22nd January 2018

mycophenolate mofetil (MMF) / mycophenolic acid (MPA): amended recommendations for contraception

Dear Healthcare Professional,

The marketing authorisation holders of mycophenolate mofetil (MMF)/mycophenolic acid (MPA) in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA) would like to inform you of the following:

Summary

- The available clinical evidence does not indicate an increased risk of malformations or miscarriage in pregnancies where the father was taking mycophenolate medicines. However MMF and MPA are genotoxic and a risk cannot be fully excluded.
- For male patients, it is recommended that **the patients or their female partner** use reliable contraception during treatment and for at least 90 days after stopping treatment.
- The risk for women is unchanged. Mycophenolate medicines remain contraindicated in women of child bearing potential who are not using reliable contraception. These medicines are also contraindicated in pregnant women unless there are no suitable alternatives to prevent transplant rejection.
- For female patients of child bearing potential, **at least one reliable form of contraception** must be used before, during and for 6 weeks after stopping treatment. Two forms of contraception are preferred but not mandatory.

Background on the safety concern

Mycophenolate, used to prevent transplant rejection, is a major human teratogen known to cause miscarriages and congenital malformation when used in pregnant women. Between 45% and 49% of cases of exposure to mycophenolate in the womb result in miscarriage, and between 23% and 27% result in malformations.

Mycophenolate medicines – both mycophenolate mofetil (MMF)[1] or mycophenolic acid (MPA) – are therefore contraindicated in women of child bearing potential not using effective contraception. Mycophenolate is also contraindicated in pregnant women unless there are no suitable alternatives to prevent transplant rejection. In addition, negative pregnancy tests are required before starting treatment (as described in the product information for these medicines).

Following a recent in depth review of non-clinical and clinical data regarding men fathering children whilst being treated with MMF and MPA, the European Medicines Agency (EMA) has updated its 2015 recommendations for MMF and MPA to prevent pregnancy.

Although the amount of mycophenolate present in semen has not been determined, calculations based on animal data show that the maximum amount of mycophenolate that could potentially be transferred to a woman is low and is unlikely to have any effect. However, mycophenolate has been shown to be genotoxic in animal studies at concentrations higher than the human therapeutic exposure levels, and the risk of genotoxic effects on sperm cells can therefore not be completely excluded.

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[1] MMF is a pro-drug of MPA

EMA now recommends that sexually active male patients or their female partners should use reliable contraception during treatment and for at least 90 days after stopping mycophenolate.

The previous recommendation that male patients should use condoms in addition to their female partners using a highly effective contraception has now been removed from the product information as this does not reflect the level of risk.

The risks for women are unchanged. Women of childbearing potential must use **at least one form of reliable contraception** before starting, during, and for 6 weeks after stopping treatment with mycophenolate unless abstinence is the chosen method of contraception. However, two complementary forms of contraception are preferred to minimise the risk of contraception failure.

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin2; Tel: +353 16764971; Fax: +353 16762517. Website: www.hpra.ie; Emails: medsafety@hpra.ie. Adverse reactions can also be reported to marketing authorisation holders for mycophenolate mofetil/ mycophenolic acid (please see contact details below)**.**

Company contact point

If you have further questions or require additional information please contact:

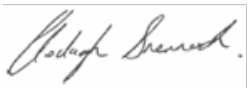
Company	**Product name**	**Email**	**Phone**	**Fax**
Roche Products (Ireland) Limited	Cellcept	ireland.drug_surveillance_centre@roche.com	+353 1 4690700	+353 1 4690793
Novartis Ireland Limited	Myfortic	medinfo.dublin@novartis.com	+353 1 2204100	+353 1 2601263
Teva	Myfenax	medinfo@tevauk.com	+44 (0)20 7540 7117	+44 (0)20 7540 7349
Accord Healthcare Limited	Mycophenolate Mofetil Accord 250 mg Capsules Mycophenolate Mofetil 500 mg Film Coated Tablets	medinfo@accord-healthcare.com	+ 44 1271385257	-
Clonmel Healthcare Ltd.	MYCOPHENOLATE MOFETIL CLONMEL	medicalinformation@clonmel-health.ie	+353 52 6177778	+353 52 6177791
Rowex Ltd.	Mycolat	pv@rowa-pharma.ie	+353 27 50077	+353 27 50417

Annexes

The relevant product information is available on www.medicines.ie, www.hpra.ie or www.ema.europa.eu/ema

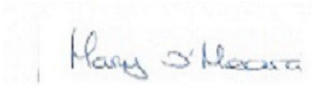
Yours sincerely,

Dr. Michal Starnawski
Medical Director (Roche)



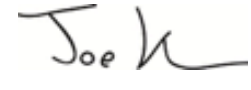
Clodagh Brennock
Medical Advisor (Novartis)

John Holmes
UK Director Medical Services (Teva)



Mary O'Meara
Head of Regulatory (Accord Healthcare)

Niall Hally
Medical Affairs Manager (Clonmel Healthcare)



Joe Keane
Marketing Manager (Rowex)