



12th November 2007

Congenital malformations observed following use of CellCept in pregnancy

Dear Health Care Professional.

Roche Products Limited wish to inform you of new safety information regarding CellCept.

Based on a review of the US National Transplantation Pregnancy Registry and a cumulative review of pregnancy outcomes from the company safety database, section 4.6 (Pregnancy and Lactation) of the Summary of Product Characteristics (SmPC) for CellCept has been updated. The section now includes the information that congenital malformations (including ear malformations, i.e. abnormally formed or absent external/middle ear) were reported in children of patients exposed to CellCept, in combination with other immunosuppressants, during pregnancy.

Post-marketing data from the US National Transplantation Pregnancy Registry (NTPR)¹ and Roche worldwide adverse event reporting system, found an increased risk of congenital malformations, including ear malformations (i.e. abnormally formed or absent external/middle ear) in children of patients treated with CellCept during pregnancy.

Since the first market approval of CellCept in 1995, 43 reports of pregnancies with live-born infants following CellCept maternal exposure have been reported to Roche. In ten reports, the outcomes of these pregnancies included structural malformations. As these numbers are subject to the usual limitations of spontaneous reporting, they should be treated with caution. However the company considers it appropriate to include wording concerning this observation in the Pregnancy section of the SmPC.

Healthcare professionals are reminded of the special precautions regarding the use of CellCept in pregnancy:

- The use of CellCept is not recommended during pregnancy unless the potential benefit outweighs the potential risk to the foetus and should therefore be reserved for cases where no more suitable alternative treatment is available;
- As CellCept may cause foetal harm when administered to a pregnant woman, female patients of childbearing potential must use effective contraception. Physicians should counsel female patients about contraceptive use and inform female patients that congenital malformations have been reported during CellCept use in pregnancy. Effective contraception must be used before initiating

CellCept therapy, during therapy, and for six weeks following discontinuation of therapy.

- It is recommended that CellCept therapy should not be initiated until a negative pregnancy test has been obtained. Patients should be instructed to consult their physician immediately should pregnancy occur.

Roche will continue to monitor the safety of CellCept through established reporting mechanisms and notify regulatory authorities of any serious adverse events. You can assist us in monitoring the safety of CellCept by reporting adverse reactions and pregnancies to us. Please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates and for pregnancy cases, details about the contraception method used.

You can assist us in monitoring the safety of CellCept by reporting adverse reactions to Roche UK Drug Safety Centre on 01707 367554.

CellCept® (mycophenolate mofetil), which has been on the market for over 10 years, is an immunosuppressive agent indicated in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in adults receiving allogeneic renal, cardiac or hepatic transplants, and in children and adolescents (2-18 years) receiving renal transplants.

Should you have any questions or require additional information regarding the use of CellCept®, please contact medicines information on 0800 328 1629



Michelle Rashford
Medical Director

References

1. Nicole M. Sifontis, Lisa A. Coscia, Serban Constantinescu, Antonella F. Lavelanet, Michael J. Moritz, and Vincent T. Armenti, Pregnancy Outcomes in Solid Organ Transplant Recipients With Exposure to Mycophenolate Mofetil or Sirolimus. *Transplantation* 2006;82: 1698–1702