Contact information
Address

Date

Important safety update for CellCept© (mycophenolate mofetil) Data Sheet: Teratogenic risk

Dear Healthcare Provider,

Roche Products New Zealand Limited ("Roche") would like to inform you of important new safety information about the use of CellCept (mycophenolate mofetil).

Summary of the safety concern

- CellCept is a powerful human teratogen, which increases the risk of spontaneous abortions and congenital malformations following exposure during pregnancy.
- A cumulative review of birth defects has confirmed CellCept as a powerful human teratogen and showed evidence of an increased rate of congenital malformations and spontaneous abortions associated with CellCept in comparison with other medicines.
- New safety information has been added to the Contraindications, Precautions and Use in Pregnancy sections of the Data Sheet for CellCept.

New safety information added to the Contraindications section:

- CellCept is contraindicated during pregnancy due to its mutagenic and teratogenic potential (see Use in Pregnancy).
- CellCept is contraindicated in women of childbearing potential not using highly effective contraceptive methods (see Use in Pregnancy).
- CellCept is contraindicated in women who are breastfeeding (see Use in Lactation).

New safety information added to the Precautions, Use in Pregnancy section:

CellCept is contraindicated during pregnancy and in women of childbearing potential not using highly effective contraceptive methods (see Contraindications).

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Before the start of treatment, female and male patients of reproductive potential must be made aware of the increased risk of pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention, and planning.

Prior to starting therapy with CellCept, female patients 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 they become pregnant.

Due to the mutagenic and teratogenic potential of CellCept, women of childbearing 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.

Congenital malformations, including multiple malformations have been reported post-marketing in children of patients exposed to mycophenolate mofetil in combination with other immunosuppressants during pregnancy.

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)

In the medical literature, malformations in children from mycophenolate mofetil exposed pregnancies have been reported in 23% to 27% of live births. For comparison, the risk of malformations is estimated at approximately 2% of live births in the overall population and at approximately 4% to 5% in solid organ transplant patients treated with immunosuppressants other than mycophenolate mofetil.

Cases of spontaneous abortions have also been reported in patients exposed to mycophenolate mofetil, mainly in the first trimester. In the medical literature, the risk has been reported at 45% to

49% following mycophenolate mofetil exposure, compared to a reported rate between 12% and 33% in solid organ transplant patients treated with other immunosuppressants.

The above information has been added to the Data Sheet for CellCept. Before prescribing CellCept, please review the full Data Sheet available on Medsafe's website at www.medsafe.govt.nz. If you have any questions or require additional information regarding the use of CellCept, please contact Roche Medical Information by telephone on 0800 276 243 or by email at auckland.medinfonz@roche.com.

Reporting Adverse Events: Roche will continue to monitor the safety of CellCept through established reporting mechanisms and notify regulatory authorities in accordance with current regulations. You can assist us in monitoring the safety of CellCept by reporting any case of exposure to CellCept during pregnancy (regardless of the outcome). Please also report any other suspected adverse events associated with the use of CellCept via email to the Roche Drug Safety Department at nz.drugsafety@roche.com.

Alternatively, this information may be reported to the Centre for Adverse Reactions Monitoring (CARM) in Dunedin by telephone on (03) 479 7247, by fax on (03) 479 7150, online at https://nzphvc.otago.ac.nz/reporting/ or by email to nzphvc@otago.ac.nz.

Yours sincerely,

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