Direct Healthcare Professional Communication:

Mycophenolate mofetil/Mycophenolic acid: serious risk of teratogenicity

Important new pregnancy prevention advice for women and men

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Dear **Pharmacist**,

In agreement with the European Medicines Agency (EMA) and the Malta Medicines Authority, *Accord Healthcare Limited, Herbert J. Passauer GmbH & Co. KG, Novartis Pharma Services Inc, Roche Registration Ltd, Teva Pharma BV and Teva BV* would like to inform you about strengthened advice for pregnancy prevention when using mycophenolate mofetil (a pro-drug of mycophenolic acid):

Summary

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:

- Mycophenolate should not be used in pregnancy unless there is no suitable alternative treatment to prevent transplant rejection
- Mycophenolate should not be given to women of childbearing potential who are not using highly effective contraception
- Mycophenolate 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 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 mycophenolate mofetil treatment, 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 25mIU/mL are recommended; the second test should be performed 8 – 10 days after the first one and immediately before starting mycophenolate mofetil. 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 mycophenolate mofetil therapy, during therapy, and for six weeks after stopping treatment

Sexually active men (including vasectomised 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 mofetil are recommended to use highly effective contraception during treatment and for a total of 90 days after the last dose of mycophenolate mofetil.

Additional precautions

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

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

The marketing authorisation holder 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 (mycophenolate mofetil and mycophenloc acid) can be found in the product information available at www.medicinesauthority.gov.mt/medicinesdatabase

Call for reporting

Any suspected adverse reactions and medication errors can be reported to the Medicines Authority or to the license holders of Mycophenolate/Mycophenolic acid products. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact points

Contact point details for further information and ADR reporting are given in the product information of the medicine (SmPC and Package Leaflet available at www.medicinesauthority.gov.mt/medicinesdatabase

Yours sincerely,

Post Licensing Directorate
Medicines Authority

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