METAPHARMACEUTICAL IND SL
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TECHNICAL DATA SHEET

0393-TDS-ENG-2025

CICLOSPORINA A (EUR. PH.)		
DESCRIPTION DCI: CICLOSPORIN	DESCRIPTION DOE: CICLOSPORINA	
CAS Nº: 59865-13-3	EC Nº: 611-907-1	AEMPS CODE: 406A
MOL. WEIGHT: 1202,63	MOL. FORMULA: C62H111N11O12	ARTICLE CODE: 0393

ATTRIBUTES	SHOULD BE
Appearance	White or almost white powder
Solubility	Practically insoluble in water, freely soluble in anhydrous ethanol and in methylene chloride
Identification A	Complies
Identification B	Complies
Appearance of solution	Clear and not more intensely coloured than ref. solution Y5, BY5 o R7
Specific optical rotation	-193 / -185
Related substances	
Sum of impurities B and E	=< 0.5 %
Impurity G	=< 0.4 %
Any other impurity	=< 0.3 %
Total impurities	=< 1.5 %
Loss on drying	=< 2.0 %
Assay	97.0 - 102.0 %

COMPLIES WITH

European Pharmacopoeia 11.0

STORAGE

Keep tightly closed, in a cool and dry place and protected from light.

REMARKS

Ciclosporin is subjected to the requirements of the ICH Q3D "Elemental Impurities" guideline and the requirements of guides EMA/CHMP/ICH/82260/2006 - ICH Q3C (R6) "Residual solvents".

Absence of N-nitrosamines impurities has been ensured after a risk evaluation according to ICH Q9, ICH M7 and in accordance with guidelines EMA/428592/2019 Rev 2 and EMA/189634/2019.

Certificates of residual solvents, allergens, non-GMO and BSE-TSE, among others, are available upon request.

All methods of analysis are validated by official pharmacopoeias or are validated by internal methods of the manufacturer, which can be obtained at specific request.

Properties and uses
CYCLOSPORIN is a metabolite of the fungi Cylindrocarpon lucidum and *Trichoderma polysporum*.
It is an immunosuppressant that acts specifically on helper T lymphocytes, decreasing the cellular immune response by inhibiting the activation of calcineurin, and therefore the production of lymphokines such as interleukin-2.
The maximum plasma concentration of an oral microemulsion dose is reached 1.5 to 2 h after ingestion. It is distributed very well throughout the body. It binds 90% to plasma proteins and the rest to erythrocytes and leukocytes. It is metabolized mainly in the liver. The elimination half-life of an oral dose of ciclosporin is between 5 - 20 h. It is excreted through the bile duct, with faeces, and a small part through the urinary tract. It crosses the placental barrier and passes into breast milk.
It is normally used in association with corticosteroids or other immunosuppressants in organ and tissue transplants for the

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prophylaxis of rejection, or in the treatment of rejection treated with other immunosuppressants.
It is also used in severe forms of atopic dermatitis, psoriasis, or rheumatoid arthritis when conventional treatment is not effective or adequate, in nephrotic syndrome, and in other diseases with autoimmune component such as aplastic anemia, Behçet's disease, active chronic hepatitis, sclerosis multiple, gravis, miscellaneous, sarcoidosis, scleritis or uveitis, scleroderma, and various skin disorders.
It is typically used in the treatment of chronic ulcers of lichen planus and inguinal psoriasis. Ophthalmic route is used in the treatment of dry eye, with an efficiency superior to that of artificial tears.

Dosage
Doses of 2 - 15 mg / Kg / day are usually taken orally, depending on the pathology.
Topically, 10% in oil solution for inguinal psoriasis.
Ophthalmic route, 0.05-2%.

Side effects
Nephrotoxicity is the main adverse effect, and appears in 1/3 of patients. Other adverse effects are hypertension, gastrointestinal disorders, hepatotoxicity, hypertrichosis, gingival hyperplasia, tremor, and a burning sensation in the hands and feet.
Occasionally, headache, rash, hyperlipidemia, anemia, electrolyte disturbances (hyperkalemia, hypomagnesemia), weight gain, edema, pancreatitis, neuropathies, paresthesias, seizures, and hyperuricemia may occur.
An increase in the incidence of some malignancies has been described.

Contraindications
It should not be administered to treat atopic dermatitis, rheumatoid arthritis, or psoriasis in patients with impaired renal function, uncontrolled hypertension, uncontrolled infections, or malignancies, except for psoriasis as a last resort in patients with premalignant or malignant skin lesions. . It is considered dangerous in patients with porphyria, since porphorogenic in animals.

Precautions
Regular monitoring of liver and kidney function, blood pressure, serum electrolytes (mainly potassium) and serum lipids is required, as well as quantification of the plasma concentration of ciclosporin in transplant patients. It is necessary to pay attention to patients with hyperuricemia. Patients with psoriasis should not avoid sun exposure and UV radiation.

Interactions
They reduce the blood levels of CYCLOSPORIN, by possible induction of their hepatic metabolism: carbamazepine, phenytoin, phenobarbital, rifampin, quinine, troglitazone, octreotide, orlistat, St. John's wort, etc.
Increase blood levels of CYCLOSPORIN, by possible inhibition of their hepatic metabolism: allopurinol, antiarrhythmics (amiodarone, propanefone), sex hormones, calcium channel blockers, erythromycin and other macrolides, carvedilol, clonidine, fluoxetine, ketoconazole and other azole antifungals, corticosteroids, chloroquine, chloramphenicol, some calcium antagonists, cisapride, glibenclamide, retinoids, grapefruit juice, etc.
It increases the plasma levels and the toxicity of doxorubicin and lovastatin. Statins may increase the risk of myopathies and rhabdomyolysis. Potassium-sparing diuretics, ACE inhibitors, and potassium-rich foods should be avoided.
Nifedipine may increase the risk of gingival hyperplasia. Co-administration with colchicine may cause myopathy.
Administration of vaccines during treatment with CYCLOSPORIN may be less effective. Caution must be exercised when administering it together with other nephrotoxic drugs (aminoglycosides, etc ...).

Incompatibilities
Do not store in PVC containers

Formulation examples

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Oral adhesive excipient with CYCLOSPORIN
CYCLOSPORIN - **3 %**
Excipient Acropic adhesive oral c.s.p. - **10 g**

Modus operandi: Moisten CYCLOSPORIN with a little liquid petrolatum in mortar. Incorporate the oral adhesive excipient little by little homogenizing with the pistil.

Alcohol solution with CYCLOSPORIN
CYCLOSPORIN - **0.025 %**
Isopropyl Alcohol c.s.p. - **50 mL**

Modus operandi: Dissolve CYCLOSPORIN in alcohol.