Accept™ (Mycophenolate Mofetil) 250mg Capsules

Mycophenolate Mofetil Guide For Healthcare Providers

This document is approved by The Executive Directorate of Pharmacovigilance at Saudi Food and Drug Authority

Risk of teratogenicity

Introduction

This Guide for Healthcare Providers, has been designed to highlight the risks associated with exposure to Mycophenolate during pregnancy, as well as the measures that should be taken to mitigate them.
It will facilitate your discussion with the patient and will help you to address any questions or concerns the patient may have.

The purpose of this Guide is to minimize the number of pregnancies during treatment with this teratogenic medicinal product. Although this Guide presents important information concerning the adverse pregnancy outcomes associated with Mycophenolate, please consult the Summary of Product Characteristics (SmPC) for full information on Mycophenolate.

The teratogenic risks of Mycophenolate

Mycophenolate is a powerful teratogen associated with an increased rate of spontaneous abortion and congenital malformation compared with other immunosuppressants. No specific mechanism of teratogenicity and mutagenicity has been identified.
However, preclinical tests showed foetal resorptions and malformations in rats and rabbits in the absence of maternal toxicity. Two genotoxicity assays indicated that Mycophenolate has the potential to cause chromosomal instability at severely cytotoxic dose levels.

A review of cumulative data found that around 45% to 49% of pregnancies in women exposed to Mycophenolate resulted in spontaneous abortion, compared with reported frequencies of 12% to 33% in solid organ transplant patients treated with other immunosuppressants. The reported incidence of malformations in the offspring of mothers exposed to Mycophenolate during pregnancy is 23% to 27% compared with 4% to 5% in transplant patients treated with other immunosuppressants, and 2% to 3% in the overall population.

Congenital malformations, including reports of multiple malformations, have been observed postmarketing in children of patients exposed to Mycophenolate during pregnancy in combination with other immunosuppressants.

The following malformations were most frequently reported:
- Abnormalities of the ear (e.g. abnormally formed or absent external/middle ear), external auditory canal artesia;
- 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.

In addition there have been isolated reports of the following malformations:
- Microphthalmia;
- Congenital choroid plexus cyst;
- Septum pellucidum agenesis;
- Olfactory nerve agenesis.

Patients at risk of adverse pregnancy outcomes following exposure to Mycophenolate include:
- Pregnant patients
- All female patients of childbearing potential
- Female partners of sexually active men treated with Mycophenolate
- Women who are breastfeeding

Patient Counseling

Before initiating or continuing treatment with Mycophenolate, female and male patients must be educated about the increased risks of spontaneous abortion and congenital malformations associated with exposure to Mycophenolate. You should ensure that women and men taking Mycophenolate understand the risk of harm to the foetus, the need for effective contraception, and the need to immediately consult their physician if there is a possibility of pregnancy. The information you share in this discussion will be supported by the Mycophenolate Guide for Patients and the Package Leaflet.

In particular, you should:
- Counsel patients at risk to make sure they understand the risks and the measures required to minimize them

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- Provide female and male patients at risk with the Mycophenolate Guide for Patients, and address any questions or concerns they might have

- Explain the importance, methods and timing of pregnancy tests prior and during treatment with Mycophenolate
- Provide counseling on the use of effective contraception prior to and during the entire duration of treatment with Mycophenolate and for 6 weeks (female patients) or 90 days (male patients) after they stop taking Mycophenolate
- Advise patients using Mycophenolate that they must let you know in advance if they are considering becoming pregnant or fathering a child so that you can discuss possible treatment alternatives with them
- Mycophenolate should not be taken by women who are breastfeeding
- Advise patients treated with Mycophenolate not to donate blood during or for 6 weeks after stopping treatment
- Advise patients that this medicine is for their own personal use, they should not give it to anyone else and should return any unused medicine to their pharmacist at the end of treatment

Pregnancy Testing

Mycophenolate must not be used during pregnancy unless there is no suitable alternative to prevent transplant rejection.

Before starting treatment with Mycophenolate, 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 to consult their physician immediately should pregnancy occur.

Contraceptive Requirements

Mycophenolate is contraindicated in **women** of childbearing potential who are not using highly effective contraception. Because of the teratogenic potential of Mycophenolate, women of childbearing potential should use **two reliable forms of contraception** imultaneously before starting Mycophenolate therapy, during therapy, and for 6 weeks after stopping the therapy; unless abstinence is the chosen method of contraception.

Sexually active **men** are recommended to use condoms during treatment and for at least 90 days after cessation of treatment. Condom use applies for both reproductively competent and vasectomised men, because the risks associated with the transfer of seminal fluid also apply to men who have had a vasectomy. In addition, female partners of male patients treated with Mycophenolate are recommended to use highly effective contraception during treatment and for a total of 90 days after the last dose of Mycophenolate.

What to do if pregnancy occurs

Patients must consult their physician immediately should pregnancy occur during treatment with Mycophenolate or within 6 weeks after the last dose (within 90 days in case of paternal exposure). It is very important that the patient does not stop Mycophenolate without speaking to a physician as transplant patients may risk graft loss. The correct course of action following exposure to Mycophenolate during pregnancy should be based on an assessment of the individual patient's benefit-risk, and determined on a case by case basis through a discussion between the treating physician and the patient.

For full information, see the Summary of Product Characteristics (SmPC) and the Package Leaflet.

Healthcare professionals should report any case of exposure to Mycophenolate during pregnancy (regardless of the outcome) to the Marketing Authorization (MA) holder. Please see covering letter for the list of MA holders and their medical information contact details.

Please continue to report suspected adverse drug reactions (ADRs) to the National Pharmacovigilance Center (NPC). Please report all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

It is easiest and quickest to report ADRs via the National Pharmacovigilance Center (NPC) at:
- SFDA call center 19999
- E-mail: npc.drug@sfda.gov.sa
- Website: https://ade.sfda.gov.sa

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

For extra copies, please contact our scientific office:
+966 114011549.

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