# הודעה על החמרה ( מידע בטיחות)

 **תאריך \_\_\_\_\_11.09.2011\_\_\_\_\_**

**שם תכשיר באנגלית Topamax tabs 25, 50, 100, 200 mg, Sprinkle caps 15, 25 mg**

**מספר רישום: 107552903100, 107562903200, 107572903300, 107582903400, 124163010222, 124173010322**

**שם בעל הרישום\_J-C Health care Ltd.**

**השינויים בעלון מסומנים ברקע צהוב**

**עלון לרופא**

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|  **פרטים על השינוי/ים המבוקש/ים** |
| **פרק בעלון** | **טקסט נוכחי** | **טקסט חדש** |
| Posology and method of administration | MigraineThe total daily dose of topiramate recommended for preventive treatment of migraine is 100 mg/day taken in two doses. Some patients may feel improvement with a total daily dose of 50 mg/day. Some patients take a total daily dose of 200 mg/day. The dosage rate and titration should be clinically monitored. | Migraine~~The total daily dose of topiramate recommended for preventive treatment of migraine is 100 mg/day taken in two doses. Some patients may feel improvement with a total daily dose of 50 mg/day. Some patients take a total daily dose of 200 mg/day. The dosage rate and titration should be clinically monitored.~~The recommended total daily dose of topiramate for prophylaxis of migraine headache is 100 mg/day administered in two divided doses. Titration should begin at 25 mg nightly for 1 week. The dosage should then be increased in increments of 25 mg/day administered at 1-week intervals. If the patient is unable to tolerate the titration regimen, longer intervals between dose adjustments can be used.Some patients may experience a benefit at a total daily dose of 50 mg/day. Patients have received a total daily dose up to 200 mg/day. Dose and titration rate should be guided by clinical outcome (See Pharmacodynamic Properties).**Special Populations****Renal Impairment**Patients with moderate and severe renal impairment may require a dose reduction. Half of the usual starting and maintenance dose is recommended (See Pharmacokinetic Properties).**Hemodialysis**Since TOPAMAX® is removed from plasma by hemodialysis, a supplemental dose of TOPAMAX® equal to approximately one-half the daily dose should be administered on hemodialysis days. The supplemental dose should be administered in divided doses at the beginning and completion of the hemodialysis procedure. The supplemental dose may differ based on the characteristics of the dialysis equipment being used (See Pharmacokinetic Properties).**Hepatic Impairment**Topiramate should be administered with caution in patients with hepatic impairment (See Pharmacokinetic Properties). |
| Pregnancy and lactation | **Pregnancy registry data suggest that there may be an association between the use of TOPAMAX® during pregnancy and congenital malformations (e.g., craniofacial defects, such as cleft lip/palate, hypospadias, and anomalies involving various body systems). This has been reported with topiramate monotherapy and topiramate as part of a polytherapy regimen.****In addition, data from these registries and other studies suggest that, compared with monotherapy, there may be an increased risk of teratogenic effects associated with the use of anti-epileptic drugs in combination therapy.** **TOPAMAX® should be used during pregnancy only if potential benefit justifies the potential risk to the fetus. In treating and counseling women of childbearing potential, the prescribing physician should weigh the benefits of therapy against the risks.** | **TOPAMAX®can cause fetal harm when administered to a pregnant woman. Data from pregnancy registries indicate that infants exposed to topiramate in utero have an increased risk of** **~~Pregnancy registry data suggest that there may be an association between the use of TOPAMAX® during pregnancy and~~ congenital malformations (e.g., craniofacial defects, such as cleft lip/palate, hypospadias, and anomalies involving various body systems). This has been reported with topiramate monotherapy and topiramate as part of a polytherapy regimen.****Compared with a reference group not taking antiepileptic drugs, registry data for TOPAMAX® monotherapy showed a higher prevalence of low birth weight (<2500 grams). A causal relationship has not been established.****In addition, data from these registries and other studies ~~suggest~~ indicate that, compared with monotherapy, there ~~may be~~ is an increased risk of teratogenic effects associated with the use of anti-epileptic drugs in combination therapy.** **TOPAMAX® should be used during pregnancy only if potential benefit justifies the potential risk to the fetus. In treating and counseling women of childbearing potential, the prescribing physician should weigh the benefits of therapy against the risks and consider alternative therapeutic options.** |
| Epilepsy Clinical Trials: | **Adjunctive Therapy:****Controlled Trials in Patients With Partial Onset Seizures Adults With Partial Onset Seizures** **Controlled Trial in Patients With Lennox-Gastaut Syndrome**The median percent reductions in seizure rates and the responder rates (fraction of patients with at least a 50% reduction) by treatment group for each study are shown below in Table 2 .**Table 2 : Efficacy Results in Double-Blind, Placebo-Controlled, Add-On Epilepsy Trials****Partial Onset Seizures****Studies in Adults****N YD** **Median % Reduction****% Responders****N YE** **Median % Reduction****% Responders****N Y1** **Median % Reduction****% Responders****N Y2** **Median % Reduction****% Responders****N Y3** **Median % Reduction****% Responders****Studies in Pediatric Patients****N YP** **Median % Reduction****% Responders****Primary Generalized Tonic‑Clonich****N YTC** **Median % Reduction****% Responders****Lennox-Gastaut Syndromei****N YL**  | **Adjunctive Therapy:****Controlled Trials in Patients With Partial Onset Seizures Adults With Partial Onset Seizures** The numbers of patients randomized to each dose, and the actual mean and median doses in the stabilization period are shown in Tables 1 and 2.**Controlled Trial in Patients With Lennox-Gastaut Syndrome**The median percent reductions in seizure rates and the responder rates (fraction of patients with at least a 50% reduction) by treatment group for each study are shown below in Table ~~2~~ 9.**Table ~~2~~ 9: Efficacy Results in Double-Blind, Placebo-Controlled, Add-On Epilepsy Trials****Partial Onset Seizures****Studies in Adults****~~N~~ YD ~~Y~~D N****Median % Reduction****% Responders****~~N~~ YE ~~YE~~ N****Median % Reduction****% Responders****~~N~~ Y1 ~~Y1~~ N****Median % Reduction****% Responders****~~N~~ Y2 ~~Y2~~ N****Median % Reduction****% Responders****~~N~~ Y3 ~~Y3~~ N****Median % Reduction****% Responders****Studies in Pediatric Patients****~~N~~ YP ~~YP~~ N****Median % Reduction****% Responders****Primary Generalized Tonic‑Clonich****~~N~~ YTC ~~YTC~~ N****Median % Reduction****% Responders****Lennox-Gastaut Syndromei****~~N~~ YL ~~YL~~ N** |
| Pharmacokinetic Properties  | The plasma and renal clearance of topiramate are decreased in patients with impaired renal function (CLCR < 60 mL/min), and the plasma clearance is decreased in patients with end-stage renal disease. As a result, higher steady-state topiramate plasma concentrations are expected for a given dose in renal-impaired patients as compared to those with normal renal function. Topiramate is effectively removed from plasma by hemodialysis. Plasma clearance of topiramate is decreased in patients with moderate to severe hepatic impairment.  | The plasma and renal clearance of topiramate ~~are~~ decreased in patients with moderate and severe impaired renal function (CLCR < ~~60~~70 mL/min)~~, and the plasma clearance is decreased in patients with end-stage renal disease~~. As a result, higher steady-state topiramate plasma concentrations are expected for a given dose in renal-impaired patients as compared to those with normal renal function. In addition, patients with renal impairment will require a longer time to reach steady-state at each dose. In patients with moderate and severe renal impairment, half of the usual starting and maintenance dose is recommended (see Posology and Method of Administratiion).Topiramate is effectively removed from plasma by hemodialysis. A prolonged period of hemodialysis may cause topiramate concentration to fall below levels that are required to maintain an anti-seizure effect. To avoid rapid drops in topiramate plasma concentration during hemodialysis, a supplemental dose of topiramate may be required. The actual adjustment should take into account 1) the duration of dialysis period, 2) the clearance rate of the dialysis system being used, and 3) the effective renal clearance of topiramate in the patient being dialyzed.Plasma clearance of topiramate ~~is~~ decreased a mean of 26% in patients with moderate to severe hepatic impairment. Therefore, topiramate should be administered with caution in patients with hepatic impairment. |