**metyrapone (mety-rap-one)**

**Indications**
- Prevention of allogenic renal, hepatic, and cardiac transplantation (used concurrently with cyclosporine and corticosteroids).

**Action**
- Inhibits the enzyme inosine monophosphate dehydrogenase, which is involved in purine synthesis. This inhibition results in suppression of T- and B-lymphocyte proliferation.

**Pharmacokinetics**
- **Absorption:** Following oral and IV administration, metyrapone is rapidly hydrolyzed to metyrapone glucuronide, the active metabolite. Absorption of enteric-coated metyrapone (Myfortic) is delayed compared with metyrapone (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.

**Contraindications/Precautions**
- **Contraindicated in:** Hypersensitivity; Hypersensitivity to polysorbate 80 (for IV metyrapone).
- **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 m2);
- Delayed graft function following transplantation (observe for toxicity);
- Geri:
- Risk of adverse reactions related to immunosuppression.
- OB: Patients with childbearing potential.

**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:** leukocytois, leukopenia, thrombocytopenia, anemia, pure red cell aplasia.
- **Resp:** cough, dyspnea.

**Interactions**
- **Drug-Drug:** Combined use with azathioprine is not recommended (effects unknown).

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

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metyrapone</td>
<td>rapid</td>
<td>0.25–1.25 hr</td>
<td>N/A</td>
</tr>
<tr>
<td>Metyrapone glucuronide</td>
<td>rapid</td>
<td>1.5–2.75 hr</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metyrapone</td>
<td>rapid</td>
<td>0.25–1.25 hr</td>
<td>N/A</td>
</tr>
<tr>
<td>Metyrapone glucuronide</td>
<td>rapid</td>
<td>1.5–2.75 hr</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Isomoprazole, omeprazole, pantoprazole, and rabeprazole may reduce the absorption of MPA (avoid concurrent use). Metoclopramide and domperidone should be used with caution. Meperidine, the antibiotic response to infection, and risk of adverse reactions from live virus vaccines, although influenza vaccine may be used. Amoxicillin/clavulanate and ciprofloxacin may increase MPA levels.

Drug-Food: When administered with food, peak plasma levels of MPA are significantly reduced (should be administered in 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 more than 14 days).

PO (Children 3 mo–18 yr): 600 mg/m² 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 more than 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 more than 14 days).

PO (Children): 50 mg/kg/dose twice daily, maximum 5 g twice daily; maximum: 5 g/day.

**Nephrotic Syndrome**

PO (Children): 12.5–18 mg/kg/dose 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 w/H11350 1.19 m²): 400–450 mg/m² 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, aphasia, confabulation, 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.
- Measure SCR with differential weekly for the 2nd and 3rd month of therapy, and then monthly during the 2nd yr. Neutropenia occurs most frequently from 35–180 days post-transplant. USOC is <10,000/mm³, dose should be reduced or discontinued.
- Measure hematocrit and renal status and electrolytes periodically during therapy. May cause q serum alkaline phosphatase, AST, ALT, BUN, and creatinine. May also cause hyperkalemia, hypocalcemia, hyperuricemia, 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 transplantation.
- Women of childbearing age 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 mofetil or enteric-coated capsules should not be inhaled or come in contact with skin or mucous membranes.

© 2021 F.A. Davis Company  
CONTINUED
CONTINUED

mycophenolic acid

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

**IV Administration**

- 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.

**Intravenous Infusion**

- **Bolus:** 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. Shake contents of 1 vial (0.5 g dose) further with 2.0 mL of D5W. Concentration: 6 mg/mL. Solution is stable for 4 hr.

- **Continuous Infusion:** Infuse: 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. Infuse each vial of 14 mL of D5W. Concentration: 6 mg/mL. Solution is stable for 4 hr.

- **Y-Site Compatibility:** adminsters include: alfentanil, amikacin, amiodarone, indole, bupivacaine, aztreonam, clindamycin, doxorubicin, dexamethasone, dexamethasone liposome, diphenhydramine, diltiazem, docusate, dopamine, doxorubicin liposomal, doxycycline, droperidol, eptifibatide, epinephrine, erythromycin, esmolol, famotidine, fenoldopam, fentanyl, fluconazole, gentamicin, glycopyrrolate, granisetron, haloperidol, hydralazine, hydromorphone, insulin, isoproterenol, labetalol, leucovorin, levofloxacin, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, meperidine, mesna, methyldopate, metoprolol, metronidazole, midazolam, milrinone, morphine, moxifloxacin, nalbufine, naloxone, nesiritide, nicardipine, nitroglycerin, norepinephrine, octreotide, ondansetron, oxytocin, pamidronate, pancuronium, pentamidine, phentolamine, phenylephrine, potassium chloride, procainamide, propofol, promethazine, propranolol, quinupristin/dalfopristin, ranitidine, remifentanil, rocuronium, succinylcholine, sufentanil, tacrolimus, theophylline, ticagrelor, 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, amphotericin, amoxicillin, calcium gluconate, cephalosporin, ciprofloxacin, citalopram, cisatracurium, clarithromycin, clofazimide, codeine, colistimethate, colistin, colcromide, colchicine, chloramphenicol, clindamycin, danazol, dexamethasone, diaspiron, epinephrine, foscarnet, fosphenytoin, furosemide, ganciclovir, heparin, hydrocortisone, imipenem/cilastatin, ketorolac, meropenem, methotrexate, methylprednisolone, mycophenolic acid, nafcillin, nitroprusside, pantoprazole, pentobarbital, 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.

- Remind the need for lifelong therapy to prevent transplant rejection. Report symptoms of rejection for the transplanted organ, and stress need to report health care professional immediately if signs of rejection occur.

- Instruct patient to notify health care professional immediately if signs and symptoms of infection (temperature >100.5°F, chills, nausea, vomiting, diarrhea, rash, headache, myalgia) or signs of rejection occur.

- 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 beginning therapy.
ning, during, and for 6 wk following discontinuation of therapy and to avoid breastfeeding. Discuss acceptable forms of contraception with health care professional. Encourage patients who become pregnant during or within 6 wk 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?**