01-March-2016

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

Dear Healthcare professional,

Hoffmann-La Roche Ltd. (hereafter referred to as Roche) in agreement with Saudi Food and Drug Authority would like to inform you about strengthened advice for pregnancy prevention when using **CellCept®**

Summary of the safety concern

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®**:

CellCept®is contraindicated:

- during pregnancy due to its mutagenic and teratogenic potential
- in women of childbearing potential not using highly effective contraceptive methods
- in women who are breastfeeding

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.***Further advice on pregnancy testing***

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.

Contraception advice for women and men

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.

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.

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®**.

Further background information to this safety update

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:

- 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.

- 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.

The following malformations were most frequently reported:

- Facial malformations such as cleft lip, cleft palate, micrognathia and hypertelorism of the orbits;
- Abnormalities of the ear (e.g. abnormally formed or absent external/middle ear) and eye (e.g. coloboma, microphthalmos);
- Malformations of the fingers (e.g. polydactyly, syndactyly, brachydactyly);
- Cardiac abnormalities such as atrial and ventricular septal defects;

- Oesophageal malformations (e.g. oesophageal atresia);
- Nervous system malformations (such as spina bifida).

NB:

CellCept® (mycophenolate mofetil) guide for patients Information about risks to the unborn baby will be distributed.

Call for reporting

As a reminder, there is a need to report any suspected adverse reactions to the National Pharmacovigilance and Drug Safety Center (NPC):

By email: npc.drug@sfda.gov.sa
Or by fax: +966 11 2057662
Or by online: https://ade.sfda.gov.sa/

Local Safety Responsible

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Yours sincerely,

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H. Dajani 22-Feb-2016	pp 22-2-2016	On his behalf: 23/2/2016