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Direct Healthcare Professional Communication

Mycophenolate Mofetil (MMF) and Mycophenolic Acid (MPA): amended recommendations for contraception

Dear Healthcare Professional

Accord Healthcare Limited UK, Actavis International Ltd, Novartis Pharmaceuticals UK Limited and Roche Products Limited in agreement with the European Medicines Agency (EMA) and the Malta Medicines Authority 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 mycophenolate mofetil (MMF) and mycophenolic acid (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).

[1] MMF is a pro-drug of MPA

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.

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

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with Mycophenolate Mofetil (MMF) and Mycophenolic Acid (MPA) in accordance with the national spontaneous reporting system. Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point

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

Company	Product name	Email	Phone
Actavis International Ltd	Axympa 180mg Gastro-resistant Tablets Axympa 360mg Gastro-resistant Tablets Mycophenolate mofetil Teva Myfenax	PHVMALTA@actavis.com	+ 30 211 8805166
Accord Healthcare Limited, UK	Mycophenolate Mofetil 250 mg Capsules Mycophenolate Mofetil 500 mg Film-coated Tablets Mycophenolate mofetil 500 mg Powder for concentrate for solution for infusion	safety@lambda-cro.com	+442089013370
Novartis	Myfortic film-coated gastro-resistant tablet 180mg Myfortic film-coated gastro-resistant tablet 360mg	*Additional Information:* novartis.malta@novartis.com *Suspected adverse reactions:* drug_safety.malta@novartis.com	+356 2122 2872
Roche Products Ltd	CellCept	*Additional Information* medinfo.uk@roche.com *Suspected adverse reactions* welwyn.uk_dsc@roche.com	+44(0)1707361010 +44(0)1707367554

Yours faithfully,

Post-Licensing Directorate
Medicines Authority

Disclaimer
This Direct Healthcare Professional Communication has been submitted to you on behalf of Accord Healthcare Limited UK, Actavis International Ltd, Novartis Pharma Services Inc. Representative office, Malta, and Roche Products Limited together with their local representatives.