

# Updated recommendations for men taking mycophenolate medicines and pregnancy following EMA recommendations.

February 2018

Dear colleagues,

The European Medicines Agency (EMA) updated their recommendations for contraception in men taking mycophenolate medicines in December 2017 to reflect **no evidence of an increased risk of malformations or miscarriages when the father has taken mycophenolate**<sup>1</sup>.

There remains substantial evidence that **maternal** exposure to mycophenolate medicines (mycophenolic acid, mycophenolate mofetil) can lead to teratogenicity in human pregnancies, and treatment with such medicines should be avoided in women for at least 6 weeks prior to attempted conception.

In principle, **paternal** exposure to teratogenic agents *may* adversely affect pregnancy in two ways:

- transmission of teratogenic agents in seminal fluid leading to local exposure of the ovum and systemic maternal exposure from maternal absorption, or
- genotoxicity in spermatozoa

Registry studies of pregnancies affected by paternal exposure to mycophenolate medicines have **not** identified an increased incidence of **teratogenicity** compared to the general population. Following exposure to seminal fluid from fathers taking mycophenolate medicines, estimated peak maternal transfer plasma concentration of mycophenolate is low, approximately 1000 times lower than therapeutic levels<sup>2</sup>, and unlikely to have any effect.

The risk of **genotoxicity** caused by paternal mycophenolate medicine exposure “cannot be completely ruled out”. For this reason the EMA recommend that *either* the male patient *or* female partner use reliable contraception during treatment and for 90 days after stopping treatment.

For stable male transplant recipients considering fathering children, or those with stable immunological renal disease taking mycophenolate medicines, conversion to alternative immunosuppressive regimes may confer significant risk of graft rejection or risk re-activation of disease.

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<sup>1</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Press\\_release/2017/12/WC500240387.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2017/12/WC500240387.pdf)

<sup>2</sup> Assuming seminal fluid concentration of mycophenolic acid equals plasma concentration, ejaculate volume of 5ml, 100% vaginal uptake and female blood volume of 5000ml

**We recommend that potential fathers taking mycophenolate medicines are informed of the *theoretical risks* of mycophenolate exposure to a fetus and be made aware of the contraceptive advice given by the EMA. We advise that these theoretical risks should be balanced against the risks of conversion to alternative immunosuppressive regimes on their kidney transplant status or immunological disease in an individualised discussion.**

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