In the immediate posttransplant phase, pharmacokinetic parameters of mycophenolate mofetil were observed to be 20% to 41% lower and mean Cmax approximately 32% to 44% lower compared to the late transplantation of the drug. Mycophenolate mofetil did not inhibit early events in the activation of human renal and rat cardiac allograft models. Mycophenolate mofetil also inhibited proliferative arteriopathy.

For a subset of patients aged 1 to <6 years, the pharmacokinetic parameters were as follows:

<table>
<thead>
<tr>
<th>Age Group (N)</th>
<th>Time (h)</th>
<th>Dose Adjusted (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to &lt; 6 yr</td>
<td>0.989</td>
<td>0.511</td>
</tr>
<tr>
<td></td>
<td>22.7</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>49.7</td>
<td>18.2</td>
</tr>
</tbody>
</table>

The pharmacokinetics of mycophenolate mofetil are not altered by hemodialysis. The pH of the reconstituted solution is 2.4 to 4.1.

Mycophenolate mofetil capsules contain FD&C blue #1, FD&C blue #3, gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The morpholino group has a pH of 5.6, and the phenolic group has a pH of 8.5.

Mycophenolate mofetil is a reversible, uncompetitive, and potent inhibitor of inosine monophosphate dehydrogenase. Mycophenolate mofetil is not metabolized by the liver, but hepatic transaminases may increase. Mycophenolate mofetil may cause anemia and neutropenia. The liver concentration of mycophenolic acid (MPA) is approximately 75% greater than peak plasma concentrations, regardless of the dose. It is recommended that mycophenolate mofetil not be administered concomitantly with azathioprine or 6-mercaptopurine.

The cumulative incidence of 12-month graft loss or patient death is presented below. No advantage was noted when comparing mycophenolate mofetil with azathioprine, as indicated in Table 6:

Table 6:

<table>
<thead>
<tr>
<th>Rejection at 6 Months/Death or Retransplantation at 1 Year</th>
<th>All Patients Treated</th>
<th>Patients with Graft Rejection</th>
<th>Patients with Graft Rejection and Death or Retransplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycophenolate Mofetil</td>
<td>33 (11.4%)</td>
<td>22 (61.2%)</td>
<td>11 (33.3%)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>18 (6.2%)</td>
<td>15 (83.3%)</td>
<td>3 (16.7%)</td>
</tr>
</tbody>
</table>

Mycophenolate mofetil is contraindicated in patients with a known hypersensitivity to its active metabolite, mycophenolic acid. It is also contraindicated in children less than 6 months of age and in patients with a known or suspected history of hemolytic anemia. Patients must be monitored for infections, especially sepsis, since they may be at increased risk of developing severe infections.

Graft rejection and death are the most common reasons for discontinuation of mycophenolate mofetil. The most common adverse effects are myelosuppression, including neutropenia and anemia. Hemorrhagic cysts have been observed in renal transplant recipients treated with mycophenolate mofetil. Mycophenolate mofetil is recommended for use during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Drug Interactions

- Discuss pregnancy plans with female patients of childbearing potential.
- The recommended dose of mycophenolate mofetil oral suspension is 600 mg/m² bid (up to a maximum for BSA). No effects on fertility or reproductive parameters were evident in the dams or in patients and 0.01 times the recommended clinical dose in cardiac transplant patients when corrected for BSA. The data were considered adequate to evaluate the potential for human risk.
- Sevelamer and other calcium free phosphate binders preferentially could be given 2 hours after administration of mycophenolate mofetil. This data suggest that sevelamer and other calcium free phosphate binders should not be administered concomitantly with mycophenolate mofetil.
- Coadministration of mycophenolate mofetil (1 g) and acyclovir (800 mg) to 12 healthy subjects resulted in a 3-fold increase in plasma MPAG AUC and a 2-fold increase in plasma MPA AUC. Thus, other cytochrome P450 inhibitors, erythromycin, and clarithromycin may significantly effect on mean MPA AUC0-48h when mycophenolate mofetil was concomitantly administered. Rifampin concomitantly unless the benefit outweighs the risk.
- Other drugs that are known to have a significant effect on mean MPA AUC0-48h when mycophenolate mofetil was concomitantly administered include: carbamazepine, cyclosporine, dehydrogenase) inhibitor, it should be avoided in patients with rare hereditary deficiency of hypoxanthine guanine phosphoribosyltransferase.
- Coadministration of mycophenolate mofetil with ganciclovir alone. The mean (±SD) AUC and Cmax of MPA (N=12) after coadministration were 80.9 ± 8.9 ng·h/mL and 52.5 ± 9.5 ng/mL, respectively. This indicates that ganciclovir concentrations, the two drugs will compete for tubular secretion and thus further increase the plasma MPA concentration.
- Clarithromycin, a CYP3A4 inhibitor, resulted in a 2-fold increase in plasma MPA AUC0-48h when mycophenolate mofetil was concomitantly administered. As clarithromycin is highly protein bound, mycophenolic acid (MPA) concentrations may be increased.
- The incidence of adverse events for mycophenolate mofetil was determined in randomized, controlled prevention trials: the incidence of sepsis was comparable in mycophenolate mofetil and in azathioprine-treated patients. Among infections, leukopenia, hypertension, diarrhea and respiratory infection, the incidence of sepsis was comparable in mycophenolate mofetil and in azathioprine-treated patients.
- Mycophenolate mofetil intravenous must be reconstituted and diluted to a concentration of 6 mg/mL (±10%). In patients receiving mycophenolate mofetil (2 g or 3 g) in controlled studies for prevention of renal, cardiac, and hepatic transplant rejection, the most frequent adverse reactions were: anemia (17.7%), hyperkalemia (10.5%), hypertension (10.4%), diarrhea, vomiting, pharyngitis, respiratory tract infection, hypertension, leukopenia, abdominal pain, fever, infection, and rash.

### Laboratory Tests

- woods/Samples/Hospital:
- Black:
- cards:
- Others:
- 1Sandimmune® is a registered trademark of Novartis Pharmaceuticals Corporation.
- Mycophenolate mofetil intravenous is an alternative dosage form to mycophenolate mofetil capsules, tablets and oral suspension recommended for patients unable to take oral medication. The recommended dose is 1 g bid for cardiac transplant and 1.5 g bid for renal transplant patients.
- Mycophenolate mofetil intravenous is usually administered as a 30 minute intravenous infusion over 1 hour. It may also be given as an intravenous bolus of 1 g over 1 minute or 1.5 g over 3 minutes. The bolus may also be followed by a 1-hour intravenous infusion of the same dose.
- Mycophenolate mofetil intravenous is usually administered as a 30 minute intravenous infusion over 1 hour. It may also be given as an intravenous bolus of 1 g over 1 minute or 1.5 g over 3 minutes. The bolus may also be followed by a 1-hour intravenous infusion of the same dose.
- Mycophenolate mofetil intravenous is usually administered as a 30 minute intravenous infusion over 1 hour. It may also be given as an intravenous bolus of 1 g over 1 minute or 1.5 g over 3 minutes. The bolus may also be followed by a 1-hour intravenous infusion of the same dose.
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- Mycophenolate mofetil is not recommended for use in adult hepatic transplant patients who are at increased risk of developing lymphomas and other malignancies, particularly of the skin and lungs.
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MYCOPHENOLATE MOFETIL
Capsules

250 mg

Each capsule contains 250 mg mycophenolate mofetil.

USUAL DOSAGE: For dosage recommendations and other important prescribing information, read accompanying insert.

Rx only

Dispense in tight, light-resistant container as defined in the USP with a child-resistant cap.

Store at 25°C (77°F). See USP Controlled Room Temperature; excursions permitted to 15° to 30°C (59° to 86°F).

Caution: Special Handling and Disposal instructions see insert.
Dispense in tight, light-resistant container as defined in the USP with a child-resistant cap.

Store at 25°C (77°F). See USP Controlled Room Temperature; excursions permitted to 15° to 30°C (59° to 86°F).

Caution: Special Handling and Disposal instructions see insert.

Roxane Laboratories, Inc.
Columbus, Ohio 43216

MYCOPHENOLATE MOFETIL
Capsules
250 mg

Each capsule contains 250 mg mycophenolate mofetil.

USUAL DOSAGE: For dosage recommendations and other important prescribing information, read accompanying insert.

Rx only

Roxane Laboratories, Inc.
Columbus, Ohio 43216

© RLI, 2006
Mycophenolate Mofetil Capsules, 250 mg / 100 Capsules / Bottle Label

10004761/01
United States
4.0” x 2.375”
1:1
23. October 2006
Roxane Approved Brown
Roxane Approved Screen
3
Boehringer Ingelheim Roxane, Inc.
UPC 3 ver A
D-72
Sales

Approvals
USP
MOFETIL
Capsules
250 mg
Each capsule contains 250 mg mycophenolate mofetil.
USUAL DOSAGE: For dosage recommendations and other important prescribing information, read accompanying insert.

Dispense in tight, light-resistant container as defined in the USP with a child-resistant cap.

Store at 25°C (77°F); See USP Controlled Room Temperature; excursions permitted to 15° to 30°C (59° to 86°F).

Caution: Special Handling and Disposal instructions see insert.

Mycophenolate Mofetil Capsules
250 mg

Roxane Laboratories, Inc.
Columbus, Ohio 43216

NDC 0054-0163-25 100 Capsules
EXP. LOT

© RLI, 2006
Each tablet contains 500 mg mycophenolate mofetil.

USUAL DOSAGE: For dosage recommendations and other important prescribing information, read accompanying insert.

Rx only

Dispense in tight, light-resistant container as defined in the USP with a child-resistant cap.

Store at 25°C (77°F). See USP Controlled Room Temperature; excursions permitted to 15° to 30°C (59° to 86°F).

Caution: Special Handling and Disposal Instructions see insert.
Dispense in tight, light-resistant container as defined in the USP with a child-resistant cap.
Store at 30°C (86°F). See USP Controlled Room Temperature: 15° to 30°C (59° to 86°F).
Caution: Special handling and Disposal instructions see insert.

Mycophenolate Mofetil Tablets, 500 mg / 100 Tablets

10004756/01
United States

2.8125” x 1.0”

Scale: 1:1

24. October 2006

Roxane Approved Brown Pan 186C
Roxane Approved Screen

4

Roxane Laboratories, Inc.
Columbus, Ohio 43216

LOT EXP.

MYCOPHENOLATE MOFETIL Tablets
500 mg

100 Tablets

Each tablet contains 500 mg mycophenolate mofetil.

USUAL DOSAGE: For dosage recommendations and other important prescribing information, read accompanying insert.

Dispense in tight, light-resistant container as defined in the USP with a child-resistant cap.
Store at 30°C (86°F). See USP Controlled Room Temperature: 15° to 30°C (59° to 86°F).
Caution: Special handling and Disposal instructions see insert.