The transient increase in the free fraction and concentration of plasma MPA in patients with delayed renal function was 6-fold higher in volunteers with severe renal impairment than in volunteers with mild renal function. Healthy volunteers (GFR >80 mL/min/1.73 m²) had mean MPA AUC values similar to those found in renal transplant patients after administration of 1 g bid intravenous mycophenolate mofetil followed by 1.5 g bid oral mycophenolate. Mean MPA AUC values following administration of 1 g bid intravenous mycophenolate mofetil over 2 and 7 days were comparable to those found in renal transplant patients. However, MPA Cmax and AUC were approximately 20% to 41% lower and mean C24h was approximately 50% lower in hepatic transplant patients compared to renal transplant patients.

Mean (±SD) apparent half-life and plasma clearance of MPA are 17.9 (±6.5) hours and 193 (±48) mL/h, respectively. Mycophenolate mofetil is metabolized principally by glucuronyl transferase to form the phenolic glucuronide of MPA (MPAG). MPAG is usually not removed by hemodialysis. However, at high MPAG plasma concentrations (>100 mcg/mL), MPAG may be removed by hemodialysis.

Increased plasma concentrations of mycophenolate mofetil metabolites (MPA 50% increase and MPAG 90% increase) were observed in patients with hepatic impairment. Mean blood to plasma ratio of radioactivity concentrations was approximately 0.6 indicating that MPA and MPAG do not extensively distribute into the cellular fractions of blood.

MPA is 97% bound to plasma albumin, while MPAG is 82% bound to plasma albumin. Pharmacologically active MPA conjugates represented 1% of the total drug present in plasma in normotensive patients. Mycophenolate mofetil clearance is approximately 50% lower in normotensive patients compared to normotensive patients. MPA at clinically relevant concentrations, is 97% bound to plasma albumin. MPAG is 82% bound to plasma albumin. The parent drug, mycophenolate mofetil, can be measured systemically as the production of interleukin-1 (IL-1) and interleukin-2 (IL-2), but did block the coupling of these cytokines.

The efficacy of mycophenolate mofetil in preventing rejection in recipients of cadaveric renal allografts has been demonstrated in controlled trials. Mycophenolate mofetil has been demonstrated in experimental animal models to prolong the survival of allografts. In vitro, mycophenolate mofetil has been shown to inhibit the activation of T, B, and natural killer cells. In addition, mycophenolate mofetil has been shown to inhibit the production of interleukin-1 (IL-1) and interleukin-2 (IL-2), but did not inhibit the coupling of these cytokines.

The metabolism of mycophenolate mofetil involves its conversion to the metabolites 2-hydroxyethylmorpholine, 4-carboxymethylmorpholine, and the N-oxide of N-(2-hydroxyethyl)carboxymethylmorpholine. Mycophenolic acid is the major metabolite of mycophenolate mofetil. Mycophenolic acid is a weak base (pKa = 8.6) and is approximately 20% bound to plasma protein. Mycophenolic acid is a major contributor to the anti-inflammatory activity of mycophenolate mofetil.

The pH of the reconstituted solution is 2.4 to 4.1. The solubility of mycophenolate mofetil in water at pH 7.4 is 1 mcg/mL. The solubility increases in acidic medium (4.27 mg/mL at pH 3.6). It is freely soluble in octanol/water (pH 7.4) buffer solution is 238. The pKa values for mycophenolate mofetil are 5.6 for the phenolic group and 9.9 for the morpholine moiety. The pKa values for mycophenolic acid are 8.6 for the carboxyl group and 5.6 for the phenolic group.
Infections

Mycophenolate mofetil (2 g or 3 g) with other immunosuppressive agents in controlled clinical trials of
appears to be related to the intensity and duration of immunosuppression rather than to the use of any
(see boxed
hours following transplantation. Mycophenolate mofetil Intravenous can be administered for upto 14

INDICATIONS AND USAGE

A double-blind, randomized, comparative, parallel-group, multicenter study in primary hepatic transplant
or retransplantation at 1 year (see
transplantation. Patients who prematurely discontinued treatment were followed for the occurrence of
proportion of patients who died or were retransplanted during the first 12 months following
hemodynamic compromise, or were retransplanted or died, within the first 6 months, and (2) the
maintenance immunosuppressive therapy. The two primary efficacy endpoints were: (1) the proportion
(n=289), in combination with cyclosporine (Sandimmune
The total number of patients enrolled was 650; 72 never received study drug and 578 received study
recipients was performed at 20 centers in the United States, 1 in Canada, 5 in Europe and 2 in Australia.
A double-blind, randomized, comparative, parallel-group, multicenter study in primary cardiac transplant

ADVERSE REACTIONS

Data obtained from several studies were pooled to look at any gender-related differences in the
Gender

Pharmacokinetics in the elderly have not been studied.

Clinical studies revealed that the plasma drug level is lower in patients with hepatic impairment than in
healthy subjects. In a study in which patients with hepatic impairment (414 subjects with alcoholic cirrhosis
in a double-blind, placebo-controlled, cross-over study) were treated with 1 g bid (up to 1 g bid) after allogeneic renal transplantation. The pharmacokinetic
study were compared. However, it should be noted that for unexplained reasons, the healthy
treatment failure within the first 6 months after transplantation (defined as biopsy-proven acute rejection
of 21 sites.

Table 4

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline MPA AUC (mg•h/L)</th>
<th>Baseline MPA Cmax (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.975 (0.484)</td>
<td>0.989 (0.511)</td>
</tr>
<tr>
<td>MMF or azathioprine/cyclosporine</td>
<td>1.63 (2.85)</td>
<td>0.978 (0.484)</td>
</tr>
<tr>
<td>Placebo</td>
<td>1.30 (0.45)</td>
<td>0.989 (0.511)</td>
</tr>
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</table>

In 8 patients with primary graft non-function following renal transplantation, plasma concentrations of

Table 3

<table>
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<tr>
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removes only small amounts of MPAG.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
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In 8 patients with primary graft non-function following renal transplantation, plasma concentrations of

Table 1

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</tr>
</tbody>
</table>

removes only small amounts of MPAG.
Mycophenolate mofetil is administered without cyclosporine compared with when mycophenolate mofetil was administered alone under fasting conditions. Mycophenolate mofetil may be administered to patients who are also taking antacids.

Patients should be advised that vaccinations may be less effective (see ADVERSE REACTIONS). Mycophenolate mofetil Oral Suspension contains aspartame, a source of phenylalanine (0.56 mg per 1 mL of Suspension).


g administered twice a day to renal transplant patients should be avoided and they should be carefully monitored.

Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate mofetil. Patients treated for prevention of renal, cardiac, and hepatic rejection.

Patients should be aware that mycophenolate mofetil reduces blood levels of the hormones in the oral contraceptive. Patients should use two methods of contraception during therapy and for 6 weeks after stopping mycophenolate mofetil.

No data are available for cardiac or hepatic transplant patients with severe chronic renal impairment.

Mycophenolate mofetil (MMF) can cause fetal harm when administered to a pregnant woman. Use of MMF during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations, especially external ear and other facial abnormalities. For comparison, the background rate for congenital anomalies in the general U.S. population is approximately 3%. Mycophenolate mofetil (MMF) was associated with a 12-fold increased risk of congenital anomalies.

In animal reproductive toxicology studies, there were increased rates of fetal resorptions and decreased fetal body weights at maternal dosages producing maternal clinical toxicities. Increased fetal resorptions were observed at a dosage of MMF that produced clinical toxicities (2.5× the maximum human dose) in the rat. In the rabbit, clinical toxicities were observed at a dosage producing 0.2× the maximum human dose. In all species, clinical toxicities consisted of diarrhea, decreased food and water consumption, and depression. Administration of cyclosporine for prevention of rejection may result in an increased risk of nephrotoxicity, mucositis, opportunistic infections, and hypertension in bone marrow transplant recipients.


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The following other opportunistic infections occurred with an incidence of less than 4% in transplant populations in the azathioprine-controlled prevention trials:

- Non-melanoma skin carcinomas occurred in 1.6% to 4.2% of patients, other types of malignancy in 0.7%

Infections eg, opportunistic infection

The principal adverse reactions associated with the administration of mycophenolate mofetil include decreased hepatic, renal or cardiac function and of concomitant or other drug therapy. Elderly patients should be cautious, reflecting the greater frequency of adverse events with concomitant or other drug therapy. Other reported clinical adverse events in pediatric patients after renal transplantation, the overall better safety profile than did patients receiving 2 g/day of mycophenolate mofetil.

Infections

The incidence of adverse events for mycophenolate mofetil was determined in randomized, active-controlled trials in renal (2 trials), cardiac (1 trial), and hepatic (1 active-controlled trial) transplant patients. The adverse event profile associated with the administration of mycophenolate mofetil.

TABLE 8 Adverse Events in Controlled Studies in Prevention of Renal, Cardiac or Hepatic Allograft Rejection (Reported in ≥20% of Patients in the Mycophenolate Mofetil Group)
What is the most important information I should know about mycophenolate mofetil?

Read the Medication Guide that comes with mycophenolate mofetil before you start taking it and each day should be avoided. These patients should also be carefully observed. No dose adjustments are needed in renal transplant patients experiencing delayed graft function postoperatively (see PHARMACOLOGY: Pharmacokinetics).

The recommended oral dose of 1 g bid for renal transplant patients, 1.5 g bid for cardiac transplant patients, and 1.5 g bid administered orally in hepatic transplant patients is appropriate for elderly patients (see PRECAUTIONS: Geriatric Use).

Mycophenolate Mofetil Capsules and Tablets

A dose of 1.5 g bid oral (daily dose of 3 g) is recommended for use in adult cardiac transplant patients. However, it is not known whether dose adjustments are needed for hepatic disease with other etiologies (see PRECAUTIONS: Hepatic Disease).

Table 10 Adverse Events Reported in 3% to <20% of Patients Treated With Mycophenolate Mofetil in Combination With Cyclosporine and Corticosteroids

<table>
<thead>
<tr>
<th>System</th>
<th>Adverse Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>Angina pectoris, arrhythmia, arterial thrombosis, atrial fibrillation, atrial flutter, bradycardia, cardiovascular collapse, chest pain, congestive heart failure, coronary artery disease, deep vein thrombosis, vasodilatation, vasospasm, ventricular extrasystole, ventricular tachycardia, venous pressure increased</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Diabetes mellitus, gout, hypoglycemia, hyperglycemia, hypokalemia, hyperlipidemia, hyperuricemia, hypophosphatemia, hyperuricemia, hypothyroidism, hypertriglyceridemia, hypocalcemia, hypercalcemia, hypomagnesemia, hypophosphatemia, hypokalemia, hyperkalemia, hypomagnesemia, hypothyroidism</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Abdominal pain, diarrhea, dyspepsia, flatulence, gastroesophageal reflux disease, gastrointestinal hemorrhage, gastrointestinal perforation, nausea, vomiting, constipation, diarrhea, abdominal pain, dyspepsia, flatulence, gastroesophageal reflux disease, gastrointestinal hemorrhage, gastrointestinal perforation, nausea, vomiting, constipation</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Anemia, leukopenia, neutropenia, decreased hemoglobin, decreased hematocrit, increased reticulocyte count, increased WBC count, increased lymphocyte count, decreased neutrophil count, increased eosinophil count</td>
</tr>
<tr>
<td>Immunological</td>
<td>Hemolytic anemia, thrombocytopenia, leukopenia, neutropenia, decreased hemoglobin, decreased hematocrit, increased reticulocyte count, increased WBC count, increased lymphocyte count, decreased neutrophil count, increased eosinophil count</td>
</tr>
<tr>
<td>Mental</td>
<td>Amnesia, confusion, depression, agitation, insomnia, nervousness, anxiety</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Back pain, myalgia, arthralgia, joint disorder, leg cramps, myasthenia, osteoporosis</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Bronchitis, cough, dyspnea, hypoxemia, pneumonia, respiratory infection, upper respiratory tract infection, sinusitis</td>
</tr>
<tr>
<td>Skin</td>
<td>Acne, skin reactions, dermatitis, eczema, gingivitis, pruritus, rash, urticaria, venous stasis ulcer, dermatitis, eczema, gingivitis, pruritus, rash, urticaria, venous stasis ulcer</td>
</tr>
<tr>
<td>Systemic</td>
<td>Anaphylaxis, angioedema, fever, hypotension, hypovolemia, sepsis, shock, septic shock, Stevens-Johnson syndrome, toxic epidermal necrolysis</td>
</tr>
</tbody>
</table>

Possible loss of a pregnancy and higher risk of birth defects.
What are the ingredients in mycophenolate mofetil?

**Inactive Ingredients:**
- aluminum lake, FD & C red #40
- aluminum lake, hypromellose
- iron oxide red
- polyethylene glycol
- gelatin
- sodium lauryl sulfate
- titanium dioxide

**Active Ingredient:**
- Mycophenolate mofetil

**What is mycophenolate mofetil?**

Mycophenolate mofetil is a medicine that is used to prevent rejection in people who have received an organ transplant. It works by reducing the activity of the immune system. This reduces the risk of your body rejecting the organ.

**How do I take mycophenolate mofetil?**

- **Oral Capsules:**
  - Take by mouth with or without food.
  - Swallow whole. Do not open, break, or chew.
  - If you miss a dose, take as soon as you remember. Do not double up your dose.

- **Oral Tablets:**
  - Take by mouth with or without food.
  - Swallow whole. Do not open, break, or chew.
  - If you miss a dose, take as soon as you remember. Do not double up your dose.

**What should I avoid while taking mycophenolate mofetil?**

- Do not take with any other medicines, vitamins, or herbal supplements. Consult your healthcare provider.

**What is the most important information I should know about mycophenolate mofetil?**

- **General Information:**
  - Mycophenolate mofetil can cause serious side effects.
  - Inform your doctor about any unexpected bruising or bleeding.
  - Inform your doctor if you have any signs of infection.

**What are the possible side effects of mycophenolate mofetil?**

- **Common side effects include:**
  - Fever
  - Stomach area pain
  - Diarrhea
  - Unusual tiredness, lack of energy, dizziness or fainting

- **Serious side effects**
  - Uncontrolled muscle twitching (myoclonus).
  - You do not care about things that you usually care about (apathy).
  - Weakness on one side of the body.

**How should I store mycophenolate mofetil?**

- Keep out of reach of children.
- Store between 15°C and 30°C (59°F and 86°F).

**How do I take treatment with mycophenolate mofetil?**

- Perform blood cell counts if necessary.
- Treatment with mycophenolate mofetil to check your blood cell counts.
- Tell your healthcare provider about any unexpected bruising or bleeding.

**Tell your healthcare provider if you:**

- Are pregnant or if you are planning to become pregnant.
- Are breastfeeding.
- Are taking any prescription or nonprescription medicines, vitamins, or herbal supplements.

**Tell your healthcare provider about all of your medical conditions, if you:**

- Have skin cancer.
- Have a bleeding disorder.
- Have a rare inherited deficiency.
- Have Lesch-Nyhan or Kelley-Seegmiller syndrome or another rare inherited deficiency.
- Have Phenylketonuria (PKU).
- Have other medical conditions.

**Tell your healthcare provider right away if you have any of the following signs and symptoms of infection:**

- Cuts, scrapes or incisions that are red, warm and oozing pus
- Earache or headache
- Unexpected bruising or bleeding
- Blindness or vision changes
- Seizures or abnormal movements
- Changes in levels of consciousness

**Tell your healthcare provider right away if you have any signs of a brain infection:**

- A brain infection called Progressive Multifocal Leukoencephalopathy (PML).
### Mycophenolate Mofetil 500 mg

#### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CROSCARMELLOSE SODIUM</td>
<td></td>
</tr>
<tr>
<td>FD&amp;C BLUE NO. 1</td>
<td></td>
</tr>
<tr>
<td>FD&amp;C RED NO. 40</td>
<td></td>
</tr>
<tr>
<td>FERRIC OXIDE</td>
<td></td>
</tr>
<tr>
<td>HYPROMELLOSE</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE</td>
<td></td>
</tr>
<tr>
<td>POLYETHYLENE GLYCOL</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE</td>
<td></td>
</tr>
<tr>
<td>POVIDONE K30</td>
<td></td>
</tr>
<tr>
<td>CELLULOSE, MICROCRYSTALLINE</td>
<td></td>
</tr>
</tbody>
</table>

#### Product Characteristics

- **Color:** Brown
- **Score:** No score
- **Shape:** Capsule
- **Size:** 18mm
- **Flavor:** Imprint Code: SAL725
- **Contains:**
- **Packaging:**
  - 100 in 1 Bottle, Plastic (NDC: 59762-0702-1)
  - 500 in 1 Bottle, Plastic (NDC: 59762-0702-3)
- **Marketing Information:** ANDA ANDA090456
  - Marketing Start Date: 06/11/2010

### Mycophenolate Mofetil 250 mg

#### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CROSCARMELLOSE SODIUM</td>
<td></td>
</tr>
<tr>
<td>FD&amp;C RED NO. 3</td>
<td></td>
</tr>
<tr>
<td>FERRIC OXIDE YELLOW</td>
<td></td>
</tr>
<tr>
<td>GELATIN</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM STEARATE</td>
<td></td>
</tr>
<tr>
<td>SODIUM LAURYL SULFATE</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE</td>
<td></td>
</tr>
<tr>
<td>POVIDONE K30</td>
<td></td>
</tr>
<tr>
<td>CELLULOSE, MICROCRYSTALLINE</td>
<td></td>
</tr>
</tbody>
</table>

#### Product Characteristics

- **Color:** White
- **Score:** No score
- **Shape:** Capsule
- **Size:** 1mm
- **Flavor:** Imprint Code: SAL726
- **Contains:**
- **Packaging:**
  - 100 in 1 Bottle, Plastic (NDC: 59762-0703-1)
  - 500 in 1 Bottle, Plastic (NDC: 59762-0703-3)
  - 120 in 1 Bottle, Plastic (NDC: 59762-0703-2)
- **Marketing Information:** ANDA ANDA090055
  - Marketing Start Date: 06/11/2010

### Labeler

- **Registrant:** Greenstone LLC
- **Address:** 825560733
- **Establishment:** Strides Arcolab Limited - KRSG
  - ID/FEI: 918513263
  - Manufacture:
    - Name: Strides Arcolab Limited - KRSG
    - ID/FEI: 918513263
  - Marketing Information: ANDA ANDA090456
    - Marketing Start Date: 06/11/2010