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DEPARTMENT OF HEALTH
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382 Nam Cheong Street, Kowloon, Hong Kong

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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

Mycophenolate: EMA recommends additional measures to prevent use in pregnancy

Your attention is drawn to the European Medicines Agency's (EMA) announcement regarding additional measures to prevent use of mycophenolate in pregnancy.

Mycophenolate (mycophenolate mofetil or mycophenolic acid) is an immunosuppressant. It is approved for use with other medicines to prevent rejection of the transplanted organ in patients given a kidney, heart or liver transplant. In the EU, mycophenolate mofetil has been authorised centrally as CellCept and other names since 1996.

Although the product information for these medicines already contains warnings against use in pregnancy, these will now be significantly strengthened in the EU by the addition of new contraindications, advice and information. Updated product information will emphasise that women and men using the medicine should use effective contraception and that pregnancy tests should be used before and during treatment as needed to rule out unintended pregnancy. In addition, doctors should properly explain the risks to patients and their partners, and educational material will be produced for patients and healthcare professionals to assist with this.

EMA's recommendations are based on the assessment of updated evidence on the teratogenic risks.

- A cumulative review found that around 45 to 49% of pregnancies in women exposed to mycophenolate resulted in spontaneous abortion, compared with reported frequencies of 12 to 33% in solid organ transplant patients treated with other immunosuppressants.
- The reported incidence of malformation in the offspring of mothers exposed to mycophenolate during pregnancy is 23 to 27% compared with 4 to 5% in transplant patients treated with other immunosuppressants, and 2 to 3% in the overall population. Malformations associated with mycophenolate have included abnormalities of the ear, eye and face, congenital heart disease including septal defects, polydactyly or syndactyly, tracheo-oesophageal malformations such as oesophageal atresia, effects on the nervous system such as spina bifida, and renal abnormalities.

Healthcare professionals are advised of the following:

- Mycophenolate is a confirmed teratogen associated with an increased rate of spontaneous abortion and congenital malformation compared with other immunosuppressants.
- It must not be used during pregnancy unless there is no suitable alternative to prevent transplant rejection. Pregnancy should be ruled out by use of a sensitive serum or urine test; one test 8 to 10 days before starting mycophenolate and another immediately before starting the medicine is recommended.
- Mycophenolate should not be used in women of childbearing potential unless they are using highly effective contraception. Women should use two reliable methods of contraception simultaneously before starting and during therapy, and for 6 weeks after stopping treatment.

- Sexually active (including vasectomised) men taking mycophenolate are recommended to use condoms for sex during treatment and for 90 days thereafter; partners of childbearing potential are also recommended to use highly effective contraception for the same period.
- Patients should be advised not to donate blood during or for 6 weeks after stopping treatment, and men should not donate sperm during therapy or for 90 days after stopping.
- Patients should be counselled to make sure they understand the risks and the measures required to minimise them. They should be advised not to stop mycophenolate without speaking to a healthcare professional, and to consult immediately if they believe they may have become pregnant.

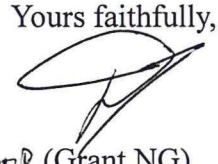
Please refer to the EMA's website for details:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/10/news_detail_002418.jsp&mid=WC0b01ac058004d5c1

In Hong Kong, there are 17 registered pharmaceutical products containing mycophenolate mofetil or mycophenolic acid. All products are prescription-only medicines. So far, the Department of Health (DH) has received three cases of adverse drug reaction on the drug, and one of them was related to missed abortion after taking the drug. In view of the EMA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,



p.p. (Grant NG)
for Assistant Director (Drug)