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CellCept® (mycophenolate mofetil): teratogenic risk- important new pregnancy prevention advice for women and men

山喜多 (mycophenolate mofetil): 致畸胎風險 - 對男性與女性重要的新的避孕建議

Dear Healthcare professional,

親愛的醫療專業人員您好，

Roche Products Ltd. would like to inform you about strengthened advice for pregnancy prevention when using CellCept

羅氏藉此通知您有關在使用 CellCept 時應避孕的加強建議

Summary of the safety concern

安全性考量概述

Mycophenolate is a powerful human teratogen, which increases the risk of spontaneous abortions and congenital malformations following exposure during pregnancy. Therefore the following new contraindications have been added to the use of CellCept:

由於 Mycophenolate 是一種強效人類致畸胎原，懷孕期間暴露將會增加流產以及先天性畸形的風險。因此已將下列新的禁忌事項加入 CellCept 的使用中。

CellCept is **contraindicated**:

CellCept 禁止使用於：

- during pregnancy due to its mutagenic and teratogenic potential
懷孕期間，由於其誘發突變和致畸胎的可能性。
- in women of childbearing potential not using highly effective contraceptive methods
具有生育能力且未使用高度有效避孕方法的女性。
- in women who are breastfeeding
哺乳女性。

Physicians should ensure that women and men taking CellCept understand the risk of harm to the baby, the need for effective contraception, and the need to immediately consult a physician if there is a possibility of pregnancy.

醫師應確保使用 CellCept 的女性與男性病患充分了解對嬰兒可能造成的傷害、需要使用有效的避孕方式、以及如果可能懷孕時需要立即諮詢醫師。

Further advice on pregnancy testing

驗孕的進一步建議

Before starting therapy with CellCept, women of childbearing potential must have two negative serum or urine pregnancy tests with a sensitivity of at least 25 mIU/mL; the second test should be performed 8-10 days after the first one and immediately before starting CellCept. Repeat pregnancy tests should be performed during routine follow-up visits. Results of all pregnancy tests should be discussed with the patient. Patients should be instructed to consult their physician immediately should pregnancy occur.

在開始接受 CellCept 治療之前，具有生育能力的女性病患，必須在兩次使用靈敏度至少 25 mIU/mL 的血清或尿液懷孕檢測中得到陰性結果；進行第二次檢測的時間，應在第一次的 8-10 天後，且在即將開始使用 CellCept 之前。在例行追蹤回診時，應重複進行懷孕檢測。應與病患討論所有的懷孕檢測結果。應指示病患如果有懷孕情形需立即向醫師諮詢。

Contraception advice for women and men

對於女性及男性的避孕建議

Women of child bearing potential should use two reliable forms of contraception simultaneously, including at least one highly effective method, before beginning CellCept therapy, during therapy, and for six weeks following discontinuation of therapy, unless abstinence is the chosen method of contraception.

在開始 CellCept 的治療之前、在治療期間以及在停止治療後的 6 週內，除非所選擇的避孕方法為禁慾，否則具有生育能力的女性應同時使用兩種可靠的避孕方法，且其中至少包含一項高度有效的方法。

Sexually active men are recommended to use condoms during treatment and for at least 90 days after cessation of treatment. Condom use applies for both reproductively competent and vasectomized men, because the risks associated with the transfer of seminal fluid also apply to men who have had a vasectomy.

在治療期間以及在停止治療後至少 90 天內，有性行為的男性建議使用保險套。使用保險套的建議適用於具有生育能力的男性以及接受過輸精管切除術的男性，因為接受過輸精管切除術的男性同樣會有傳遞精液的風險。

In addition, female partners of male patients are recommended to use highly effective contraception during treatment and for a total of 90 days after the last dose of CellCept.

此外，在治療期間以及在最後一劑 CellCept 後總計 90 天內，建議男性病患的女性伴侶應使用高度有效避孕方法。

Further background information to this safety update

此項安全性資訊更新的進一步背景說明

The above recommendations are made following a cumulative review of birth defects which confirmed mycophenolate as a powerful human teratogen and showed evidence of an increased rate of congenital malformations and spontaneous abortions associated with mycophenolate in comparison with other medicines. Based on literature evidence:

上述是基於一項針對出生缺陷的累積案例評估後所做出的建議。該評估確認 mycophenolate 是一種強效人類致畸胎原，且證據顯示相較於其他藥品，發生與 mycophenolate 相關的先天性畸形及流產的比例增加。基於下列文獻證據：

- Spontaneous abortions have been reported in 45 to 49% of patients exposed to mycophenolate mofetil during pregnancy, compared to a reported rate between 12 and 33% in solid organ transplant patients treated with other immunosuppressants.
- 曾有報導指出，暴露於 mycophenolate mofetil 後，發生自然流產的風險為 45 至 49%，相較於接受其他免疫抑制劑治療的臟器器官移植病患，據報告此比率約為 12 至 33%
- Malformations occurred in 23-27% of live births in women exposed to mycophenolate mofetil during pregnancy, compared to 2 to 3 % of live births in the overall population and approximately 4 to 5% in solid organ transplant patients treated with immunosuppressants other than mycophenolate mofetil.
- 女性懷孕期暴露於 mycophenolate mofetil 而導致的活產兒童畸形為 23 至 27%，相較於整體人口的活產畸形約為 2 至 3 %，而接受非 mycophenolate mofetil 的免疫抑制劑治療的臟器器官移植病患則約為 4 至 5 %。

The following malformations were most frequently reported:

最常通報的畸形如下：

- Facial malformations such as cleft lip, cleft palate, micrognathia and hypertelorism of the orbits;

- 臉部畸形，如唇裂、齶裂、小顎症以及眼距過寬；
- Abnormalities of the ear (e.g. abnormally formed or absent external/middle ear) and eye (e.g. coloboma, microphthalmos);
- 耳部異常(如外/中耳形態異常或缺失)和眼睛異常(如眼器官裂開、小眼症)；
- Malformations of the fingers (e.g. polydactyly, syndactyly, brachydactyly);
- 手指畸形(如多指、併指、短指)；
- Cardiac abnormalities such as atrial and ventricular septal defects;
- 心臟異常，如心房和心室中膈缺陷；
- Oesophageal malformations (e.g. oesophageal atresia);
- 食道畸形(如食道閉鎖)；
- Nervous system malformations (such as spina bifida).
- 神經系統畸形(如脊柱裂)。

Roche is working closely with health authorities to update the product information. Once approved by the health authorities, the revised CellCept product information will be available on <http://www.roche.com.tw>.

羅氏與衛生主管機關正密切合作於更新產品仿單訊息。一旦衛生主管機關核准後，更新的山喜多產品仿單資訊將可於羅氏官網 <http://www.roche.com.tw> 獲得。

Call for reporting

通報專線

Healthcare professionals should report any case of exposure to mycophenolate during pregnancy (regardless of the outcome) according to national reporting requirements, in addition to any adverse events suspected to be associated with the use of CellCept.

醫藥專業人員除了應通報任何疑似與使用 CellCept 相關的不良反應外，在得知任何於懷孕期間暴露於 mycophenolate 之案例 (不論結果為何)，亦應依國家通報相關規定進行通報。

Taiwan National Adverse Drug Reaction Reporting System

全國藥物不良反應通報系統

Postal address: 10F, 22, Aiguo E. Rd., Zhongzheng Dist., Taipei City, Taiwan.

地址：台北市中正區愛國東路 22 號 10 樓
Phone: 02-23960100 Fax: 02-23584100
E-mail: adr@tdrf.org.tw
Website: <http://adr.fda.gov.tw/>

Company contact point

公司聯絡人

Should you have any questions or require additional information regarding the use of CellCept please feel free to contact

若您有關於使用 CellCept 上的任何問題，或需要進一步的資訊，敬請聯絡

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Yours sincerely,



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