衛生局　藥物事務廳

季度藥訊 Quarterly Drug Newsletter

2009　No. 2

本季度藥訊的內容主要摘錄自世界各國藥政部門所公佈及在本澳所收集有關藥物安全性的資訊，目的是通知本澳的衛生專業人士最新的藥物安全性資訊，從而推廣安全及合理用藥。

The content of this Quarterly Drug Newsletter originates as compilation of the adverse drug reactions (ADR) and drug safety issues published by various drug regulatory authorities as well as those reported locally. With this information, we aim at disseminating the latest adverse drug reaction alerts, safety and efficacy issues to our healthcare professionals with the ultimate goal to encourage safe and rational use of pharmaceuticals.

熱點關注藥物 ***DRUGS OF CURRENT INTEREST***

熱點關注藥物泛指一些近期在國內外及本地曾被報告發生藥物不良反應的藥物，以及最近獲批准進口本澳的新藥，訂定熱點關注藥物的目的是提醒衛生專業人士尤其關注及通報該等藥物所引起的不良反應，如　閣下察覺病人在服用以下及其他藥物後產生任何不良反應，請向藥物事務廳通報。

Generally speaking, ¡Drugs of Current Interest¡ are defined as those drugs of which adverse drug reaction(s) (ADRs) was (were) experienced and had been reported recently at international, national and local levels. In addition, drugs that have received recent approval for importation into Macao are also being incorporated into this list. The purpose of including this column serves to remind all healthcare professionals to pay special attention to ADRs and report them. If you observe any adverse reaction on your patient subsequent to the use of the following or any other drugs, please report all suspected reactions to the Department of Pharmaceutical Affairs.

Abacavir	Entecavir	Metoclopamide
Adalimumab	Erlotinib	Moxifloxacin
Aliskiren	Eszopiclone	Metoclopamide
Allopurinol	Etanercept	Moxifloxacin
Atorvastatin	Etoricoxib	Mycophenolate mofetil
Bisphosphonates	Ezetimibe	Norfloxacin
Bevacizumab	Ezetimibe/Simvastatin	Oseltamivir
Botulinum toxins	Flucloaxillin	Phenytoin
Bortezomib	Fluoroquinolones	Propranolol
Carbamazepine	Fosaprepitant dimeglmine	Raltegravir
Carbimazole	Fulvestrant	Rimonbant
Certolizumab pegol	Gadobenate dimeglumine	Rituximab
Clopidgrel	Heparin sodium	Rosiglitazone
Darunavir	Iloprost trometamol	Simvastatin
Decitabine	Infliximab	Sunitinib malate
Deferasirox	Ivabradine	Tinzaparin sodium
Desflurane	Lamotrigine	Tiotropium bromide
Diacerein	Lapatinib	Trabectedin
Didanosine	Levofloxacin	Zanamuvir
Docetaxel	Leukotriene inhibitors -montelukast	Zonisamide
Drotrecogin alfa	Methylphenidate	

通報及聯絡資料 ***Reporting and Contact Information:***

通報表格：在 http://www.ssm.gov.mo/design/services/serpt_chn.pdf 下載或向藥物事務廳索取。
網上通報：登入 http://www.ssm.gov.mo。
如有任何疑問，請致電 85983517(辦公時間)或傳呼 85008068(非辦公時間)。
Report form: access http://www.ssm.gov.mo/design/services/serpt_chn.pdf to download or obtain from Dept. of Pharmaceutical Affairs. Internet reporting: access http://www.ssm.gov.mo. Any query, call 85983517(office hrs) or pager 85008068 (off-duty hrs).

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有關醋酸環丙孕酮**(cyproterone acetate)**（商品名：**Androcur R** ）安全性的最新資訊

Latest safety update on cyproterone acetate (AndrocurR）

資料來源: 新加坡藥物監管局
Source： Singaporean Health Science Authority (HSA)
http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/safety_information/product_safety_alerts/safety_alerts_2009.html

自 1972 年起，新加坡拜耳先靈藥廠(Bayer Schering Pharm)共接獲 24 宗（ 20 名女性、4 名男性）懷疑服用醋酸環丙孕酮(cyproterone acetate) （商品名： Androcur R ）或併用雌激素後引發腦膜瘤(meningiomas)的個案，當中 9 個案例的病人在接受第一次腦膜瘤診斷時，已出現了多發性腦膜瘤的情況。而上述所有個案均與病人曾高劑量及長時間（4-24 年）服用醋酸環丙孕酮有關。而 Froelich 等人亦曾報導 9 宗有關年齡介乎 33 至 62 歲的女病人，在 10 至 20 年期間每日服用醋酸環丙孕酮，而產生多發性腦膜瘤的個案。故此，當醫生需處方高劑量的醋酸環丙孕酮給予病人前，應考慮上述安全訊息。

Bayer Schering Pharma, Singapore has received 24 reports (20 females, four males) of meningiomas suspected to be associated with its product cyproterone acetate either used singly or in combination with estrogens since 1972. In nine of the 24 patients, multiple meningiomas were present at the time of the first meningioma diagnosis. All the cases were associated with high doses of cyproterone acetate and after long treatment periods of four to 24 years. Froelich et al also reported nine case studies of female patients, aged between 33 to 62 years old, who presented with multiple meningiomas after receiving daily cyproterone acetate treatments for durations of between 10 to 20 years. Therefore, healthcare professionals are advised to take into consideration the above safety information when prescribing high dosages of cyproterone acetate to their patients.

有關哺乳嬰兒可引致可待因中毒的最新資訊

Latest update on codeine toxicity in breastfed infants

資料來源: 新加坡藥物監管局
Source： Singaporean Health Science Authority (HSA)
http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/safety_information/product_safety_alerts/safety_alerts_2009.html

新加坡藥物監管局亦提醒醫療專業人仕，屬可待因快速代謝型的授乳婦女，在使用可待因後可能引致嬰兒產生既罕見又嚴重的可待因中毒。據有限的證據顯示，帶有 CYP2D6 酶活基因或其他快速代謝者會比其他人更迅速及完整地將可待因轉化爲嗎啡，因而導致授乳婦女血清及母乳內的嗎啡含量比預期高，增加哺乳嬰兒嗎啡中毒的風險。倘醫生需向授乳婦女處方可待因藥物時，須選擇最低有效劑量及最短療程的治療方案。

Health Science Authority (HSA) would like to bring the attention of healthcare professionals to a very rare, but serious risk of toxicity in breastfed babies posed by codeine use in nursing mothers who are ultra-rapid metabolisers of codeine. Limited evidence suggests that individuals with a specific CYP2D6 genotype or otherwise known as ultra-rapid metabolisers, may convert codeine to morphine more rapidly and completely than other people. Therefore, in nursing mothers, this metabolism can result in a higher than expected levels of morphine in serum and breast milk, putting nursing infants at increased risk for morphine overdose. When prescribing codeine to a nursing mother, physicians are advised to choose the lowest effective dose for the shortest period of time.

有關抗癲癇藥物 **(antiepileptics)**引發骨質不良反應安全性的最新資訊

Latest safety update on antiepileptics and adverse effects on bones

資料來源：英國藥物與健康產品監管局
Source ： Medicines and Healthcare products Regulatory Agency (MHRA)
http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON043809
Drug Safety, Volume 2 Issue 9 April 2009 from MHRA and CHM Pages 2-3

最新研究報告指出，長期服用卡馬西平(carbamazepine)、苯妥英(phenytoin)、樸米酮(primidone)及丙戊酸鈉(sodium valproate)可能引發骨質密度降低，從而導致骨質減少、增加骨質疏鬆以及引致長期卧床、缺乏陽光照曬及缺鈣一類高危病人骨折的風險。雖然目前對抗癲癇藥物作用於骨骼的認識有限，但某些證據指出這可能與抗癲癇藥物，包括苯妥英、苯巴比妥(Phenobarbital)、卡馬西平及樸米酮誘發細胞色素 P450 酶系統有關，從而增加維生素 D 的排出，引致繼發性甲狀腺功能亢進、增加骨質轉換以及降低骨質密度。而非酶誘導藥物丙戊酸鈉引致骨質密度降低之機理尚未明確。直到目前爲止，尚未有足夠的數據證明其他抗癲癇藥物與骨質密度降低、骨質減少、骨質疏鬆及骨質軟化症有直接關係。基於上述情況，MHRA 向醫療專業人士提出下列建議：

1. 現有資料顯示苯妥英、卡馬西平、樸米酮及丙戊酸鈉會降低骨質密度，從而增加引發骨質減少、骨質疏鬆以及令高危病人骨折的機會。
2. 苯妥英、卡馬西平 、苯巴比妥、樸米酮會增加骨質軟化症的風險。
3. 對於長期服用樸米酮、苯妥英、卡馬西平、苯巴比妥及丙戊酸鈉的高危病人，醫生應考慮處方維生素 D 給該類病人服用。

Latest results from published studies indicated that long-term treatment with carbamazepine, phenytoin, primidone, and sodium valproate, is associated with decreased bone mineral density that results in an increased risk of developing osteopenia, osteoporosis, and fractures in the following patients who are at-risk e.g. those who are immobilized for long periods, those who have inadequate

sun exposure and those who take insufficient dietary calcium. There is limited understanding of the effects of antiepileptics on bone but some evidence suggests that antiepileptics (including phenytoin, phenobarbital, carbamazepine, and primidone) induce the cytochrome P450 enzyme system, which results in increased clearance of vitamin D, leading to secondary hyperparathyroidism, increased bone turnover, and reduced bone density. The mechanism by which sodium valproate, a non-enzyme-inducing drug, causes decreased bone mineral density is unclear. At present there are insufficient data to support an association between decreased bone mineral density, osteopenia, osteoporosis, and osteomalacia and other antiepileptic drugs. With the above information, the MHRA offered the following advice for healthcare professionals:

1. The available data suggest that phenytoin, carbamazepine, primidone, and sodium valproate are associated with decreased bone mineral density, which may lead to osteopenia, osteoporosis, and increased fractures in at-risk patients.
2. Phenytoin, carbamazepine, phenobarbital, and primidone are associated with an increased risk of osteomalacia.
3. Vitamin D supplementation should be considered for at-risk patients who receive long-term treatment with primidone, phenytoin, carbamazepine, phenobarbital, or sodium valproate.

有關含水楊酸局部口腔藥物安全性的最新資訊

Latest safety update on oral topical preparations containing salicylate salts

資料來源： 英國藥物與健康產品監管局

Source ：Medicines and Health-product Regulatory Agency (MHRA)

http://www.mhra.gov.uk/PrintPreview/PressReleaseSP/CON044014

http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON044014

由於含水楊酸的藥物理論上具引發瑞氏綜合症(Reye¡s Syndrome)的風險，故英國人用藥物委員會(Commission on Human Medicines - CHM)建議，含有水楊酸作舒緩局部口腔痛楚的藥物不可用於 16 歲以下孩童及年輕病人。對於出牙時痛楚或口腔潰瘍問題，英國藥物與健康產品監管局(MHRA)建議下列鎮痛替代療法：

1. 嬰兒出牙痛楚，以冷凍物品輕壓可幫助緩解出牙痛楚。
2. 市面其他不含水楊酸的局部麻醉劑或溫和抗菌劑可治療孩童和年輕病人出牙痛楚及口腔潰瘍。
3. 以鹽水漱口方式舒緩由矯牙裝置引致的痛楚。以撲熱息痛(paracetamol)止痛藥舒緩牙齒移位所引致的不適。
4. 如家長/孩童監護人或年輕病人對治療有任何疑問，應向主診醫生查詢。

The Commission on Human Medicines (CHM), U.K. recommended that oral topical pain relief products containing salicylate salts should be contraindicated in children and young people under the age of 16 years as there is a theoretical risk of Reye¡s syndrome with these oral topical preparations. In light of the above, the MHRA suggested the following alternative treatments to pains due to teething or ulceration problems:

1. For infant teething, gentle pressure with something cool may be helpful in relieving teething pain.
2. There are a number of alternative products on the market which contain a local anaesthetic/mild antiseptic which can be used for the treatment of teething pain or mouth ulcers in children and young people and which do not contain a salicylate.
3. For pain associated with orthodontic devices, salt water mouthwashes are recommended for sore areas. For discomfort arising from tooth movement a paracetamol based painkiller is recommended.
4. If parents/carers or young people are in doubt over which treatment to use, then they should consult their physicians.

有關甲狀腺機能亢進藥物 **propylthiouracil** 安全性的最新資訊

Latest safety update on the antithyroid propylthiouracil.

資料來源： 新英格蘭醫學雜誌

Source ：New England Journal of Medicines

http://www.doh.gov.tw/CHT2006/DM/DM2_p01.aspx?class_no=25&now_fod_list_no=10402&level_no=2&doc_no=71000

http://ovidsp.tx.ovid.com/spa/ovidweb.cgi?&S=BDEPFPFFCDDDNBOKNCGLMFJLNNLJAA00&Link+Set=S.sh.15.16.18%7c28%7csl_10

Rivkees, Scott A. M.D.; Mattison, Donald R. M.D., Ending Propylthiouracil-Induced Liver Failure in Children, Volume 360(15), 9 April 2009, p 1574¡ 1575, the New England Journal of Medicine, Massachusetts Medical Society, Boston, Massachusetts, USA

根據一份發表於 2009 年 4 月 9 日新英格蘭醫學雜誌（NEJM 360:1574）之研究報告，用於治療罹患葛瑞夫氏病（Graves¡ disease）病童的兩種首選藥物 propylthiouracil 及 methimazole，在過去 60 多年的使用中，由 propylthiouracil 誘發肝衰竭、導致需要肝臟移植及致命性的個案與日俱增，但卻沒有小孩因服用 methimazole 而引起上述不良反應。在 2007 年，美國的醫生向病童發出超過 9000 張 propylthiouracil 的處方，估計當中超過 1000 名病童正服用該藥。除停藥外，尚沒有處理由 propylthiouracil 引致的肝毒性的其他方案，按近期的數據，作者估計如醫生繼續處方 propylthiouracil，由該藥誘發肝衰竭而導致需要肝臟移植的個案會繼續增加。基於此，建議醫生不要以 propylthiouracil 作爲治療葛瑞夫氏病童的首選藥物。對現正服用該藥的病童，醫生應考慮另覓其他治療方案。

According to the latest published article on the April 9th 2009 issue of the New England Journal of Medicines, reports indicated that propylthiouracil and methimazole are the two antithyroid drugs widely used in children as a first-line therapy for Graves¡ disease. Over the past 60 years of propylthiouracil and methimazole uses, reports of propylthiouracil-related liver failures, transplantations and deaths have accumulated. In contrast, this problem has not

been reported with methimazole use in children. In 2007, more than 9000 prescriptions were written for propylthiouracil for use in children and is estimated that more than 1000 pediatric patients are currently receiving propylthiouracil in the United States. As there is no other alternative to manage the risk of hepatotoxicity in a patient receiving propylthiouracil, other than not using the drug. On the basis of recent data, the authors estimated that if propylthiouracil continues to be used, it is likely that propylthiouracil-induced liver failure requiring transplantation will be increased. In light of the above, it is suggested that propylthiouracil should no longer be used as first-line treatment for Graves' disease in children. Alternative treatments should be considered for children currently on propylthiouracil.

有關甲基藍 **(methylthioninium chloride, methylene blue)**安全性的最新資訊

Latest safety update on methylthioninium chloride (methylene blue)

資料來源： 英國藥物與健康產品監管局
Source ：Medicines and Health-product Regulatory Agency (MHRA)
http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON043809
Drug Safety, Volume 2 Issue 9 April 2009 from MHRA and CHM Pages 2-3

甲基藍獲准用於治療因藥物引致的血紅蛋白貧血症（methaemoglobinaemia）的成年病人，根據最近的觀察，MHRA 公佈有關上述藥物與血清素（如：SSRIs、clomipramine 及 venlafaxine）作非合理併服時可能引發病人產生中樞神經中毒現象，其症狀包括思想混亂、定向障礙、激動不安、表達性失語、四肢肌肉張力改變、缺氧、眼部症狀及精神欠佳。上述沒有按批准用途使用甲基藍所產生的中樞神經中毒個案，皆發生於甲狀旁腺或甲狀腺手術中以該藥作顯影劑以及在心臟手術過程中以該藥治療不可控制的低血壓。以上資料足以支持血清素藥物與甲基藍併用時引發中樞神經中毒的可能性。有見及此，MHRA 向衛生專業人士提出下列建議：

1. 甲基藍注射劑只獲批准用於治療因藥物引發血紅蛋白貧血症的成年病人，其使用劑量爲每公斤體重靜脈注射 1-2 毫克。
2. 當甲基藍用於未獲批准的情況時（包括甲狀旁腺局部手術時或其他超出批准劑量的情況），應謹慎評估以免引發中樞神經中毒。
3. 正服用血清素抗抑鬱藥物（包括 SSRIs、clomipramine 及 venlafaxine）的病人應避免使用甲基藍靜脈注射劑。
4. 在無可避免的情況下而必須使用甲基藍注射劑時，醫生應盡量使用最低劑量及在注射該藥後 4 小時內密切觀察該藥對病人中樞神經的影響。
5. 如病人在使用甲基藍後產生中樞神經系統毒性，醫生應密切監察病人情況，並給予支持性照護。

Methylthioninium chloride (methylene blue) is approved for the management of drug-induced methaemoglobinaemia in adults. On the basis of the latest observation, MHRA issued an update about the possibility of CNS toxicity associated with the off-labeled uses of methylthioninium chloride in patients who are also being treated with serotonergic drugs such as selective serotonin reuptake inhibitor (SSRI) antidepressants, clomipramine, and venlafaxine. Features of such toxicity include confusion, disorientation, agitation, expressive aphasia, altered muscle tone in limbs, hypoxia, ocular symptoms, and depressed level of consciousness. All cases described CNS toxicity after the off-labelled uses of methylthioninium as a visualising agent in parathyroid or thyroid surgery and in the management of uncontrollable hypotension during cardiac surgery. Such information reinforces the possibility that CNS toxicity results from an interaction between a serotonergic drug and methylthioninium. In light of the above, MHRA offered the following advice for healthcare professionals:

1. Methylthioninium chloride by the intravenous route is approved only for drug-induced methaemoglobinaemia in adults at a dose of 1¡2 mg/kg.
2. Off-label uses of methylthioninium (including use in parathyroid localization or its use at doses exceeding the licensed dose) should be carefully evaluated in view of the potential for CNS toxicity
3. Intravenous methylthioninium chloride should be avoided in patients who have been treated recently with serotonergic antidepressants, including SSRIs, clomipramine, and venlafaxine.
4. If use of intravenous methylthioninium chloride cannot be avoided, the lowest possible dose should be used and the patient observed closely for CNS effects for up to 4 hours after administration
5. If features of CNS toxicity develop after use of methylthioninium, the patient should be monitored closely and given supportive care.

有關肉毒桿菌毒素注射劑產品安全性的最新資訊

Latest safety update on injectable botulinium toxin products

資料來源： 美國食物及藥物管理局
中國台灣行政院衛生署
澳門特別行政區衛生局藥物事務廳
Sources ：United States Food and Drug Administration (USFDA)
Department of Health, Executive Yuan, Taiwan, China
Department of Pharmaceutical Affairs, Health Bureau, Macao S.A.R.
http://www.fda.gov/medwatch/safety/2009/safety09.htm#Botox
http://www.fda.gov/cder/drug/early_comm/botulinium_toxins200904.htm
http://www.doh.gov.tw/CHT2006/other/ShowCopy.aspx?doc_no=71322&class_no=25

近期，本廳接獲兩宗關於本澳市民在國內使用肉毒桿菌毒素(botulinium toxins)注射劑美容後，產生藥物不良反應的本地通報個案，患者出現語言不清、吞咽困難、眼瞼下垂、氣促、肌肉無力、頭暈及複視的不良反應。此外，中國台灣衛生署亦接獲 28 例通報，出現之不良反應包括胸悶、尿滯留等。肉毒桿菌毒素注射劑用於治療眼瞼痙攣、半面痙攣、局部肌肉痙攣、斜視、痙攣性斜

頸、小兒腦性麻痺引起之肌肉痙攣、皺眉紋及原發性腋窩多汗症。近日，美國食物及藥物管理局（USFDA）經評估此藥物上市後的安全性資料後，要求肉毒桿菌毒素產品生產商須在說明書內加註關於毒素自注射部位擴散至其他部位而導致不良反應風險之警示，從而提醒醫生及患者有關使用此類藥物之危險性。

基於以上所述，建議醫生、藥劑師及其他衛生專業人士注意以下事項：

- 應清楚明白不同肉毒桿菌毒素的產品，以 ¡Units¡ 或 ¡U¡ 所標示的單位劑量的強度存有差異，即以單位標示的臨床劑量不可在肉毒桿菌毒素產品間互換。
- 向病人解釋有關局部注射肉毒桿菌毒素後，可能會因注射液擴散而可能引發不良事件，當中包括肌肉無力、構音困難、對膀胱失去控制、呼吸困難、吞嚥困難、複視、視力模糊及眼瞼下垂。
- 上述不良事件在病人接受注射後可最早於數小時或遲至於數星期內出現。
- 提醒病人如發現上述任何症狀，立即向醫生求診。

Lately, Department of Pharmaceutical Affairs has received 2 locally reported cases whereby two residents from Macao experienced adverse drug effects after they were being administered with injectable botulinium toxins for cosmetic purposes in Mainland China. The reported adverse effects included speech disorder, dysphagia, blepharoptosis, rapid respiration, muscle weakness, headache and double vision. In addition, the Taiwanese Department of Health, China also received 28 reported cases associating to the use of injectable botulinium toxins. The most common adverse reactions are chest tightness, urinary retention etc.. Injectable botulinium toxin products are indicated for the treatments of blepharospasm, hemifacial spasm, localized muscle spasm, strabismus, spasmodic torticollis, muscle spasm subsequent to cerebral palsy in children, glabellar lines and primary hyperhidrosis of the axillae. After a recent assessment of the post-marketing safety data for the injectable botulinium toxin, the United States Food and Drug Administration (USFDA) ordered the manufacturers for all botulinium toxin products to strengthen warnings on the prescribing information regarding the risk of adverse events when the effects of the toxin spread beyond the site where it was injected. This serves to notify the physicians and the patients about the risk of using this class of medications.

In light of the above, we would like to inform all physicians, pharmacists and other healthcare professionals to take note about the following recommendations：

- Understand that dosage strength expressed in ¡Units¡ or ¡U¡ is different among the botulinum toxin products, clinical doses expressed in units are not interchangeable from one botulinum toxin product to another.
- Educate patients about potential adverse events due to distant spread of botulinum toxin effects following local injections including: muscle weakness, dysarthria, loss of bladder control, trouble breathing, trouble swallowing, double vision, blurred vision and drooping eyelids.
- The above adverse events have been reported as early as several hours and as late as several weeks after treatment.
- Advise patients to seek immediate medical attention if they develop any of these symptoms.

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有關埃羅替尼 **erlotinib(**特羅凱^{R}, **Tarceva^{R})**安全性的最新資訊

Latest safety update on erlotinib (Tarceva^{R})

資料來源： 美國食物及藥物管理局及星加坡藥監局

Sources ：United States Food and Drug Administration (USFDA) and the Singaporean Health Science Authority (HSA)

http://www.fda.gov/medwatch/safety/2009/safety09.htm#Tarceva

http://www.fda.gov/medwatch/safety/2009/Tarceva_DHCP_Letter_April09.pdf

http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/safety_information/DHCPL.html

美國食物及藥物管理局（USFDA）及星加坡藥監局(HSA)通知衛生專業人士一則有關埃羅替尼(erlotinib)(特羅凱R, TarcevaR)安全性的最新資訊。單獨使用特羅凱R可治療曾接受化療而失敗的局部晚期或轉移性非小細胞肺癌患者。當特羅凱R 與吉西他濱尼(gemcitabine)併用時，特羅凱R 可作爲局部晚期、不能切除或已轉移胰腺癌的第一線用藥。根據臨床研究以及上市後藥物監測的最新資料顯示，患者在接受特羅凱R治療後會增加胃腸穿孔的風險（包括某些死亡案例）。此外，亦有患者在服用特羅凱R後，出現擬似史帝文生綜合症(Stevens Johnson Syndrome ¡ SJS)/中毒性表皮壞死(Toxic Epidermal Necrolysis - TENs)的大疱性、水疱性以及剝脫性皮膚症狀，以及出現角膜穿孔或潰瘍。如患者在服用特羅凱R 後，出現胃腸穿孔、嚴重大疱性、水疱性、脫落性皮膚症狀、急性或惡化的眼疾，如眼痛，應停用上述藥物。

The United States Food and Drug Administration (USFDA) and the Singaporean Health Science Authority (HSA) notified healthcare professionals about the latest safety update on erlotinib (Tarceva^{R}). Tarceva monotherapy is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen. In combination with gemcitabine, Tarceva is also indicated for the first-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer. According to the latest information, which comes from routine pharmacovigilance activities of clinical study and postmarketing reports, there is an increased risk of developing gastrointestinal perforations (including fatalities) in patients receiving erlotinib (TarcevaR). Additionally, there have also been occurrences of bullous, blistering and exfoliative skin conditions suggestive of Stevens-Johnson syndrome/toxic epidermal necrolysis as well as corneal perforation or ulceration in patients receiving TarcevaR. This treatment should be discontinued in patients who develop gastrointestinal perforation, severe bullous, blistering or exfoliative skin conditions or acute/worsening ocular disorders such as eye pain.

有關左氧氟沙星注射液的嚴重不良反應狀
Serious adverse drug reactions associated with levofloxacin injectable solution

資料來源：國家食品藥品監督管理局
Source ：Chinese State Food and Drug Administration (SFDA)
http://www.sfda.gov.cn/WS01/CL0051/38034.html

左氧氟沙星（levofloxacin）爲廣效的第三代喹諾酮類（fluoroquinolone）抗菌藥物，用於治療成人因 levofloxacin 感受性致病菌所引起之社區性肺炎、複雜性泌尿道感染（包括：腎盂腎炎、皮膚和軟組織感染）。在國家食品藥品監督管理局(State Food and Drug Administration-SFDA)轄下國家藥品不良反應監測中心(National Adverse Drug Monitoring Center) 的病例報告資料庫中，與左氧氟沙星注射液相關的嚴重病例報告在諾酮類品種中較爲突出，由該藥引致的嚴重不良反應/事件包括：

- 全身性損害：過敏性休克、過敏樣反應、寒戰、高熱等
- 中樞及外周神經系統損害：抽搐、癲癇大發作、意識模糊、精神異常、譫妄等
- 皮膚損害：皮疹、多形性紅斑型藥疹等
- 呼吸系統損害：呼吸困難、喉水腫、呼吸抑制等
- 其他損害：肝功能異常、腎功能異常、血尿、紫紺、白細胞減少、血小板減少、血糖異常、嘔吐、腹瀉等。

鑑於上述不良反應/事件個案可由不合理用藥而引致，因此該中心建議：

- 臨床醫生應按文獻記載的方法使用左氧氟沙星注射液，避免配伍禁忌，確需聯合使用其他抗菌藥物時應合理選擇，對喹諾酮類藥物過敏者、癲癇患者、妊娠及哺乳期婦女、18 歲以下患者禁用。腎功能不全者、老年患者、神經系統疾病患者應慎用或在嚴格監護下使用。用藥過程中醫護人員應仔細觀察測患者的症狀和體徵，一旦發現異常，應立即停藥，並儘快明確診斷，及時對症治療。
- 藥品生產、經營企業和醫療機構加強臨床合理使用抗菌藥物的教育與宣傳，充分告知醫生和患者可能潛在的風險，避免嚴重不良反應的重複發生。

Levofloxacin is a third generation broad spectrum fluoroquinolone antimicrobial and is indicated for treating infections due to levofloxacin-susceptible microorganisms in adult patients with community-acquired pneumonia, complicated urinary tract infections including pyelonephritis, skin & soft tissue infections. Reported cases obtainable from the database, administered by the Chinese State Food and Drug Administration (SFDA) National Adverse Drug Reaction Monitoring Center, indicated that there were more cases of serious adverse drug reactions associated with levofloxacin than any other fluoroquinolone of the same class. The serious adverse reactions/events manifested chiefly as follows：

- systemic damages ： anaphylactic shock, allergic reaction, chills, fever, etc.
- central & peripheral nervous damages：convulsions, grand mal epilepsy, vague sense of mental abnormalities, delirium, etc
- dermatological damages ： main rash, erythema multiforme type drug eruption
- respiratory system damages：difficulty in breathing, throat edema, respiratory depression
- other damages ： abnormal liver function, renal dysfunction, hematuria, cyanosis, leukopenia, thrombocytopenia, blood glucose abnormalities, vomiting and diarrhea.

In view of the occurrence of above adverse drug reactions/events, which were possibly caused by the irrational use of drugs, the National ADR Monitoring Center offers recommendations as listed below：

- For the clinicians：any consideration to use injectable levofloxacin onto a patient should follow the prescribing methodologies documented on the literature references. Avoid using levofloxacin in conditions listed on the contraindication section. Do not use levofloxacin in patients who have previous history of fluoroquinolone allergies, epilepsy, pregnant and nursing women, patients who are under 18 years of age. Cautioning uses and strict monitoring of patients who are renally-compromised, elderly and those inflicted with nervous system disorders. During the course of levofloxacin treatment healthcare professionals should carefully observe any sign or symptom experienced by the patient. If any abnormality is perceived, discontinue therapy immediately, initiate a swift and clear diagnosis and provide symptomatic treatment in a timely manner.
- For the manufacturers, sales and healthcare facilities：they should strengthen the rational uses of antimicrobials in clinical settings for the healthcare professionals as well as on the educational and promotional leaflets. Fully inform the prescribers and patients about possible underlying potential risks and how to avoid the repeated occurrences of adverse drug reactions.

有關麥考酚酸酯**(mycophenolate mofetil)(**商品名：**CellceptR)**安全性資訊
Latest safety update on mycophenolate mofetil, MMF (CellceptR)

資料來源： 香港羅氏有限公司通報藥物事務廳
Source： Roche Hong Kong Limited reported to Department of Pharmaceutical Affairs

香港羅氏有限公司(Roche Hong Kong Limited)通報藥物事務廳，最近出現多宗因併用 CellceptR (麥考酚酸酯，mycophenolate mofetil)及其他免疫抑制劑而產生單純紅血球再生不良（Pure Red Blood Cell Aplasia - PRCA）的個案。目前由麥考酚誘發 PRCA 的機理尚未清楚，某些個案中隨著 CellceptR 劑量的降低或停用，由該藥引致的 PRCA 是可逆轉的，但是，對於已接受移植手術的患者，

降低免疫抑制劑的劑量可能會增加由移植物所引發的風險。

Roche Hong Kong Limited reported to Department of Pharmaceutical Affairs cases of pure red cell aplasia (PRCA) in patients having been treated with CellceptR (mycophenolate mofetil) in combination with other immunosuppressive agents. The mechanism for mycophenolate mofetil-induced PRCA is unknown. In some cases, PRCA was found to be reversible with dose reduction or cessation of CellceptR therapy. In transplant patients, however, reduced immunosuppression may place the graft at risk.

有關白三烯類受體抑制劑**(leukotriene inhibitors)**安全性的資訊
Latest safety update on leukotriene inhibitors

資料來源： 美國食物及藥物管理局
中國台灣行政院衛生署
Sources ：United States Food and Drug Administration (USFDA)
Department of Health, Executive Yuan, Taiwan, China
http://www.doh.gov.tw/CHT2006/other/ShowCopy.aspx?doc_no=71713&class_no=25
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm166246.htm
http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm165489.htm

藥物事務廳接獲一宗本地不良反應通報，個案涉及一名小孩在服用 4 毫克孟魯司特 montelukast(SingulairR)口嚼錠劑後出現焦慮及發惡夢的不良反應。Montelukast 是用於治療間歇性哮喘、過敏性鼻炎及過敏性皮膚瘙癢。早前，中國台灣衛生署亦發現曾有病人疑似使用 montelukast 後導致做惡夢的不良反應，而美國食物及藥物管理局（USFDA）亦向衛生專業人士發佈一則有關白三烯類受體抑制劑(leukotriene inhibitors)包括孟魯司特 montelukast (SingulairR)、扎魯司特 zafirlukast (AccolateR)及齊留通 zileuton (ZyfloR、Zyflo CRR)安全性的資訊，當中指出某些病人在服用上述藥物後產生神經性精神方面的不良反應，包括激動不安、侵犯性行爲、焦慮、異常夢境、幻覺、抑鬱、失眠、易怒、煩躁不安、自殺傾向及行爲。

基於以上所述，建議醫生、藥劑師及其他衛生專業人士注意以下事項：

- 應警惕上述藥物可能引發潛伏性的神經性精神方面的不良反應。
- 教育病人如出現上述不良反應，應向醫生求診。
- 醫生如發覺患者出現上述神經性精神方面的不良反應 ，應考慮要求患者停藥。

Department of Pharmaceutical Affairs received 1 locally reported case on adverse drug reaction, a child was prescribed with 4mg montelukast chewable tablet (SingulairR) orally once daily. Days later, this patient developed anxiety and nightmares as the observable adverse reactions. Montelukast was started on to treat his intermittent asthmatic condition, atopic allergic rhinitis and itchy skin. In addition, the Taiwanese Department of Health, China also found that patients experienced nightmares as an adverse drug reaction subsequent to the use of montelukast. Besides, the United States Food and Drug Administration (USFDA) had also recently notified healthcare professionals about the latest safety update on leukotriene inhibitors including montelukast (SingulairR), zafirlukast (AccolateR) and zileuton (ZyfloR , Zyflo CRR). Neuropsychiatric events have been reported in some patients taking the above medications and they include cases of agitation, aggression, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behavior (including suicide).

In light of the above, we would like to inform all physicians, pharmacists and other healthcare professionals to take note about the following recommendations：

- Be aware of the potential for neuropsychiatric adverse reactions with these medications.
- Educate their patients to notify their prescribers should the neuropsychiatric reactions ever occur.
- Prescribers should inform the patients to discontinue the above medications if patients develop neuropsychiatric symptoms.

有關 **sirolimus** 安全性的最新資訊
Latest safety update on sirolimus

資料來源： 美國食物及藥物管理局
Source： United States Food and Drug Administration (USFDA)
http://www.doh.gov.tw/CHT2006/DM/DM2_p01.aspx?class_no=25&level_no=1&doc_no=71714
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm165731.htm
http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm165015.htm

美國食物及藥物管理局（USFDA）通知衛生專業人士一則有關免疫抑制劑安全性的資訊，根據惠氏藥廠(Wyeth)進行的一項名爲〝A randomized, open-label, comparative evaluation of conversion from calcineurin inhibitor treatment to sirolimus treatment versus continuation of calcineurin inhibitor treatment in liver allograft recipients undergoing maintenance therapy〞的臨床試驗，以抑制 calcineurin 爲主的免疫抑制劑(CIN-based immunosuppressants)（如 tacrolimus）控制排斥的肝臟移植病人，倘若將 CIN 類免疫抑制劑轉換成含 sirolimus 的藥物治療，可能會增加病人之死亡風險。基於此，USFDA 正匯集惠氏藥廠之臨床試驗結果及 sirolimus 上市後使用資料進行再評估，在未有進一步評估結果之前，USFDA 建議醫生依照 sirolimus 原有的治療指引使用該藥物。本廳會密切監測該藥的安全性及密切注意 USFDA 針對 sirolimus 之評估結果，並會將最新結果通知衛生專業人士。

United States Food and Drug Administration (USFDA) notified healthcare professionals about the latest safety update on immunosuppresants. According to the results of

a clinical trial conducted by Wyeth which was titled as ¡A randomized, open-label, comparative evaluation of conversion from calcineurin inhibitor treatment to sirolimus treatment versus continuation of calcineurin inhibitor treatment in liver allograft recipients undergoing maintenance therapy¡, suggested that stable liver transplant patients who had been using calcineurin (CIN-based immunosuppressants）can control the incidence of organ rejection. Nevertheless, there may be increased mortality in patients converted from calcineurin inhibitor (CNI) therapy e.g. tacrolimus to sirolimus usage. Therefore, USFDA will compile the results of this clinical trial with those data obtained from the postmarketing utilization of sirolimus in order to conduct further re-evaluation. Prior to the arrival of any conclusion and in the interim USFDA would recommend that physicians should continue to follow the prescribing information of sirolimus as a guide to therapy.

The Department of Pharmaceutical Affairs will keep a close vigilance and attention on the safety and results of the USFDA assessment on this drug. We are dedicated to inform all healthcare professionals once the latest update is being announced.

- 完 END-

有關吡羅昔康**(piroxicam)**安全性的最新資訊
Latest safety update on piroxicam

資料來源： 加拿大藥監局
Source： Health Canada
http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_102-eng.php

加拿大藥監局(Health Canada)通知衛生專業人士一則有關吡羅昔康(piroxicam)安全性的最新資訊。 最近，該局剛完成了一項有關吡羅昔康用於治療急性及短暫性痛楚風險的安全性回顧，結果顯示相對於其他非選擇性非甾體抗炎藥(NSAIDs)，由於 piroxicam 會增加引發嚴重皮膚反應及胃腸道問題的風險，因此服用該藥所得的好處不再高於其風險。基於此，該局認爲吡羅昔康不應再用於治療短暫性痛症及炎症，但對於患有慢性關節炎如骨性關節炎、類風濕關節炎及強直性脊柱炎的病人，醫生仍可處方吡羅昔康直以舒緩此類病人的慢性痛症及炎症。

Health Canada notified healthcare professionals about the latest safety update on piroxicam. The Agency had recently completed a safety review on this medication evaluating the risks associated with its use in treating acute and short-term pain. Results indicated that the use of this drug no longer outweighs the benefits relative to other non-selective NSAIDs because of an increased risk of serious skin reactions and gastrointestinal problems relative to other similar drugs. Therefore, the Agency concluded that piroxicam should no longer be used to treat short-term pain and inflammation, however, this drug can still be prescribed for the symptomatic relief of chronic pain and inflammation in patients suffering from certain types of chronic arthritis namely osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.