NOVARTIS

Sandimmun® Neoral

Film coated tablets
Oral solution
Oral solution in ready-to-use ampoules

Composition:
Soft gelatin capsule:
Active substance: ciclosporin
Excipients: ethanol, alpha-tocopherol, ethanol anhydrous, propylene glycol, corn oil, macrogolglycerol, macrogolglycerol hydroxystearate (PhEur) polysorp 80 (polysorbate 80)
(INN), Sandimmun Neoral soft gelatin capsules contain 11.88% v/v ethanol (9.4% w/w).
Film coated tablets:
Active substance: ciclosporin
Excipients: pregelatinised starch, colloidal silicon dioxide, talcum, magnesium stearate, glycerol 85%, propylene glycol, hypromellose, macrogol 6000, titanium dioxide (E171), iron oxide yellow (E172), iron oxide red (E172).
Oral solution:
Active substance: ciclosporin
Excipients: ethanol, corn oil, propylene glycol, sorbitan oleate, polysorbate 80 (INN), macrogolglycerol hydroxystearate (PhEur) polysorp 40 (polyoxyl 40 castor oil) (INN), Sandimmun Neoral oral solution contains 12% v/v ethanol (9.6% w/w) (see section 4 **Warnings and precautions**).
Sandimmun Neoral oral solution in ampoules:
Excipients: ethanol, corn oil, propylene glycol, sorbitan oleate, polysorbate 80 (INN), macrogolglycerol hydroxystearate (PhEur) polysorp 40 (polyoxyl 40 castor oil) (INN), Sandimmun Neoral oral solution contains 12% v/v ethanol (9.6% w/w) (see section 4 **Warnings and precautions**).

Pharmaceutical form and quantity of active substance per unit

Soft gelatin capsules 25, 50, or 100 mg
Film coated tablets 100 mg
Oral solution 50 mg/ml, 100 mg/ml
Oral solution in ampoules 50 mg/ml, 250 mg/ml of a concentrate for intravenous infusion (see separate prescribing information)

Indications / Potential uses

Transplantation
Prevention of rejection of kidney, liver, heart, combined heart/lung, lung and pancreas/kidney grafts.
Treatment of Transplant rejection in patients previously treated with other immunosuppressive agents.
Bone marrow transplantation
Prevention of graft rejection
Prevention of graft versus host disease (GVHD)
Severe psoriasis
Endogenous uveitis
Nephrotic syndrome including intermittent or persistent cases of nonfibrotic etiology in which Steroid or Cytotoxic Drugs are proved ineffective or inappropriate.
Uveitis in Behcet's disease, with recurrent inflammatory attacks involving the retina, when conventional treatment has failed or when it is not tolerated.
Psoriasis
Severe cases in which alternative therapies are ineffective or inappropriate.
Rheumatoid arthritis
Severe cases in which standard specific disease-related therapies are ineffective or inappropriate.
Nephrotic syndrome
Idiopathic steroid-dependent or steroid-resistant nephrotic syndrome (drugs other than corticosteroids or steroids) in focal segmental glomerulosclerosis (FSGS) in children who are at risk of developing chronic renal failure, in adult patients with stable therapy, but who have persistent nephrotic syndrome and at least 50% of normal glomerular filtration rate.
Maintenance of corticosteroid-induced remission, in order to enable corticosteroids to be withdrawn.

Dosage / Administration

The dose of Sandimmun Neoral is expressed in mg/kg bodyweight and the dosage of all other products refers to mg/mg ciclosporin therapy. Consultation with the prescribing information for Sandimmun is compulsory for its dosage, the following information is for Sandimmun Neoral only.
The total daily dose of Sandimmun Neoral should always be divided into two doses (morning and evening). If the prescribed dose cannot be precisely adjusted by using the capsules, the film coated tablets or the oral solution, a change of formulation is recommended.

A) Transplantation
Sandimmun Neoral formulations given before are intended as guidelines only. Routine monitoring of blood ciclosporin levels is mandatory. Dosage may be adjusted on individual basis in accordance with clinical response and ciclosporin blood levels.

1. Organ transplantation
The starting dose is 12.15 mg/kg, given in two divided doses within 12 hours before transplantation. This dose should be adjusted to the individual immunological response. The dosage may then be gradually reduced to a maintenance dose of 2-6 mg/kg/day (depending on blood ciclosporin levels). In the liver no fixed dosage can be recommended. Ciclosporin blood levels should be monitored. The dose should result in trough blood levels below 500-1000 ng/ml, as associated with an increase risk of nephrotoxicity.
Triple therapy with Sandimmun Neoral is given in conjunction with other immunosuppressive agents (e.g. corticosteroids, or as part of a 4 or fivefold regimen). Lower ciclosporin dosages are used when ciclosporin is used in combination.
Bone marrow transplantation in combination with azathioprine:
A ciclosporin dose of 5 mg/kg/day is recommended for a prolonged period, as all bone marrow transplant recipients are exposed to ciclosporin. Reduction of ciclosporin dosage should be made if necessary, depending on individual response. Higher dosages for ciclosporin regulation are recommended.
In very severe cases, rapid and adequate control of the disease may be achieved with a starting dose of 5 mg/kg/day.
Ciclosporin therapy in bone marrow transplants is taken as sufficient improvement in graft versus host disease if the severity of symptoms, it must be proved that severe graft versus host disease (GVHD) is prevented.
Ciclosporin should be continued for a long period after the prophylaxis of graft rejection, continuation of prophylaxis treatment must be recommended. Further Reduction the risk of relapse in efficacy, it is important to ensure that neither exceptional nor ciclosporin blood levels are reached, because of the risk of toxic side effects.
Data on renal function, liver function and blood pressure should be taken before starting Sandimmun Neoral therapy. However, they are not necessarily a reason for drug withdrawal. If they occur during treatment, unless infection is severe.
Patients who are receiving Sandimmun Neoral should not receive concomitantly administration of live attenuated vaccines (e.g. vaccine against poliomyelitis).
Co-medications should be avoided, however, as it may increase blood ciclosporin levels and thus increase the risk of side effects, particularly nephrotoxicity and hepatotoxicity.
Co-medications should be avoided, if possible, or should be closely monitored.

2. Rheumatoid arthritis
Treatment:
Treatment should only be started and treated by physicians experienced in the use of immunosuppressive drugs. Treatment should be initiated with appropriate antibiotics. Sandimmun Neoral should be given in divided doses, preferably twice daily, with a total daily dose of 2.5 mg/kg bodyweight. Ciclosporin blood levels should be monitored. The dose should be gradually increased if ciclosporin blood levels are not achieved