

## mycophenolate mofetil

(mye-koe-fee-noe-late moe-fe-til)  
CellCept

## mycophenolic acid (mye-koe-fee-noe-lik)

Myfortic

### Classification

*Therapeutic:* immunosuppressants

### Pregnancy Category D

### Indications

**Mycophenolate mofetil:** Prevention of rejection in allogenic renal, hepatic, and cardiac transplantation (used concurrently with cyclosporine and corticosteroids).

**Mycophenolic acid:** Prevention of rejection in allogenic renal transplantation (used concurrently with cyclosporine and corticosteroids). **Unlabeled Use:** Nephrotic syndrome.

### Action

Inhibits the enzyme inosine monophosphate dehydrogenase, which is involved in purine synthesis. This inhibition results in suppression of T- and B-lymphocyte proliferation. **Therapeutic Effects:** Prevention of heart, kidney, or liver transplant rejection.

### Pharmacokinetics

**Absorption:** Following oral and IV administration, mycophenolate mofetil is rapidly hydrolyzed to mycophenolic acid (MPA), the active metabolite. Absorption of enteric-coated mycophenolic acid (Myfortic) is delayed compared with mycophenolate mofetil (CellCept).

**Distribution:** Cross the placenta and enter breast milk.

**Protein Binding:** MPA—97%.

**Metabolism and Excretion:** MPA is extensively metabolized; <1% excreted unchanged in urine. Some enterohepatic recirculation of MPA occurs.

**Half-life:** MPA—8–18 hr.

✱ = Canadian drug name.

⊠ = Genetic Implication.

CAPITALS indicate life-threatening, underscores indicate most frequent.

~~Strikethrough~~ = Discontinued.

### TIME/ACTION PROFILE (blood levels of MPA)

ROUTE	ONSET	PEAK	DURATION
mycophenolate mofetil- rapid PO		0.25–1.25 hr	N/A
mycophenolic acid rapid		1.5–2.75 hr	N/A

### Contraindications/Precautions

**Contraindicated in:** Hypersensitivity; Hypersensitivity to polysorbate 80 (for IV mycophenolate mofetil); **OB, Lactation:** ↑ risk of congenital anomalies or spontaneous abortion.

**Use Cautiously in:** Active serious pathology of the GI tract (including history of ulcer disease or GI bleeding); Phenylketonuria (oral suspension contains aspartame); Severe chronic renal impairment (dose not to exceed 1 g twice daily (CellCept) if CCr <25 mL/min/1.73 m<sup>2</sup>); careful monitoring recommended; Delayed graft function following transplantation (observe for ↑ toxicity); **Geri:** ↑ risk of adverse reactions related to immunosuppression; **OB:** Patients with childbearing potential; **Pedi:** Mycophenolate mofetil approved in children ≥3 mo for renal transplant; mycophenolic acid approved in children ≥5 yr for renal transplant; safety not established for other age groups.

### Adverse Reactions/Side Effects

**CNS:** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY, anxiety, dizziness, headache, insomnia, paresthesia, tremor. **CV:** edema, hypertension, hypotension, tachycardia. **Derm:** rashes. **Endo:** hypercholesterolemia, hyperglycemia, hyperkalemia, hypocalcemia, hypokalemia, hypomagnesemia. **GI:** GI BLEEDING, anorexia, constipation, diarrhea, nausea, vomiting, abdominal pain. **GU:** renal dysfunction. **Hemat:** leukocytosis, leukopenia, thrombocytopenia, anemia, pure red cell aplasia. **Resp:** cough, dyspnea. **Misc:** fever, infection (including activation of latent viral infections such as Polymavirus-associated nephropathy or Hepatitis B/C), ↑ risk of malignancy.

### Interactions

**Drug-Drug:** Combined use with **azathioprine** is not recommended (effects unknown). **Acyclovir** and **ganciclovir** compete with MPA for renal excretion and, in patients with renal dysfunction, may ↑ each other's toxicity. **Magnesium and aluminum hydroxide** antacids ↓ the absorption of MPA (avoid simultaneous administration). **Proton pump inhibitors**, including **dexlansoprazole**, **esomeprazole**,

lansoprazole, omeprazole, pantoprazole, and rabeprazole may ↓ levels. Cholestyramine and colestipol ↓ the absorption of MPA (avoid concurrent use). May ↓ the effectiveness of oral contraceptives (additional contraceptive method should be used). May ↓ the antibody response to and ↑ risk of adverse reactions from live-virus vaccines, although influenza vaccine may be useful. Amoxicillin/clavulanic acid or ciprofloxacin may ↓ MPA trough levels.

**Drug-Food:** When administered with food, peak blood levels of MPA are significantly ↓ (should be administered on an empty stomach).

### Route/Dosage

#### Mycophenolate Mofetil (CellCept)

##### Renal Transplantation

**PO, IV (Adults):** 1 g twice daily; IV should be started ≤24 hr after transplantation and switched to PO as soon as possible (IV not recommended for ≥14 days).

**PO (Children 3 mo–18 yr):** 600 mg/m<sup>2</sup> twice daily (not to exceed 2 g/day).

##### Hepatic Transplantation

**PO, IV (Adults):** 1 g twice daily IV, or 1.5 g twice daily PO. IV should be started ≤24 hr after transplantation and switched to PO as soon as possible (IV not recommended for ≥14 days).

##### Cardiac Transplantation

**PO, IV (Adults):** 1.5 g twice daily; IV should be started ≤24 hr after transplantation and switched to PO as soon as possible (IV not recommended for ≥14 days).

##### Nephrotic syndrome

**PO (Children):** *Frequent relapses*—12.5–18 mg/kg/dose twice daily; maximum: 2 g/day. *Steroid-dependent*—12–18 mg/kg/dose or 600 mg/m<sup>2</sup> twice daily; maximum: 2 g/day.

##### Renal Impairment

**PO, IV (Adults):** *CCr <25 mL/min*—daily dose should not exceed 2 g.

##### Mycophenolic Acid (Myfortic)

Mycophenolate mofetil and mycophenolic acid should not be used interchangeably without the advice of a health care professional.

### Renal Transplantation

**PO (Adults):** 720 mg twice daily.

**PO (Children 5–16 yr and ≥1.19 m<sup>2</sup>):** 400–450 mg/m<sup>2</sup> twice daily (not to exceed 720 mg twice daily).

### NURSING IMPLICATIONS

#### Assessment

- Assess for symptoms of organ rejection throughout therapy.
- **Assess for signs of progressive multifocal leukoencephalopathy (hemiparesis, apathy, confusion, cognitive deficiencies, and ataxia) periodically during therapy.**
- **Lab Test Considerations:** Obtain a urine pregnancy test with a specificity of 25 mIU/mL immediately prior to beginning therapy and again 8–10 days later. Repeat pregnancy tests should be performed during routine follow-up visits.
- Monitor CBC with differential weekly during the 1st month, twice monthly for the 2nd and 3rd month of therapy, and then monthly during the 1st yr. Neutropenia occurs most frequently from 31–180 days post-transplant. If ANC is <1000/mm<sup>3</sup>, dose should be reduced or discontinued.
- Monitor hepatic and renal status and electrolytes periodically during therapy. May cause ↑ serum alkaline phosphatase, AST, ALT, LDH, BUN, and creatinine. May also cause hyperkalemia, hypokalemia, hypocalcemia, hypomagnesemia, hyperglycemia, and hyperlipidemia.

#### Potential Nursing Diagnoses

Risk for infection (Adverse Reactions)

#### Implementation

- The initial dose of mycophenolate (usually IV) should be given within 24 hr of transplant.
- Women of childbearing yr should have a negative serum or urine pregnancy test within 1 wk prior to initiation of therapy.
- Mycophenolate mofetil (CellCept) and mycophenolic acid (Myfortic) are not interchangeable; rate of absorption is different.
- **PO:** Administer on an empty stomach, 1 hr before or 2 hr after meals. Capsules and delayed-release tablets should be swallowed whole; do not open, crush, or chew. Mycophenolate may be teratogenic; contents of capsules should not be inhaled or come in contact with skin or mucous membranes.

## CONTINUED

**mycophenolic acid**

- Do not administer mycophenolate concurrently with antacids containing magnesium or aluminum.

**IV Administration**

- IV:** IV route should only be used for patients unable to take oral medication and should be switched to oral dose form as soon as patient can tolerate capsules or tablets.
- Intermittent Infusion:** *Diluent:* Reconstitute each vial with 14 mL of D5W. Shake gently to dissolve. Solution is slightly yellow; discard if solution is discolored or contains particulate matter. Dilute contents of 2 vials (1-g dose) further with 140 mL of D5W or 3 vials (1.5-g dose) with 210 mL of D5W. *Concentration:* 6 mg/mL. Solution is stable for 4 hr. *Rate:* Administer via slow IV infusion over 2 hr. Do not administer as a bolus or via rapid infusion.
- Y-Site Compatibility:** alemtuzumab, alfentanil, amikacin, amiodarone, anidulafungin, argatroban, bivalirudin, bumetanide, buprenorphine, butorphanol, calcium chloride, caspofungin, chlorpromazine, ciprofloxacin, cisatracurium, daptomycin, dexmedetomidine, dexrazoxane, digoxin, diltiazem, diphenhydramine, dobutamine, dolasetron, dopamine, doxorubicin liposomal, doxycycline, droperidol, enalaprilat, ephedrine, epinephrine, erythromycin, esmolol, famotidine, fenoldopam, fentanyl, fluconazole, gentamicin, glycopyrrolate, granisetron, haloperidol, hydralazine, hydromorphone, insulin, isporoterol, labetalol, leucovorin, levofoxacin, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, meperidine, mesna, methylodopate, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, morphine, moxifloxacin, nalbuphine, naloxone, nesiritide, nicardipine, nitroglycerin, norepinephrine, octreotide, ondansetron, oxytocin, pamidronate, pancuronium, pentamidine, phenolamine, phenylephrine, potassium chloride, procainamide, prochlorperazine, promethazine, propranolol, quinupristin/dalfopristin, ranitidine, remifentanyl, rocuronium, succinylcholine, sufentanil, tacrolimus, theophylline, tigecycline, tirofiban, tobramycin, vancomycin, vasopressin, vecuronium, verapamil, voriconazole, zidovudine, zoledronic acid.

- Y-Site Incompatibility:** acyclovir, allopurinol, amifostine, aminophylline, amphotericin B colloidal, amphotericin B lipid complex, amphotericin B liposome, ampicillin, ampicillin/sulbactam, azithromycin, aztreonam, calcium gluconate, cefazolin, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, chloramphenicol, clindamycin, danrolene, dexamethasone, diazepam, eptifibatide, foscarnet, fosphenytoin, furosemide, ganciclovir, heparin, hydrocortisone, imipenem/cilastatin, ketorolac, meropenem, methotrexate, methylprednisolone, mycalfungin, nafcillin, nitroprusside, pantoprazole, pentobarbital, phenobarbital, phenytoin, piperacillin/tazobactam, potassium acetate, potassium phosphates, sodium acetate, sodium phosphates, ticarcillin/clavulanate, trimethoprim/sulfamethoxazole.

**Patient/Family Teaching**

- Instruct patient to take medication as directed, at the same time each day. Take missed dose as soon as remembered, but not if almost time for next dose. Do not skip or double up on missed doses. Do not discontinue without consulting health care professional.
- Reinforce the need for lifelong therapy to prevent transplant rejection. Review symptoms of rejection for the transplanted organ, and stress need to notify health care professional immediately if signs of rejection or infection occur.
- Instruct patient to notify health care professional immediately if signs and symptoms of infection (temperature  $\geq 100.5^{\circ}\text{F}$ , cold symptoms [runny nose, sore throat], flu symptoms [upset stomach, stomach pain, vomiting, diarrhea], earache or headache, pain during urination, frequent urination, white patches in mouth or throat, unexpected bruising or bleeding, cuts, scrapes, or incisions that are red, warm, and oozing pus) or multifocal leukoencephalopathy.
- Advise patient to avoid contact with persons with contagious diseases.
- Advise patient to avoid vaccinations with live attenuated virus during therapy.
- Inform patient of the increased risk of lymphoma and other malignancies. Advise patient to use sunscreen and wear protective clothing to decrease risk of skin cancer.
- Advise patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult with health care professional before taking other medications.
- Inform female patients of the importance of simultaneously using two reliable forms of contraception, unless abstinence is the chosen method, prior to begin-

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ning, during, and for 6 wk following discontinuation of therapy and to avoid breast feeding. Discuss acceptable forms of contraception with health care professional. Encourage patients who become pregnant during or within 6 wks after therapy to enroll in the Pregnancy Registry by calling 1–800–617–8191 to help the Health Care Community better understand the effects of mycophenolate during pregnancy.

- Emphasize the importance of routine follow-up laboratory tests.

### **Evaluation/Desired Outcomes**

- Prevention of rejection of transplanted organs.

### **Why was this drug prescribed for your patient?**