

Prior Authorization DRUG Guidelines

**CELLCEPT®; MYFORTIC®
(Mycophenolate)**

Effective Date: 7/28/05

Date Developed: 7/28/05 by C. Wilhelmy MD

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Mycophenolate is an immunosuppressant agent. MPA exhibits a cytostatic effect on T and B lymphocytes. It is an inhibitor of inosine monophosphate dehydrogenase (IMPDH) which inhibits de novo guanosine nucleotide synthesis. T and B lymphocytes are dependent on this pathway for proliferation.

Pre-Authorization Criteria:

prophylaxis of organ rejection concomitantly with cyclosporine and corticosteroids in patients receiving allogeneic renal cardiac or hepatic transplants

Off-Label: acute graft-versus-host disease, refractory (treatment); chronic graft-versus-host disease, refractory (treatment); graft-versus-host disease (prevention); hepatitis (autoimmune, refractory); lupus nephritis; myasthenia gravis; psoriasis (moderate-to-severe); rejection in heart transplant patients (recurrent or persistent); rejection in liver transplant patients unable to tolerate tacrolimus or cyclosporine due to toxicity

MONITORING PARAMETERS — Complete blood count; signs and symptoms of infection

DOSING: ADULTS — The initial dose should be given as soon as possible following transplantation; intravenous solution may be given until the oral medication can be tolerated (up to 14 days).

Renal transplant:

CellCept®: Oral: 1 g twice daily.

Myfortic®: Oral: 720 mg twice daily (1440 mg/day)

Cardiac transplantation:

Oral (CellCept®): 1.5 g twice daily

I.V. (CellCept®): 1.5 g twice daily

Hepatic transplantation:

Oral (CellCept®): 1.5 g twice daily

I.V. (CellCept®): 1 g twice daily

Dosing adjustment for toxicity (neutropenia): ANC $<1.3 \times 10^3/\mu\text{L}$: Dosing should be interrupted or the dose reduced, appropriate diagnostic tests performed and patients managed appropriately

DOSING: PEDIATRIC

Renal transplant: Oral:

CellCept® suspension: 600 mg/m²/dose twice daily; maximum dose: 1 g twice daily

Alternatively, may use solid dosage forms according to BSA as follows:

BSA 1.25-1.5 m²: 750 mg capsule twice daily

BSA >1.5 m²: 1 g capsule or tablet twice daily

Myfortic®:

BSA <1.19 m²: Use of this formulation is not recommended

BSA 1.19-1.58 m²: 400 mg/m² twice daily (maximum: 1080 mg/day)

BSA >1.58 m²: 400 mg/m² twice daily (maximum: 1440 mg/day)

DOSING: ELDERLY — Dosage is the same as younger patients, however, dosing should be cautious due to possibility of increased hepatic, renal, or cardiac dysfunction. Elderly patients may be at an increased risk of certain infections, gastrointestinal hemorrhage, and pulmonary edema, as compared to younger patients.

DOSING: RENAL IMPAIRMENT

Renal transplant: GFR <25 mL/minute in patients outside the immediate post-transplant period:

CellCept®: Doses of >1 g administered twice daily should be avoided; patients should also be carefully observed; no dose adjustments are needed in renal transplant patients experiencing delayed graft function postoperatively

Myfortic®: Clcr <25 mL/minute: Monitor carefully

Cardiac or liver transplant: No data available; mycophenolate may be used in cardiac or hepatic transplant patients with severe chronic renal impairment if the potential benefit outweighs the potential risk.

DOSING: HEPATIC IMPAIRMENT — No dosage adjustment is recommended for renal patients with severe hepatic parenchymal disease; however, it is not currently known whether dosage adjustments are necessary for hepatic disease with other etiologies.

DOSAGE FORMS

Capsule, as mofetil (CellCept®): 250 mg

Injection, powder for reconstitution, as mofetil hydrochloride (CellCept®): 500 mg [contains polysorbate 80]

Powder for oral suspension, as mofetil (CellCept®): 200 mg/mL (225 mL) [provides 175 mL suspension following reconstitution; contains phenylalanine 0.56 mg/mL; mixed fruit flavor]

Tablet, as mofetil [film coated] (CellCept®): 500 mg [may contain ethyl alcohol]

Tablet, delayed release, as mycophenolic acid [film coated] (Myfortic®): 180 mg, 360 mg [formulated as a sodium salt]

ADMINISTRATION

Oral dosage formulations (tablet, capsule, suspension) should be administered as soon as possible following transplantation. Oral dosage forms should be administered on an empty stomach to avoid variability in MPA absorption.

ADVERSE REACTIONS SIGNIFICANT — As reported in adults following oral dosing of CellCept® alone in renal, cardiac, and hepatic allograft rejection studies. In general, lower doses used in renal rejection patients had less adverse effects than higher doses. Rates of adverse effects were similar for each indication, except for those unique to the specific organ involved. The type of adverse effects observed in pediatric patients was similar to those seen in adults; abdominal pain, anemia, diarrhea, fever, hypertension, infection, pharyngitis, respiratory tract infection, sepsis, and vomiting were seen in higher proportion; lymphoproliferative disorder was the only type of malignancy observed. Percentages of adverse reactions were similar in studies comparing CellCept® to Myfortic® in patients following renal transplant.

CONTRAINDICATIONS — Hypersensitivity to mycophenolate mofetil, mycophenolic acid, mycophenolate sodium, or any component of the formulation; intravenous formulation is contraindicated in patients who are allergic to polysorbate 80

WARNINGS / PRECAUTIONS — Risk for infection and development of lymphoproliferative disorders is increased. Patients should be monitored appropriately and given supportive treatment should these conditions occur. Toxicity may be increased in patients with renal impairment. Use caution with active peptic ulcer disease.

DRUG INTERACTIONS Multiple drug-drug interactions have been reported. Consult the Cellcept website for more information.

Herb/Nutraceutical: Avoid cat's claw, echinacea (have immunostimulant properties)

PREGNANCY RISK FACTOR — C

PREGNANCY IMPLICATIONS — There are no adequate and well-controlled studies using mycophenolate in pregnant women, however, it may cause fetal harm. Women of childbearing potential should have a negative pregnancy test prior to beginning therapy. Two reliable forms of contraception should be used prior to, during, and for 6 weeks after therapy.

LACTATION — Excretion in breast milk unknown/not recommended

BREAST-FEEDING CONSIDERATIONS — It is unknown if mycophenolate is excreted in human milk. Due to potentially serious adverse reactions, the decision to discontinue the drug or discontinue breast-feeding should be considered. Breast-feeding is not recommended during therapy or for 6 weeks after treatment is complete.

DIETARY CONSIDERATIONS — Oral dosage formulations should be taken on an empty stomach to avoid variability in MPA absorption. However, in stable renal transplant patients, may be administered with food if necessary. Oral suspension contains 0.56 mg phenylalanine/mL; use caution if administered to patients with phenylketonuria.

PATIENT EDUCATION — Take as directed, preferably 1 hour before or 2 hours after meals. Do not take within 1 hour before or 2 hours after antacids or cholestyramine medications. Do not alter dose and do not discontinue without consulting prescriber. Maintain adequate hydration (2-3 L/day of fluids unless instructed to restrict fluid intake) during entire course of therapy. You will be susceptible to infection (avoid crowds and people with infections or contagious diseases). If you are diabetic, monitor glucose levels closely (may alter glucose levels). You may experience dizziness or trembling (use caution until response to medication is known); nausea or vomiting (frequent small meals, frequent mouth care may help); diarrhea (boiled milk, yogurt, or buttermilk may help); sores or white plaques in mouth (frequent rinsing of mouth and frequent mouth care may help); or muscle or back pain (mild analgesics may be recommended). Report chest pain; acute headache or dizziness; symptoms of respiratory infection, cough, or difficulty breathing; unresolved gastrointestinal effects; fatigue, chills, fever, unhealed sores, white plaques in mouth; irritation in genital area or unusual discharge; unusual bruising or bleeding; or other unusual effects related to this medication. May be at increased risk for skin cancer; wear protective clothing and use sunscreen with high protective factor to help limit exposure to sunlight and UV light. Two reliable forms of contraception should be used prior to, during, and for 6 weeks after therapy.

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