הודעה על החמרה (מידע בטיחות)

תאריך: 30.04.2012

שם תכשיר באנגלית: Sandimmun concentrate for infusion

מספר רישום: 042 39 22691 00

שם בעל הרישום: Novartis Pharma Services AG

השינויים בעלון מסומנים על רקע צהוב

בעלון לרופא

פרטים על השינוי/ים המבוקש/ים		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Special population ***Renal impairment*** Ciclosporin undergoes minimal renal elimination and its pharmacokinetics is not affected by renal impairment (see section 11 Clinical pharmacology). However, due to its nephrotic potential, (see section 7 Adverse drug reactions), a careful monitoring of the renal function is recommended (see section 6 Warnings and precautions subsection all indications). ***Hepatic impairment*** Ciclosporin is extensively metabolized by the liver. The terminal half-life varied between 6.3 hours in healthy volunteers to 20.4 hours in severe liver patients (see section 11 Clinical pharmacology). Dose reduction may be necessary in patients with severe liver impairment to maintain blood levels within the recommended target range (see section 6 Warnings and precautions) and section 11 Clinical pharmacology).		**Dosage and administration**
Acute and chronic nephrotoxicity A frequent and potentially serious complication, an increase in serum creatinine and urea, may occur during the first few weeks of Sandimmun therapy. These functional changes are dose-dependent and reversible, usually responding to dose reduction. During long-term treatment, some patients may develop structural changes in the kidney (e.g. arteriolar hyalinosis, tubular atrophy and interstitial fibrosis) which, in renal transplant patients, must be differentiated from changes due to chronic rejection (see section 7 Adverse drug reactions). Close monitoring of parameters that assess renal function is required. Abnormal values may necessitate dose reduction (see section 4 Dosage and administration and section 11 Clinical pharmacology). ...	A frequent and potentially serious complication, an increase in serum creatinine and urea, may occur during the first few weeks of Sandimmun therapy. These functional changes are dose-dependent and reversible, usually responding to dose reduction. During long-term treatment, some patients may develop structural changes in the kidney (e.g. interstitial fibrosis) which, in renal transplant patients, must be differentiated from changes due to chronic rejection. ... Since, on rare occasions, Sandimmun has been reported to induce a reversible slight increase in blood lipids, it is advisable to perform lipid determinations before treatment and after the first month of therapy. In the event of increased lipids being found, restriction of dietary fat and, if appropriate, a dose reduction, should be considered.	**Warnings and precautions**

Monitoring ciclosporin levels in transplant patients Routine monitoring of ciclosporin blood levels is an important safety measures (see section 4 Dosage and administration). ... ***Blood lipid increased*** Since Sandimmun has been reported to induce a reversible slight increase in blood lipids, it is advisable to perform lipid determinations before treatment and after the first month of therapy. In the event of increased lipids being found, restriction of dietary fat and, if appropriate, a dose reduction, should be considered (see section 7 Adverse drug reactions).		
Summary of the safety profile The principal adverse reactions observed in clinical trials and associated with the administration of ciclosporin include renal dysfunction, tremor, hirsutism, hypertension, diarrhea, anorexia, nausea and vomiting. **Table 7-1** **Blood and lymphatic system disorders** Common Anaemia, Leucopenia ... **Metabolism and nutrition disorders** Very common Anorexia, hyperglycemia ... **Nervous system disorders** Common Convulsions, paraesthesia ... **Vascular disorders** Common Flushing ... **Gastrointestinal disorders** Very common Nausea, vomiting, abdominal discomfort, diarrhea, gingival hyperplasia Common Peptic ulcer ... **Skin and subcutaneous tissue disorders** Very common Hirsutism Common Acne, rash ... **Reproductive system and breast disorders** Common Perexia, edema ... **Table 7-2 adverse drug reactions from spontaneous reports and literature (frequency not known)** ***Blood and lymphatic system disorders*** Thrombotic microangiopathy, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura;	**Table 1** **Blood and lymphatic system disorders** Uncommon Anaemia, thrombocytopenia. ... **Metabolism and nutrition disorders** Common Anorexia, hyperuricaemia, hyperkalaemia, hypomagnesaemia. ... **Nervous system disorders** Common Paraesthesia. ... **Gastrointestinal disorders** Common Nausea, vomiting, abdominal pain, diarrhoea, gingival hyperplasia. ... **Skin and subcutaneous tissue disorders** Common Hypertrichosis.Uncommon Allergic rashes. ... **Reproductive system and breast disorders** Common Fatigue. **Table 1** **Blood and lymphatic system disorders** Uncommon Anaemia, thrombocytopenia. Rare Microangiopathic haemolytic anaemia, haemolytic uraemic syndrome.	**Adverse drug interactions**

anemia; thrombocytopenia ... **Nervous system disorders** 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 edema including papilledema, with possible visual impairment secondary to benign intracranial hypertension; peripheral neuropathy; migraine. **Gastrointestinal disorders** Pancreatitis acute **Hepatobiliary disorders** Hepatotoxicity and liver injury including cholestasis, jaundice, hepatitis and liver failure with some fatal outcome (see section 6 Warnings and precautions) ... ***Acute and chronic nephrotoxicity*** Patients receiving calcineurin inhibitors (CNIs therapies, including ciclosporin and ciclosporin-containing regimens, are at increased risk of acute or chronic nephrotoxicity. There have been reports from clinical trials and from the post marketing setting associated with the use of Sandimmun. Cases of acute nephrotoxicity reported disorders of ion homestasis, such as hyperkalemia, hypomagnesemia, hyperuricemia. Cases reporting chronic morphological changes included arteriolar hyalinosis, tubular atrophy and interstitial fibrosis (see section 6 Warnings and precautions).	... **Nervous system disorders** Very common Tremor, headache including migraine. Common Paraesthesia. Uncommon Signs of encephalopathy such as convulsions, confusion, disorientation, decreased responsiveness, agitation, insomnia, visual disturbances, cortical blindness, coma, paresis, cerebellar ataxia. Rare Motor polyneuropathy. Very rare Optic disc oedema including papilloedema, with possible visual impairment secondary to benign intracranial hypertension. ... **Gastrointestinal disorders** Common Nausea, vomiting, abdominal pain, diarrhoea, gingival hyperplasia. Rare Pancreatitis. **Hepatobiliary disorders** Common Hepatic function abnormal (see section 4.4 Special warnings and precautions for use).	
... Co-administration of bosentan and ciclosporin in healthy volunteers resulted in an approximately 2-fold increase in bosentan exposure and a 35% decrease in ciclosporin exposure (see above subsection drug interactions decreasing ciclosporin levels). Multiple dose administration of ambrisentan and ciclosporin in healthy volunteers resulted in an approximately 2-fold increase in ambrisentan exposure while the ciclosporin exposure was marginally increased (approximately 10%). A significant increased exposure in anthracycline antibiotics (e.g. doxorubicine, mitoxanthrone, daunorubicine) was observed in oncology patients with the intravenous co-administration of anthracycline antibiotics and very high doses of		**Interactions**

ciclosporin.		
Breast-feeding Ciclosporin passes into breast milk. The ethanol content of Sandimmun should also be taken into account (see section 6 Warnings and precautions). Mothers receiving treatment with Sandimmun should not breast-feed. Because of the potential of Sandimmun to cause serious adverse drug reactions in breastfed newborns/infants, a decision should be made whether to abstain from breast-feeding or to abstain from using the medicinal drug, taking into account the importance of the medicinal product to the mother.	**Lactation** Ciclosporin passes into breast milk. Mothers receiving treatment with Sandimmun should not breast-feed.	**Women of child-bearing potential, pregnancy, breast-feeding and fertility**
Hepatic impairment In a study performed in severe liver disease patients with biopsy-proven cirrhosis, the terminal half-life was 20.4 hours (range between 10.8 to 48.0 hours) compared to 7.4 to 11.0 hours in healthy subjects.		**Clinical pharmacology**