

Ciclosporin (cyclosporin), a calcineurin inhibitor, is a potent immunosuppressant which is virtually non-myelotoxic but markedly nephrotoxic. It may be used in organ and tissue transplantation, for prevention of graft rejection following bone marrow, kidney, liver, pancreas, heart, lung, and heart-lung transplantation, and for prophylaxis and treatment of graft-versus-host disease. Ciclosporin also has a role in steroid-sensitive and steroid-resistant nephrotic syndrome; in corticosteroid-sensitive nephrotic syndrome it may be given with prednisolone.

Tacrolimus is also a calcineurin inhibitor. Although not chemically related to ciclosporin it has a similar mode of action and side-effects.

Other drugs used for immune system disorders and transplantation Anakinra, p. 691 · Chloroquine, p. 429 · Everolimus, p. 605 · Hydroxychloroquine sulfate, p. 690 · Rituximab, p. 574

IMMUNE SERA AND IMMUNOGLOBULINS > IMMUNOGLOBULINS

Antithymocyte immunoglobulin (rabbit)

28-Nov-2017

● INDICATIONS AND DOSE

Prophylaxis of organ rejection in heart allograft recipients

▶ BY INTRAVENOUS INFUSION

- ▶ Child: 1–2.5 mg/kg daily for 3–5 days, start treatment on day of transplantation, to be given over at least 6 hours

Prophylaxis of organ rejection in renal allograft recipients

▶ BY INTRAVENOUS INFUSION

- ▶ Child 1–17 years: 1–1.5 mg/kg daily for 3–9 days, start treatment on day of transplantation, to be given over at least 6 hours

Treatment of corticosteroid-resistant allograft rejection in renal transplantation

▶ BY INTRAVENOUS INFUSION

- ▶ Child 1–17 years: 1.5 mg/kg daily for 7–14 days, to be given over at least 6 hours

DOSES AT EXTREMES OF BODY-WEIGHT

- ▶ To avoid excessive dosage in obese patients, calculate dose on the basis of ideal body weight.

- **CONTRA-INDICATIONS** Infection

- **INTERACTIONS** → Appendix 1: immunoglobulins

● **SIDE-EFFECTS**

- ▶ **Common or very common** Chills · diarrhoea · dysphagia · dyspnoea · fever · hypotension · infection · lymphopenia · myalgia · nausea · neoplasm malignant · neoplasms · neutropenia · reactivation of infection · secondary malignancy · sepsis · skin reactions · thrombocytopenia · vomiting

- ▶ **Uncommon** Cytokine release syndrome · hepatic disorders · hypersensitivity · infusion related reaction

SIDE-EFFECTS, FURTHER INFORMATION

Tolerability is increased by pretreatment with an intravenous corticosteroid and antihistamine; an antipyretic drug such as paracetamol may also be beneficial.

- **PREGNANCY** Manufacturer advises use only if potential benefit outweighs risk—no information available.

- **BREAST FEEDING** Manufacturer advises avoid—no information available.

- **MONITORING REQUIREMENTS** Monitor blood count.

- **DIRECTIONS FOR ADMINISTRATION** For *continuous intravenous infusion* reconstitute each vial with 5 mL water for injections to produce a solution of 5 mg/mL; gently rotate to dissolve. Dilute requisite dose with Glucose 5% or

Sodium Chloride 0.9% to an approx. concentration of 0.5 mg/mL; begin infusion immediately after dilution; give through an in-line filter (pore size 0.22 micron); incompatible with unfractionated heparin and hydrocortisone in glucose infusion—precipitation reported.

● **NATIONAL FUNDING/ACCESS DECISIONS**


NICE decisions

- ▶ **Immunosuppressive therapy for kidney transplant in children and young people (October 2017) NICE TA482** Antithymocyte immunoglobulin (rabbit) is not recommended as an initial treatment to prevent organ rejection in patients having a kidney transplant. Patients whose treatment was started within the NHS before this guidance was published should have the option to continue treatment, without change to their funding arrangements, until they and their NHS clinician consider it appropriate to stop. www.nice.org.uk/guidance/TA482

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

- ▶ **Grafalon** (Imported (Germany))

Antithymocyte immunoglobulin (rabbit) 20 mg per 1 ml Grafalon 100mg/5ml concentrate for solution for infusion vials | 1 vial [PoM] 

Powder and solvent for solution for infusion

- ▶ **Thymoglobulin** (Sanofi)

Antithymocyte immunoglobulin (rabbit) 25 mg Thymoglobuline 25mg powder and solvent for solution for infusion vials | 1 vial [PoM] £158.77 (Hospital only)

IMMUNOSUPPRESSANTS > ANTIMETABOLITES

Azathioprine

13-Jun-2018

- **DRUG ACTION** Azathioprine is metabolised to mercaptopurine.

● **INDICATIONS AND DOSE**

Severe ulcerative colitis | Severe Crohn's disease

▶ BY MOUTH

- ▶ Child 2–17 years: Initially 2 mg/kg once daily, then increased if necessary up to 2.5 mg/kg once daily

Systemic lupus erythematosus | Vasculitis | Autoimmune conditions usually when corticosteroid therapy alone has proved inadequate

▶ BY MOUTH

- ▶ Child: Initially 1 mg/kg daily, then adjusted according to response to 3 mg/kg daily, consider withdrawal if no improvement within 3 months; maximum 3 mg/kg per day

Suppression of transplant rejection

▶ BY MOUTH, OR BY INTRAVENOUS INFUSION

- ▶ Child: Maintenance 1–3 mg/kg daily, adjusted according to response, consult local treatment protocol for details, oral route preferred, but if oral route is not possible then can be given by intravenous infusion, the total daily dose may alternatively be given in 2 divided doses

DOSE ADJUSTMENTS DUE TO INTERACTIONS

- ▶ Manufacturer advises reduce dose to one-quarter of the usual dose with concurrent use of allopurinol.

- **CAUTIONS** Reduced thiopurine methyltransferase activity

- **INTERACTIONS** → Appendix 1: azathioprine

● **SIDE-EFFECTS**

GENERAL SIDE-EFFECTS

- ▶ **Common or very common** Bone marrow depression (dose-related) · increased risk of infection · leucopenia · pancreatitis · thrombocytopenia
- ▶ **Uncommon** Anaemia · hepatic disorders · hypersensitivity