

季度藥訊 Quarterly Drug Newsletter

2010 No. 1

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

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).

有關秋水仙鹼(colchicine)和 P-糖蛋白或 CYP3A4 強效抑制劑相互作用的最新資訊 Updates on drug interaction between colchicine and P-glycoprotein or strong CYP3A4 inhibitors

資料來源：星加坡藥監局

Source : Health Science Authority (HSA)

http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/safety_information/product_safety_alerts/safety_alerts_2009/import_ant_drug_interactions.html

星加坡藥監局 (HSA) 通知衛生專業人士一則有關秋水仙鹼(colchicine)與 P-糖蛋白(P-glycoprotein, P-gp)或 CYP3A4 強效抑制劑相互作用的資訊。據述, 美國食物及藥物管理局 (USFDA) 過去曾接獲 169 宗與口服 colchicine 有關的死亡個案。在這些個案中, 117 宗發生在 colchicine 的標準治療劑量以內(≤ 2 毫克/天), 當中超過 60 例的病人同時服用抑制 CYP3A4 的克拉霉素(clarithromycin)。分析指出, 影響 colchicine 胃腸道吸收及/或肝代謝的藥物相互作用是產生 colchicine 中毒的主要原因。Colchicine 從胃腸道中的吸收會受外排載體 P-gp 所影響, 而 colchicine 在小腸和肝中由 P450 色素酶 CYP3A4 轉化為無活性的代謝物。Colchicine 主要通過肝膽分泌至糞便中排除, 在腎功能正常的病人中腎排泄只佔 10%~20%的排除量。現有併用 Colchicine 和其他 P-gp 或 CYP3A4 抑制劑而出現致命或非致命的個案, 足以支持改變 P-gp 或 CYP3A4 活性的藥物會造成 colchicine 中毒的論點, 這些藥物包括環孢素(cyclosporin)、紅霉素(erythromycin)以及鈣通道阻斷劑(calcium channel blockers), 如維拉帕米(verapamil)和地爾硫草(diltiazem), 其他 P-gp 或 CYP3A4 強效抑制劑包括泰利霉素(telithromycin)、酮康唑(ketoconazole)、伊曲康唑(itraconazole)、HIV 蛋白酶抑制劑以及奈非西坦(nefazodone)。

基於以上事實, USFDA 總結認為, 同時服用 colchicine 以及 P-gp 或 CYP3A4 強效抑制劑具有嚴重藥物相互作用的風險, 並作出下列建議:

- P-gp 或 CYP3A4 強效抑制劑不可用於正在服用 colchicine 兼有肝腎功能損傷的病人。
- 對於需要使用 P-gp 或 CYP3A4 強效抑制劑但肝腎功能正常的病人, 醫生應考慮降低 colchicine 的劑量或暫停 colchicine 的治療。

The Singaporean Health Sciences Authority (HSA) notified healthcare professionals about the drug interaction between colchicine and P-glycoprotein (P-gp) or strong CYP3A4 inhibitors. Latest data from the United States Food and Drug Administration (USFDA) indicated that there have been 169 deaths associated with the use of oral colchicines. Of these, 117 cases occurred within the standard therapeutic doses of colchicine (≤ 2 mg/day) and 60 out of these 117 cases patients also had concomitant clarithromycin, a CYP3A4 inhibitor. Analysis findings suggested that drug interactions affecting gastrointestinal absorption and/or hepatic metabolism of colchicine play a central role in the development of colchicine toxicity. The absorption of colchicine from the gastrointestinal tract is affected by the efflux transporter P-glycoprotein (P-gp), while the metabolism of colchicine to inactive metabolites is catalyzed by intestinal and hepatic cytochrome P450

CYP3A4. Colchicine is primarily eliminated by hepatobiliary excretion through the stool. Renal excretion accounts for 10% to 20% of colchicine elimination in patients with normal renal function. The theoretical risk of colchicine toxicity through the modulation of P-gp and CYP3A4 activity is further supported by the presence of fatal and non-fatal cases of colchicine toxicity reported in literature with concomitant use of other CYP3A4 and P-gp inhibitors such as cyclosporin, erythromycin and calcium channel blockers e.g. verapamil and diltiazem. Other examples of P-gp and strong CYP3A4 inhibitors include telithromycin, ketoconazole, itraconazole, HIV protease inhibitors, and nefazodone.

In view light of the above, USFDA concluded that there is a risk for severe drug interactions in certain patients treated with colchicine and concomitant P-gp or strong CYP3A4 inhibitors. Hence, she offered the following advice:

- Avoid the use of P-gp or strong CYP3A4 inhibitors in patients with renal or hepatic impairment who are currently taking colchicine.
- Prescribing physician should consider a dose reduction or interruption of colchicine in patients with normal renal and hepatic function if treatment with a P-gp or strong CYP3A4 inhibitor is required.

有關硼替佐米(bortezomib, Velcade®)安全性的最新資訊

Latest safety update for bortezomib (Velcade®)

資料來源：美國食物及藥物管理局

Source : United States Food and Drug Administration (USFDA)

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm198424.htm>

<http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM198426.pdf>

美國食物及藥物管理局 (USFDA) 通知衛生專業人士一則有關硼替佐米(bortezomib, Velcade®)注射液的最新資訊。Bortezomib 用於治療患上多發性骨髓瘤(multiple myeloma)的病人, 亦用於已接受一種藥物治療的套細胞淋巴瘤(mantle cell lymphoma)的病人。根據一項隨機及開放式的臨床研究, 得出以下關於 bortezomib 的最新資訊:

- 在還未接受過治療的多發性骨髓瘤病人中, bortezomib 能顯著提高病人的生存率。
- 對於輕度肝功能損傷的病人, 不需調整起始劑量。
- 因為 bortezomib 經肝臟代謝, 肝功能損傷會增加藥物在體內的濃度, 對於中、重度肝功能損傷的病人需使用較低的起始劑量, 在第一階段的治療中, 初始劑量應為每劑 0.7 毫克/平方米身體表面積, 其後每劑增至 1.0 毫克/平方米身體表面積, 或根據病人的耐受情況減至 0.5 毫克/平方米身體表面積。此外, 應密切監察病人發生不良反應的情況。
- 由於 bortezomib 能引起血小板減少和中性粒細胞減少, 因此應經常監測全血細胞數。

The United States Food and Drug Administration (USFDA) notified healthcare professionals about the latest updates on bortezomib (Velcade®) for injections. Bortezomib is indicated for the treatments of patients with multiple myeloma and, also, those patients with mantle cell

lymphoma who have received at least one prior therapy. According to a randomized, open-label clinical study, the new updates include :

- The overall survival in patients with previously untreated multiple myeloma showed a statistically significant survival benefit for the bortezomib.
- Do not require a starting dose adjustment for patients with mild hepatic impairment.
- Use a lower starting dose for patients with moderate to severe hepatic impairment since bortezomib is metabolized by liver enzymes and hepatic impairment will have an increased exposure of this drug. The initial dose should be 0.7 mg/m² per injection during the first cycle, and a subsequent dose escalation to 1.0 mg/m² or further dose reduction to 0.5 mg/m² may be considered based on the patient tolerance. Besides, close monitoring on these patients for toxicities should also be warranted.
- Bortezomib is associated with thrombocytopenia and neutropenia, thus complete blood counts should be monitored frequently.

有關去羥肌苷(didanosine, Videx[®]/Videx EC[®])安全性的最新資訊 Latest safety updates on didanosine(Videx[®]/Videx EC[®])

資料來源：美國食物及藥物管理局

Sources : United States Food and Drug Administration (USFDA)
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm199343.htm>
<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm199169.htm>

美國食物及藥物管理局 (USFDA) 通知衛生專業人士關於去羥肌苷(didanosine(DDI), Videx[®]/VidexEC[®])安全性的最新資訊, 簡述如下:

經分析 42 宗關於服用 didanosine 的病人發生罕見但嚴重的非肝硬化門靜脈高壓症的通報個案後, USFDA 總結出使用 didanosine 與發生此症狀存在因果關係。由於非肝硬化門靜脈高壓症具有造成食管靜脈曲張出血等可能導致死亡的潛在風險, USFDA 決定修改 didanosine 說明書中的警告及注意事項部分, 以確保使用該藥的安全性。然而, USFDA 認為在受 HIV 感染的某些病人中, didanosine 的臨床效益依然大於潛在的風險, 因此, 必須根據醫生和病人的個別情況而決定是否使用該藥。此外, USFDA 對衛生專業人士作出下列建議:

- 須留意使用 didanosine 有可能發生非肝硬化門靜脈高壓症。
- 與病人討論使用 didanosine 的臨床效益及潛在風險, 包括非肝硬化門靜脈高壓症。
- 持續監測病人發生門脈高壓及食管靜脈曲張的情況。
- 注意 didanosine 已有乳酸性酸中毒及脂肪性肝腫大的特別警告。
- Didanosine 與其他抗逆轉錄病毒藥物及羥基脲(hydroxyurea)或利巴韋林(ribavirin)併用時可能增加肝毒性。

The United States Food and Drug Administration (USFDA) notified healthcare professionals about the latest update on didanosine(DDI)(Videx[®]/VidexEC[®]). Summaries are listed as follows:

Upon analysis of the 42 post-marketing reports concerning patients, who were on didanosine, developed a rare, but serious, liver complication known as non-cirrhotic portal hypertension, USFDA concluded a causal association between the use of didanosine and development of this liver condition. As the potential severity of this non-cirrhotic portal hypertension including death from hemorrhaging esophageal varices, the Agency decided to revise the Warning and Precautions section of the didanosine drug label to assure safe use of this medication. However, USFDA believes the clinical benefits of didanosine for certain patients with HIV continue to outweigh its potential risks, hence, the decision to use this drug must be made on an individual basis between the prescribing physician and the patient. Besides, the USFDA also offered the following additional reminders for healthcare professionals:

- Be aware that didanosine use has been associated with the development of non-cirrhotic portal hypertension.
- Discuss with patients the clinical benefits and potential risks, including the risk of non-cirrhotic portal hypertension, with the use of didanosine.
- Continue to monitor patients for the development of portal hypertension and esophageal varices.
- Be aware that didanosine already has a Boxed Warning for lactic acidosis and hepatomegaly with steatosis.
- Didanosine in combination with other antiretroviral agents as well as hydroxyurea or ribavirin has been associated with the development of liver toxicity.

有關奧氮平(olanzapine, Zyprexa[®])安全性的最新資訊 Latest safety update on olanzapine (Zyprexa[®])

資料來源：美國食物及藥物管理局

Sources : United States Food and Drug Administration (USFDA)
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm198402.htm>
<http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM198412.pdf>

美國食物及藥物管理局 (USFDA) 通知衛生專業人士關於奧氮平(olanzapine, Zyprexa[®])安全性的最新資訊, 簡述如下:

- Olanzapine 可用於 13 至 17 歲青少年的精神分裂症和第一類雙極症(躁狂或混合發作)。醫生在決定治療方案前應注意, 相對於成人, olanzapine 在青少年中更易引起高血糖、高血脂、體重增加、高泌乳素血症、與鎮靜有關的不良反應、肝轉氨酶升高以及其他潛在的長期毒性。在多數情況下, 醫生應優先考慮對青少年病人處方其他藥物。
- 當 olanzapine 用於兒科病人時, 需要全面的治療方案。Olanzapine 只是治療兒科病人精神分裂症和雙極症的其中一個療程, 對於這類疾病還需要配合心理方面、教育方面以及社會方面的措施, 但是

olanzapine 對小於 13 歲的兒童病人中的有效性和安全性尚未確立。

The United States Food and Drug Administration (USFDA) notified healthcare professionals about the latest update on olanzapine(Zyprexa[®]) medications. Summaries are listed as follows:

- Olanzapine is indicated for use for schizophrenia and bipolar I disorder (manic or mixed episodes) in adolescents ages 13 – 17. Before the physicians decide among the alternative treatments, the clinician should note that olanzapine has an increased potential for causing hyperglycemia, hyperlipidemia, weight gain, hyperprolactinemia, increased frequencies of sedation-related adverse events, increased hepatic transaminase levels and other potential long-term risks when this medication is prescribed to the adolescents as compared to their adult counterparts. In many cases this may lead them to consider prescribing other drugs first in adolescents.
- There is a need for comprehensive Treatment Program in Pediatric Patients when olanzapine is being used in this population. Olanzapine is indicated as an integral part of a total treatment program for pediatric patients with schizophrenia and bipolar disorder that may include other measures (psychological, educational, social) for patients with the disorders. Effectiveness and safety of olanzapine have not been established in pediatric patients less than 13 years of age.

有關長效 β 受體激動劑(Long-Acting Beta Agonists, LABAs)安全性的最新資訊 Latest safety update on Long-Acting Beta Agonists(LABAs)

資料來源：美國食物及藥物管理局

Source : United States Food and Drug Administration (USFDA)

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm201003.htm>

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm200776.htm>

美國食物及藥物管理局 (USFDA) 通知衛生專業人士關於長效 β 受體激動劑(Long-Acting Beta Agonists, LABAs)安全性的最新資訊。USFDA 在分析臨床研究的結果後，認為 LABAs 可能會增加哮喘病人病情惡化的風險、導致住院甚至死亡，基於安全方面的考慮，USFDA 更新使用該類藥物的指引。

為確保安全使用此類藥物，衛生專業人士應注意以下事項：

- 含單一成份的 LABAs 只可與其他控制哮喘的藥物併用，不能單獨使用。
- 只有服用治療哮喘的藥物後仍不能有效控制症狀的病人才可長期使用 LABAs。
- 儘可能以最短的 LABAs 使用時間來控制哮喘的症狀，當哮喘受到控制後，應停用 LABAs。而病人應繼續使用原來的藥物控制病情。
- 對於有使用類固醇吸入劑的兒童和青少年病人，如需要增加一種 LABA，應使用含有一種類固醇及

一種 LABA 的複方製劑，以增加病人服藥的順從性。

USFDA 認為，對於需要加入 LABA 來控制哮喘病情的病人，適當地使用 LABAs 對改善哮喘症狀的效益將大於其潛在風險。

United States Food and Drug Administration(USFDA) notified healthcare professionals about the latest safety update on Long-Acting Beta Agonists(LABAs) Due to safety concerns, FDA is class-labeling changes for all LABAs. These changes are based on FDA's analyses of studies showing an increased risk of severe exacerbation of asthma symptoms, leading to hospitalizations in patients as well as death in some patients using LABAs for the treatment of asthma.

Healthcare professionals are reminded that to ensure the safe use of these products:

- Single-ingredient LABAs should only be used in combination with an asthma controller medication; they should not be used alone.
- LABAs should only be used long-term in patients whose asthma cannot be adequately controlled on asthma controller medications.
- LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved. Patients should then be maintained on an asthma controller medication.
- Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure compliance with both medications.

USFDA has determined that the benefits of LABAs in improving asthma symptoms outweigh the potential risks when used appropriately with an asthma controller medication in patients who need the addition of LABAs.

有關 deferasirox (商品名：Exjade[®])安全性的最新資訊

Latest safety updates on deferasirox (Exjade[®])

資料來源：美國食物及藥物管理局

Source : United States Food and Drug Administration (USFDA)

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm200850.htm>

<http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM200858.pdf>

美國諾華公司(Novartis)與USFDA發出的通告指 Exjade[®]有可能引起腎功能損傷(包括腎衰竭)、肝功能損傷(包括肝衰竭)以及胃腸道出血等不良反應。上述不良反應於年長患者、骨髓異常增生綜合症(myelodysplastic syndrome, MDS)的高危病患、潛在的腎臟、肝臟損傷患者以及血小板過低的人士中更易發生，且有可能是致命的。因此，美國諾華公司(Novartis)和USFDA決定在此藥物的說明書中加入以下的禁忌症資訊：

- 肌酐清除率小於40 mL/min或血清肌酐大於兩倍與年齡相應的正常值上限。

- 骨髓異常增生綜合症病情危急或惡化，以及晚期惡性腫瘤。
 - 血小板數少於 $50 \times 10^9/L$ 。
 - 已知對deferasirox或Exjade®中任一成份過敏者。
- 此外，需對使用Exjade®的病人進行密切監測，包括以下措施：
- 於開始治療前檢測血清肌酐和/或肌酐清除率，然後每月檢測一次；對於具有潛在腎功能損傷或危險因子的病人，首月每星期檢測一次肌酐和/或肌酐清除率，然後每月檢測一次。
 - 於開始治療前檢測血清轉氨酶和膽紅素，首月每兩個星期檢測一次，然後每月檢測一次。

Novartis Oncology and USFDA notified that the product may cause renal impairment(including failure), hepatic impairment(including failure) and gastrointestinal hemorrhage. These reactions were more frequently observed in patients with advanced age, high risk myelodysplastic syndromes, underlying renal or hepatic impairment or low platelet counts, and they could be fatal. Therefore Novartis and USFDA have decided to add the followings on contraindications:

- Creatinine clearance <40 mL/min or serum creatinine >2 times the age-appropriate upper limit of normal.
- Poor performance status and high-risk myelodysplastic syndromes or advanced malignancies.
- Platelet counts $<50 \times 10^9/L$.
- Known hypersensitivity to deferasirox or to any other component of Exjade®.

In addition, Exjade® therapy requires close patient monitoring, including measurement of:

- serum creatinine and/or creatinine clearance prior to initiation of therapy and monthly thereafter; in patients with underlying renal impairment or risk factors for renal impairment, monitor creatinine and/or creatinine clearance weekly for the first month, then monthly thereafter.any risk associated with Byetta.
- serum transaminases and bilirubin prior to initiation of therapy, every two weeks during the first month and monthly thereafter.

有關異維 A 酸(isotretinoin)安全性的最新資訊 Latest safety updates on isotretinoin

資料來源：加拿大衛生部

Sources : Health Canada

http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/advisories-avi/s/prof/2010/accutane_2_hpc-cps-eng.pdf

加拿大衛生部向衛生專業人士發出關於 isotretinoin 安全性的最新資訊，簡述如下：

- 上市後通報的個案中，發現十分罕見的嚴重皮膚反應，如多形性紅斑(erythema multiforme, EM)、史提芬-強生綜合症(Stevens-Johnson syndrome, SJS)及毒性表皮溶解症(toxic epidermal necrolysis, TEN)，與服用 isotretinoin 存在關聯性。
- 上述不良反應可能很嚴重，並足以導致住院、殘疾

或死亡。

- 應密切監測病人發生的不良反應，一旦出現嚴重皮膚反應，應考慮停藥。

Health Canada informed prescribers of important new safety information regarding the use of isotretinoin:

- There have been very rare post-marketing reports of severe skin reactions (e.g. erythema multiforme [EM], Stevens-Johnson syndrome [SJS], and toxic epidermal necrolysis [TEN]) associated with isotretinoin use.
- These events may be serious and result in hospitalization, disability or death.
- Patients should be monitored closely for severe skin reactions and discontinuation of isotretinoin should be considered if warranted.

有關沙奎那韋(saquinavir)安全性的最新資訊 Latest safety update on saquinavir

資料來源：美國食物及藥物管理局

Sources : United States Food and Drug Administration (USFDA)

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm201221.htm>

美國食物及藥物管理局 (USFDA) 正回顧關於併用沙奎那韋(saquinavir)和利托那韋(ritonavir)對心臟可能產生嚴重不良反應的臨床試驗，資料顯示併用兩藥可能會引起 QT 或 PR 間期延長。QT 間期延長會增加出現心律失常的風險，甚至導致 torsades de pointes, PR 間期延長可能會造成心臟傳導阻滯，因此，請衛生專業人士：

- 密切留意併用 saquinavir 與 ritonavir 的病人是否出現有關的不良反應。
- 對於有 QT 間期延長病史、罹患心臟傳導系統疾病、缺血性心臟病、心肌病或潛在的結構性心臟病的病人，不要使用 saquinavir。
- 對於正在服用可能延長 QT 或 PR 間期的藥物，包括服用第 IA 類(如奎尼丁(quinidine))或第 III 類(如胺碘酮(amiodarone))抗心律失常藥物的病人，不要併用 saquinavir。

The U.S. Food and Drug Administration (USFDA) is reviewing clinical trial data about a potentially serious effect on the heart from the use of saquinavir in combination with ritonavir. The data suggest that together the two drugs may affect the electrical activity of the heart, causing prolonged QT or PR intervals. A prolonged QT interval can increase the risk for abnormal heart rhythms, including a serious abnormal rhythm called torsades de pointes. A prolonged PR interval can cause heart block. Therefore, healthcare professionals are recommended:

- Closely monitor if any adverse drug reaction occurs in patients using saquinavir with ritonavir.
- Not use saquinavir in patients with a history of QT interval prolongation, preexisting conduction system disease, ischemic heart disease, cardiomyopathy, or underlying structural heart disease.
- Not use saquinavir in patients who are currently using Class IA (such as quinidine) or Class III (such as amiodarone) antiarrhythmic drugs or other drugs that

may prolong the QT or PR interval.

有關 WinRho[®] SDF(Rh₀(D))人類免疫球蛋白注射劑安全性的最新資訊

Latest safety update on WinRho[®] SDF(Rh₀(D)) Immune Globulin Intravenous (Human)

資料來源：美國食物及藥物管理局

Sources : United States Food and Drug Administration (USFDA)

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm203739.htm>

<http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM198725.pdf>

Cangene Corporation 與美國食物及藥物管理局 (USFDA) 通知衛生專業人士，過去有數宗關於免疫性血小板減少性紫癍 (immune thrombocytopenic purpura, ITP) 的病人在使用 WinRho[®] SDF(Rh₀(D)) 人類免疫球蛋白注射劑後出現血管內溶血 (intravascular hemolysis, IVH) 及併發症的報告，當中包括致死個案。IVH 可引致貧血和多器官衰竭，包括急性呼吸窘迫綜合症。其他曾報告的嚴重不良反應包括嚴重貧血、急性腎功能不全、腎衰竭以及彌漫血管內凝血。在出現 IVH 的病人中，致命個案多發生於併有其他疾病的年長病人 (大於 65 歲)。因此，Cangene Corporation 與 USFDA 對衛生專業人士作出下述建議：

- 病人於注射上述藥物後，需於具有相應設備的醫療機構內密切監視最少 8 小時。
- 在注射後 2 小時、4 小時以及監視期結束前，需使用尿液試紙進行分析。
- 應提醒病人注意 IVH 的症狀，包括背痛、寒戰、尿液變色或血尿。即使於 8 小時內沒有出現這些症狀，也不表示隨後並不會發生 IVH。
- 如果於注射 WinRho[®] SDF 後出現了 IVH 的症狀，或者懷疑出現相關症狀，便需要進行實驗室檢驗，包括血漿血紅蛋白、尿液分析、結合珠蛋白、乳酸脫氫酶 (LDH) 以及血漿膽紅素。

Cangene Corporation and United States Food and Drug Administration (USFDA) notified healthcare professionals that cases of intravascular hemolysis (IVH) and its complications, including fatalities, have been reported in patients treated for immune thrombocytopenic purpura (ITP) with WinRho[®] SDF(Rh₀(D)) Immune Globulin Intravenous (Human)). IVH can lead to anemia and multi-system organ failure including acute respiratory distress syndrome. Serious complications including severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation have also been reported. Fatal outcomes associated with IVH and its complications have occurred most frequently in patients of advanced age (age over 65) with co-morbid conditions. Therefore, Cangene Corporation and USFDA informed healthcare professionals that:

- Patients should be closely monitored in a health care setting for at least eight hours after administration.
- A dipstick urinalysis should be performed at baseline, 2 hours, 4 hours after administration and prior to the end of the monitoring period.

- Patients should be alerted to and monitor for signs and symptoms of IVH, including back pain, shaking chills, fever, and discolored urine or hematuria. Absence of these signs and/or symptoms of IVH within eight hours do not indicate IVH cannot occur subsequently.
- If signs and/or symptoms of IVH are present or if IVH is suspected after WinRho[®] administration, post-treatment laboratory tests should be performed including plasma hemoglobin, urinalysis, haptoglobin, LDH and plasma bilirubin.

- 完 END-