For the use of Registered Medical Practitioner only

1. GENERIC NAME AND BRAND NAME

Mycophenolic Acid Delayed-Release Tablets USP 180 mg
Renfor® 180

Mycophenolic Acid Delayed-Release Tablets USP 360 mg
Renfor®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Renfor® 180 mg
Each Delayed-Release tablet contains:
Mycophenolate Sodium USP
Equivalent to Mycophenolic Acid 180mg
Colour: Titanium Dioxide IP

Renfor®
Each Delayed-Release tablet contains:
Mycophenolate Sodium USP
Equivalent to Mycophenolic Acid 360mg
Colours: Red Oxide of Iron, Yellow Oxide of Iron & Titanium Dioxide IP

3. DOSAGE FORM AND STRENGTH

Refer section 1 & 2

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATION

For the prophylaxis of acute organ rejection and for the treatment of refractory organ rejection in patients receiving allogeneic renal transplants increased graft and patient's survival receiving allogeneic cardiac transplants and used concomitantly with cyclosporine and cortico-steroids.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Dosage in Adult Kidney Transplant Patients
The recommended dose of Mycophenolate sodium is 720 mg administered twice daily (1440 mg total daily dose).

Dosage in Pediatric Kidney Transplant Patients
The recommended dose of Mycophenolate sodium in conversion (at least 6 months post-transplant) pediatric patients age 5 years and older is 400 mg/m2 by mouth administered twice daily (up to a maximum dose of 720 mg administered twice daily).

METHOD OF ADMINISTRATION
To be taken 1 or 2 hours after food intake. Mycophenolate sodium tablets should be taken on an empty stomach.

Prior to ingesting Mycophenolate sodium tablets should not be chewed, crushed, or cut. In order to maintain the integrity of the enteric coating, the tablets should be swallowed whole.
Patients with a BSA of >1.58 m2 may be dosed either with four Mycophenolate sodium 180 mg tablets, or two Mycophenolate sodium 360 mg tablets twice daily (1440 mg daily dose).

Patients with a BSA of 1.19 to 1.58 m2 may be dosed either with three Mycophenolate sodium 180 mg tablets, or one 180 mg tablet plus one 360 mg tablet twice daily (1080 mg daily dose). Pediatric doses for patients with BSA <1.19 m2 cannot be accurately administered using currently available formulations of Mycophenolate sodium tablets.

4.3 CONTRAINDICATIONS

Hypersensitivity Reactions

In patients with a hypersensitivity to mycophenolic acid, mycophenolate sodium, mycophenolate mofetil, or to any of its excipients, Mycophenolate sodium is contraindicated. Reactions like rash, hypotension, pruritus, and chest pain have been observed in clinical trials and post marketing reports.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Pregnancy Exposure Prevention and Planning

Females of reproductive potential must be aware of the increased risk of congenital malformations and first trimester pregnancy loss and must be counseled regarding pregnancy planning and prevention.

Embryo fetal Toxicity

Use of Mycophenolate sodium 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, esophagus, heart, and kidney.

Lymphoma and Other Malignancies

Patients receiving immune suppressants, including Mycophenolate sodium, are at increased risk of developing lymphomas and other malignancies, particularly of the skin. The risk appears to be related to the duration and intensity of immune suppression rather than to the use of any specific agent.

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

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

Management of Immunosuppression

Mycophenolate sodium should be prescribed only by physicians experienced in immunosuppressive therapy and management of organ transplant patients. Patients receiving the drug should be managed in facilities staffed and equipped with adequate laboratory and supportive medical resources. The physicians responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.

Serious Infections

Patients receiving immunosuppressants, including Mycophenolate sodium, are at increased risk of developing bacterial, fungal, viral, and protozoal infections, and new or reactivated viral infections including opportunistic infections.

Combination immunosuppressant therapy should be used with caution; these infections may lead to serious, including fatal outcomes. Because of the danger of over suppression of the immune system which can increase susceptibility to infection.

New or Reactivated Viral Infections
Polyomavirus associated nephropathy (PVAN), JC virus associated progressive multifocal leukoencephalopathy (PML), reactivation of hepatitis B (HBV) or hepatitis C (HCV), cytomegalovirus (CMV) infections have been reported in patients treated with immunosuppressants, including the mycophenolic acid (MPA) derivatives Mycophenolate sodium 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.

Among transplant recipients seronegative for CMV at time of transplant who receives a graft from a CMV seropositive donor, the risk of CMV viremia and CMV disease is highest. Therapeutic approaches to limiting CMV disease exist and should be routinely provided.

Patient monitoring may help detect patients at risk for CMV disease.
PML, which is sometimes fatal, commonly presents with hemiparesis, confusion, cognitive deficiencies, apathy, and ataxia. Risk factors for PML include treatment with immunosuppressant therapies and impairment of immune function. In immune suppressed 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.
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.

Serious GI Tract Complications
Gastrointestinal bleeding (requiring hospitalization), intestinal perforations, gastric ulcers, and duodenal ulcers have been reported in patients treated with Mycophenolate sodium. Mycophenolate sodium should be administered with caution in patients with active serious digestive system disease.

Blood Dyscrasias Including Pure Red Cell Aplasia
In patients treated with MPA derivatives in combination with other immunosuppressive agents, cases of pure red cell aplasia (PRCA) have been reported. 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. With dose reduction or cessation of therapy with MPA derivatives, in some cases PRCA was found to be reversible. In transplant patients, however, reduced immune suppression may place the graft at risk. Changes to Mycophenolate sodium therapy should only be undertaken under appropriate supervision in transplant recipients in order to minimize the risk of graft rejection. Patients receiving Mycophenolate sodium should be monitored for blood dyscrasias (e.g., neutropenia or anemia). The development of neutropenia may be related to Mycophenolate sodium itself, concomitant medications, viral infections, or some combination of these reactions. During the first month, complete blood count should be performed weekly, for the second twice monthly and the third month of treatment, then monthly through the first year. If blood dyscrasias occur [neutropenia develops (ANC <1.3 × 103/mcL) or anemia], dosing with Mycophenolate sodium

should be interrupted or the dose reduced, appropriate tests performed, and the patient managed accordingly.

Immunizations
During treatment with Mycophenolate sodium, the use of live attenuated vaccines should be avoided; examples include (but not limited to) the following: measles, intranasal influenza, mumps, oral polio, BCG, rubella, yellow fever, varicella, and TY21a typhoid vaccines.

Rare Hereditary Deficiencies
Mycophenolate sodium is an inosine monophosphate dehydrogenase inhibitor (IMPDH Inhibitor). In patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Leschnyhan and Kelley-Seegmiller syndromes, Mycophenolate sodium should be avoided 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, nephrolithiasis, tophi or urolithiasis and renal disease including renal failure.

4.5 DRUG INTERACTIONS

No	Drug	Drug interaction	Remark
1.	Azathioprine	Given that azathioprine and MMF inhibit purine metabolism	It is recommended that Mycophenolate sodium not be administered concomitantly with azathioprine or MMF.
2.	Antacids with Magnesium and Aluminum Hydroxides	Concomitant use of Mycophenolate sodium and antacids decreased plasma concentrations of mycophenolic acid (MPA).	It is recommended that Mycophenolate sodium and antacids not be administered simultaneously.
3.	Acyclovir (Valacyclovir), Ganciclovir (Valganciclovir), and Other Drugs that Undergo Renal Tubular Secretion	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 also increased in the presence of renal impairment.	Acyclovir/valacyclovir/ganciclovir/ valganciclovir may be taken with Mycophenolate sodium; however, during the period of treatment, physicians should monitor blood cell counts`.
4.	Cholestyramine, Bile Acid Sequestrates, Oral Activated Charcoal and Other Drugs that Interfere with Enterohepatic Recirculation	Drugs that interrupt enterohepatic recirculation may decrease MPA plasma concentrations when coadministered with MMF.	do not administer Mycophenolate sodium with cholestyramine or other agents that may interfere with enterohepatic recirculation or drugs that may bind bile acids, e.g., bile acid sequestrates or

			oral activated charcoal, because of the potential to reduce the efficacy of Mycophenolate sodium.
5.	Cyclosporine	Cyclosporine inhibits the enterohepatic recirculation of MPA, and therefore, MPA plasma concentrations may be decreased when Mycophenolate sodium is coadministered with cyclosporine.	Clinicians should be aware that there is also a potential change of MPA plasma concentrations after switching from cyclosporine to other immunosuppressive drugs or from other immunosuppressive drugs to cyclosporine in patients concomitantly receiving Mycophenolate sodium
6.	Sevelamer	Concomitant administration of sevelamer and MMF may decrease MPA plasma concentrations.	Sevelamer and other calcium free phosphate binders should not be administered simultaneously with Mycophenolate sodium.
7.	Rifampin	The concomitant administration of MMF and rifampin may decrease MPA plasma concentrations.	Mycophenolate sodium is not recommended to be given with rifampin concomitantly unless the benefit outweighs the risk
8.	Norfloxacin and Metronidazole	MPA plasma concentrations may be decreased when MMF is administrated with norfloxacin and metronidazole. Therefore, Mycophenolate sodium is not recommended to be given with the combination of norfloxacin and metronidazole.	Although there will be no effect on MPA plasma concentrations when Mycophenolate sodium is concomitantly administered with norfloxacin or metronidazole when given separately
9.	Ciprofloxacin, Amoxicillin plus Clavulanic Acid and Other Drugs that Alter the Gastrointestinal Flora	Drugs that alter the gastrointestinal flora such as ciprofloxacin or amoxicillin plus clavulanic acid may interact with MMF by disrupting enterohepatic recirculation. Interference of MPAG hydrolysis may lead to less MPA available for absorption when Mycophenolate sodium is concomitantly administered with ciprofloxacin or amoxicillin plus clavulanic acid.	The clinical relevance of this interaction is unclear; however, no dose adjustment of Mycophenolate sodium is needed when coadministered with these drugs.

10.	Hormonal Contraceptives	In a drug interaction study, mean levonorgestrel AUC was decreased by 15% when coadministered with MMF. Mycophenolate sodium may not have any influence on the ovulation-suppressing action of oral contraceptives	It is recommended to coadminister Mycophenolate sodium with hormonal contraceptives (e.g., birth control pill, transdermal patch, vaginal ring, injection, and implant) with caution, and additional barrier contraceptive methods must be used.
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 Mycophenolate sodium	

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

Pregnancy

Pregnancy Category D

The healthcare practitioner should report the pregnancy to the Mycophenolate, pregnancy Registry For those females using Mycophenolate sodium at any time during pregnancy and those becoming pregnant within 6 weeks of discontinuing therapy. 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 Mycophenolate sodium 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, esophagus, heart, and kidney.

Risks and benefits of Mycophenolate sodium should be discussed with the patient. Consider alternative immune suppressants with less potential for embryofetal toxicity, when appropriate. In certain situations, the patient and her healthcare practitioner may decide that the maternal benefits outweigh the risks to the fetus. The patient should be apprised of the potential hazard to the fetus, if this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug.

Nursing Mothers

Whether MPA is excreted in human milk, it is not known. A decision should be made whether to discontinue nursing or discontinue the drug, because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Mycophenolate sodium, considering the importance of the drug to the mother.

Females of Reproductive Potential Pregnancy Exposure Prevention and Planning

Awareness of the increased risk of first trimester pregnancy loss and congenital malformations and must be counselled regarding pregnancy prevention and planning must be made in females of reproductive potential.
Females of reproductive potential include all women who have a uterus and have not passed through menopause and girls who have entered puberty and. Menopause are the permanent end of menstruation and fertility. By a patient's healthcare practitioner, menopause should be clinically confirmed. Some commonly used diagnostic criteria include

1. 12 months of spontaneous amenorrhea (not amenorrhea induced by a medical condition or medical therapy), or
2. Postsurgical from a bilateral oophorectomy.

Pregnancy Testing
To prevent unplanned exposure during pregnancy, immediately before starting Mycophenolate sodium females of reproductive potential should have a urine or serum pregnancy test with a sensitivity of at least 25 mIU/mL. With the same sensitivity another pregnancy test should be done 8 to 10 days later. During routine follow-up visits repeat pregnancy tests should be performed. With the patient, results of all pregnancy tests should be discussed.
In the event of a positive pregnancy test, with regard to whether the maternal benefits of mycophenolate treatment may outweigh the risks to the fetus in certain situations, females should be counseled.

Contraception
Females of reproductive potential must receive contraceptive counseling and use acceptable contraception who are taking Mycophenolate sodium. During entire Mycophenolate sodium therapy, patients must use acceptable birth control, and for 6 weeks after stopping Mycophenolate sodium, unless the patient chooses abstinence (she chooses to avoid heterosexual intercourse completely).
Patients should be aware that Mycophenolate sodium reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness.

Pregnancy Planning
Consider alternative immune suppressants with less potential for embryofetal toxicity, for patients who are considering pregnancy. With the patient risks and benefits of Mycophenolate sodium should be discussed.

Geriatrics
Clinical studies of Mycophenolate sodium 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 Mycophenolate sodium 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. In responses between the elderly and younger patients, other reported clinical experience has not identified differences. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased renal, hepatic, or cardiac function, and of concomitant disease or other drug therapy.

Pediatrics
In pediatric kidney transplant patients 5 to 16 years of age who were initiated on Mycophenolate sodium at least 6 months post-transplant, the effectiveness and safety of Mycophenolate sodium have been established. In this age group, use of Mycophenolate sodium is supported by evidence from adequate and well-controlled studies of Mycophenolate sodium

in a similar population of adult kidney transplant patients with additional pharmacokinetic data in pediatric kidney transplant patients. Pediatric doses for patients with BSA <1.19 m2 cannot be accurately administered using currently available formulations of Mycophenolate sodium tablets.

The effectiveness and safety of Mycophenolate sodium in de novo pediatric kidney transplant patients and in pediatric kidney transplant patients below the age of 5 years have not been established.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Mycophenolate Mofetil has a moderate influence on the ability to drive and use machines. Mycophenolate Mofetil may cause somnolence, confusion, dizziness, tremor or hypotension and therefore patients are advised to use caution when driving or using machines.

4.8 UNDESIRABLE EFFECTS

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

- Blood Dyscrasias Including Pure Red Cell Aplasia
- Serious GI Tract Complications
- Embryofetal Toxicity
- Serious Infections
- Lymphomas and Other Malignancies
- New or Reactivated Viral Infections
- Rare Hereditary Deficiencies

Post-marketing Experience

During post-approval use of Mycophenolate sodium or other MPA derivatives, the following adverse reactions have been identified. It is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure, because these reactions are reported voluntarily from a population of uncertain size.

- Following exposure to MMF during pregnancy, congenital malformations and an increased incidence of first trimester pregnancy loss have been reported.
- Infections
    - Cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal.
    - Polyomavirus associated nephropathy (PVAN), especially due to BK virus infection, associated with serious outcomes, including deteriorating renal function and renal graft loss.
    - In patients infected with HBV or HCV, viral reactivation.
- In patients treated with MPA derivatives in combination with other immunosuppressive agents, cases of pure red cell aplasia (PRCA) have been reported.

The following additional adverse reactions have been identified during post approval use of Mycophenolate sodium: asthenia, agranulocytosis, osteomyelitis, lymphopenia, wheezing, dry mouth, lymphadenopathy, gastritis, anorexia, alopecia, peritonitis, Kaposi's sarcoma, pulmonary edema.

4.9 OVERDOSE

Signs and Symptoms

With Mycophenolate sodium, there have been anecdotal reports of deliberate or accidental overdoses, whereas not all patients experienced related adverse reactions. The reactions fall

within the known safety profile of the class in those overdose cases in which adverse reactions were reported. Accordingly, an overdose of Mycophenolate sodium could possibly result in over suppression of the immune system and may increase the susceptibility to infection including fatal infections, opportunistic infections and sepsis. If blood dyscrasias occur, it may be appropriate to interrupt or discontinue Mycophenolate sodium.
Possible signs and symptoms of acute overdose could include the following: hematological abnormalities such as neutropenia and leukopenia, and gastrointestinal symptoms such as diarrhea, abdominal pain, nausea and vomiting, and dyspepsia.

Treatment and Management
In all cases of overdosage, general supportive measures and symptomatic treatment should be followed. 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 although dialysis may be used to remove the inactive metabolite mycophenolic acid glucuronide (MPAG). Activated charcoal or bile sequestrates, such as cholestyramine, may reduce the systemic mycophenolic acid exposure, by interfering with enterohepatic circulation of mycophenolic acid.

5.0 PHARMACOLOGIC PROPERTIES
5.1 MECHANISM OF ACTION
An immunosuppressant, Mycophenolic acid (MPA), is reversible and an uncompetitive inhibitor of inosine monophosphate dehydrogenase (IMPDH), and therefore inhibits the de novo pathway of guanosine nucleotide synthesis without incorporation to DNA. T- and B-lymphocytes are critically dependent for their proliferation on de novo synthesis of purines, whereas other cell types can utilize salvage pathways. MPA has cytostatic effects on lymphocytes. In rat models of kidney and heart allotransplantation, Mycophenolate sodium has been shown to prevent the occurrence of acute rejection. Mycophenolate sodium also decreases in mice antibody production.

5.2 PHARMACODYNAMIC PROPERTIES
Mycophenolate mofetil is rapidly absorbed following oral administration and hydrolyzed to form MPA, which is the active metabolite. MPA is a potent, selective, uncompetitive, and reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH), and therefore inhibits the de novo pathway of guanosine nucleotide synthesis without incorporation into DNA. Because T- and B-lymphocytes are critically dependent for their proliferation on de novo synthesis of purines, whereas other cell types can utilize salvage pathways, MPA has potent cytostatic effects on lymphocytes. MPA inhibits proliferative responses of T- and B-lymphocytes to both mitogenic and allospecific stimulation. Addition of guanosine or deoxyguanosine reverses the cytostatic effects of MPA on lymphocytes. MPA also suppresses antibody formation by B-lymphocytes. MPA prevents the glycosylation of lymphocyte and monocyte glycoproteins that are involved in intercellular adhesion to endothelial cells and may inhibit recruitment of leukocytes into sites of inflammation and graft rejection. Mycophenolate mofetil did not inhibit early events in the activation of human peripheral blood mononuclear cells, such as the production of interleukin-1 (IL-1) and interleukin-2 (IL-2) but did block the coupling of these events to DNA synthesis and proliferation.

5.3 PHARMACOKINETIC PROPERTIES
Mycophenolate sodium exhibits dose-proportional and linear pharmacokinetics over the dose-range (360 to 2160 mg) evaluated. The absolute bioavailability of Mycophenolate sodium in stable renal transplant patients on cyclosporine was 72%. MPA is highly protein bound (>98%

bound to albumin). The predominant metabolite of MPA is the phenolic glucuronide (MPAG) which is pharmacologically inactive. A minor metabolite AcMPAG which is an acyl glucuronide of MPAG is also formed and has pharmacological activity comparable to MPA. MPAG undergoes renal elimination. A fraction of MPAG also undergoes biliary excretion, followed by deconjugation by gut flora and subsequent reabsorption as MPA. The mean elimination half-lives of MPA and MPAG ranged between 8 and 16 hours, and 13 and 17 hours, respectively.

Absorption	The median delay (Tlag) in the rise of MPA concentration ranged between 0.25 and 1.25 hours The median time to maximum concentration (Tmax) of MPA ranged between 1.5 and 2.75 hours. In comparison, following the administration of MMF, the median Tmax ranged between 0.5 and 1.0 hours.
Distribution	The mean (± SD) volume of distribution at steady state and elimination phase for MPA is 54 (± 25) L and 112 (± 48) L, respectively. MPA is highly protein bound to albumin, >98%. The protein binding of mycophenolic acid glucuronide (MPAG) is 82%. The free MPA concentration may increase under conditions of decreased protein binding (uremia, hepatic failure, and hypoalbuminemia).
Metabolism	MPA is metabolized principally by glucuronyltransferase to glucuronidase metabolites. The mean clearance of MPA was 140 (± 30) mL/min
Excretion	The majority of MPA dose administered is eliminated in the urine primarily as MPAG (>60%) and approximately 3% as unchanged MPA. The mean renal clearance of MPAG was 15.5 (± 5.9) mL/min. MPA resulting from the deconjugation may then be reabsorbed and produce a second peak of MPA approximately 6 to 8 hours after Mycophenolate sodium dosing.
Half life	The mean elimination half-life of MPA and MPAG ranged between 8 and 16 hours, and 13 and 17 hours, respectively.
Plasma protein binding	98%

6. NONCLINICAL PROPERTIES

6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

In experimental models, Mycophenolate Mofetil was not tumorigenic. The highest dose tested in the animal carcinogenicity studies resulted in approximately 2 – 3 times the systemic exposure (AUC or Cmax) observed in renal transplant patients at the recommended clinical dose of 2 g/day and 1.3 – 2 times the systemic exposure (AUC or Cmax) observed in cardiac transplant patients at the recommended clinical dose of 3 g/day.

Two genotoxicity assays (in vitro mouse lymphoma assay and in vivo mouse bone marrow micronucleus test) showed a potential of Mycophenolate Mofetil to cause chromosomal aberrations. These effects can be related to the pharmacodynamic mode of action, i.e. inhibition of nucleotide synthesis in sensitive cells. Other in vitro tests for detection of gene mutation did not demonstrate genotoxic activity.

Mycophenolate Mofetil had no effect on fertility of male rats at oral doses up to 20mg/kg/day The systemic exposure at this dose represents 2 – 3 times the clinical exposure at the recommended clinical dose of 2 g/day in renal transplant patients and 1.3 – 2 times the clinical exposure at the recommended clinical dose of 3 g/day in cardiac transplant patients.

In a female fertility and reproduction study conducted in rats, oral doses of 4.5 mg/kg/day caused malformations (including anophthalmia, agnathia, and hydrocephaly) in the first generation offspring in the absence of maternal toxicity. The systemic exposure at this dose was approximately 0.5 times the clinical exposure at the recommended clinical dose of 2 g/day for renal transplant patients and approximately 0.3 times the clinical exposure at the recommended clinical dose of 3 g/day for cardiac transplant patients. No effects on fertility or reproductive parameters were evident in the dams or in the subsequent generation.

In teratology studies in rats and rabbits, foetal resorptions and malformations occurred in rats at 6 mg/kg/day (including anophthalmia, agnathia, and hydrocephaly) and in rabbits at 90 mg/kg/day (including cardiovascular and renal anomalies, such as ectopia cordis and ectopic kidneys, and diaphragmatic and umbilical hernia), in the absence of maternal toxicity. The systemic exposure at these levels is approximately equivalent to or less than 0.5 times the clinical exposure at the recommended clinical dose of 2 g/day for renal transplant patients and approximately 0.3 times the clinical exposure at the recommended clinical dose of 3 g/day for cardiac transplant patients.

The haematopoietic and lymphoid systems were the primary organs affected in toxicology studies conducted with Mycophenolate Mofetil in the rat, mouse, dog and monkey. These effects occurred at systemic exposure levels that are equivalent to or less than the clinical exposure at the recommended dose of 2 g/day for renal transplant recipients. Gastrointestinal effects were observed in the dog at systemic exposure levels equivalent to or less than the clinical exposure at the recommended doses. Gastrointestinal and renal effects consistent with dehydration were also observed in the monkey at the highest dose (systemic exposure levels equivalent to or greater than clinical exposure). The Nonclinical toxicity profile of Mycophenolate Mofetil appears to be consistent with adverse events observed in human clinical trials, which now provide safety data of more relevance to the patient population.

7. DESCRIPTION

Renfor 180 - RENFOR is supplied for oral administration, as a delayed - release tablet of Mycophenolic Acid. Each delayed - release tablet of RENFOR contains Mycophenolate Sodium USP equivalent to Mycophenolic Acid 180mg.

Renfor - RENFOR is supplied for oral administration, as a delayed - release tablet of Mycophenolic Acid. Each delayed - release tablet of RENFOR contains Mycophenolate Sodium USP equivalent to Mycophenolic Acid 360mg.

8. PHARMACEUTICAL PARTICULARS

8.1 INCOMPATIBILITIES

Not Applicable

8.2 SHELF-LIFE

Refer pack

8.3 PACKAGING INFORMATION
Refer pack

8.4 STORAGE CONDITION AND HANDING INSTRUCTIONS
Refer pack

9. PATIENT COUNSELLING INFORMATION

- Patient should be informed that a possible loss of a pregnancy and higher risk of birth defects are associated with women who take MPA during pregnancy have a higher risk of losing a pregnancy (miscarriage) during the first 3 months (first trimester), and a higher risk that their baby will be born with birth defect.
- Patient should inform their healthcare provider incase planning pregnancy.
- Patient should not stop taking MPA incase they become pregnant while taking medication.
- Patient should be informed that MPA weakens the bodies immunity and may make them more prone to viral and fungal infections.
- Patients should be informed that MPA may cause an infection of the brain that can be fatal. They should inform their healthcare provider right away incase of developing any of the following
- Weakness on one side of the body • Lack of care about things that they may usually care about (apathy) • Confusion

10. DETAILS OF MANUFACTURER
Refer Pack for manufacturer details.

Marketed By:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 3 &
11 to 13 Ground Floor, 101 to 106 &
111 to 116 First Floor, 201 to 206 & 211 to 216
2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302,
Maharashtra, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER
Refer Pack for Permission/License details.

12. DATE OF REVISION
Version 5.0 Dated 16th May 2025

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