

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†; Expectorali†; **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; Lišć babki lancetowatej; Plantaginifolium; Plantaginifolium; Plantaginifolium lanceolatae folium; Plantain Herb; Plantain lanceolé; Sauralapij gysoelőj lapai; Spitzwegerich; Spitzwegerichkraut; Svartkämparblad.

Pharmacopoeias. *Eur.* (see p.vii) includes the leaf.

Ph. Eur. 6.2 (Ribwort Plantain; Plantaginifolium 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 acetoiside (C₂₉H₃₆O₁₅ = 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; Plantagan.

Multi-ingredient: **Austria:** Brust- und Hustentee St Severin; Grippeteer St Severin; Pneumopan; Scottopect; **Canada:** Original Herb Cough Drops; **Cz.:** Biotussil; Bronchiattee N†; Cajova Smes pri Nachlazení; Detsky Caj s Hermankem; Dr Theiss Spitzwegerich Hustensaft†; Mucoplant Jitrocelovy; Naturident†; Pruduškova; 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; Echinasil; Flegatussin; Gwajatussin; Pectobonisol; Plantifor; Saponarex; **Rus.:** Eucabal (Эукабал); Herbi-on Plantain Syrup (Гербион Сируп Подорожника); Stoptussin-Fito (Стоптуссин-Фито); **Spain:** Llantusil†; Natusor Farinol†; Natusor Gastrolen†; Natusor Inferol†; **Switz.:** Bronchifluid N†; Gouttes contre la toux 'S'; Neo-DPT; 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 ab-

sorbed 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 reviews²⁻⁴ 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-dglycosylated 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 Muckle-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; Rilutsoil; Riluzol; Riluzolum; RP-54274. 2-Amino-6-(trifluoromethoxy) benzothiazole; 6-Trifluoromethoxy-1,3-benzothiazol-2-ylamine.

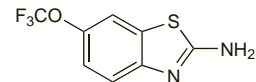
Рилузол

C₈H₅F₃N₂OS = 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 reported¹ 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 reported¹ 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 cited¹ 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 reported² 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 methylnthionium 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.

The symbol † denotes a preparation no longer actively marketed