that reducing the dosing interval to once every 3 months is less satisfactory than monthly injections, although tailoring the treatment to morphological parameters was as effective at 1 year as giving a fixed dosage regimen. However, ranibizumab in combination with photodynamic therapy does not necessarily result in better visual acuity outcomes and may even be worse than ranibizumab alone. A systematic review[5] of 5 randomised controlled studies found that ranibizumab was effective in reducing the risk of loss of visual acuity, and also improved visual acuity in a significant proportion of eyes.

1. Blick SKA, *et al.* Ranibizumab. *Drugs* 2007; **67:** 1199–1206.
2. Rosenfeld PJ, *et al.* for the MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006; **355:** 1419–31.
3. Brown DM, *et al.* for the ANCHOR Study Group. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *N Engl J Med* 2006; **355:** 1432–44.
4. Rosenfeld PJ, *et al.* Ranibizumab: phase III clinical trial results. *Ophthalmol Clin North Am* 2006; **19:** 361–72.
5. Vedula SS, Krzystolik MG. Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 06/06/08).

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Lucentis; ***Cz.:*** Lucentis; ***Fr.:*** Lucentis; ***Gr.:*** Lucentis; ***Indon.:*** Lucentis; ***Malaysia:*** Lucentis; ***Port.:*** Lucentis; ***UK:*** Lucentis; ***USA:*** Lucentis.

Rapeseed Oil

Colza, aceite de; Colza, huile de; Colza Oil; Olej rzepakowy; Oleum Rapae; Rapae oleum; Rape Oil; Rapsolja; Rapsų aliejus; Repceolaj; Řepkový olej; Rypsiöljy.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*. *USNF* includes fully hydrogenated rapeseed oil and superglycerinated fully hydrogenated rapeseed oil.
Ph. Eur. 6.2 (Rapeseed Oil, Refined). The fatty oil obtained from the seeds of *Brassica napus* and *Brassica campestris* by mechanical expression or extraction and then refined. A suitable antoxidant may be added. It contains not more than 2% of erucic acid. A clear light yellow liquid. Practically insoluble in water and in alcohol; miscible with petroleum spirit. Store in well-filled airtight containers. Protect from light.
USNF 26 (Fully Hydrogenated Rapeseed Oil). A mixture of triglycerides in which the fatty acid composition is a mixture of saturated fatty acids. It is obtained by refining and hydrogenating oil obtained from the seeds of *Brassica napus* and *Brassica campestris*. It contains not more than 1% of erucic acid. A white, waxy solid. Insoluble in water and in alcohol. Store in airtight containers. Protect from light.
USNF 26 (Superglycerinated Fully Hydrogenated Rapeseed Oil). A mixture of mono-, di-, and triglycerides, with triglycerides as a minor component. It is obtained by refining, hydrogenating, and glycerinating oil obtained from the seeds of *Brassica napus* and *Brassica campestris*. It contains not more than 1% of erucic acid. A white solid. Insoluble in water and in alcohol. Store in airtight containers. Protect from light.

Profile

Rapeseed oil has been used in liniments in place of olive oil. It is used in some countries as an edible oil but the erucic acid ($C_{22}H_{42}O_2$ = 338.6) content of the oil has been implicated in muscle damage. The erucic acid content of oils and fats intended for human consumption and of foodstuffs containing oil or fat is subject to legal control. Contaminated rapeseed oil was the cause of the toxic oil syndrome that affected thousands of Spanish citizens in early 1981. Rapeseed oil is also used in industrial manufacturing.

There has been some debate whether the frequency of allergic respiratory symptoms in sensitive individuals is increased in areas in which oilseed rape is cultivated.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Gr.:*** Fissan-Pate†.

Raspberry Leaf

Frambuesa, hoja de; Rubi Idaei Folium.

Profile

Raspberry leaf consists of the dried leaflets of *Rubus idaeus* (Rosaceae). It contains a principle, readily extracted with hot water, which relaxes the smooth muscle of the uterus and intestine of some *animals*.

Raspberry 'tea' has been a traditional remedy for painful and profuse menstruation and for use before and during labour. The infusion has also been used as an astringent gargle.

◊ References.

1. Simpson M, *et al.* Raspberry leaf in pregnancy: its safety and efficacy in labor. *J Midwifery Womens Health* 2001; **46:** 51–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Rubus Complex†; ***Cz.:*** Detsky Caj s Hermankem; Diabetan; Hertz- und Kreislauftee†; Hypotonicka; Species Cholagogae Planta.

Relaxin

Relaxina.
CAS — 9002-69-1.

Profile

Relaxin is a polypeptide hormone that has been extracted from the corpus luteum of the ovaries of pregnant sows, although a human recombinant form is also now available. It is reported to be related structurally to insulin and has a molecular weight of about 6000.

Relaxin is secreted by the human corpus luteum during pregnancy and is thought to interact with other reproductive hormones. It acts on connective tissue, including collagen, and causes relaxation of the pubic symphysis and softening of the uterine cervix. In many *animal* species relaxin appears to play a major part in cervical ripening before parturition; significant species difference is shown. It has been studied for cervical ripening in humans. Recombinant human relaxin has also been investigated in infertility, cardiovascular disorders, and scleroderma (p.1817).

◊ References.

1. Seibold JR, *et al.* Safety and pharmacokinetics of recombinant human relaxin in systemic sclerosis. *J Rheumatol* 1998; **25:** 302–7.
2. Seibold JR, *et al.* Recombinant human relaxin in the treatment of scleroderma: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2000; **132:** 871–9.
3. Kelly AJ, *et al.* Relaxin for cervical ripening and induction of labour. Available in The Cochrane Database of Systematic Reviews; Issue 2. John Wiley; Chichester; 2001 (accessed 28/04/06).

Resveratrol

NSC-327430; 3,4′,5-Stilbenetriol; 3,4′,5-Trihydroxystilbene. (E)-5-[2-(4-Hydroxyphenyl)ethenyl]-1,3-benzenediol.
$C_{14}H_{12}O_3$ = 228.2.
CAS — 501-36-0.

Profile

Resveratrol is a phytoalexin present in a range of plant sources including species of *Arachis*, *Pinus*, *Polygonum*, *Veratrum*, and *Vitis*. It is thought to be one of the compounds responsible for the cardioprotective action of wine (see Grape, p.2316, and Flavonoid Compounds, p.2304).

Resveratrol used in commercial preparations is often derived from the root of Japanese knotweed, *Fallopia japonica* (*Polygonum cuspidatum*; *Reynoutria japonica*) (Polygonaceae) often as the racemate although the *trans*-isomer is also promoted.

Resveratrol is promoted as an antoxidant for the prevention of atherosclerosis. It also has mixed agonist/antagonist activity at oestrogen receptors and some anti-inflammatory and antiproliferative activity, and is under investigation in the prevention and treatment of malignancy.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Resvelife†.

Rhamnose

Ramnosa; Ramnoza; L-Rhamnose. 6-Deoxy-L-mannose.
$C_6H_{12}O_5$ = 164.2.
CAS — 3615-41-6.

Profile

Rhamnose is a monosaccharide used to assess intestinal permeability.

For reference to the use of rhamnose in the differential sugar absorption test, see Diagnosis and Testing under Lactulose, p.1739.

◊ References.

1. van Nieuwenhoven MA, *et al.* The sensitivity of the lactulose/rhamnose gut permeability test. *Eur J Clin Invest* 1999; **29:** 160–5.
2. Haase AM, *et al.* Dual sugar permeability testing in diarrheal disease. *J Pediatr* 2000; **136:** 232–7.
3. van Nieuwenhoven MA, *et al.* Effects of pre- and post-absorptive factors on the lactulose/rhamnose gut permeability test. *Clin Sci* 2000; **98:** 349–53.

Rhatany Root

Krameria; Krameria Root; Ratanhia, racine de; Ratanhiae radix; Ratanhiagyökér; Ratanhový kořen; Ratania, raíz de; Ratanianjuuri; Rataniarot; Ratanijų šaknys.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Rhatany Root). The dried, usually fragmented, underground organs of *Krameria triandra*. It contains not less than 5% of tannins, expressed as pyrogallol, calculated with reference to the dried drug. It is known as Peruvian rhatany. Protect from light.

Profile

Rhatany root has astringent properties and is used in herbal preparations for a variety of disorders, including oropharyngeal inflammation.

Homoeopathy. Rhatany root has been used in homoeopathic medicines under the following names: Ratanhia; Krameria triandra; Ratanhiae radix; Ratania peruviana; Ratan.

Preparations

Ph. Eur.: Rhatany Tincture.

Proprietary Preparations (details are given in Part 3)
Ger.: ratioSept.

Multi-ingredient: ***Arg.:*** Esculeol P; Parodontax Fluor; ***Austria:*** Parodontax; ***Braz.:*** Malvatricin Natural Organic; Parodontax; ***Chile:*** Hemorrol†; ***Fr.:*** Delabarre Bio-adhesif; ***Ger.:*** Ratanhia comp; Repha-Os; ***Israel:*** Parodontax†; ***Ital.:*** Gengivario†; ***Spain:*** Encialina†; ***Switz.:*** Eubucal†; GU Eau†; Parodontax F†; Parodontax†; Sanogencive.

Rhus

Sumach Berries; Zumaque.

Pharmacopoeias. *Br.* includes Toxicodendron Quercifolium for Homoeopathic Preparations.
BP 2008 (Toxicodendron Quercifolium for Homoeopathic Preparations). Fresh, young, not yet lignified shoots, with leaves, of *Toxicodendron quercifolium*. The shoots contain a yellowish-white milky sap that is a strong cutaneous irritant and darkens the skin. Contact with the skin and mucous membranes is to be avoided.

Profile

Rhus consists of the dried fruits of the smooth or Pennsylvanian sumach, *Rhus glabra* (Anacardiaceae). It has astringent and reputed diuretic properties. *R. aromatica* has been used similarly to *R. glabra*.

Poison ivy (*R. radicans*) and poison oak (*R. toxicodendron*), species growing in the USA, contain irritant poisons, such as urushiol, that produce severe contact dermatitis. Extracts of poison ivy and poison oak have been used for the prophylaxis of poison ivy dermatitis but their effectiveness has not been proved. The spice sumac is prepared from the berries of *R. coriaria*.

Homoeopathy. Some *Rhus* spp. are used in homoeopathic medicine. Poison oak has been used in homoeopathic medicines under the following names: Toxicodendron quercifolium; Rhus toxicodendron; Rhus. tox.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Joint & Muscle Cream; ***Chile:*** Rhus Opodeldoc; ***Ger.:*** Hicoton†; Rhus-Rheuma-Gel N.

Ribonuclease

Ribonucleasa; RNase.
CAS — 9001-99-4.

Profile

Ribonuclease is an enzyme present in most mammalian tissue, and it is involved in the catalytic cleavage of ribonucleic acid. It

has been applied, alone or with other drugs, for its supposed anti-inflammatory properties.

Preparations

Proprietary Preparations (details are given in Part 3)
Mex.: Cro 50.

Multi-ingredient: ***Braz.:*** Bromelin†; Expectoral†; ***Fr.:*** Ribatran; ***Mex.:*** Ofzim; Ridasa.

Ribonucleic Acid

ARN; Plant Nucleic Acid; Ribonucleico, ácido; Ribose Nucleic Acid; RNA; Yeast Nucleic Acid.

Рибонуклеиновая Кислота

Profile

Ribonucleic acid (RNA) is a nucleic acid (p.2355) in which the pentose sugar moiety of the nucleotides is ribose, the purine bases are adenine (p.2247) and guanine, and the pyrimidine bases are cytosine and uracil (p.2407). RNA exists as a single polynucleotide strand that replicates using DNA as a template during which process the pairing of bases between the complementary strands of RNA and DNA is always the same: adenine with uracil and cytosine with guanine. RNA is present in cell nuclei and cytoplasm and is directly involved in protein synthesis; it also plays a part in encoding genetic information. RNA also carries the genetic material of RNA viruses. Gene suppression by RNA interference (RNAi), using specific double-stranded ribonucleic acid sequences, is under investigation. For the role of RNA as a tool in gene therapy, see p.2310.

Proprietary preparations containing RNA are marketed in some countries for a variety of asthenic and convalescent conditions. RNA has also been tried in the treatment of mental retardation and to improve memory in senile dementia. It may also have a role in enteral feeds under some circumstances.

Immune RNA (extracted from the spleens and lymph nodes of immunised animals) has been tried in the immunotherapy of hepatitis and cancer.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: AU 4 Regeneresen; Osteochondrin S; Regeneresen; RN13 Regeneresen.

Multi-ingredient: ***India:*** Placentrex; ***Spain:*** Dertrase; Nucleserina; Policolinosil.

Ribwort Plantain

Heinäratamonlehti; Jitrocelový list; Liść babki lancetowatej; Plantaginis Folium; Plantaginis Lanceolatae; Plantaginis lanceolatae folium; Plantain Herb; Plantain lancéolé; Siauralapių gysločių lapai; Spitzwegerich; Spitzwegerichkraut; Svartkämparblad.

Pharmacopoeias. *Eur.* (see p.vii) includes the leaf.
Ph. Eur. 6.2 (Ribwort Plantain; Plantaginis Lanceolatae Folium). The whole or fragmented, dried leaf and scape of *Plantago lanceolata*. It contains not less than 1.5% of total *ortho*-dihydroxycinnamic acid derivatives expressed as acteoside ($C_{29}H_{36}O_{15}$ = 624.6) with reference to the dried drug. Protect from light.

Profile

Ribwort plantain is an ingredient in herbal remedies used for catarrh and inflammation of the upper respiratory tract.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Jitrocel v Nalevovych†; Jitrocelovy; ***Fr.:*** Sensivision au plantain; ***Ger.:*** Broncho-Sern; Proguval†; Tetesept Husten Saft; Tetesept Husten Tropfen; ***Pol.:*** Lancetan; Lanceticum; Plantagen.

Multi-ingredient: ***Austria:*** Brust- und Hustentee St Severin; Grippetee St Severin; Pneumopan; Scottopect; ***Canad.:*** Original Herb Cough Drops; ***Cz.:*** Biotussil; Bronchialtee N†; Cajova Smes pri Nachlazeni; Detsky Caj s Hermankem; Dr Theiss Spitzwegerich Hustensaft†; Mucoplant Jitrocelovy; Naturident†; Prudušková; Pulmoran; Species Pectorales Planta; Thymomel; ***Ger.:*** Bronchicum Elixir Plus†; Equisil N; Eucabal†; Kneipp Husten- und Bronchial-Tee; ***Hong Kong:*** Pectoral†; ***Ital.:*** Altea (Specie Composta)†; Timo (Specie Composta)†; ***Pol.:*** Babicum; Echinasal; Flegatussin; Gwajatussin; Pectobonisol; Plantifort; Saponarex; ***Rus.:*** Eucabal (Эвкабал); Herbion Plantain Syrup (Гербион Сироп Подорожника); Stoptussin-Fito (Стоптуссин-фито); ***Spain:*** Llantusil†; Natusor Farinol†; Natusor Gastrolen†; Natusor Infenol†; ***Switz.:*** Bronchofluid N†; Gouttes contre la toux "S"; Neo-DP†; Nican; Pastilles bronchiques S nouvelle formule; Thymodrosin N†; Wala Pulmonium suc contre la toux.

Ricin

Ricino.

CAS — 9009-86-3.

NOTE. The title ricin is used for the castor seed in *Chin.* and *Fr.*

Profile

Ricin is a lectin present in castor seeds, the seeds of *Ricinus communis* (Euphorbiaceae). It is extremely toxic when given parenterally and the fatal dose by injection has been reported to be around 1 microgram/kg. The toxicity of orally ingested beans depends on how thoroughly they are chewed since the hard seed coat prevents absorption. Ingestion of as few as 3 castor seeds by a child and 4 by an adult may be fatal. Ricin may also be absorbed through abraded skin. It has potential use in aerosol form as an agent of chemical warfare. Toxic effects may be delayed for several days after exposure by any route. Early symptoms include severe gastrointestinal irritation, haemorrhage, vomiting, and diarrhoea, which may result in circulatory collapse. Abnormal liver function tests and pulmonary oedema have been reported. Ophthalmological disturbances ranging from irritation and conjunctivitis to optic nerve damage may occur; miosis and mydriasis have also been reported. Proteinuria, haematuria, and renal impairment may develop and serum creatinine levels may be raised. In severe cases haemolysis of the red blood cells with subsequent acute renal failure may occur. Fatalities due to multi-organ failure have occurred. If the patient presents within 1 hour of ingestion any seeds may be removed by gastric lavage and activated charcoal given. Treatment thereafter is symptomatic.

After expression of the oil from castor seeds (see p.2278), the ricin remaining in the seed cake or 'pomace' is destroyed by steam treatment. The detoxified pomace is used as a fertiliser.

Ricin conjugated with monoclonal or polyclonal antibodies is being studied in the treatment of cancers; zolimomab aritox is an example of such a conjugate. Some of these conjugates have been investigated for various malignancies, particularly leukaemias and lymphomas.

Toxicity. A report of ricin toxicity after partial chewing and ingestion of 10 to 15 castor oil seeds,[1] and reviews[2-4] of ricin toxicity, including its potential as an agent of chemical warfare.

1. Aplin PJ, Eliseo T. Ingestion of castor oil plant seeds. *Med J Aust* 1997; **167:** 260–1.
2. Bradberry SM, *et al.* Ricin poisoning. *Toxicol Rev* 2003; **22:** 65–70.
3. Lord MJ, *et al.* Ricin: mechanisms of cytotoxicity. *Toxicol Rev* 2003; **22:** 53–64.
4. Audi J, *et al.* Ricin poisoning: a comprehensive review. *JAMA* 2005; **294:** 2342–51.

Uses. References to the use of ricin conjugates with monoclonal antibodies in the treatment of cancer.

1. Byers VS, *et al.* Phase I study of monoclonal antibody-ricin A chain immunotoxin XomaZyme-791 in patients with metastatic colon cancer. *Cancer Res* 1989; **49:** 6153–60.
2. Oratz R, *et al.* Antimelanoma monoclonal antibody-ricin A chain immunoconjugate (XMMME-001-RTA) plus cyclophosphamide in the treatment of metastatic malignant melanoma: results of a phase II trial. *J Biol Response Mod* 1990; **9:** 345–54.
3. Anonymous. Application considered for immunotoxin in treatment of graft-vs-host disease. *JAMA* 1991; **265:** 2041–2.
4. Amlot PL, *et al.* A phase I study of an anti-CD22-deglycosylated ricin A chain immunotoxin in the treatment of B-cell lymphomas resistant to conventional therapy. *Blood* 1993; **82:** 2624–33.
5. Senderowicz AM, *et al.* Complete sustained response of a refractory, post-transplantation, large B-cell lymphoma to an anti-CD22 immunotoxin. *Ann Intern Med* 1997; **126:** 882–5.
6. Multani PS, *et al.* Phase II clinical trial of bolus infusion anti-B4 blocked ricin immunoconjugate in patients with relapsed B-cell non-Hodgkin's lymphoma. *Clin Cancer Res* 1998; **4:** 2599–2604.
7. Dinndorf P, *et al.* Phase I trial of anti-B4-blocked ricin in pediatric patients with leukemia and lymphoma. *J Immunother* 2001; **24:** 511–16.
8. Schnell R, *et al.* Clinical evaluation of ricin A-chain immunotoxins in patients with Hodgkin's lymphoma. *Ann Oncol* 2003; **14:** 729–36.
9. Tsimberidou AM, *et al.* Anti-B4 blocked ricin post chemotherapy in patients with chronic lymphocytic leukemia—long-term follow-up of a monoclonal antibody-based approach to residual disease. *Leuk Lymphoma* 2003; **44:** 1719–25.

Ricinoleic Acid

Kwas rycynolowy; Ricinoleico, ácido.

CAS — 141-22-0.

Profile

Ricinoleic acid is a mixture of fatty acids obtained by the hydrolysis of castor oil. It is an ingredient of some proprietary vaginal jellies used to maintain or restore normal vaginal acidity.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Aci-Jel†; ***Israel:*** Glovan; ***NZ:*** Aci-Jel†; ***USA:*** Acid Jelly.

Rilonacept *(USAN, rINN)*

IL-1 Trap; Interleukin-1 Receptor; Interleukin-1 Trap; Rilonaceptum.

Рильонацепт

CAS — 501081-76-1.

Profile

Rilonacept is an interleukin-1 blocker used in the treatment of cryopyrin-associated periodic syndromes (CAPS) including familial cold auto-inflammatory syndrome (FCAS) and Muckel-Wells syndrome (MWS), which are rare inherited auto-inflammatory disorders. Rilonacept is a soluble decoy interleukin-1 receptor that binds interleukin-1_{beta} (p.2325) and blocks its actions at cell surfaces.

Rilonacept is given by subcutaneous injection. The solution, when prepared according to the manufacturer's directions, contains 160 mg per 2 mL and this is the maximum amount that should be given as a single injection or at a single site; if a larger dose is required (as at loading) two separate injections should be given on the same day at two different sites.

The loading dose is 320 mg (as two separate injections). A single injection of 160 mg is then given once weekly. The loading dose for children aged 12 to 17 years is 4.4 mg/kg up to a maximum of 320 mg (given as one or two injections depending on the dose). A single injection of 2.2 mg/kg up to a maximum of 160 mg is then given once weekly.

Preparations

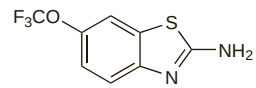
Proprietary Preparations (details are given in Part 3)
USA: Arcalyst.

Riluzole *(BAN, USAN, rINN)*

PK-26124; Rilutsoli; Riluzol; Riluzolum; RP-54274. 2-Amino-6-(trifluoromethoxy) benzothiazole; 6-Trifluoromethoxy-1,3-benzothiazol-2-ylamine.

Рилузол

$C_8H_5F_3N_2OS$ = 234.2.
CAS — 1744-22-5.
ATC — N07XX02.
ATC Vet — QN07XX02.



Adverse Effects and Treatment

Adverse effects associated most commonly with riluzole are asthenia, nausea, elevations in liver enzyme values, headache, and abdominal pain. Other gastrointestinal effects may include diarrhoea or constipation, anorexia, and vomiting. There may be tachycardia, dizziness, vertigo, or somnolence. Circumoral paraesthesia has been reported and decreased lung function and rhinitis may occur. Anaphylactoid reactions, angioedema, pancreatitis, and neutropenia have all been reported rarely.

Effects on the blood. Severe neutropenia has been reported[1] in a 71-year old patient with amyotrophic lateral sclerosis receiving standard doses of riluzole. The neutrophil count returned to normal on cessation of riluzole.

See also under Overdosage, below.

1. Weber G, Bitterman H. Riluzole-induced neutropenia. *Neurology* 2004; **62:** 1648.

Effects on the kidneys. A 44-year-old patient developed renal tubular impairment 3 months after starting riluzole for amyotrophic lateral sclerosis.[1] Tubular function recovered 1 month after stopping riluzole.

1. Poloni TE, *et al.* Renal tubular impairment during riluzole therapy. *Neurology* 1999; **52:** 670.

Effects on the liver. Icteric toxic hepatitis, with jaundice and elevated liver enzyme values, has been reported[1] in an elderly woman receiving riluzole for amyotrophic lateral sclerosis (ALS). Acute hepatitis developed in 2 patients several weeks after starting therapy with riluzole for ALS.[2] Liver histology showed hepatocellular damage with inflammatory infiltration and microvesicular steatosis without fibrosis. Hepatotoxicity was reversed in all these cases when riluzole was stopped.

1. Castells LI, *et al.* Icteric toxic hepatitis associated with riluzole. *Lancet* 1998; **351:** 648.
2. Remy A-J, *et al.* Acute hepatitis after riluzole administration. *J Hepatol* 1999; **30:** 527–30.

Effects on the pancreas. Riluzole was cited[1] as the most likely cause of severe pancreatitis that developed in a 77-year-old woman 6 months after starting therapy for sporadic amyotrophic lateral sclerosis; pancreatic symptoms improved when riluzole was stopped.

1. Drory VE, *et al.* Riluzole-induced pancreatitis. *Neurology* 1999; **52:** 892–3.

Hypersensitivity. A severe life-threatening systemic inflammatory reaction occurred in a patient 2 weeks after starting treatment with riluzole for amyotrophic lateral sclerosis.[1] Symptoms resolved spontaneously on stopping riluzole.

1. Sorenson EJ. An acute, life-threatening, hypersensitivity reaction to riluzole. *Neurology* 2006; **67:** 2260–1.

Overdosage. Severe neutropenia developed in a 63-year-old woman receiving riluzole for amyotrophic lateral sclerosis 10 days after inadvertent dose increase to 200 mg daily (twice the standard recommended dose).[1]

Methaemoglobinaemia has been reported[2] in a 43-year-old patient with amyotrophic lateral sclerosis after intentional overdose with 2.8 g of riluzole. The patient was treated with gastric lavage followed by activated charcoal; intravenous methylthioninium chloride successfully reversed the methaemoglobinaemia. However, the patient died of respiratory failure related to her underlying disease 7 days after the overdose.

An amnesic syndrome that persisted for over a year developed in a woman 4 days after ingestion of 3 g of riluzole.[3]

1. North WA, *et al.* Reversible granulocytopenia in association with riluzole therapy. *Ann Pharmacother* 2000; **34:** 322–4.