NOVARTIS

IMPORTANT PRESCRIBING INFORMATION ABOUT *myfortic*® (mycophenolic acid) delayed-release tablet

Subject: **Important Change in the *myfortic* Prescribing Information – Postmarketing Reports of Pure Red Cell Aplasia (PRCA)**

August 2009

Dear Healthcare Professional:

Novartis Pharmaceuticals Corporation would like to inform you that new postmarketing safety information has been added to the **WARNINGS** and **ADVERSE REACTIONS** sections of the *myfortic* Prescribing Information. Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate mofetil (MMF) in combination with other immunosuppressive agents. MMF is converted to mycophenolic acid (MPA), the active ingredient in *myfortic*, following oral or IV administration.

The new important safety information in the *myfortic* Prescribing Information includes:

> **"WARNINGS (SEE BOXED WARNING)**
>
> **Pure Red Cell Aplasia**
> Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate mofetil (MMF) in combination with other immunosuppressive agents. MMF is metabolized to mycophenolic acid (MPA), the active ingredient in Myfortic and the active form of the drug. The mechanism for MMF induced PRCA is unknown; the relative contribution of other immunosuppressants and their combinations in an immunosuppressive regimen are also unknown. In some cases PRCA was found to be reversible with dose reduction or cessation of MMF therapy. In transplant patients, however, reduced immunosuppression may place the graft at risk. Changes to Myfortic therapy should only be undertaken under appropriate supervision in transplant recipients in order to minimize the risk of graft rejection (see ADVERSE REACTIONS, Postmarketing Experience).

ADVERSE REACTIONS
Postmarketing Experience

Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate mofetil in combination with other immunosuppressive agents (see WARNINGS)."

We'd also like to inform you that the "**What are the possible side effects of Myfortic?**" section of the *myfortic* Medication Guide has been updated to include the following information:

"Your healthcare provider will do blood tests before you start taking Myfortic and during treatment with Myfortic to check your blood cell counts. Tell your healthcare provider right away if you have any signs of infection (see **"What is the most important information I should know about Myfortic?"**), or any unexpected bruising or bleeding. Also, tell your healthcare provider if you have unusual tiredness, dizziness or fainting."

The complete revised Prescribing Information and Medication Guide can be found on the Internet at http://www.myfortic.com. Contact Novartis if you have any questions about this information or the safe and effective use of *myfortic*.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of *myfortic* to Novartis Pharmaceuticals Corporation, One Health Plaza, East Hanover, NJ 07936 or by phone at 1-888-NOW-NOVA (1-888-669-6682), Monday through Friday from 8:30 AM - 5:00 PM EST.

Alternatively, this information may be reported to the FDA's MedWatch Reporting System by phone at 1-800-FDA-1088, by facsimile at 1-800-FDA-0178, or by mail using the form 3500 available at http://www.fda.gov/medwatch/index.html.

Important Information About *myfortic*® (mycophenolic acid) delayed-release tablet

Indication:
myfortic is indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine and corticosteroids.

Contraindications:
myfortic is contraindicated in patients with a hypersensitivity to mycophenolate sodium, mycophenolic acid, mycophenolate mofetil, or to any of its excipients.

Important Safety Information:

WARNING: Immunosuppression may lead to increased susceptibility to infection and possible development of lymphoma and other neoplasms. Only physicians experienced in immunosuppressive therapy and management of organ transplant recipients should use *myfortic*® (mycophenolic acid) delayed-release tablet. Patients receiving *myfortic*® should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.

Female users of childbearing potential must use contraception. Use of *myfortic*® during pregnancy is associated with increased risks of pregnancy loss and congenital malformations.

- *myfortic*® is contraindicated in patients with a hypersensitivity to mycophenolate sodium, mycophenolic acid, mycophenolate mofetil, or to any of its excipients
- Patients receiving immunosuppressive regimens involving combinations of drugs, including *myfortic*®, as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin
- Oversuppression of the immune system can also increase susceptibility to infection, including opportunistic infections, fatal infections, and sepsis
- Cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal, have been reported in patients treated with mycophenolate mofetil (MMF). Hemiparesis, apathy, confusion, cognitive deficiencies, and ataxia were the most frequent clinical features observed. MMF is metabolized to MPA, the active ingredient in *myfortic*® and the active form of the drug. The reported cases generally had risk factors for PML, including treatment with immunosuppressant therapies and impairment of immune functions. In immunosuppressed patients, physicians should consider PML in the differential diagnosis in patients reporting neurological symptoms and consultation with a neurologist should be considered as clinically indicated. Consideration should be given to reducing the amount of immunosuppression in patients who develop PML. In transplant patients, physicians should also consider the risk that reduced immunosuppression represents to the graft (See **WARNINGS**, **Infections**)
- Cases of pure red cell aplasia (PRCA) have been reported in patients treated with MMF in combination with other immunosuppressive agents. In some cases PRCA was found to be reversible with dose reduction or cessation of MMF therapy. In transplant patients, however, reduced immunosuppression may place the graft at risk (see **ADVERSE REACTIONS, Postmarketing Experience**)
- Mycophenolic acid can cause fetal harm when administered to a pregnant woman. A patient who is planning a pregnancy should not use *myfortic*® unless she cannot be successfully treated with other immunosuppressant drugs. Risks and benefits of *myfortic*® and alternative immunosuppressants should be discussed with the patient. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus

- Women of childbearing potential (including pubertal girls and peri-menopausal women) taking *myfortic*® must receive contraceptive counseling and use effective contraception. The patient should begin using her two chosen contraceptive methods 4 weeks prior to starting *myfortic*® therapy, unless abstinence is the chosen method. She should continue contraceptive use during therapy and for 6 weeks after stopping *myfortic*®. Patients should be aware that *myfortic*® reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness
- Patients receiving *myfortic*® should be monitored for neutropenia. If neutropenia develops (ANC $<1.3 \times 10^3/\mu L$), dosing with *myfortic*® should be interrupted or the dose reduced, appropriate diagnostic tests performed, and the patient managed appropriately (see **DOSAGE AND ADMINISTRATION**)
- Gastrointestinal bleeding (requiring hospitalization) has been reported in *de novo* renal transplant patients (1.0%) and maintenance patients (1.3%) treated with *myfortic*® (mycophenolic acid) (up to 12 months)
- The principal adverse reactions associated with the administration of *myfortic*® include constipation, nausea, and urinary tract infection in *de novo* patients and nausea, diarrhea, and nasopharyngitis in maintenance patients. Common adverse events reported in ≥20% of patients receiving *myfortic*® or mycophenolate mofetil in the 12-month *de novo* renal study and maintenance renal study, when used in combination with cyclosporine, USP (MODIFIED) and corticosteroids, are listed in Table 4 of the **ADVERSE REACTIONS** section of the *myfortic*® Prescribing Information

Please see the enclosed *myfortic* Prescribing Information, which includes additional information for **Warnings**, **Precautions**, and **Adverse Reactions**.

If you have any questions about this information or the safe and effective use of *myfortic*, please contact Novartis Pharmaceuticals Corporation at 1-888-NOW-NOVA (1-888-669-6682), Monday through Friday from 8:30 AM - 5:00 PM EST.

Sincerely,

✍ John Orloff, MD
Senior Vice President
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