מרץ 2016

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

הנדון: Sandimmun Concentrate For Infusion
סנדאימון תמיסה מרוכזת לאינפוזיה

התכשיר שבנדון רשום בישראל להתוויה הבאה:

Prophylaxis of organ rejection in kidney liver heart allogenic transplants in conjunction with corticosteroids.
May also be used in the treatment of chronic rejection in patients previously treated with other immuno-suppressive agents.
Bone marrow transplantation.

המרכיב הפעיל: Ciclosporin 50mg/ml

ברצוננו להודיעכם על עדכונים בעלון לרופא של התכשיר בנדון (עדכונים מסומנים עם קו תחתי).

בהודעה זו מצויינים הסעיפים בהם נעשה שינוי אשר מהווה החמרה או שינוי מהותי. עידכונים נוספים, אינם נכללים בהודעה זו.

למידע מלא יש לעיין בעלון העדכני כפי שאושר ע"י משרד הבריאות הישראלי.
העלון נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על-ידי פניה לבעל הרישום.

בברכה,
ויקי יוסף יאבו
רוקחת ממונה

Novartis Israel Ltd.
36 Shaham St., Kiryat Matalon, Petach-Tikva
P.O.B 7759, Petach Tikva 49250, Israel
Tel: 972-3-9201111 Fax: 972-3-9229230

נוברטיס ישראל בע"מ.
רח' שחם 36 קריית מטלון פתח-תקוה
ת.ד. 7759 פתח-תקוה 49250
טלפון: 03-9201111 פקס: 03-9229230

תחת סעיף Warnings עודכן המלל הבא:

…

Interactions

Caution should be observed while co-administering lercanidipine with ciclosporin (see section 8 Interactions).
Ciclosporin may increase blood levels of concomitant medications that are substrates for the multidrug efflux transporter P-glycoprotein or the organic anion transporter protein (OATP) such as aliskiren, dabigatran or bosentan. Co-administration of ciclosporin with aliskiren is not recommended. Co-administration of ciclosporin together with dabigatran or bosentan should be avoided. These recommendations are based upon the potential clinical impact of these interactions (see section 8 Interactions).

…

תחת סעיף Adverse Drug Reactions עודכן המלל הבא:

…..

Table 7-2 Adverse drug reactions from spontaneous reports and literature (frequency not known)

……

Musculoskeletal and connective tissue disorders

Myopathy; muscle spasm; myalgia; muscular weakness; pain of lower extremities

…….

Description of selected adverse drug reactions

….

Pain of lower extremities

Isolated cases of pain of lower extremities have been reported in association with ciclosporin. Pain of lower extremities has also been noted as part of Calcineurin-Inhibitor Induced pain syndrome (CIPS) as described in the literature.

….

תחת סעיף Interactions עודכן המלל הבא:

….

Interactions resulting in an increase of other drugs

Ciclosporin is also an inhibitor of CYP3A4 and of the multidrug efflux transporter P-glycoprotein and may increase plasma levels of co-medications that are substrates of this enzyme and/or transporter.
Ciclosporin may reduce the clearance of digoxin, colchicine, and prednisolone, HMG-CoA reductase inhibitors (statins), etoposide, aliskiren, bosentan or dabigatran.
Severe digitalis toxicity has been seen within days of starting ciclosporin in several patients taking digoxin. There are also reports on the potential of ciclosporin to enhance the toxic effects of colchicine such as myopathy and neuropathy, especially in patients with renal dysfunction. If digoxin or colchicine is used concurrently with ciclosporin, close clinical observation is required in order to enable early detection of toxic manifestations of digoxin or colchicine, followed by reduction of dosage or its withdrawal.
Literature and post-marketing cases of myotoxicity, including muscle pain and weakness, myositis, and rhabdomyolysis, have been reported with concomitant administration of ciclosporin with lovastatin, simvastatin, atorvastatin, pravastatin, and, rarely, fluvastatin. When concurrently administered with ciclosporin, the dosage of these statins should be reduced according to label recommendations. Statin therapy needs to be temporarily withheld or discontinued in patients with signs and symptoms of myopathy or those with risk factors predisposing to severe renal injury, including renal failure, secondary to rhabdomyolysis.
If digoxin, colchicines, or HMG-CoA reductase inhibitors (statins) are used concurrently with ciclosporin, close clinical observation is required in order to enable early detection of toxic manifestations of the drugs, followed by reduction of its dosage or its withdrawal.
Elevations in serum creatinine were observed in the studies using everolimus or sirolimus in combination with full-dose ciclosporin for microemulsion. This effect is often reversible with ciclosporin dose reduction. Everolimus and sirolimus had only a minor influence on ciclosporin pharmacokinetics. Co-administration of ciclosporin significantly increases blood levels of everolimus and sirolimus.
Ciclosporin may increase the plasma concentrations of repaglinide and thereby increase the risk of hypoglycemia.
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 and section 6 warnings and precautions).

Novartis Israel Ltd.
36 Shaham St., Kiryat Matalon, Petach-Tikva
P.O.B 7759, Petach Tikva 49250, Israel
Tel: 972-3-9201111 Fax: 972-3-9229230

נוברטיס ישראל בע"מ.
רח' שחם 36 קריית מטלון פתח-תקוה
ת.ד. 7759 פתח-תקוה 49250
טלפון: 03-9201111 פקס: 03-9229230

Following concomitant administration of ciclosporin and aliskiren, the Cmax of aliskiren was increased by approximately 2.5 fold and the AUC by approximately 5 fold. However, the pharmacokinetic profile of ciclosporin was not significantly altered (see section 6 Warnings and precautions).
Concomitant administration of dabigatran and ciclosporin leads to increased plasma level of dabigatran due to P-gp inhibitory activity of ciclosporin (see section 6 Warnings and precautions). Dabigatran has a narrow therapeutic index and an increase in plasma level may be associated with an increased risk of bleeding.

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 ciclosporin.
….

Novartis Israel Ltd.
36 Shaham St., Kiryat Matalon, Petach-Tikva
P.O.B 7759, Petach Tikva 49250, Israel
Tel: 972-3-9201111 Fax: 972-3-9229230

נוברטיס ישראל בע"מ.
רח' שחם 36 קריית מטלון פתח-תקוה
ת.ד. 7759 פתח-תקוה 49250
טלפון: 03-9201111 פקס: 03-9229230