NOVARTIS

SANDIMMUN® NEORAL® (ciclosporin)

100 mg/mL oral solution

10 mg, 25 mg, 50 mg and 100 mg soft gelatin capsules

SANDIMMUN® (ciclosporin)

50 mg/mL concentrate for solution for infusion

Basic Succinct Statement

Version 2.1

Code: BSS RD 14 JUL 20; APPR 01 NOV 20

This material is only meant for Healthcare Professionals

SANDIMMUN NEORAL® 100 mg/mL oral solution
SANDIMMUN NEORAL® 10 mg, 25 mg, 50 mg, 100 mg soft gelatin capsules
SANDIMMUN® 50 mg/mL concentrate for solution for infusion

Important note: Before prescribing, consult full prescribing information.

Presentation: ♦Oral solution containing 100 mg/mL ciclosporin. ♦Soft gelatin capsules containing 10 mg, 25 mg, 50 mg and 100 mg ciclosporin. ♦Concentrate for solution for infusion containing 50 mg/mL ciclosporin (contains polyoxyl castor oil as excipients).

Indications: ♦**Transplantation:** Solid organ transplantation (kidney, liver, heart, combined heart-lung, lung, pancreas); bone marrow transplantation ♦**Non transplantation:** endogenous uveitis; nephrotic syndrome; severe active rheumatoid arthritis; severe psoriasis; severe atopic dermatitis.

Dosage: ♦Depending upon indication and route of administration. ♦**Use in** children for non-transplant indications other than nephrotic syndrome is not recommended. ♦**Conversion from Sandimmun® to Sandimmun Neoral®:** the recommended dose ratio is 1:1. For specific safety measures in transplantation and autoimmune diseases see full prescribing information. ♦**Conversion between oral ciclosporin formulations:** For specific safety measures in transplantation and autoimmune diseases see full prescribing information.

Contraindications: ♦Known hypersensitivity to ciclosporin or any other component of the formulation. ♦For Sandimmun concentrate for solution for infusion, in addition: hypersensitivity to polyoxyl castor oil (e.g. Cremophor® EL).

Warnings/Precautions: ♦Sandimmun Neoral and Sandimmun concentrate should only be used by physicians experienced in immunosuppressive therapy after they have consulted the full prescribing information. ♦Monitor closely kidney and liver function, blood pressure, blood lipids and ciclosporin blood levels in transplant patients. ♦Caution is required when using concentrate for solution for infusion due to the polyoxyl castor oil as this could lead to anaphylactoid reactions. ♦Avoid excessive immunosuppression, as this could lead to lymphoproliferative disorders, other malignancies and may result in an increased risk of infection. Avoid excess unprotected sun exposure and UV light therapy. ♦Activation of latent polyomavirus infections that may lead to Polyomavirus associated nephropathy, especially BK virus nephropathy, or to JC virus associated progressive multifocal leukoencephalopathy. ♦Renal function should be monitored with particular care in elderly patients. ♦Caution is required with potassium-containing medication or potassium-sparing drugs, avoid high dietary potassium intake. ♦Monitoring of serum potassium and magnesium is recommended. ♦Caution is required in treating patients with hyperuricaemia. ♦Caution is required when vaccinating (avoid live-attenuated vaccines), and when co-administering with lercanidipine ♦ Ciclosporin increases blood levels of concomitant medications that are substrates for the multidrug efflux transporter P-glycoprotein such as aliskiren (co-administration not recommended) or dabigatran (avoid co-administration) or the organic anion transporter proteins such as bosentan (avoid co-administration). ♦Alcohol (ethanol) content should be

taken into account when given to pregnant or breast feeding women, in patients presenting with liver disease or epilepsy, in alcoholic patients or if the medicine is being given to a child. ♦For non-transplant indications do not use Sandimmun concentrate. ♦For non-transplant indications, caution is required in case of impaired renal function (for nephrotic syndrome see full prescribing information), uncontrolled hypertension, uncontrolled infection, history or presence of malignancy. ♦For atopic dermatitis, psoriasis and rheumatoid arthritis, if hypertension develops and cannot be controlled by appropriate antihypertensives, Sandimmun Neoral treatment should be discontinued. ♦Caution should be observed in patients treated for rheumatoid arthritis in combination with methotrexate. ♦Patients treated for psoriasis should not receive concomitant ultraviolet irradiation or PUVA photochemotherapy. ♦For atopic dermatitis, skin infections should be controlled by appropriate antibacterial agents. ♦For endogenous uveitis, caution is required in patients with neurological Behcet's syndrome. ♦Sandimmun Neoral should not be used during pregnancy unless the expected benefit to the mother outweighs the potential risk to the fetus. ♦Mothers treated with Sandimmun Neoral should not breast feed.

Interactions: ♦**Not recommended:** live-attenuated vaccines ♦**To be considered:** potassium sparing drugs and potassium containing drugs and lercanidipine ♦**Increasing or decreasing ciclosporin levels:** barbiturates, carbamazepine, oxcarbazepine, phenytoin, rifampicin, nafcillin, sulfadimidine i.v., octreotide, probucol, orlistat, *hypericum perforatum* (St. John's wort), ticlopidine, sulfinpyrazone, terbinafine, bosentan, macrolides (e.g. erythromycin, azithromycin, clarithromycin), ketoconazole, fluconazole, itraconazole, voriconazole, diltiazem, nicardipine, verapamil, metoclopramide, oral contraceptives, danazol, methylprednisolone (high dose), allopurinol, amiodarone, cholic acid and derivatives, protease inhibitors, imatinib, nefazodone. ♦**Potential increased nephrotoxicity:** aminoglycosides, amphotericin B, ciprofloxacin, vancomycin, melphalan, trimethoprim (+ sulfamethoxazole), NSAIDs (including diclofenac), histamine H2-receptor antagonists, tacrolimus, methotrexate, fibric acid derivatives (e.g. bezafibrate, fenofibrate). ♦Nifedipine due to an increase rate of gingival hyperplasia. ♦**Increase of other drug levels:** HMG-CoA reductase inhibitors (statins), colchicine, digoxin, etoposide, everolimus, sirolimus, repaglinide, aliskiren, dabigatran, bosentan, ambrisentan and anthracyclines antibiotics (e.g. doxorubicine).

Adverse reactions: ♦**Very common:** anorexia, hyperglycaemia, tremor, headache, hypertension,, nausea, vomiting, abdominal discomfort, diarrhoea, gingival hyperplasia, hirsutism and renal dysfunction. ♦**Common:** leucopenia, convulsions, paraesthesia, flushing, peptic ulcer, hepatotoxicity, acne, rash, pyrexia and oedema ♦**Rare**: menstrual disturbances ♦**Frequency unknown:** thrombotic microangiopathy, haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura, anaemia, thrombocytopenia, hyperlipidemia, hyperuricaemia, hyperkalaemia, hypomagnesaemia, encephalopathy including Posterior Reversible Encephalopathy Syndrome (PRES), signs and symptoms such as convulsions, confusion, disorientation, decreased responsiveness, agitation, insomnia, visual disturbances, cortical blindness, coma, paresis cerebellar ataxia; optic disc oedema including papilloedema, with possible visual impairment secondary to benign intracranial hypertension; peripheral neuropathy, migraine, pancreatitis, hepatotoxicity and liver injury including cholestasis, jaundice, hepatitis and liver failure with some fatal outcome, hypertrichosis, myopathy,

muscle spasm, myalgia, muscular weakness, pain of lower extremities, gynecomastia, fatigue, weight increase and acute and chronic nephrotoxicity.

Take note: Approved PI and BSS of this 14-Jul-2020 version is only applicable for Sandimmun Neoral Oral Solution, the same version of PI has been submitted to HA for Sandimmun Neoral Capsules and Sandimmun Concentrate and pending for approval.