HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use mycophenolic acid delayed-release tablets safely and effectively. See full prescribing information for mycophenolic acid delayed-release tablets.

MYCOPHENOLIC ACID delayed-release tablets, for oral use

WARNING: EMBRYOFETAL TOXICITY, MALIGNANCIES, AND SERIOUS INFECTIONS

See full prescribing information for complete boxed warning

- Use during pregnancy is associated with increased risks of pregnancy loss and congenital malformations. Females of reproductive potential must be counseled regarding pregnancy prevention and planning. (5.1, 8.1, 8.6)
- Increased risk of development of lymphoma and other malignancies, particularly of the skin, due to immunosuppression. (5.4)
- Increased susceptibility to bacterial, viral, fungal, and protozoal infections, including opportunistic infections. (5.5, 5.6)
- Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe mycophenolic acid delayed-release tablets. (5.3)

RECENT MAJOR CHANGES

Warnings and Precautions, New or Reactivated Viral Infections (5.6) 09/2013

INDICATIONS AND USAGE

- Mycophenolic acid delayed-release tablets are an antimetabolite immunosuppressant indicated for prophylaxis of organ rejection in adult patients receiving kidney transplants and in pediatric patients at least 5 years of age and older who are at least 6 months post kidney transplant. (1.1)
- Use in combination with cyclosporine and corticosteroids. (1.1)
- Limitations of Use:
  - Mycophenolic acid delayed release tablets and mycophenolate mofetil tablets and capsules should not be used interchangeably. (1.2)

DOSAGE AND ADMINISTRATION

- In adults: 720 mg by mouth, twice daily (1440 mg total daily dose) on an empty stomach, one hour before or 2 hours after food intake. (2.1)
- In children: 5 years of age and older who are at least 6 months post kidney transplant), 400 mg/m² by mouth, twice daily (up to a maximum of 720 mg twice daily). (2.2)
- Do not crush, chew, or cut tablet prior to ingestion. (2.3)

DOSAGE FORMS AND STRENGTHS

Mycophenolic acid delayed-release tablets are available as 180 mg and 360 mg tablets. (3)

CONTRAINDICATIONS

Known hypersensitivity to mycophenolate sodium, mycophenolic acid, mycophenolate mofetil, or to any of its excipients. (4.1)

WARNINGS AND PRECAUTIONS

- New or Reactivated Viral Infections: Consider reducing immunosuppression. (5.6)
- Blood Dyscrasias including Pure Red Cell Aplasia (PRCA): Monitor for neutropenia or anemia; consider treatment interruption or dose reduction. (5.7)
- Serious GI Tract Complications (gastrointestinal bleeding, perforations and ulcers): Administer with caution to patients with active digestive system disease. (5.8)
- Immunosuppression: Avoid live vaccines. (5.9)
- Patients with Hereditary Deficiency of Hypoxanthine-guanine Phosphoribosyl-transferase (HPRT): May cause exacerbation of disease symptoms; avoid use. (5.10)

ADVERSE REACTIONS

Most common adverse reactions (≥ 20%): anemia, leukopenia, constipation, nausea, diarrhea, vomiting, dyspepsia, urinary tract infection, CMV infection, insomnia, and postoperative pain. (6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Mylan Pharmaceuticals Inc. at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Antacids with Magnesium and Aluminum Hydroxides: Decreases concentrations of mycophenolic acid (MPA); concomitant use is not recommended. (7.1)
- Azathioprine: Competition for purge metabolism; concomitant administration is not recommended. (7.2)
- Cholestyramine, Bile Acid Sequestrates, Oral Activated Charcoal, and Other Drugs that Interfere with Enterohepatic Recirculation: May decrease MPA concentrations; concomitant use is not recommended. (7.3)
- Sevelamer: May decrease MPA concentrations; concomitant use is not recommended. (7.4)
- Cyclosporine: May decrease MPA concentrations; exercise caution when switching from cyclosporine to other drugs or from other drugs to cyclosporine. (7.5)
- Norfloxacin and Metronidazole: May decrease MPA concentrations; concomitant use with both drugs is not recommended. (7.6)
- Rifampin: May decrease MPA concentrations; concomitant use is not recommended unless the benefit outweighs the risk. (7.7)
- Hormonal Contraceptives: Additional barrier contraceptive methods must be used. (5.2, 7.8)
- Acyclovir, Valacyclovir, Ganciclovir, Valganciclovir, and Other Drugs that Undergo Renal Tubular Secretion: May increase concentrations of mycophenolic acid glucuronide (MPAG) and coadministered drug; monitor blood cell counts. (7.9)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

REVISED OCTOBER 2013

MYCODR.R4m/NS;MYCODR.R3m

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1 INDICATIONS AND USAGE

1.1 Prophylaxis of Organ Rejection in Kidney Transplant

Mycophenolic acid delayed-release tablets are indicated for the prophylaxis of organ rejection in adult patients receiving a kidney transplant.

Mycophenolic acid delayed-release tablets are indicated for the prophylaxis of organ rejection in pediatric patients 5 years of age and older who are at least 6 months post kidney transplant.

Mycophenolic acid delayed-release tablets are to be used in combination with cyclosporine and corticosteroids.

1.2 Limitations of Use

Mycophenolic acid delayed-release tablets and mycophenolate mofetil (MMF) tablets and capsules should not be used interchangeably without physician supervision because the rate of absorption following the administration of these two products is not equivalent.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage in Adult Kidney Transplant Patients

The recommended dose of mycophenolic acid delayed-release tablets is 720 mg administered twice daily (1440 mg total daily dose).

2.2 Dosage in Pediatric Kidney Transplant Patients

The recommended dose of mycophenolic acid delayed-release tablets in conversion (at least 6 months post-transplant) pediatric patients age 5 years and older is 400 mg/m² body surface area (BSA) administered twice daily (up to a maximum dose of 720 mg administered twice daily).

2.3 Administration

Mycophenolic acid delayed-release tablets should be taken on an empty stomach, one hour before or 2 hours after food intake [See Clinical Pharmacology (12.3)].

Mycophenolic acid delayed-release tablets should not be crushed, chewed, or cut prior to ingesting. The tablets should be swallowed whole in order to maintain the integrity of the enteric coating.

Pediatric patients with a BSA of 1.19 to 1.58 m² may be dosed either with three mycophenolic acid delayed-release 180 mg tablets, or one 180 mg tablet plus one 360 mg tablet twice daily (1080 mg daily dose). Patients with a BSA of > 1.58 m² may be dosed either with four mycophenolic acid delayed-release 180 mg tablets, or two mycophenolic acid delayed-release 360 mg tablets twice daily (1440 mg daily dose). Pediatric doses for patients with BSA < 1.19 m² cannot be accurately administered using currently available formulations of mycophenolic acid delayed-release tablets.

3 DOSAGE FORMS AND STRENGTHS

Mycophenolic acid delayed-release tablets are available as 180 mg and 360 mg tablets.

Table 1. Description of Mycophenolic Acid Delayed-Release Tablets

<table>
<thead>
<tr>
<th>Dosage Strength</th>
<th>180 mg tablet</th>
<th>360 mg tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active ingredient</td>
<td>mycophenolic acid</td>
<td>mycophenolic acid</td>
</tr>
<tr>
<td></td>
<td>as mycophenolate sodium</td>
<td>as mycophenolate sodium</td>
</tr>
<tr>
<td>Appearance</td>
<td>sage green, film-coated, round tablet</td>
<td>redish-orange, film-coated, modified capsule shaped tablet</td>
</tr>
<tr>
<td>Imprint</td>
<td>M over MC1 on one side of the tablet and blank on the other side</td>
<td>M MC2 on one side of the tablet and blank on the other side</td>
</tr>
</tbody>
</table>

4 CONTRAINDICATIONS

4.1 Hypersensitivity Reactions

Mycophenolic acid delayed-release tablets are contraindicated in patients with a hypersensitivity to mycophenolic acid, mycophenolate mofetil, or to any of its excipients. Reactions like rash, pruritus, hypotension, and chest pain have been observed in clinical trials and post-marketing reports [see Adverse Reactions (6)].

5 WARNINGS AND PRECAUTIONS

5.1 Embryofetal Toxicity

Use of mycophenolic acid delayed-release tablets 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 including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney [see Use in Specific Populations (8.1, 8.6)].

5.2 Pregnancy Exposure Prevention and Planning

Females of reproductive potential must be aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning. For recommended pregnancy testing and contraception methods [see Use in Specific Populations (8.6)].

5.3 Management of Immunosuppression

Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe mycophenolic acid delayed-release tablets. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient [see Boxed Warning].

5.4 Lymphoma and Other Malignancies

Patients receiving immunosuppressants, including mycophenolic acid delayed-release tablets, are at increased risk of developing lymphomas and other malignancies, particularly of the skin [see Adverse Reactions (6)]. The risk appears to be related to the intensity and duration of immunosuppression rather than to the use of any specific agent.

As usual for patients with increased risk for skin cancer, exposure to sunlight and UV light should be limited by wearing protective clothing and using a sunscreen with a high protection factor.

Post-transplant lymphoproliferative disorder (PTLD) has been reported in immunosuppressed organ transplant recipients. The majority of PTLD events appear related to Epstein Barr Virus (EBV) infection. The risk of PTLD appears greatest in those individuals who are EBV seronegative, a population which includes many young children.

5.5 Serious Infections

Patients receiving immunosuppressants, including mycophenolic acid delayed-release tablets, are at increased risk of developing bacterial, viral, fungal, and protozoal infections, and new or reactivated viral infections including opportunistic infections [see Warnings and Precautions (5.6)]. These infections may lead to serious, including fatal outcomes. Because of the danger of oversuppression of the immune system which can increase susceptibility to infection, combination immunosuppressant therapy should be used with caution.

5.6 New or Reactivated Viral Infections

Polyomavirus associated nephropathy (PVAN), JC virus associated progressive multifocal leukoencephalopathy (PML), cytomegalovirus (CMV) infections, reactivation of hepatitis B (HBV) or hepatitis C (HCV) have been reported in patients treated with immunosuppressants, including the mycophenolic acid (MPA) derivatives mycophenolic acid delayed-release tablets and MMF. Reduction in immunosuppression should be considered for patients who develop evidence of new or reactivated viral infections. Physicians should also consider the risk that reduced immunosuppression represents to the functioning allograft.

PVAN, especially due to BK virus infection, is associated with serious outcomes, including deteriorating renal function and renal graft loss. Patient monitoring may help detect patients at risk for PVAN.

PML, which is sometimes fatal, commonly presents with hemiparesis, apathy, confusion, cognitive deficiencies, and ataxia. Risk factors for PML include treatment with immunosuppressant therapies and impairment of immune function. In immunosuppressed patients, physicians should consider PML in the differential diagnosis in patients reporting neurological symptoms and consultation with a neurologist should be considered as clinically indicated.

The risk of CMV viremia and CMV disease is highest among transplant recipients seronegative for CMV at time of transplant who receive a graft from a CMV seropositive donor. Therapeutic approaches to limiting CMV disease exist and should be routinely provided. Patient monitoring may help detect patients at risk for CMV disease [see Adverse Reactions (6.1)].

Viral reactivation has been reported in patients infected with HBV or HCV. Monitoring infected patients for clinical and laboratory signs of active HBV or HCV infection is recommended.

5.7 Blood Dyscrasias Including Pure Red Cell Aplasia

Cases of pure red cell aplasia (PRCA) have been reported in patients treated with MPA derivatives in combination with other immunosuppressive agents. The mechanism for MPA derivatives induced PRCA is unknown; the relative contribution of other immunosuppressants and their combinations in an immunosuppressive regimen is also unknown. In some cases PRCA was found to be reversible with dose reduction or cessation of therapy with MPA derivatives. In transplant patients, however, reduced immunosuppression may place the graft at risk. Changes to mycophenolic acid delayed-release tablet therapy should only be undertaken under appropriate supervision in transplant recipients in order to minimize the risk of graft rejection.

Patients receiving mycophenolic acid delayed-release tablets should be monitored for blood dyscrasias (e.g., neutropenia or anemia). The development of neutropenia may be related to mycophenolic acid delayed-release tablets itself, concomitant medications, viral infections, or some combination of these reactions. Complete blood count should be performed.
weekly during the first month, twice monthly for the second and the third month of treatment, then monthly through the first year. If blood dyscrasias occur (neutropenia develops (ANC < 1.3x10^9/mcL) or anemia), dosing with mycophenolic acid delayed-release tablets should be interrupted or the dose reduced, appropriate tests performed, and the patient managed accordingly.

5.8 Serious GI Tract Complications
Gastrointestinal bleeding (requiring hospitalization), intestinal perforations, gastric ulcers, and duodenal ulcers have been reported in patients treated with mycophenolic acid delayed-release tablets. Mycophenolic acid delayed-release tablets should be administered with caution in patients with active serious digestive system disease.

5.9 Immunizations
The use of live attenuated vaccines should be avoided during treatment with mycophenolic acid delayed-release tablets; examples include (but not limited to) the following: intranasal influenza, measles, mumps, rubella, oral polio, BCG, yellow fever, varicella, and TY21a typhoid vaccines.

5.10 Rare Hereditary Deficiencies
Mycophenolic acid delayed-release tablets are an inosine monophosphate dehydrogenase inhibitor (IMPDH Inhibitor). Mycophenolic acid delayed-release tablets should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndromes because it may cause an exacerbation of disease symptoms characterized by the overproduction and accumulation of uric acid leading to symptoms associated with gout such as acute arthritis, tophi, nephrolithiasis or urolithiasis and renal disease including renal failure.

6 ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in other sections of the label.

- Embryofetal Toxicity [see Boxed Warning, Warnings and Precautions (5.1)]
- Lymphomas and Other Malignancies [see Boxed Warning, Warnings and Precautions (5.4)]
- Serious Infections [see Boxed Warning, Warnings and Precautions (5.5)]
- New or Reactivated Viral Infections [see Warnings and Precautions (5.6)]
- Blood Dyscrasias Including Pure Red Cell Aplasia [see Warnings and Precautions (5.7)]
- SeriousGI Tract Complications [see Warnings and Precautions (5.8)]
- Rare Hereditary Deficiencies [see Warnings and Precautions (5.10)]

6.1 Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below derive from two randomized, comparative, active-controlled, double-blind, double-dummy trials in prevention of acute rejection in de novo and converted stable kidney transplant patients.

In the de novo trial, patients were administered either mycophenolic acid delayed-release tablets 1.44 grams per day (n = 213) or MMF 2 grams per day (n = 210) within 48 hours post-transplant for 12 months in combination with cyclosporine, USP MODIFIED and corticosteroids. Forty-one percent of patients also received antibody therapy as induction treatment. In the conversion trial, renal transplant patients who were at least 6 months post-transplant and receiving 2 grams per day MMF in combination with cyclosporine USP MODIFIED, with or without corticosteroids for at least 2 weeks prior to entry into the trial were randomized to mycophenolic acid delayed-release tablets 1.44 grams per day (n = 159) or MMF 2 grams per day (n = 163) for 12 months.

The average age of patients in both studies was 47 years and 48 years (de novo study and conversion study, respectively), ranging from 22 to 75 years. Approximately 66% of patients were male; 82% were white, 12% were black, and 6% other races. About 40% of patients were from the United States and 60% from other countries.

In the de novo trial, the overall incidence of discontinuation due to adverse reactions was 18% (39/213) and 17% (35/210) in the mycophenolic acid delayed-release tablets and MMF arms, respectively. The most common adverse reactions leading to discontinuation in the mycophenolic acid delayed-release tablets arm were graft loss (2%), diarrhea (2%), vomiting (1%), renal impairment (1%), CMV infection (1%), and leukopenia (1%). The overall incidence of patients reporting dose reduction at least once during the 0 to 12 month study period was 59% and 60% in the mycophenolic acid delayed-release tablets and MMF arms, respectively. The most frequent reasons for dose reduction in the mycophenolic acid delayed-release tablets arm were adverse reactions (44%), dose reductions according to protocol guidelines (17%), dosing errors (11%) and missing data (2%).

The most common adverse reactions (≥ 20%) associated with the administration of mycophenolic acid delayed-release tablets were anemia, leukopenia, constipation, nausea, diarrhea, vomiting, dyspepsia, urinary tract infection, CMV infection, insomnia and postoperative pain.

The adverse reactions reported in ≥ 10% of patients in the de novo trial are presented in Table 2 below.

Table 2. Adverse Reactions (%) in Reported in ≥ 10% of De Novo Kidney Transplant Patients in Either Treatment Group

<table>
<thead>
<tr>
<th>System organ class</th>
<th>de novo Renal Trial</th>
<th>Mycophenolate Mofetil (MMF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Gastrointestinal System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>Nausea</td>
<td>29</td>
<td>27</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>Vomiting</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>23</td>
<td>19</td>
</tr>
<tr>
<td>Abdominal pain upper</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Flatulence</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>General and Administrative Site Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edema</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Edema lower limb</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased blood creatinine</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>CMV Infection</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Hyperlipedemia</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>Musculoskeletal, Connective Tissue and Bone Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Tremor</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Headache</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>18</td>
<td>18</td>
</tr>
</tbody>
</table>

* The trial was not designed to support comparative claims for mycophenolic acid delayed-release tablets for the adverse reactions reported in this table.

Table 3 summarizes the incidence of opportunistic infections in de novo transplant patients.

Table 3. Viral and Fungal Infections (%) Reported Over 0 to 12 Months

<table>
<thead>
<tr>
<th>de novo Renal Trial</th>
<th>Mycophenolic Acid Delayed-release Tablets</th>
<th>Mycophenolate Mofetil (MMF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.44 grams per day (n = 213)</td>
<td>(%)</td>
<td>(n = 210)</td>
</tr>
<tr>
<td>Any Cytomegalovirus</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>Cytomegalovirus Disease</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Herpes Simplex</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Any Fungal Infection</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>-Candida NOS</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>-Candida albicans</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Lymphoma developed in two de novo patients (1%), one diagnosed 9 days after treatment initiation and in two conversion patients (1%) receiving mycophenolic acid delayed-release tablets with other immunosuppressive agents in the 12-month controlled clinical trials. Nonmelanoma skin carcinoma occurred in 1% de novo and 12% conversion patients. Other types of malignancy occurred in 1% de novo and 1% conversion patients [see Warnings and Precautions (5.4)].

The adverse reactions reported in < 10% of de novo or conversion patients treated with mycophenolic acid delayed-release tablets in combination with cyclosporine and corticosteroids are listed in Table 4.
Infections that Interfere with Enterohepatic Recirculation

7.3 Cholestyramine, Bile Acid Sequestrates, Oral Activated Charcoal and Other Drugs

Avoid concomitant use with MMF. Given that azathioprine and MMF inhibit purine metabolism, it is recommended that mycophenolic acid (MPA) plasma concentrations may be decreased when MMF is administered with norfloxacin and metronidazole. Therefore, mycophenolic acid delayed-release tablets are not recommended to be given with the combination of norfloxacin and metronidazole. Although there will be no effect on MPA plasma concentrations when mycophenolic acid delayed-release tablets are concomitantly administered with norfloxacin or metronidazole when given separately [see Clinical Pharmacology (12.3)].

7.10 Ciprofloxacin, Amoxicillin plus Clavulanic Acid and Other Drugs that Alter the Gastrointestinal Flora

The coadministration of MMF and acyclovir or ganciclovir may increase plasma concentrations of mycophenolic acid glucuronide (MPAG) and acyclovir/valacyclovir/ganciclovir/valganciclovir as their coexistence competes for tubular secretion. Both acyclovir/valacyclovir/ganciclovir/valganciclovir and MPAG concentrations will be increased in the presence of renal impairment. Acyclovir/valacyclovir/ganciclovir/valganciclovir may be taken with mycophenolic acid delayed-release tablets; however, during the period of treatment, physicians should monitor blood cell counts [see Clinical Pharmacology (12.3)].

7.11 Pantoprazole

Administration of a pantoprazole at a dose of 40 mg twice daily for 4 days to healthy volunteers did not alter the pharmacokinetics of a single dose of mycophenolic acid delayed-release tablets [see Clinical Pharmacology (12.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects. Pregnancy Category D: [see Warnings and Precautions (5.1).] For those females using mycophenolic acid delayed-release tablets at any time during pregnancy and those becoming pregnant within 6 weeks of discontinuing therapy, the healthcare practitioner should report the pregnancy to the Mycophenolate Pregnancy Registry (1-800-617-8191). The healthcare practitioner should strongly encourage the patient to enroll in the pregnancy registry. The information provided to the registry will help the Health Care Community to better understand the effects of mycophenolate in pregnancy.

Risk Summary: Following oral or intravenous (IV) administration, MMF is metabolized to mycophenolic acid (MPA), the active ingredient in mycophenolic acid delayed-release tablets and the active form of the drug. 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 including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney. In animal studies, congenital malformations and an increased incidence of first trimester pregnancy loss occurred when pregnant rats and rabbits received mycophenolic acid at dose multiples similar to and less than clinical doses. Risks and benefits of mycophenolic acid delayed-release tablets should be discussed with the patient. When appropriate, consider alternative immunosuppressants with less potential for embryofetal toxicity. In certain situations, the patient and her healthcare practitioner may

Table 4. Adverse Reactions Reported in < 10% of Patients Treated with Mycophenolic Acid Delayed-release Tablets in Combination with Cyclosporine and Corticosteroids

<table>
<thead>
<tr>
<th>Condition</th>
<th>Blood and Lymphatic Disorders</th>
<th>Cardiac Disorder</th>
<th>Eye Disorder</th>
<th>Gastrointestinal Disorders</th>
<th>General Disorders and Administration Site Conditions</th>
<th>Infections and Infestations</th>
<th>Metabolism and Nutrition Disorders</th>
<th>Musculoskeletal and Connective Tissue Disorders</th>
<th>Nervous System Disorders</th>
<th>Psychiatric Disorders</th>
<th>Renal and Urinary Disorders</th>
<th>Respiratory, Thoracic and Mediastinal Disorders</th>
<th>Skin and Subcutaneous Tissue Disorders</th>
<th>Vascular Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lymphocite, thrombocytopenia</td>
<td>Tachycardia</td>
<td>Vision blurred</td>
<td>Abdominal pain, abdominal distension, gastroesophageal reflux disease, gingival hyperplasia</td>
<td>Fatigue, peripheral edema</td>
<td>Nasopharyngitis, herpes simplex, upper respiratory infection, oral candidiasis, herpes zoster, sinusitis, influenza, wound infection, implant infection, pneumonia, sepsis</td>
<td>Hypercholesterolemia, hyperkaemia, hypomagnesemia, diabetes mellitus, hyperglycemia</td>
<td>Arthralgia, pain in limb, peripheral swelling, muscle cramps, myalgia</td>
<td>Dizziness (excluding vertigo)</td>
<td>Anxiety</td>
<td>Renal tubular necrosis, renal impairment, hematuria, urinary retention</td>
<td>Cough, dyspnea, dyspnea exertional</td>
<td>Acne, pruritus, rash</td>
<td>Hypertension aggravated, hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
decide that the maternal benefits outweigh the risks to the fetus. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

**Data:**

**Human Data:** In the National Transplantation Pregnancy Registry (NTPR), there were data on 33 MMF-exposed pregnancies in 24 transplant patients; there were 15 spontaneous abortions (45%) and 18 live-born infants. Four of these 18 infants had structural malformations (22%). In post-marketing data (collected from 1995 to 2007) on 77 women exposed to systemic MMF during pregnancy, 25 had spontaneous abortions and 14 had a malformed infant or fetus. Six of 14 malformed offspring had ear abnormalities. Because these post-marketing data are reported voluntarily, it is not always possible to reliably estimate the frequency of particular adverse outcomes. These malformations are similar to findings in animal reproductive toxicology studies. For comparison, the background rate for congenital anomalies in the United States is about 3%, and NTPR data show a rate of 4% to 5% among babies born to organ transplant patients using other immunosuppressive drugs. There are no relevant qualitative or quantitative differences in the teratogenic potential of mycophenolate sodium and MMF.

**Animal Data:** In a teratology study performed with mycophenolate sodium in rats, at a dose as low as 1 mg per kg, malformations in the offspring were observed, including anophthalmia, exencephaly, and umbilical hernia. The systemic exposure at this dose represents 0.05 times the clinical exposure at the dose of 1440 mg per day mycophenolic acid delayed-release tablets. In teratology studies in rabbits, fetal resorptions and malformations occurred at doses equal to or greater than 80 mg per kg per day, in the absence of maternal toxicity (which corresponds to about 1.1 times the recommended clinical dose, based on body surface area).

### 8.3 Nursing Mothers

It is not known whether MPA is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from mycophenolic acid delayed-release tablets, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

### 8.4 Pediatric Use

The safety and effectiveness of mycophenolic acid delayed-release tablets have been established in pediatric kidney transplant patients 5 to 16 years of age who were initiated on mycophenolic acid delayed-release tablets at least 6 months post-transplant. Use of mycophenolic acid delayed-release tablets in this age group is supported by evidence from adequately and well controlled studies of mycophenolic acid delayed-release tablets in a similar population of adult kidney transplant patients with additional pharmacokinetic data in pediatric kidney transplant patients (see Dosage and Administration [2.2, 2.3], Clinical Pharmacology [12.3]). Pediatric doses for patients with BSA < 1.19 m² cannot be accurately administered using currently available formulations of mycophenolic acid delayed-release tablets.

The safety and effectiveness of mycophenolic acid delayed-release tablets in de novo pediatric kidney transplant patients and in pediatric kidney transplant patients below the age of 5 years have not been established.

### 8.5 Geriatric Use

Clinical studies of mycophenolic acid delayed-release tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Of the 372 patients treated with mycophenolic acid delayed-release tablets in the clinical trials, 6 % (n = 21) were 65 years of age and older and 0.3 % (n = 1) were 75 years of age and older. Among these patients, 8% (2) had been treated with mycophenolic acid delayed-release tablets.

### 8.6 Females of Reproductive Potential

#### Pregnancy Exposure Prevention and Planning

Females of reproductive potential must be made aware of the increased risk of first trimester pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning. Females of reproductive potential include girls who have entered puberty and all women who have a uterus and have not passed through menopause. Menopause is the permanent end of menstruation and fertility. Menopause should be medically confirmed by a patient's healthcare practitioner. Some commonly used diagnostic criteria include 1) 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy), or 2) post-surgical sterility from a bilateral oophorectomy.

#### Pregnancy Testing

To prevent unplanned exposure during pregnancy, females of reproductive potential should have a serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL immediately before starting mycophenolic acid delayed-release tablets. Another pregnancy test with the same sensitivity should be done 8 to 10 days later. Repeat pregnancy tests should be performed during routine follow-up visits. Results of all pregnancy tests should be discussed with the patient.

In the event of a positive pregnancy test, females should be counseled with regard to whether the maternal benefits of mycophenolate treatment may outweigh the risks to the fetus in certain situations.

#### Contraception

Females of reproductive potential taking mycophenolic acid delayed-release tablets must receive contraceptive counseling and use acceptable contraception (see Table 5 for Acceptable Contraception Methods). Patients must use acceptable birth control during entire mycophenolic acid delayed-release tablets therapy, and for 6 weeks after stopping mycophenolic acid delayed-release tablets, unless the patient chooses abstinence (she chooses to avoid heterosexual intercourse completely).

Patients should be aware that mycophenolic acid delayed-release tablets reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness [see Patient Counseling Information (17), Drug Interactions (7.8)].

### Table 5. Acceptable Contraception Methods for Females of Reproductive Potential

**Pick from the following birth control options:**

#### Option 1

<table>
<thead>
<tr>
<th>Methods to Use Alone</th>
<th>Intrauterine devices (IUDs)</th>
<th>Tubal sterilization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s partner had a vasectomy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Option 2

<table>
<thead>
<tr>
<th>Choose One Hormone Method</th>
<th>Barrier Methods from each column (must choose two methods)</th>
<th>AND</th>
<th>Barrier Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Contraceptive Pill</td>
<td>Diaphragm with spermicide and contraceptive sponge</td>
<td>Cervical cap with spermicide</td>
<td></td>
</tr>
<tr>
<td>Transdermal Patch</td>
<td>Male condom</td>
<td>Female condom</td>
<td></td>
</tr>
<tr>
<td>Vaginal ring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progesterone-only Injection</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Option 3

<table>
<thead>
<tr>
<th>Choose One Barrier Method</th>
<th>Barrier Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male condom</td>
<td>AND Male condom</td>
</tr>
</tbody>
</table>

**Pregnancy Planning:** For patients who are considering pregnancy, consider alternative immunosuppressants with less potential for embryofetal toxicity. Risks and benefits of mycophenolic acid delayed-release tablets should be discussed with the patient.

### 10 OVERDOSAGE

#### Signs and Symptoms

There have been anecdotal reports of deliberate or accidental overdoses with mycophenolic acid delayed-release tablets, whereas not all patients experienced related adverse reactions.

In those overdose cases in which adverse reactions were reported, the reactions fall within the known safety profile of the class. Accordingly an overdose of mycophenolic acid delayed-release tablets could possibly result in oversuppression of the immune system and may increase the susceptibility to infection including opportunistic infections, fatal infections and sepsis. If blood dyscrasias occur (e.g. neutropenia with absolute neutrophil count < 1.5 x 10⁹/mL or anemia), it may be appropriate to interrupt or discontinue mycophenolic acid delayed-release tablets.

Possible signs and symptoms of acute overdose could include the following: hematological abnormalities such as leukopenia and neutropenia, and gastrointestinal symptoms such as abdominal pain, diarrhea, nausea and vomiting, and dyspepsia.

#### Treatment and Management

General supportive measures and symptomatic treatment should be followed in all cases of overdosage. Although dialysis may be used to remove the inactive metabolite mycophenolic acid glucuronide (MPAG), it would not be expected to remove clinically significant amounts of the active moiety, mycophenolic acid, due to the 98% plasma protein binding of mycophenolic acid. By interfering with enterohpatic circulation of mycophenolic acid, activated charcoal or bile sequestrants, such as cholestyramine, may reduce the systemic mycophenolic acid exposure.

### 11 DESCRIPTION

Mycophenolic acid delayed-release tablets are an enteric formulation of mycophenolate sodium that delivers the active moiety mycophenolic acid (MPA). Mycophenolic acid is an immunosuppressive agent. As the sodium salt, MPA is chemically designated as Sodium 4(E)-6-(4-hydroxy-6-ethyl-7-methyl-3-oxo-1,3-dinhydrobenzozuran-5-y1)-4-methylhex-4-enenate. Its molecular formula is C₂₁H₂₉O₇Na. The molecular weight is 342.32 and the structural formula is:

![Structural formula of mycophenolic acid](image)

Mycophenolic acid, as the sodium salt, is a white to off-white, crystalline powder and is highly soluble in aqueous media at physiological pH and practically insoluble in 0.1 N hydrochloric acid.

Mycophenolic acid is available for oral use as delayed-release tablets containing either 180 mg or 360 mg of mycophenolic acid.

Inactive ingredients include colloidal silicon dioxide, croscarmellose sodium, crospovidone, FD&C Blue No. 2 Aluminum Lake, hypromellose, hypromellose acetate succinate, magnesium
Pharmacokinetics in Renal Transplant Patients: failure, and hypoalbuminemia. The protein binding of mycophenolic acid glucuronide (MPAG) is 82%. The free MPA dose pharmacokinetics. However, in the early post-transplant period, mean MPA AUC and Cmax were 15% and 22% lower in Japanese subjects compared to Caucasians. The respective mean Cmax and AUC of MPA determined in children were higher by 33% and 18%, in the intestine [see Drug Interactions (7.3)].

**Ethnicity:** Following a single dose administration of 720 mg of mycophenolic acid delayed-release tablets to 18 Japanese and 18 Caucasian healthy subjects, the exposure (AUCinf) for MPA and MPAG were 15% and 22% lower in Japanese subjects compared to Caucasians. The peak concentrations (Cmax) for MPAG were similar between the two populations, however, Japanese subjects had 9.6% higher Cmax for MPA. These results do not suggest any clinically relevant differences.

**Drug Interactions:** Antacids with Magnesium and Aluminum Hydroxides: Absorption of a single oral mycophenolic acid delayed-release tablet was decreased when administered to 12 stable kidney transplant patients also taking magnesium-aluminum-containing antacids (30 mL); the mean Cmax and AUC(0-12) values for MPA were 25% and 37% lower, respectively, than when mycophenolic acid delayed-release tablets was administered alone under fasting conditions [see Drug Interactions (7.1)].

**Pentobarbital:** In a trial conducted in 12 healthy volunteers, the pharmacokinetics of MPA were observed to be similar when a single dose of 720 mg of mycophenolic acid delayed-release tablets was administered alone and following concomitant administration of mycophenolic acid delayed-release tablets and pentobarbital, which was administered at a dose of 40 mg twice daily for 4 days [see Drug Interactions (7.1)].

The following drug interaction studies were conducted following the administration of MMF: Cholestyramine: Following single-dose oral administration of 1.5 grams MMF to 12 healthy volunteers pretreated with 4 grams 3 times daily of cholestyramine for 4 days, MPA AUC decreased approximately 40%. This decrease is consistent with interruption of enterohepatic recirculation which may be the binding of recirculating MMF with cholestyramine in the intestine [see Drug Interactions (7.3)].

**Sevelamer:** Concomitant administration of sevelamer and MMF in stable adult and pediatric

**Table 6: Mean ± SD Pharmacokinetic Parameters for MPA Following the Oral Administration of Mycophenolic Acid Delayed-release Tablets to Renal Transplant Patients on Cyclosporine, USP MODIFIED Based Immunosuppression**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mycophenolic Acid Dose</th>
<th>n</th>
<th>Dose (mg)</th>
<th>Tmax (hr)</th>
<th>Cmax (mcg/mL)</th>
<th>AUCinf (mcg*hr/mL)</th>
<th>AUC0-12 (mcg*hr/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>Single</td>
<td>24</td>
<td>720</td>
<td>2 (0.8 to 3)</td>
<td>26.1 ± 12</td>
<td>66.5 ± 22.6*</td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>Multiple x 6 days, twice daily</td>
<td>10</td>
<td>720</td>
<td>2 (1.5 to 3)</td>
<td>37 ± 13.3</td>
<td>67.9 ± 20.3</td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>Multiple x 28 days, twice daily</td>
<td>26</td>
<td>720</td>
<td>2 (1.5 to 8)</td>
<td>31.2 ± 18.1</td>
<td>71.2 ± 26.3</td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>Chronic, multiple dose, twice daily</td>
<td>18</td>
<td>720</td>
<td>1.5 (6 to 10)</td>
<td>18.3 ± 7.9</td>
<td>57.4 ± 15</td>
<td></td>
</tr>
</tbody>
</table>

* median (range), ** AUC0-12, *** age range of 5 to 16 years
kidney transplant patients decreased the mean MPA C\text{max} and AUC\text{(0-12h)} by 36% and 26% respectively [see Drug Interactions (7.4)].

Cyclosporine: Cyclosporine (Sandimmune\textsuperscript{®}) pharmacokinetics (at doses of 75 to 415 mg/day) were unchanged by single- or multiple-dose of 1.5 g/myd for 7 or at least 14 days. Approximately 50% reductions in cyclosporine concentrations were seen in 48 hours post-transplant for 12 months in combination with cyclosporine, USP MODIFIED and corticosteroids. The genotoxic potential of mycophenolate sodium was determined in five assays. Mycophenolate sodium was genotoxic in the mouse lymphoma/lymphid kinase assay, the micronucleus test in V79 Chinese hamster cells, and the in vivo mouse micronucleus assay. Mycophenolate sodium was not genotoxic in the bacterial mutation assay (Salmonella typhimurium 18 1535, 97a, 98, 100, and 102) or the chromosomal aberration assay in human lymphocytes. Mycophenolate moftel generated similar genotoxic activity. The genotoxic activity of mycophenolic acid (MPA) is probably due to the depletion of the nucleotide pool required for DNA synthesis as a result of the pharmacodynamic mode of action of MPA (inhibition of nucleotide synthesis).

Mycophenolate sodium had no effect on male rat fertility at daily oral doses as high as 18 mg per kg and exhibited no testicular or spermatogenic effects at daily oral doses of 20 mg per kg for 13 weeks (approximately 2 times the systemic exposure of MPA at the recommended therapeutic dose). No effects on female fertility were seen up to a daily dose of 20 mg per kg (approximately 3 times the systemic exposure of MPA at the recommended therapeutic dose).

14 CLINICAL STUDIES

14.1 Prophylaxis of Organ Rejection in Patients Receiving Allogeneic Renal Transplantation

The safety and efficacy of mycophenolic acid delayed-release tablets in combination with cyclosporine, USP MODIFIED and corticosteroids for the prevention of organ rejection was assessed in two multicenter, randomized, double-blind active-controlled trials in de novo and conversion renal transplant patients compared to MMF.

The de novo trial was conducted in 423 renal transplant patients (ages 18 to 75 years) in Austria, Canada, Germany, Hungary, Italy, Norway, Spain, UK, and USA. Eighty-four percent of randomized patients received kidneys from deceased donors. Patients were excluded if they had second or multi-organ (e.g., kidney and pancreas) transplants, or previous transplant with any other organs; kidneys from non-heart beating donors; panel reactive antibodies (PRA) of > 50% at last assessment prior to transplantation, and presence of severe diabetes, active peptic ulcer disease, or uncontrolled diabetes mellitus. Patients were administered either mycophenolic acid delayed-release tablets 1.44 g/myd per day or MPA 750 mg/day with in 48 hours post-transplant for 12 months in combination with cyclosporine, USP MODIFIED and corticosteroids. Forty-one percent of patients received antibody therapy as induction treatment. Treatment failure was defined as the first occurrence of biopsy proven acute rejection, graft loss, death or loss to follow-up at 6 months.

The incidence of treatment failure was similar in mycophenolic acid delayed-release tablets - and MMF-treated patients at 6 and 12 months (Table 7). The cumulative incidence of graft loss, death and lost to follow-up at 12 months is also shown in Table 7.

## Table 7: Treatment Failure in de novo Renal Transplant Patients (Percent of Patients) at 6 and 12 Months of Treatment When Administered in Combination with Cyclosporine\textsuperscript{a} and Corticosteroids

<table>
<thead>
<tr>
<th></th>
<th>Mycophenolic Acid</th>
<th>Mycophenolate Mofetil (MMF)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.44 grams per day</td>
<td>2 grams per day</td>
</tr>
<tr>
<td>n = 213</td>
<td>n = 210</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment failure*</td>
<td>55 (25.8)</td>
<td>55 (26.2)</td>
</tr>
<tr>
<td>Biopsy-proven acute rejection</td>
<td>46 (21.6)</td>
<td>48 (22.9)</td>
</tr>
<tr>
<td>Graft loss</td>
<td>7 (3.3)</td>
<td>9 (4.3)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.5)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Lost to follow-up**</td>
<td>3 (1.4)</td>
<td>0</td>
</tr>
<tr>
<td>12 Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment failure*</td>
<td>61 (28.6)</td>
<td>59 (28.1)</td>
</tr>
<tr>
<td>Biopsy-proven acute rejection</td>
<td>48 (22.5)</td>
<td>51 (24.3)</td>
</tr>
<tr>
<td>Graft loss</td>
<td>9 (4.2)</td>
<td>9 (4.3)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (0.9)</td>
<td>5 (2.4)</td>
</tr>
<tr>
<td>Lost to follow-up**</td>
<td>5 (2.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

\* USP MODIFIED
** Lost to follow-up indicates patients who were lost to follow-up without prior biopsy-proven acute rejection, graft loss or death
*** Treatment failure indicates patients who were lost to follow-up without prior graft loss or death (nine mycophenolic acid patients and four MMF patients) [95% confidence interval of the difference in treatment failure at 6 months (mycophenolic acid – MMF) is (-8.7%, 8%)].

The genotoxic potential of mycophenolate sodium was determined in five assays. Mycophenolate sodium was genotoxic in the mouse lymphoma/lymphid kinase assay, the micronucleus test in V79 Chinese hamster cells, and the in vivo mouse micronucleus assay. Mycophenolate sodium was not genotoxic in the bacterial mutation assay (Salmonella typhimurium 18 1535, 97a, 98, 100, and 102) or the chromosomal aberration assay in human lymphocytes. Mycophenolate moftel generated similar genotoxic activity. The genotoxic activity of mycophenolic acid (MPA) is probably due to the depletion of the nucleotide pool required for DNA synthesis as a result of the pharmacodynamic mode of action of MPA (inhibition of nucleotide synthesis).

Mycophenolate sodium had no effect on male rat fertility at daily oral doses as high as 18 mg per kg and exhibited no testicular or spermatogenic effects at daily oral doses of 20 mg per kg for 13 weeks (approximately 2 times the systemic exposure of MPA at the recommended therapeutic dose). No effects on female fertility were seen up to a daily dose of 20 mg per kg (approximately 3 times the systemic exposure of MPA at the recommended therapeutic dose).
or without corticosteroids for at least 2 weeks prior to entry in the trial. Patients were ran-
domized to mycophenolic acid delayed-release tablets 1.44 grams per day or MMF 2 grams per
day for 12 months. The trial was conducted in Austria, Belgium, Canada, Germany, Italy, Spain,
and USA. Treatment failure was defined as the first occurrence of biopsy-proven acute
rejection, graft loss, death, or lost to follow-up at 6 and 12 months.

The incidences of treatment failure at 6 and 12 months were similar between mycophenolic
acid delayed-release tablets- and MMF-treated patients (Table 8). The cumulative incidence
of graft loss, death and lost to follow-up at 12 months is also shown in Table 8.

**Lost to follow-up** indicates patients who were lost to follow-up without prior biopsy-proven acute rejec-
tion, graft loss, or death

**Lost to follow-up indicates patients who were lost to follow-up without prior graft loss or death (eight
mycophenolic acid patients and 12 MMF patients)**

<table>
<thead>
<tr>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure#</td>
<td>7 (4.4)</td>
</tr>
<tr>
<td>Biopsy-proven acute rejection</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Graft loss</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Lost to follow-up*</td>
<td>5 (3.1)</td>
</tr>
<tr>
<td>Graft loss or death or lost to follow-up***</td>
<td>10 (6.3)</td>
</tr>
<tr>
<td>Treatment Failure##</td>
<td>12 (7.5)</td>
</tr>
<tr>
<td>Biopsy-proven acute rejection</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Graft loss</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Lost to follow-up**</td>
<td>8 (5)</td>
</tr>
</tbody>
</table>

### HOW SUPPLIED/STORAGE AND HANDLING

Mycophenolic Acid Delayed-release Tablets are available containing mycophenolate sodium equivalent to 180 mg or 360 mg of mycophenolic acid.

The 180 mg tablets are sage green film-coated, round tablets with M over MC1 imprinted in
black ink on one side of the tablet and blank on the other side. They are available as follows:

- **NDC 0378-4201-78** bottles of 240 tablets
- **NDC 0378-4201-24** bottles of 240 tablets

The 360 mg tablets are reddish-orange, film-coated, modified capsule-shaped tablets with M
MC2 imprinted in black ink on one side of the tablet and blank on the other side. They are available as follows:

- **NDC 0378-4202-78** bottles of 120 tablets
- **NDC 0378-4202-24** bottles of 240 tablets

### Storage: Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]Pro-
tect from moisture.

Dispense in a tight, light resistant container as defined in the USP using a child-resistant clo-
sure.

### Handling: Keep out of reach and sight of children. Mycophenolic acid delayed-release tablets
should not be crushed or cut in order to maintain the integrity of the enteric coating [See Dosage and Administration (2.3.1)].

### Teratogenic effects have been observed with mycophenolate sodium [see Warnings and Pre-
cautions (5.1)]. If for any reason, the mycophenolic acid delayed-release tablets must be
chewed, avoid inhalation of the powder, or direct contact of the powder, with skin or mucous
membranes.

### PHARMACIST: Dispense a Medication Guide with each prescription.

### MEDICATION GUIDE

**MYCOPHENOLIC ACID® DELAYED-RELEASE TABLETS**

<table>
<thead>
<tr>
<th>(mye koe fe nole' ik as' id)</th>
</tr>
</thead>
<tbody>
<tr>
<td>180 mg and 360 mg</td>
</tr>
</tbody>
</table>

*as mycophenolate sodium

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Read the Medication Guide that comes with mycophenolic acid delayed-release tablets before you start taking it and each time you get a refill. There may be new information. This Medica-
tion Guide does not take the place of talking with your healthcare provider about your medical
condition or treatment. If you have any questions about mycophenolic acid delayed-release tablets, ask your doctor.

### What is the most important information I should know about mycophenolic acid delayed-
release tablets? Mycophenolic acid delayed-release tablets can cause serious side effects
including:

- Increased risk of loss of pregnancy (miscarriage) and higher risk of birth defects.

Females who take mycophenolic acid delayed-release tablets during pregnancy, have a higher
risk of miscarriage during the first 3 months (first trimester), and a higher risk that
their baby will be born with birth defects.

If you are a female who can become pregnant:

- your doctor must talk with you about acceptable birth control methods (contraceptive counseling) while taking mycophenolic acid delayed-release tablets.
- you should have a pregnancy test immediately before starting mycophenolic acid delayed-
release tablets and another pregnancy test 8 to 10 days later. Pregnancy tests should be
repeated during routine follow-up visits with your doctor. Talk to your doctor about the
results of all of your pregnancy tests.
Mycophenolic acid delayed-release tablets are used with other medicines containing (antirejection medicine) in people who have received a kidney transplant. Rejection is Mycophenolic acid delayed-release tablets are a prescription medicine given to prevent rejection. See the section "What are the possible side effects of mycophenolic acid delayed-release tablets?"

- Increased risk of getting serious infections. Mycophenolic acid delayed-release tablets weakens the body’s immune system and affects your ability to fight infections. Serious infections can happen with mycophenolic acid delayed-release tablets and can lead to death. These serious infections can include:
  - Viral infections. Certain viruses can live in your body and cause active infections when your immune system is weak. Viral infections that can happen with mycophenolic acid delayed-release tablets include:
    - Shingles, other herpes infections, and cytomegalovirus (CMV). CMV can cause serious tissue and blood infections.
    - BK virus. BK virus can affect how your kidney works and cause your transplanted kidney to fail.
    - Hepatitis B and C viruses. Hepatitis viruses can affect how your liver works. Talk to your doctor about how hepatitis viruses may affect you.
  - A brain infection called Progressive Multifocal Leukoencephalopathy (PML). In some patients mycophenolic acid delayed-release tablets may cause an infection of the brain that may cause death. You are at risk for this brain infection because you have a weakened immune system. You should tell your healthcare provider right away if you have any of the following symptoms:
    - Weakness on one side of the body
    - You do not care about things that you usually care about (apathy)
    - You are confused or have problems thinking
    - You cannot control your muscles
  - Fungal infections. Yeast and other types of fungal infections can happen with mycophenolic acid delayed-release tablets and cause serious tissue and blood infections. See “What are the possible side effects of mycophenolic acid delayed-release tablets?”

Call your doctor right away if you have any of these signs and symptoms of infection:
- Temperature of 100.3°F or greater
- Cold symptoms, such as a runny nose or sore throat
- Flu symptoms, such as an upset stomach, stomach pain, vomiting, or diarrhea
- Earache or headache
- Pain during urination or you need to urinate often
- White patches in the mouth or throat
- Unexpected bruising or bleeding
- Cuts, scrapes, or incisions that are red, warm, and oozing pus
- Increased risk of getting certain cancers. People who take mycophenolic acid delayed-release tablets have a higher risk of getting lymphoma, and other cancers, especially skin cancer. Tell your doctor if you have:
  - unexplained fever, tiredness that does not go away, weight loss, or lymph node swelling
  - a brown or black skin lesion with uneven borders, or one part of the lesion does not look like other parts
  - a change in the size or color of a mole
  - a new skin lesion or bump
  - any other changes to your health

See the section “What are the possible side effects of mycophenolic acid delayed-release tablets?” for other serious side effects.

Who should not take mycophenolic acid delayed-release tablets?
Do not take mycophenolic acid delayed-release tablets if you are allergic to mycophenolic acid, mycophenolate sodium, mycophenolate mofetil, or any of the ingredients in mycophenolic acid delayed-release tablets. See the end of this Medication Guide for a complete list of ingredients in mycophenolic acid delayed-release tablets.

What should I tell my doctor before I start taking mycophenolic acid delayed-release tablets?
Tell your healthcare provider about all of your medical conditions, including if you:
- have any digestive problems, such as ulcers
- plan to receive any vaccines. You should not receive live vaccines while you take mycophenolic acid delayed-release tablets. Some vaccines may not work as well during treatment with mycophenolic acid delayed-release tablets.
- have Lesch-Nyhan syndrome or another rare inherited deficiency of hypoxanthine-guanine phosphoribosyltransferase (HGPRT). You should not take mycophenolic acid delayed-release tablets if you have one of these disorders.
- are pregnant or planning to become pregnant. See “What is the most important information I should know about mycophenolic acid delayed-release tablets?”
- are breast-feeding or plan to breast-feed. It is not known if mycophenolic acid passes into breast milk. You and your doctor will decide if you will take mycophenolic acid delayed-release tablets or breast-feed.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements.
Some medicines may affect the way mycophenolic acid delayed-release tablets work and mycophenolic acid delayed-release tablets may affect how some medicines work. Especially tell your doctor if you take:
- birth control pills (oral contraceptives). See “What is the most important information I should know about mycophenolic acid delayed-release tablets?”
- antacids that contain aluminum or magnesium. Mycophenolic acid delayed-release tablets and antacids should not be taken at the same time.
- alogliptin (Zanaflex®), Ganciclovir (Cytovene® W, Valcyte®)
- azathioprine (Azasan®, Imuran®)
- chloroquine (Quastra® Light, Questar®, Locholest Light, Prevalite®)

Know the medicines you take. Keep a list of your medicines with you to show your healthcare provider and pharmacist when you get a new medicine. Do not take any new medicine without talking to your doctor.

How should I take mycophenolic acid delayed-release tablets?
- Take mycophenolic acid delayed-release tablets exactly as prescribed. Your healthcare provider will tell you how much mycophenolic acid to take.
- Do not stop taking or change your dose of mycophenolic acid delayed-release tablets without talking to your healthcare provider.
- Take mycophenolic acid delayed-release tablets on an empty stomach, either one hour before or 2 hours after a meal.
- Swallow mycophenolic acid delayed-release tablets whole. Do not crush, chew, or cut mycophenolic acid delayed-release tablets. The mycophenolic acid delayed-release tablets have a coating so that the medicine will pass through your stomach and dissolve in your intestine.
- If you forget to take mycophenolic acid delayed-release tablets, take it as soon as you remember and then take your next dose at its regular time. If it is almost time for your next dose, skip the missed dose. Do not take two doses at the same time. Call your doctor or pharmacist if you are not sure what to do.
- If you take more than the prescribed dose of mycophenolic acid delayed-release tablets, call your doctor right away.
- Do not change (substitute) between using mycophenolic acid delayed-release tablets and mycophenolate mobilti tablets, capsules, or oral suspension for one another unless your healthcare provider tells you to. These medicines are absorbed differently. This may affect the amount of medicine in your blood.
- Be sure to keep all appointments at your transplant clinic. During these visits, your doctor may perform regular blood tests.

What should I avoid while taking mycophenolic acid delayed-release tablets?
Avoid pregnancy. See “What is the most important information I should know about mycophenolic acid delayed-release tablets?”
- Limit the amount of time you spend in sunlight. Avoid using tanning beds and sunlamps. People who take mycophenolic acid delayed-release tablets have a higher risk of getting skin cancer. See “What is the most important information I should know about mycophenolic acid delayed-release tablets?” Wear protective clothing when you are in the sun and use a sunscreen with a high sun protection factor (SPF 30 and above). This is especially important if your skin is fair (light colored) or you have a family history of skin cancer.
- Elderly patients 65 years of age or older may have more side effects with mycophenolic acid delayed-release tablets because of a weaker immune system.

What are the possible side effects of mycophenolic acid delayed-release tablets?
Mycophenolic acid delayed-release tablets can cause serious side effects. See “What is the most important information I should know about mycophenolic acid delayed-release tablets?”

Stomach and intestinal bleeding can happen in people who take mycophenolic acid delayed-release tablets. Bleeding can be severe and you may have to be hospitalized for treatment.
The most common side effects of taking mycophenolic acid delayed-release tablets include:

- low blood cell counts
- red blood cells
- white blood cells
- platelets
- constipation
- nausea
- vomiting
- urinary tract infections
- stomach upset

In people with a new transplant:
- low blood cell counts
- red blood cells
- white blood cells
- platelets
- constipation
- nausea
- vomiting
- urinary tract infections
- stomach upset

In people who take mycophenolic acid delayed-release tablets for a long time (long-term) after transplant:
- low blood cell counts
- red blood cells
- white blood cells
- constipation
- nausea
- vomiting
- urination

Your healthcare provider will do blood tests before you start taking mycophenolic acid delayed-release tablets and during treatment with mycophenolic acid delayed-release tablets to check your blood cell counts. Tell your healthcare provider right away if you have any signs of infection (see “What is the most important information I should know about mycophenolic acid delayed-release tablets?”), or any unexpected bruising or bleeding. Also, tell your healthcare provider if you have unusual tiredness, dizziness, or fainting.

These are not all the possible side effects of mycophenolic acid delayed-release tablets. Your healthcare provider may be able to help you manage these side effects.

Call your doctor for medical advice about side effects.

You may report side effects to
- FDA MedWatch at 1-800-FDA-1088 or
- Mylan Pharmaceutical Inc. at 1-877-446-3679 (1-877-4-INFO-RX)

How should I store mycophenolic acid delayed-release tablets?
- Store mycophenolic acid delayed-release tablets at room temperature, 20º to 25ºC (68º to 77ºF). Mycophenolic acid delayed-release tablets do not need to be refrigerated.
- Keep the container tightly closed. Store mycophenolic acid delayed-release tablets in a dry place.
- Keep mycophenolic acid delayed-release tablets and all medicines out of the reach of children.

General information about mycophenolic acid delayed-release tablets
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use mycophenolic acid delayed-release tablets for a condition for which it was not prescribed. Do not give mycophenolic acid delayed-release tablets to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about mycophenolic acid delayed-release tablets. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about mycophenolic acid delayed-release tablets that is written for healthcare professionals. You can also call Mylan Pharmaceuticals Inc. at 1-877-446-3679 (1-877-4-INFO-RX).

What are the ingredients in mycophenolic acid delayed-release tablets?
**Active ingredient:** mycophenolic acid (as mycophenolate sodium)

**Inactive ingredients:** colloidal silicon dioxide, croscarmellose sodium, crospovidone, FD&C Blue No. 2 Aluminum Lake, hypromellose, hypromellose acetate succinate, magnesium stearate, maltodextrin, microcrystalline cellulose, polyethylene glycol, polyvinyl alcohol, pregelatinized starch (corn), propylene glycol, sodium lauryl sulfate, talc, titanium dioxide and triethyl citrate. In addition, the 180 mg strength contains yellow iron oxide and the 360 mg strength contains FD&C Red No. 40 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake.

The black imprinting ink contains the following: black iron oxide, hypromellose and propylene glycol.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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