

Ciclosporin

Current Indication

No longer a first line agent but some transplant patients will still have Neoral (previous formulation Sandimmun but nearly all patients are on Neoral) as the lead agent in their immunosuppression regime.

Dose

Starting dose is 8 mg/kg/day in 2 divided doses.

Preparation

Ciclosporin is available 10 mg (yellow / white), 25 mg (blue / grey), 50 mg (yellow / white) and 100 mg (blue / grey) capsules and as a 100 mg/ml oral solution.

Different generic preparations of ciclosporin may vary in bioavailability and should not be considered interchangeable.

Within NHS Lothian the formulation in use for solid organ transplantation is Neoral[®]. As ciclosporin is a drug with a narrow therapeutic index drug it is vital that patients are not switched between formulations. Therefore care must be taken to prescribe and dispense ciclosporin by BRAND name to avoid potential toxicity or potential graft rejection.

Administration

Oral route in most instances.

It is administered usually at 10 am and 10 pm.

Oral solution should be diluted immediately before taking. It may be diluted in orange juice or squash, apple juice or water (not grapefruit juice – see interactions) and needs to be stirred well. Measuring device should not come into contact within the diluent.

One third of the oral dose can be given as a slow intravenous infusion in normal saline or dextrose 5% over 2-6 hours if absolutely necessary.

N.B the injection is only available in the Sandimmun brand and care should be

taken if switching patients who are on the Neoral brand.

Contra-indications/Cautions

Live vaccines are not to be given to immunocompromised patients.

Neoral should be used with caution during pregnancy.

Ciclosporin passes into breast milk so mothers should not breast feed their infants.

Side effects

The most frequent side effects seen with Ciclosporin include:

abnormal kidney function	hepatic dysfunction
hypertrichosis	gingival hypertrophy
tremor	gastrointestinal disturbances
hypertension	burning sensation of hands and feet

Less common side effects are:

headaches	oedema
mild anaemia	pancreatitis
hyperkalaemia	neuropathy
Hyperuricaemia	reversible dysmenorrhoea
hypomagnesaemia	muscle weakness, cramps, myopathy
hypercholesterolaemia	

Interactions

Potential interactions due to effects on hepatic microsomal enzymes:

Inhibitors of cytochrome P450 which may decrease metabolism of ciclosporin and thus increase ciclosporin blood levels include:

- Clarithromycin,
- Erythromycin,
- Nicardipine

- Danazol
- Fluconazole
- Ketoconazole
- Oral contraception
- Diltiazem
- Verapamil

Inducers of cytochrome P450 which may increase metabolism of ciclosporin and thus decrease blood levels include:

barbiturates	phenytoin
carbamazepine	rifampicin

Interactions due to cumulative toxicity / synergistic effects:

- Take care when using ciclosporin in combination with compounds known to have nephrotoxic effects, e.g.: aminoglycosides, ciprofloxacin, trimethoprim, amphotericin B, melphalan and NSAIDs.
- Concurrent administration of ciclosporin with HMG-CoA reductase inhibitors may enhance risk of rhabdomyolysis.
- Concomitant administration of nifedipine and ciclosporin increases the rate of gingival hyperplasia when compared to that for ciclosporin alone, particularly in the presence of poor oral hygiene.
- Since ciclosporin may cause hyperkalaemia, potassium sparing diuretics, potassium supplements and high potassium intake should be avoided.

Other interactions:

- Vaccines may be less effective and the use of live attenuated vaccines should be avoided.
- Owing to its possible interference with the gastrointestinal cytochrome P450 enzyme system, grapefruit or grapefruit juice should not be taken 1 hour prior to ciclosporin dosing and grapefruit juice should not be used as a diluent for the oral solution.
- This is not a comprehensive list of all potential interactions with ciclosporin. For further information please ask senior members of staff or consult the transplant unit pharmacist.

Levels: 12 hour trough levels should be sent, similar to tacrolimus. Early post

transplant levels should be maintained in the 200-300 ng/ml range. However, almost all patients currently on ciclosporin will be far out post transplantation. For these patients a level in the 50-150 ng/ml range is desirable.