Uses and Administration

Sulfinpyrazone is a uricosuric drug used to treat hyperuricaemia associated with chronic gout (p.552). It also has some antiplatelet activity.

Sulfinpyrazone is used in chronic gout to inhibit the renal tubular reabsorption of uric acid so increasing the urinary excretion of uric acid, lowering plasma-urate concentrations, and eventually reducing urate deposits in the tissues. It is therefore of value in hyperuricaemia caused by decreased uric acid excretion rather than increased urate production and is not used for hyperuricaemia associated with cancer or cancer therapy.

Sulfinpyrazone has little analgesic or anti-inflammatory action and is of no value in acute gout. Initially, it may increase plasma concentrations of urate and uric acid by dissolving deposits. This can trigger or exacerbate acute attacks, hence sulfinpyrazone should not be given until an acute attack has completely subsided, and an NSAID or colchicine may be given during the first few months.

The initial oral dose of sulfinpyrazone in the UK is 100 to 200 mg daily (the USA allows up to 200 mg twice daily), taken with meals or milk. This may be gradually increased over 1 to 3 weeks until a daily dosage of 600 mg is reached; up to 800 mg daily may be given if necessary. After the plasma-urate concentration has been controlled, the daily maintenance dose may be reduced to as low as 200 mg. An adequate fluid intake is required to prevent formation of uric acid renal calculi.

Antiplatelet therapy. Sulfinpyrazone inhibits platelet function, thereby inhibiting thrombosis. A meta-analysis of studies, conducted by the Antiplatelet Trialists' Collaboration, has shown that it reduces the risk of myocardial infarction, stroke, or vascular death in patients at high risk of occlusive vascular disease[1] and also reduces the risk of occlusion in patients undergoing arterial reperfusion and revascularisation procedures.[2] However, aspirin is the most widely used antiplatelet therapy, as discussed under Cardiovascular Risk Reduction, on p.1164.

1. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy—I: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ* 1994; **308:** 81–106.
2. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy—II: maintenance of vascular graft or arterial patency by antiplatelet therapy. *BMJ* 1994; **308:** 159–68.

Preparations

BP 2008: Sulfinpyrazone Tablets;
USP 31: Sulfinpyrazone Capsules; Sulfinpyrazone Tablets.

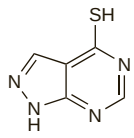
Proprietary Preparations (details are given in Part 3)
Ital.: Enturen; ***Port.:*** Sulfinona†; ***UK:*** Anturan; ***USA:*** Anturane.

Tisopurine *(rINN)*

MPP; Thioallopurinol; Thiopurinol; Tisopurina; Tisopurinum. 1*H*-Pyrazolo[3,4-*d*]pyrimidine-4-thiol.

Тизопурин

$C_5H_4N_4S$ = 152.2.
CAS — 5334-23-6.
ATC — M04AA02.
ATC Vet — QM04AA02.



Profile

Tisopurine, an analogue of allopurinol, is an inhibitor of uric acid synthesis. It is used orally in the treatment of disorders associated with hyperuricaemia (p.552), including gout, in doses of 100 to 400 mg daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Exuracid.

Urate Oxidase

CB-8129; Uricasa; Uricase.

Уратоксидаза
CAS — 9002-12-4.
ATC — M04AX01.
ATC Vet — QM04AX01.

Rasburicase *(BAN, USAN, rINN)*

Rasburicasa; Rasburicasum; Rasburikaasi; Rasburikas; Rasburikaz; SR-29142.

Разбуриказа
CAS — 134774-45-1.
ATC — V03AF07.
ATC Vet — QV03AF07.

Description. Rasburicase is a recombinant form of the enzyme urate oxidase.

Adverse Effects

The most serious adverse effects of rasburicase involve hypersensitivity reactions, including anaphylaxis, rashes, bronchospasm, rhinitis, urticaria, hypotension, dyspnoea, and chest pain and tightness. Haemolysis and methaemoglobinaemia have also been reported. Other adverse effects are nausea, vomiting, abdominal pain, constipation, diarrhoea, headache, fever, respiratory distress, sepsis, neutropenia, and mucositis.

Precautions

Treatment with rasburicase should be immediately and permanently stopped if hypersensitivity reactions, methaemoglobinaemia, or haemolysis develop. Rasburicase is contra-indicated in patients with G6PD deficiency or other cellular metabolic disorders known to cause haemolytic anaemia; hydrogen peroxide, which is produced during oxidation of uric acid to allantoin, can induce haemolytic anaemia in these patients. Patients at higher risk of having G6PD deficiency should be screened before receiving rasburicase.

Uses and Administration

Rasburicase is a recombinant form of the enzyme urate oxidase, which oxidises uric acid to allantoin. It is used in the treatment and prophylaxis of severe hyperuricaemia (p.552) associated with the treatment of malignancy. It is given by intravenous infusion before and during the start of chemotherapy, in a dose of 150 or 200 micrograms/kg daily over 30 minutes. Duration of treatment may vary from 5 to 7 days.

The native form of urate oxidase has also been used.

Gout. Rasburicase has been used successfully to treat gout in patients allergic to allopurinol.[1,2]

1. Vogt B. Urate oxidase (rasburicase) for treatment of severe tophaceous gout. *Nephrol Dial Transplant* 2005; **20:** 431–3.
2. Richette P, Bardin T. Successful treatment with rasburicase of a tophaceous gout in a patient allergic to allopurinol. *Nat Clin Pract Rheumatol* 2006; **2:** 338–42.

Tumour lysis syndrome. The tumour lysis syndrome (p.639) represents a biochemical disturbance after massive release of cellular breakdown products from tumour cells sensitive to therapy; hyperuricaemia is a cardinal feature. Rasburicase was effective in the prophylaxis or treatment of hyperuricaemia in children and young adults with leukaemia or lymphoma who either presented with abnormally high plasma concentrations of uric acid or had large tumour cell burdens.[1] Treatment was mostly well tolerated; one patient developed nausea and vomiting and one experienced bronchospasm and hypoxaemia 3 hours after infusion. Antibodies to rasburicase were seen in 17 of 121 assessable patients. Safety and efficacy were confirmed in further studies of children[2] and adults[2,3] considered to be at particularly high risk of tumour lysis syndrome. In children[4] with haematologic malignancies at high risk for tumour lysis, rasburicase given intravenously achieved more rapid control and lower levels of plasma uric acid than oral allopurinol. No antibodies to rasburicase were detected at day 14. In 3 children with acute lymphoblastic leukaemia, hyperuricaemia was reportedly controlled with oral allopurinol and a single dose of rasburicase, although subclinical tumour lysis was apparent.[5] Rasburicase has also been used for tumour lysis syndrome in neonates. One infant was given a single dose of rasburicase after 2 days of induction chemotherapy for neuroblastoma, started on day 21 of life; serum urate normalised and chemotherapy was completed without further incident. A second infant, with acute lymphoblastic leukaemia and renal dysfunction, presented with tumour lysis syndrome, and had 6 doses of intravenous rasburicase plus aggressive supportive therapy, but died of complications on day 7 of life.[6] Reviews[7,8] have concluded that rasburicase is highly effective at decreasing uric acid concentrations rapidly and thoroughly; there is some suggestion that shorter durations of treatment (between 1 and 3 days as opposed to 5 days) may be sufficient even in high-risk patients.

1. Pui C-H, *et al.* Recombinant urate oxidase for the prophylaxis or treatment of hyperuricemia in patients with leukaemia or lymphoma. *J Clin Oncol* 2001; **19:** 697–704.
2. Pui C-H, *et al.* Recombinant urate oxidase (rasburicase) in the prevention and treatment of malignancy-associated hyperuricemia in pediatric and adult patients: results of a compassionate-use trial. *Leukemia* 2001; **15:** 1505–9.
3. Coiffier B, *et al.* Efficacy and safety of rasburicase (recombinant urate oxidase) for the prevention and treatment of hyperuricemia during induction chemotherapy of aggressive non-Hodgkin's lymphoma: results of the GRAAL1 (Groupe d'Etude des Lymphomes de l'Adulte Trial on Rasburicase Activity in Adult Lymphoma) study. *J Clin Oncol* 2003; **21:** 4402–6.
4. Goldman SC, *et al.* A randomized comparison between rasburicase and allopurinol in children with lymphoma or leukemia at high risk for tumor lysis. *Blood* 2001; **97:** 2998–3003.
5. Lee ACW, *et al.* Treatment of impending tumor lysis with single-dose rasburicase. *Ann Pharmacother* 2003; **37:** 1614–17.
6. McNutt DM, *et al.* Rasburicase for the management of tumor lysis syndrome in neonates. *Ann Pharmacother* 2006; **40:** 1445–50.
7. Bessmertny O, *et al.* Rasburicase: a new approach for preventing and/or treating tumor lysis syndrome. *Curr Pharm Des* 2005; **11:** 4177–85.
8. Oldfield V, Perry CM. Rasburicase: a review of its use in the management of anticancer therapy-induced hyperuricaemia. *Drugs* 2006; **66:** 529–45.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Fasturtec; ***Belg.:*** Fasturtec; ***Braz.:*** Fasturtec; ***Canad.:*** Fasturtec; ***Chile:*** Fasturtec†; ***Cz.:*** Fasturtec; ***Denm.:*** Fasturtec; ***Fin.:*** Fasturtec; ***Fr.:*** Fasturtec; ***Ger.:*** Fasturtec; ***Gr.:*** Fasturtec; ***Hong Kong:*** Fasturtec; ***Hung.:*** Fasturtec; ***Irl.:*** Fasturtec; ***Ital.:*** Fasturtec; Uricozyme†; ***Neth.:*** Fasturtec; ***Norw.:*** Fasturtec; ***NZ:*** Fasturtec; ***Pol.:*** Fasturtec; ***Port.:*** Fasturtec; ***Singapore:*** Fasturtec; ***Spain:*** Fasturtec; ***Swed.:*** Fasturtec; ***Switz.:*** Fasturtec; ***UK:*** Fasturtec; ***USA:*** Elitek; ***Venez.:*** Fasturtec.