

27 November 2015

Myfortic (sodium mycophenolate): serious risk of teratogenicity - important new pregnancy prevention advice for women and men

Dear Healthcare Professional,

Novartis would like to inform you about strengthened advice for pregnancy prevention when using mycophenolate sodium. This communication is in accordance with the European Medicines Agency (EMA) notification to Roche on 23 October 2015 for CellCept (mycophenolate mofetil):

Summary of the safety concern

Mycophenolate is a powerful human teratogen, which increases the risk of spontaneous abortions and congenital malformations in case of exposure during pregnancy.

The following new contraindications have been added to section 4.3 of the SmPC of the mycophenolate Cellcept (mycophenolate mofetil). The SmPCs of Cellcept and Myfortic will be harmonised:

- Mycophenolate sodium should not be used in pregnancy unless there is no suitable alternative treatment to prevent transplant rejection;
- Mycophenolate sodium should not be given to women of childbearing potential who are not using highly effective contraception;
- Mycophenolate sodium treatment should not be initiated in women of child bearing potential without providing a pregnancy test result to rule out unintended use in pregnancy.

Additionally:

- Physicians should ensure that women and men taking mycophenolate sodium 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;
- Educational materials will be provided.

Further advice on pregnancy testing

Before starting treatment with mycophenolate sodium, women of child bearing potential should have a pregnancy test in order to exclude unintended exposure of the embryo to mycophenolate.

Two serum or urine pregnancy tests with a sensitivity of at least 25 mIU/mL are recommended; the second test should be performed 8 to 10 days after the first one and immediately before starting mycophenolate sodium.

Pregnancy tests should be repeated as clinically required (e.g. after any gap in contraception is reported). Results of all pregnancy tests should be discussed with the patient. Patients should be instructed not to stop treatment but to consult their physician immediately should pregnancy occur.

Contraception advice for women and men

Women of childbearing potential should use two reliable forms of contraception simultaneously before starting therapy, during therapy, and for six weeks after stopping treatment with mycophenolate sodium.

Sexually active men (including vasectomized men) are recommended to use condoms during treatment and for at least 90 days after cessation of treatment. In addition, female partners of male patients treated with mycophenolate sodium are recommended to use highly effective contraception during treatment and for a total of 90 days after the last dose.

Additional precautions

Patients should not donate blood during therapy or for at least 6 weeks following discontinuation of mycophenolate sodium. Men should not donate semen during therapy or for 90 days following discontinuation of mycophenolate sodium.

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:

- Spontaneous abortions have been reported in 45 to 49% of pregnant women exposed to mycophenolate mofetil, compared to a reported rate of between 12 and 33% in solid organ transplant patients treated with immunosuppressants other than mycophenolate mofetil.
- Based on literature reports, malformations occurred in 23 to 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% of live births in solid organ transplant recipients treated with immunosuppressants other than mycophenolate mofetil).

The following malformations (including multiple malformations) were most frequently reported:

- Abnormalities of the ear (e.g. abnormally formed or absent external/middle ear), external auditory canal atresia;
- Congenital heart disease such as atrial and ventricular septal defects;
- Facial malformations such as cleft lip, cleft palate, micrognathia and hypertelorism of the orbits;
- Abnormalities of the eye (e.g. coloboma);
- Malformations of the fingers (e.g. polydactyly, syndactyly);
- Tracheo-oesophageal malformations (e.g. oesophageal atresia);
- Nervous system malformations such as spina bifida;
- Renal abnormalities.

Educational materials

Novartis will provide educational materials to healthcare professionals. The educational materials will reinforce the warnings about the teratogenicity of mycophenolate, provide advice on contraception before, during and after therapy and reinforce the need for pregnancy testing. Full information about the teratogenic risk and the pregnancy prevention measures should be given to women of childbearing potential and, as appropriate, to men.

Full prescribing and adverse event information for Myfortic (mycophenolate sodium) can be found in the product information available via the following:

- www.medicines.ie
- www.hpra.ie


Call for reporting

Healthcare professionals should report any serious adverse events suspected to be associated with the use of mycophenolate sodium according to national reporting requirements. Healthcare professionals are asked to report any suspected adverse reactions via HPRAs Pharmacovigilance, Earlsfort Terrace, Dublin 2; [Tel:+353 16764971](tel:+35316764971); [Fax:+3531 6762517](tel:+35316762517). Website: www.hpra.ie; Adverse events should also be reported to Novartis Ireland Limited, Vista Building, Elm Park Business Park, Merrion Road, Dublin 4
Tel: 01-2204100; Fax: 01-2838777; Email: drugsafety.dublin@novartis.com.

Company contact point

Should you have any questions or require additional information regarding the use of mycophenolate sodium, please feel free to contact via Medical Information by email (medinfo.dublin@novartis.com).

Yours sincerely,



Dr Eva Lindgren

Chief Scientific Officer

Novartis Ireland Limited