**CMEO Podcast Transcript**

**Diana M. Girnita, MD, PhD:**

Hello, I'm Dr. Diana Girnita, and I would like to welcome you to “Preventing the Preventable, Safe Mycophenolate Practices in Patients of Childbearing Potential.” This CME activity is supported by an independent educational grant from the Mycophenolate REMS Group, a consortium of more than 20 companies that provide branded and generic forms of mycophenolate. This CME activity is provided by CME Outfitters, a jointly accredited provider of CME and CE for clinicians. During our discussion today, we will disclose if any therapies or procedures mentioned here are off-label or investigational. And here they are our disclosures.

Once again, I'm Dr. Diana Girnita. I'm the CEO and founder of Rheumatologist OnCall, and I'm also a volunteer assistant professor for many years at University of Cincinnati Medical Center. And I'm pleased to be joined today by two esteemed colleagues that I will ask them to introduce themselves. And I will start with Dr. Shah.

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

Hi, I'm Dr. Silvi Shah. I'm a transplant nephrologist at the University of Cincinnati, and I'm very excited to be here.

**Amanuel Kehasse, PharmD, PhD:**

Hello, my name is Amanuel Kehasse. I am the director of clinical programs and drug information at Clearway Health, a subsidiary of Boston Medical Center Health Systems. I'm also assistant professor of medicine at Boston University's School of Medicine, the rheumatologist section. Pleasure to be here.

**Diana M. Girnita, MD, PhD:**

Thank you so much to both of you. I'm looking forward to our conversation today. So, let's start by asking us this question. Why are we still talking about Mycophenolate REMS? And the reason is, there is a lot of evidence that Mycophenolate REMS, it's suboptimal at best in preventing prenatal exposure. Yes, we know awareness is very high, but clinical implementation remains low. And with the new and evolving abortion laws that are very strict, those will be important for our patients with accidental prenatal exposure. There are absolute or six weeks abortion bans that will limit the opportunity to consider pregnancy termination if that's desired. And there is also an increased potential for malformation that is not recognized in these abortion laws as exceptions.

And here are the goals for healthcare providers with regard to Mycophenolate REMS. We need to mitigate the risk of embryo-fetal toxicity associated with the use of these drugs, and we need to educate the healthcare providers about this increased risk in the first trimester, and especially about the pregnancy loss and about congenital malformations with exposure to mycophenolate during pregnancy. We also need to counsel patients of reproductive potential on the importance of pregnancy prevention, and also planning when taking mycophenolate. And we also need to report pregnancies to the Mycophenolate Pregnancy Registry. But not only that, we also have goals for our patients. We need to inform our patients of reproductive potential who are prescribed this kind of medication about their increased risk for miscarriages and birth defects. And we also need to make them understand about the importance of pregnancy prevention and planning when taking this medication.

And now, let's turn to our first of the three learning objectives that we'll address today, and we are going to talk about identifying the teratogenic risk associated with mycophenolate use during pregnancy. Dr. Kehasse, can you provide us with a little bit of background on mycophenolate?

**Amanuel Kehasse, PharmD, PhD:**

Thank you, Dr. Girnita for the great introduction about this session. And yes, I'd be happy to provide some introductory information.

In this slide, we are looking at the two major formulation of mycophenolate commonly used in transplant medicine. As we know, mycophenolate mofetil comes in several dosage forms. We have the IV formulation or intravenous formulation. We also have the oral formulation as capsules, tablets, or oral suspensions.

Mycophenolate carries FDA approval for the prevention of organ rejection in kidney, heart, and liver transplant recipients, and it's always used in combination with other immunosuppressive agents as well. Next, we have the delayed release formulation of mycophenolic acid sodium. This product is available as an oral tablet only, and it's FDA approved for the kidney transplant rejection prophylaxis at this time. The most common side effect that we see of mycophenolate are mostly gastrointestinal, such as diarrhea, stomach upset, nausea, and vomiting. And given the drug's immunosuppressive mechanism, we also see leukopenia quite frequently in patients taking mycophenolate as well.

In order to address the GI tolerability issues that we see with mycophenolate, an enteric-coated mycophenolate sodium tablets were introduced into the market in 2004. This formulation was designed to reduce the irritation to the stomach, and thereby hoping to improve the patient adherence and ultimately support better grafts arrival outcomes.

Mycophenolic acid journey in medicine is quite unique, as you know. Starting from being the very first purified antibiotic in 1893, to the decades long of exploration for its anti-microbial, anti-cancer activity among the few, and finally to the key discovery of its immunosuppressive potential in 1960s. That breakthrough ultimately transformed mycophenolate into becoming a cornerstone of modern transplant pharmacotherapy.

And here we are looking at the immunosuppressive effect of mycophenolates, or speaking of the mechanism of action. To our right side, we are looking at the de novo DNA synthesis pathway. As we know, most of our cells utilize both the de novo and the salvage pathways to generate their purines. Purines are one of the building blocks of DNA synthesis. However, our activated T and B lymphocytes rely heavily on the de novo pathway for their DNA synthesis and proliferation.

Here we are looking at the de novo pathway, right? And I want to draw your attention to a key enzyme in this pathway, which is the inosine monophosphate dehydrogenase. This is an enzyme that converts inosine monophosphate into xanthosine monophosphate, which is a critical step in the guanosine nucleotide production pathway thereby in the DNA synthesis end cell proliferation process. Now, mycophenolate is a prodrug as we know, right? And it has to be converted into its active metabolite, which is mycophenolic acid by the action of the plasma esterases. Once we have the active form created, it selectively and reversibly inhibit the inosine monophosphate dehydrogenase enzyme leading to the depletion of guanosine nucleotides resulted in impaired DNS synthesis as well as reduced lymphocyte proliferation and antibody formation as well.

That lends into its mechanism of action or its effect as an immunosuppressive because now you have the key players of the immune system lymphocytes production lowered and the antibody or autoantibody generation will also be reduced as a result of that. Now, we know mycophenolate is still remaining as the anti-metabolite of choice in solid organ transplants. For example, in the year 2023, nearly 15,000 adult female patients underwent solid organ transplantation. Among these patients, over 90% of these patients were maintained on mycophenolate-based regimens as part of their long-term immunosuppressive strategy. This highlights the central role of mycophenolate in preventing solid organ rejection.

And as you know, while mycophenolate is primarily approved for the prevention of post-transplant solid organ rejection, it is frequently used as an off-label basis across multiple therapeutic areas. This include multiple other solid organ transplants that we didn't talk about yet, and bone marrow transplantation as well. It's also used in range of autoimmune or inflammatory conditions such as rheumatoid arthritis, systemic sclerosis, lupus vasculitis, psoriasis and inflammatory bowel disease to name a few. With that, I'm going to transfer you back to Dr. Girnita to take us to the next slides.

**Diana M. Girnita, MD, PhD:**

Thank you so much for this introduction on the mycophenolate history and what mycophenolate does. I would like to continue now, and let's get our audience involved. I'm going to ask a question, what percentage of infants born to a mother exposed to mycophenolate during pregnancy are born with congenital malformalities? And the answer are, A, 10% to 15%. B, 20% to 25%. C, 45% to 50%. D, more than 50%, and E, I'm not sure. And I would like to ask you to go ahead and register your answers now.

And the correct answer is B, 20% to 25%. Dr. Shah, can you describe these abnormalities when were they discovered and how do they look like?

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

So, human teratogenicity of mycophenolate was first described in 2001 and it was described in a child who was born with hypoplastic nails and shortened fingers to a mother who had been exposed to mycophenolate. This was the tip of the iceberg as many other subsequent reports have followed since then. So, mycophenolate usually causes facial and limb anomalies. The common teratogenic effects which are seen with mycophenolate includes microtia or anotia, auditory canal atresia or conductive deafness, cleft lip and palate, congenital heart defects, tracheoesophageal malformations. The other frequent manifestations include dysmorphic features of the face and distal limb anomalies. Now let's discuss what we know with the transplantation community.

So, this is a report which was published in 2006 by the National Transplantation Pregnancy Registry, which is a voluntary registry which collects information on all pregnancy from solid organ transplants. What they reported, 24 female transplant patients and 33 mycophenolate exposed pregnancies in them. Of these pregnancies, about 45% had spontaneous miscarriages, and four out of 18, which is 22%, has structural malformations in live-born infants. The post-marketing data of 77 patients who were exposed to systemic mycophenolate during pregnancy between 1995 and 2007 showed that 25 patients, which is around 32% had spontaneous abortions and 14 patients, which is around 22% had a malformed fetus or infant.

**Diana M. Girnita, MD, PhD:**

So, Dr. Kehasse, we have here the mycophenolate FDA box warning. And as you see here, we also know that in 2008, pharmacists were also required to distribute a medication guide to patients. Is that correct?

**Amanuel Kehasse, PharmD, PhD:**

That's right, doctor. As mycophenolate use has been expanding year after year, the safety concerns came into really a crystal focus as well, particularly the risk of teratogenicity, bone marrow suppression and serious infection. So, as a result, patients deserve and it's their right to know about all these things. So, patients need to be counseled first at the site of medication pickup at the pharmacy or during the pharmacy consultation time in the clinics. Now we have pharmacists operating at the clinic as an extension of the care team. So that can happen then, or if not, it could also happen during the dispensing of this medication. But that's a requirement now at the very least when the patients are picking their first medication, they need to have the label insert that outlines the benefits and risks associated with mycophenolate as well. At the same time, the manufacturers of mycophenolate were also required to come with the mycophenolate risk evaluation and mitigation strategy proposals.

And as a result, the FDA have determined that additional safeguards were necessary which led to creation of the formal and first Mycophenolate REMS program in 2012. This REMS program is designed to educate patients of reproductive potential and healthcare providers about the embryo-fetal risks associated with mycophenolate, with more emphasis on the importance of pregnancy prevention and ensuring safe and consistent use of this medication. And this portal also provides a tailored information for prescribers as you can see in this slide for patients and other healthcare professionals that may interact with the patients. So, I would highly encourage every healthcare professionals to at least review these documents and understand the content so that we can actually guide our patients and our co-workers into the right platform when and if we have a patient of reproductive health taking or starting on mycophenolate.

**Diana M. Girnita, MD, PhD:**

And also the Mycophenolate REMS also provides a portal for the Mycophenolate Pregnancy Registry that we will discuss later on in this program. And now as we implement the Mycophenolate REMS in practice, we have to understand and we have to note that they define the persons of reproductive potential and also specifies the need for pregnancy testing. And those persons of reproductive potential or childbearing potential, they do include adolescents who have entered puberty, but also all the persons who have a uterus and ovaries and have not passed through menopause. And we also need two negative pregnancy tests with a high sensitivity of at least 25 milli-international units per ML, one before we start the therapy and then another one eight to 10 days after. But we also need pregnancy tests during follow-ups. And that is why testing and counseling is critical because the National Transplantation Pregnancy Registry actually compare the pregnancies conceived on mycophenolate to those conceived when mycophenolate was discontinued at least six weeks prior to conception.

And the findings were actually striking. The risk of miscarriages in pregnancies with mycophenolate was as high as 48% compared to 22% when the medication was discontinued prior to conception. So, that's why selection of adequate contraception remains critical. And now in terms of male exposure, there were observable risk of negative fetal and pregnancy outcomes when a man using mycophenolate fathers a child, but there is available prescribing information that sexually active male patients and or their female partners should use effective contraception during the treatment of a male patient and for at least three months after the last dose. So, a natural question is to ask what are the safer alternatives to mycophenolate products? Dr. Shah, would you like to answer this question in terms of organ transplantation?

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

So, the safer alternative to mycophenolate with regards to organ transplantation is azathioprine, and we often use it in our patients for our female patients who would like to get pregnant. And what we usually do is that we change mycophenolate to Imuran and then tell them that they should wait at least six weeks before they try to attempt conception. And in my clinical experience and what even the data shows, pregnancy in solid organ transplants is safe with azathioprine. So, it's a safe alternative to mycophenolate for our women patients who are of childbearing age and who would like to pursue pregnancy.

**Diana M. Girnita, MD, PhD:**

Dr. Kehasse.

**Amanuel Kehasse, PharmD, PhD:**

We should also note that there is data to show that azathioprine is a safer alternative to mycophenolate. Again, the trade-off here is especially in the organ transplantation setting, that azathioprine may have slightly lower efficacy compared to mycophenolic acid. Most immunosuppressants in the clinical practice have very limited human embryo-fetal safety data, but azathioprine being one of the oldest agents with long-standing pregnancy experience, while there is animal study that shows certain level of teratogenicity, the human data however are more reassuring. For instance, here we're looking at the data results of a retrospective cohort study. Pregnancy loss was observed in about 50% of patients exposed to mycophenolate versus 24% pregnancy loss in patients exposed to azathioprine during their first trimester. If you take a look at the risk or adjusted relative risk of these loss of pregnancy, mycophenolate-exposed patients have at least two-fold higher risk of pregnancy loss compared to azathioprine.

All right. So, now that we have this data reviewed in terms of the pregnancy loss in the first trimester, this seems to be assuring patients will have a better pregnancy outcomes while they're on azathioprine, right? So, Dr. Shah, I just want to understand from your perspective the slightly less efficacy that I mentioned earlier with azathioprine in terms of organ rejection, how concerning is that in terms of your clinical practice in the renal clinics?

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

So, thanks for the question, and this is one of the very frequent question which patients ask as well because as we discussed, azathioprine is a weaker immunosuppression as compared to mycophenolate. Also, pregnancy in solid organ transplants is associated with higher risk of adverse fetal and maternal outcomes. So, I always tell patients that they will have a higher risk of preeclampsia, higher risk of cesarean sections and a higher risk of preterm births. It also depends what your baseline organ function is. For example, if you are a kidney transplant recipient, what your baseline creatinine is prior to conception that may impact your graft function during the course of pregnancy and after delivery. So, if you have a lower baseline creatinine to start with, like if you have creatinine less than 1.4, majority the fetal outcomes are good, the live birth rates are comparable to the general population.

However, if your baseline creatinine is higher than 1.4, the risk of graft rejection may be higher. So, this is the counseling which I always do with all my patients. However, if you do not have risk factors, for example, your blood pressure is well-controlled, your creatinine is less than 1.4, then in my clinical practice and what the data shows patients do well with switching off mycophenolate to azathioprine. So, although it is a weaker immunosuppression, this is our best option for our female patients of childbearing age who would try to attempt conception provided their creatinine is at baseline, they had no recent episodes of rejection, their blood pressure is well controlled. So, overall the outcomes are favorable.

**Amanuel Kehasse, PharmD, PhD:**

Thank you, Dr. Shah. And in my clinical pharmacy service is well, I practice at the rheumatologic clinic also caring for lupus and lupus nephritis patients. So, always in my counseling points, I try to keep the balance of the benefit and the risk associated with it and mainly engaging patients in the shared decision-making process so that they can actually take part in the discussion and decision-making so that they can actually feel comfortable in the process of taking the medication that the provider is recommending. So, thank you so much for that explanation.

**Diana M. Girnita, MD, PhD:**

And thank you both for explaining those things. And now we are going to move on to our second learning objective, which is about counseling patients of childbearing potential before and during mycophenolate administration on appropriate pregnancy testing and acceptable methods of contraception. And I will start by asking the audience another question. Which of the following is a positive impact of Mycophenolate REMS to date? A, decrease MMF initiation during pregnancy. B, improve contraception during MMF therapy. C, decrease MMF initiation during pregnancy and improve contraception during MMF therapy. D, 90% participation in the Mycophenolate REMS Pregnancy Registry and E, I don't know.

And the correct answer is A, decrease mycophenolate initiation during pregnancy. We would have hoped that the correct answer is C, but it is not. And now we're going to talk about counseling and education efforts that are very needed. So, Dr. Shah, how do you determine who is at risk and what kind of education does your team provide to your patients?

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

So, we do contraceptive counseling for patients who are of childbearing age and who are of reproductive potential, which is starting from the onset of puberty and before the menopause sets in. We do exclude patients who have had hysterectomy, oophorectomy or premature menopause since they will not be able to get pregnant. When to start contraception? So, as we discussed, mycophenolate is teratogenic and is associated with higher risk of miscarriages. So, contraception should be started during treatment and at least six weeks after ending medication. And what should be the frequency of pregnancy screening? So, pregnancy should be screened at the start of the treatment, then eight to 10 days after starting mycophenolate and at every follow-up encounter.

What is the birth control guide for Mycophenolate REMS? So, the contraceptive choice is impacted by cost, access, compliance, the expected date for desired pregnancy, insurance coverage and comorbidities of the patient. And we have three options to choose from depending upon the failure rate and their effectiveness. Option one is use one method only, and the reason is because they are most effective with the least failure rate of less than one pregnancy per 100 women in one year. And we can tell patients to choose from either intrauterine device, which is temporary or permanent methods of contraception, which is tubal sterilization or vasectomy. The option two is to use a combination of a hormone and a barrier method. And these are moderately effective and that is why patients have to be on two methods and it can cause four to seven pregnancies per 100 women in one year. So, from B, for the hormonal method, they can either choose from progesterone only injection, the birth control pill, the birth control progesterone patch, vaginal ring or progesterone-only implant.

And one of the items should be chosen from the option C, which can either be a female or a male condom or female diaphragm with spermicide, female birth control sponge or cervical cap with spermicide. The option three is to have two barrier methods and this is the least effective with 13 or more pregnancies per 100 women in one year. And patients can pick one item from C1, which can either be a female condom or a male condom, and they can pick one item from C2, which can be a female diaphragm with spermicide, female birth control sponge or cervical cap with spermicide.

What options patients have for emergency contraception? Again, there are three options for our patients. The first type of emergency contraception is plan B or levonorgestrel. And it is ideally for patients weighing less than 165 pounds. It can be started within three days after sexual encounter. And the mechanism of its action is that it prevents ovulation or prevents an egg from attaching to uterus. It is available over the counter. So, this is one of the options which has very easy access and it has a four-year shelf life. The second option is Ella or ulipristal. However, this is only available with a prescription and has a three-year shelf life. It can be used for patients weighing less than 195 pounds and can be used within five days after unprotected sexual encounter. And it works by preventing ovulation.

The third type of emergency contraception is a copper intrauterine device. And patients of any weight can use this. It is a 100% effective. It can be used within five days of unprotected sexual encounter. It's also a non-hormonal method, and the copper ions mainly affects sperm mortality and that is its mechanism of action as emergency contraception. However, it does require a referral to a healthcare provider.

**Diana M. Girnita, MD, PhD:**

Thank you very much, Dr. Shah for this explanation. And now we are going to move to our last learning objective, which is to monitor and report relevant pregnancies to the Mycophenolate Pregnancy Registry. And I'm going to start again with a question. This is our last question. What percent of pregnancies are unplanned? And the answers are A, 18%. B, 25%. C, 40%. D, 54%, and E, I'm not sure.

And the correct answer is C, 40%. And because this number is quite large, we need to report that. And as we mentioned before, we are going to talk a little bit about this registry. There is a website that they offer, www.mycophenolaterems.com where patients can go and report the pregnancy or healthcare providers can go and report the pregnancy. But the question is, when we have such an event, who is on the team responsible to report a pregnancy to the registry? Do you have an answer in your teams, Dr. Shah and Dr. Kehasse?

**Amanuel Kehasse, PharmD, PhD:**

In the clinical practice that I practice at, which is at Boston Medical Center Health Systems, I think anyone in the care team is responsible to report this one. But we also understand rheumatologists have a very limited bandwidth and this adds additional logistical burden into their workload. So, the clinical pharmacist embedded in the clinic and the nursing team that are working alongside with the providers usually take up this responsibility and make sure that the patient understand why we are actually referring them to this registry. The key information here is what you mentioned, you're being registered, some people will automatically associate that they're enrolled into a research project.

**Diana M. Girnita, MD, PhD:**

Correct.

**Amanuel Kehasse, PharmD, PhD:**

And that gives them anxiety, so we have to make sure that they understand why. Partly this data will be used to elevate our understanding of the teratogenicity of this medication because it's going to be unethical to use clinical trial to identify the teratogenicity of this medication. We know that. But by enrolling this patient and by reporting this outcome, pregnancy outcome or untoward effect of this medication, it gives us a pool of data for us to understand better so that we can better provide better care for our patients, including the patient that we are talking about right now.

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

So, I agree. Again, anybody from the team can report. And as a transplant nephrologist, we do have a multidisciplinary team which includes right from a pharmacist to a coordinator, medical assistant, social worker, a physician, a nurse practitioner, and any one of us can report if we do see a pregnancy on mycophenolate. So, it's just any member of the team, but we do [inaudible 00:35:12]-

**Diana M. Girnita, MD, PhD:**

I'm glad that you made those comments because indeed any member of this multidisciplinary teams that you work through may take the lead and report it. And there is also important to emphasize that communication and coordination amongst the team members is highly recommended. And as Dr. Kehasse mentioned, the Mycophenolate Pregnancy Registry, it'll assess just the risk and the outcomes. It's not a research product, it creates a framework for education for other patients, for clinicians, for other healthcare providers. And the purpose is to mitigate and eliminate exposure to mycophenolate in pregnancy. Everybody has a role from our nurses to clinicians, to patients to coordinate this kind of communication. And that's why it's important for our nurses and even for non-clinical administrators to be on top of these things. And when applicable, to report the pregnancy and to even follow the patients after the pregnancy. And we can use many options.

We can use a phone call. There is this phone number that we have it here, 1800-617-8191. We can use also the website, www.mycophenolaterems.com. We can also use certain tips for patient communications from using an email to link that website to our patients. We can use social media posts to share this general information about the registry. We can also use reminders to the patient electronic health record notes. And we can also remind patients or we can take the lead to register these patients during our clinic visits. But of course there are many, many challenges that will remain. There is still suboptimal participation patients that we have up to date. And this REMS assessment surveys of patients taking mycophenolate during reproductive age, they still indicate actually that there are many patients that do not understand their risk in the first trimester of pregnancy and they don't understand the risk that they have towards congenital malformation. So, that's why I think we are all in agreement that participation remains critical. Any thoughts that you have, Dr. Shah, and Dr. Kehasse before we close this meeting?

**Silvi Shah, MD, MS, FAST, FASN, FNKF, FACP:**

It has been a great discussion and just I would like to emphasize that it is very important for, again, to remind our patients and physicians and healthcare providers that if they are on mycophenolate, they should be on an appropriate contraceptive method and mycophenolate should be changed to safer immunosuppression or alternative immunosuppression like azathioprine if patients would like to get pregnant, again, counseling them of risks and benefits with regards to their health condition and status of organ transplant if they have an organ transplant.

**Amanuel Kehasse, PharmD, PhD:**

I think that's really important. I wanted to emphasize the role of pharmacists on this one. And that's coming from the fact that unlike other REMS programs, for example, we have multiple REMS programs for multiple therapeutic options. In some cases, the pharmacists have to ensure certain steps are taken before they even dispense this medication. They have to go to the registry sometimes, check if that is done. They have to go to the EMR or maybe call the provider if the pregnant tests are done and documented before they proceed on the dispensing process. However, in mycophenolate it's all voluntary. There is no hard stop for the pharmacist to double-check before they dispense that medication. So, as a good clinical practice, what I usually advise to my team is we have access to the EMR, especially if you're practicing in the healthcare system as integrated pharmacists, we want to make sure that we review all the clinical notes and the active medication list.

If you are in a dispensing setting, if you have a patient who is refilling mycophenolate month after month, but you don't see birth controls in their active medication base, that's perfect opportunity to engage with the patient. What other system that they might be using to make sure that they are properly counseled to make sure that they understand the risk and the benefits of mycophenolate. So, when I highlight that, my pharmacists will have a key role to play because we are at the very end of the medication dispensing. So, taking all this into consideration as a multidisciplinary team, everyone have a role and we all should take this one very seriously.

**Diana M. Girnita, MD, PhD:**

I would like to thank you both, Dr. Shah and Dr. Kehasse for our conversation today. And I would also like to thank our audience for participating. And by the way of summary, I would like to offer four SMART goals. You'll know that SMART stands for specific, measurable, attainable, relevant, and timely. And with that, let me introduce you to these four SMART goals. Number one, it's important to educate and remind everyone, every person of reproductive potential about the risk that they have. Number two, we need to engage in pregnancy prevention and planning, which will include discussions of acceptable methods of contraception while they're taking the mycophenolate treatment. We need to introduce them to alternative immunosuppressive medications with less potential for embryo-fetal toxicity if pregnancy is desired. Number three, we need to report to the Mycophenolate Pregnancy Registry, any pregnancies that will occur or encourage also our patients to participate in the registry because once again, that will support the collection of evidence and it will support our understanding about REMS failure and it'll enhance the prevention of prenatal exposure to this medication, mycophenolate.

And last but not least, it's important to read and to share educational resources with other healthcare providers and also with our patients. Now, to receive credit for this activity, please complete the post-test and evaluation. Thank you very much for participating. Have a wonderful day.