裕利股份有限公司　　函

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受　文　者：臺中榮民總醫院

發文日期：中華民國 114 年 08 月 28 日

發文字號：114-裕利-001392

主　　旨：本公司銷售嬌生股份有限公司之產品「TOPAMAX FILM-COATED TABLETS 25MG，妥泰膜衣錠25毫克(衛署藥輸字第022509號)、TOPAMAX FILM-COATED TABLETS 50MG，妥泰膜衣錠50毫克(衛署藥輸字第022507號)、TOPAMAX FILM-COATED TABLETS 100MG，妥泰膜衣錠100毫克(衛署藥輸字第022508號)及TOPAMAX SPRINKLE CAPSULES 25MG，妥泰分散型膠囊25毫克(衛署藥輸字第023381號)」DHPC信函事宜，詳如說明段，請查照。

說　　明：

一、本公司銷售嬌生股份有限公司之產品「TOPAMAX FILM-COATED TABLETS 25MG，妥泰膜衣錠25毫克(衛署藥輸字第022509號)、TOPAMAX FILM-COATED TABLETS 50MG，妥泰膜衣錠50毫克(衛署藥輸字第022507號)、TOPAMAX FILM-COATED TABLETS 100MG，妥泰膜衣錠100毫克(衛署藥輸字第022508號)及TOPAMAX SPRINKLE CAPSULES 25MG，妥泰分散型膠囊25毫克(衛署藥輸字第023381號)」，承蒙貴院採用，特此致謝。

二、原廠預計發送DHPC信函(附件一)通知醫療相關人員，旨揭藥品之懷孕預防計劃(pregnancy prevention programme)，信函內容詳如附件，請先行知悉。

三、有關此懷孕預防計劃，除了通知醫療相關人員 topiramate 成分藥品之安全性資訊，也告知未來嬌生公司將在仿單增列病人用藥指引，並新增一份HCP指引。此仿單變更已於 114年6月20日送件至 食藥署審查(案號1149043013、1149043016、1149043018-19)。

四、嬌生公司領有含 topiramate 成分藥品許可證請詳如附件，其中「妥泰膜衣錠200毫克」、「妥泰分散型膠囊15毫克」及「妥泰分散型膠囊50毫克」並未實際輸台。

五、特此通知，敬請轉知 貴院相關單位，造成不便之處懇請見諒，並請繼續支持本公司為禱。

附件：原廠公文、原廠通知食藥署函文、DHPC Letter

裕利股份有限公司
負責人：　葛約翰

嬌生股份有限公司 函

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受文者：裕利股份有限公司
發文日期：中華民國 114 年 8 月 21 日
發文字號：(一一四)台嬌字第 0176 號
速別：
密等：
附件：

主　旨：函告本公司產品「妥泰®膜衣錠25、50、100毫克(Topamax® film-coated tablets)(衛署藥輸字第022509、022507、022508號)及妥泰®分散型膠囊25毫克(Topamax® Sprinkle Capsules 25mg)(衛署藥輸字第023381號)」DHPC信函事宜，煩請 貴公司代為發函至各醫院，函文如下：

「主　旨：函告本公司產品「妥泰®膜衣錠25、50、100毫克(Topamax® film-coated tablets)(衛署藥輸字第022509、022507、022508號)及妥泰®分散型膠囊25毫克(Topamax® Sprinkle Capsules 25mg)(衛署藥輸字第023381號)」DHPC信函事宜，詳如說明段，請查照。

說　明：

一、 本公司產品「妥泰®膜衣錠25、50、100毫克(Topamax® film-coated tablets)(衛署藥輸字第022509、022507、022508號)及妥泰®分散型膠囊25毫克(Topamax® Sprinkle Capsules 25mg)(衛署藥輸字第023381號)」DHPC信函事宜。DHPCC信函摘要如下：

一、 孕期風險與限制
- Topiramate 孕期使用可導致：
- 嚴重先天缺陷（如：唇顎裂、尿道下裂）
- 胎兒生長限制
- 可能增加胎兒日後發展出 神經發展疾患的風險，如自閉症、智能障礙與注意力不足過動症（ADHD）

二、 偏頭痛預防用途的禁忌
- 懷孕中及未使用有效避孕的育齡女性，不可使用 Topiramate 預防偏頭痛。

三、 懷孕預防計畫（Pregnancy Prevention Program）

- 針對所有女性孩童與育齡女性：
- 治療需由有癲癇或偏頭痛治療經驗的醫師開始施行和監督。
- 至少每年重新評估治療的必要性。
- 整個治療期間和停止治療後4週內必須使用高度有效避孕方式（如子宮內避孕器）或兩種避孕方式搭配（例如荷爾蒙避孕+阻隔避孕法）。
- 若使用系統性荷爾蒙避孕，建議同時加用阻隔避孕法。
- 懷孕前應考慮改用其他藥物；若為癲癇治療，需提醒未控制癲癇對懷孕本身也有風險。
- 若懷孕，偏頭痛治療需立刻停藥，癲癇治療應轉診專科進行監測與評估是否更換藥物。

四、 教育與溝通

- 針對病患與醫師提供：
- 醫師用風險認知查核表，治療起始與每年需填寫。
- 告知女性病患與照顧者用之衛教手冊列在仿單章節病人指引資訊。
- 包裝上將加入致畸形警語與圖示標示。

五、 不良反應通報

- 可通報至台灣藥物不良反應通報系統：http://adr.fda.gov.tw

如需協助與更多資訊，可聯絡J&JIM Taiwan電話 0800-211-688。

二、 隨函檢附相關附件如下：

(一) 衛生福利部核准函

(二) DHPC letter

三、 特此通知　貴院。懇請　貴院持續支持與愛護，無任感荷。

」

嬌生股份有限公司

負責人 古佳成

<2-July-2025>

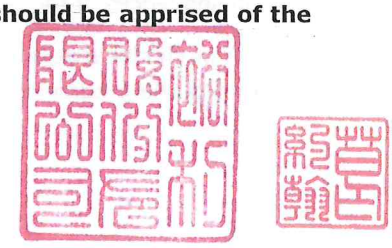
Topiramate:
New restrictions to prevent exposure during pregnancy

Dear healthcare professional,

This letter is sent in agreement with the Taiwan FDA to inform you of the implementation of a **pregnancy prevention programme for topiramate-containing medicinal products.**

Summary

- **Topiramate can cause major congenital malformations and foetal growth restriction when used during pregnancy. Recent data also suggest a possibly increased risk of neurodevelopmental disorders (NDD) including autism spectrum disorders, intellectual disability and attention deficit hyperactivity disorder (ADHD) following topiramate use during pregnancy.**
- **Topiramate for prophylaxis of migraine is already contraindicated in pregnancy and in women of childbearing potential not using highly effective contraception.**
- **The need for treatment should be reassessed at least annually.**
- **Due to a potential interaction, women using systemic hormonal contraceptives should be advised to also use a barrier method.**
- **For women of childbearing potential currently using topiramate, the treatment should be re-evaluated to confirm that the pregnancy prevention programme is adhered to.**
- **Topiramate should be used during pregnancy only if the 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. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.**



Background on the safety concern

The approved indication in Taiwan for Topamax is:

Adjunctive therapy for adults and children aged 2 and above with partial onset seizures or combined with seizures associated with Lennox Gastaut syndrome, and generalized tonic clonic seizures. Monotherapy in patients with partial onset seizure. Prophylaxis of migraine headache.

Data from two observational population-based registry studies (1, 2) undertaken in largely the same dataset from the Nordic countries suggest that there may be a 2- to 3-fold higher prevalence of autism spectrum disorders, intellectual disability or attention deficit hyperactivity disorder (ADHD) in almost 300 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to an anti-epileptic drug (AED).

A third observational cohort study (3) from the U.S.A. did not suggest an increased cumulative incidence of these outcomes by 8 years of age in 1030 children of mothers with epilepsy exposed to topiramate in utero, compared with children of mothers with epilepsy not exposed to topiramate, after adjustment for indication and other confounders.

It is already well known that topiramate can cause major congenital malformations and foetal growth restriction when used during pregnancy. Clinical data from pregnancy registries indicate that infants exposed to topiramate monotherapy have:

- An increased risk of congenital malformations (particularly cleft lip/palate, hypospadias, and anomalies involving various body systems) following exposure during the first trimester. The North American Antiepileptic Drug pregnancy registry data for topiramate monotherapy showed an approximate 3-fold higher prevalence of major congenital malformations (4.3%), compared with a reference group not taking AEDs (1.4%). In addition, data from other studies indicate that, compared with monotherapy, there is an increased risk of teratogenic effects associated with the use of AEDs in combination therapy. The risk has been reported to be dose dependent; effects were observed in all doses. (4)
- A higher prevalence of low birth weight (< 2500 grams) compared with a reference group. (5)
- An increased prevalence of being small for gestational age (SGA; defined as birth weight below the 10th percentile corrected for their gestational age, stratified by sex). The long term consequences of the SGA findings could not be determined. (5)

For women of childbearing potential currently using topiramate, the treatment should be re-evaluated to confirm that the pregnancy prevention programme is adhered to (described below).

Key elements of the pregnancy prevention programme

In female children and women of childbearing potential:

- Treatment with topiramate should be initiated and supervised by a physician experienced in the management of epilepsy or migraine, respectively.
- Alternative therapeutic options should be considered.
- The need for topiramate treatment in these populations should be reassessed at least annually.

In women of childbearing potential:

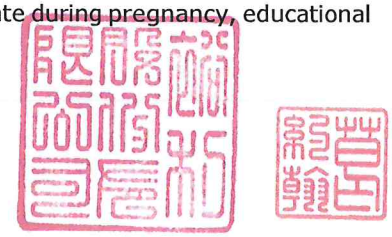
- Topiramate for migraine prophylaxis is contraindicated:
  - in pregnancy,
  - in women of childbearing potential not using highly effective contraception.
- Pregnancy testing should be performed before initiating treatment.
- The patient must be fully informed and understand the potential risks related to the use of topiramate during pregnancy. This includes the need for a specialist consultation if the woman is planning a pregnancy and for prompt contact with a specialist if she becomes pregnant or thinks she may be pregnant.
- At least one highly effective method of contraception (such as an intrauterine device) or two complementary forms of contraception including a barrier method should be used during treatment and for at least 4 weeks after stopping treatment. Women using systemic hormonal contraceptives should be advised to also use a barrier method.
- If a woman is planning to become pregnant, efforts should be made to switch to an appropriate alternative <epilepsy or migraine> treatment before contraception is discontinued. For the treatment of epilepsy, the woman must also be informed about the risks of uncontrolled epilepsy to the pregnancy.
- If a woman being treated with topiramate for epilepsy becomes pregnant, she should promptly be referred to specialists to reassess topiramate treatment and consider alternative treatment options, as well as for careful antenatal monitoring and counselling.
- If a woman being treated with topiramate as migraine prophylaxis becomes pregnant, treatment should be stopped immediately. The woman should be referred to a specialist for careful antenatal monitoring and counselling.

In female children (for epilepsy <and migraine> only):

- Prescribers must ensure that parent(s)/caregiver(s) of female children using topiramate understand the need to contact a specialist once the child experiences menarche.
- At that time, the patient and parent(s)/caregiver(s) should be provided with comprehensive information about the risks due to topiramate exposure in utero, and the need for using highly effective contraception.

Educational material

In order to assist healthcare professionals and patients in avoiding exposure to topiramate during pregnancy and to provide information about the risks of taking topiramate during pregnancy, educational materials will be put in place including:



- a guide for healthcare professionals involved in the care of female children and women of childbearing potential using topiramate including a risk awareness form, which must be used {and signed} at the time of treatment initiation and during each annual review of topiramate treatment by the treating physician,
- a patient guide will be incorporated into the sections of "Patient using information" in Topamax package insert which should be informed of all female children or their parent(s)/caregiver(s) and women of childbearing potential using topiramate.

A textual warning <and a pictogram> on the teratogenic risk will be added to the outer package of all topiramate containing medicinal products.

Call for reporting

Any suspected adverse events should be reported to Taiwan National Adverse Drug Reactions Reporting System (http://adr.fda.gov.tw/).

Company contact point

If you have further questions or require additional information, please contact Johnson & Johnson Medical Information Department at 0800-211-688.

Your faithfully,

Electronically signed by: Chih-Lin Chiang
Reason: I am certifying this document
Chih-Lin Chiang *Date: Jul 2, 2025 19:19 GMT+8*

Medical Director Taiwan
Johnson & Johnson Taiwan Ltd.

References

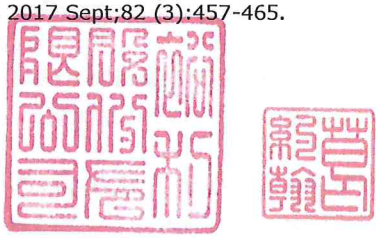
[1]**Bjørk** M, Zoega H, Leinonen MK, et al. Association of Prenatal Exposure to Antiseizure Medication With Risk of Autism and Intellectual Disability. JAMA Neurol. Published online May 31, 2022. doi:10.1001/jamaneurol.2022.1269.

[2]**Dreier** JW, Bjørk M, Alvestad S, et al. Prenatal Exposure to Antiseizure Medication and Incidence of Childhood- and Adolescence-Onset Psychiatric Disorders. JAMA Neurol. Published online April 17, 2023. doi: 10.1001/jamaneurol.2023.0674. Online ahead of print. PMID: 37067807.

[3]**Hernández-Díaz** S, Straub L, Bateman BT, et al. Risk of Autism after Prenatal Topiramate, Valproate, or Lamotrigine Exposure. N Engl J Med. 2024 Mar 21;390(12):1069-1079. doi: 10.1056/NEJMoa2309359. PMID: 38507750; PMCID: PMC11047762.

[4]**Cohen** JM, Alvestad S, Cesta CE, et al. Comparative Safety of Antiseizure Medication Monotherapy for Major Malformations. Ann Neurol. 2023; 93(3):551-562.

[5]**Hernandez-Diaz** S, McElrath TF, Pennell PB et al. Fetal Growth and Premature Delivery in Pregnant Women on Anti-epileptic Drugs. North American Antiepileptic Drug Pregnancy Registry. Ann Neurol. 2017 Sept;82 (3):457-465. doi:10.1002/ana.25031. PMI:28856694.



Topamax DHPC letter_clean

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