Ceptimmun™-S 360

Mycophenolate Sodium 360 mg Tablets

Maximize Acceptance, Better Compliance

Product Description:

Ceptimmun-S 360: Each delayed release tablet containsMycophenolate Sodium U.S.P. 360 mg

General Information:

Ceptimmun-S(mycophenolic acid) isdelayed release enteric coated formulation of mycophenolate sodium that delivers the active moiety mycophenolic acid (MPA). Mycophenolate sodium is an immunosuppressive agent. As the sodium salt, MPA is chemically designatedas (E)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3dihydroisobenzofuran5-yl)-4-methylhex-4-enoic acid sodium salt.
Its empirical formula is $C_{17}H_{19}O_6Na$.

Mycophenolate sodium is an immunosuppressants used in combination with cyclosporine or tacrolimus and corticosteroids, as well as in steroid-free regimens. Mycophenolate sodium is therapeutically equivalent to mycophenolate mofetil in renal transplant recipients.

Indication & Usage:

Ceptimmun-S is indicated for the prophylaxisof organ rejection in patientsreceiving allogeneic transplants.

Ceptimmun-Sshould be used concomitantly with cyclosporine and corticosteroids.

DOSAGE AND ADMINISTRATION:

- **Adult kidney transplant patients:**
  - Recommended dose is 720 mg administered twice daily(1440 mg total daily dose)
- **Paediatric kidney transplant patients: (Patients 5 yrs& older)**
  - The recommended dose is 400 mg/m^2body surface area(BSA) administered twice daily(upto a maximum dose of 720 mg administered twice daily)

Mechanism of action:

MPA is an uncompetitive and reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH), and therefore inhibits the *de novo* pathway of guanosine nucleotide synthesis without incorporation to 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.

Pharmacokinetic:

Absorption:

Enteric-coated mycophenolic acid tablet does not release MPA under acidic conditions (pH <5) as in the stomach but is highly soluble in neutral pH conditions as in the intestine.

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 (uraemia, hepatic failure, and hypoalbuminemia).

Metabolism:

Mycophenolic acid is metabolized mainly by glucuronyl transferase to glucuronidated metabolites, predominantly the phenolic glucuronide, mycophenolic acid glucuronide (MPAG). MPAG does not manifest pharmacological activity. The acyl glucuronide minor metabolite has pharmacological activity similar to mycophenolic acid. The AUC ratio of Mycophenolic acid:MPAG:acyl glucuronide is approximately 1:24:0.28 at steady state.

Excretion:

The majority of MPA dose administered is eliminated in the urine primarily as MPAG (>60%) and approximately 3% as unchanged MPA after administration to stable renal transplant patients.

Use in Specific Population:

Pregnancy: Mycophenolate Sodium (MPS) can cause fetal harm when administered to a pregnant woman. Use of MPS during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations

Nursing Mother: It is not known whether this drug 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 mycophenolate sodium, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Paediatric Use: The safety and effectiveness of mycophenolate sodium have been established in paediatric kidney transplant patients 5 to 16 years of age who were initiated on mycophenolate sodium at least 6 months post-transplant.

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

Geriatric Use: Use of mycophenolate sodium in elderly patients should be with caution. There may be decreased hepatic, renal or cardiac function in elderly patients and they may be on concomitant or other drug therapy.

Contraindication: Ceptimmun-S is contraindicated in patients with hypersensitivity to mycophenolic acid or any component of drug product.

Warning & Precaution:

Lymphoma & other malignancies: Patients receiving mycophenolic acid or any other immunosuppressant are at the risk of developing lymphomas & other malignancies, particularly of skin

Serious Infection: Patients receiving mycophenolic acid are at high risk of developing various infection like opportunistic infection, fatal infection & sepsis.

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).

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. 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.

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

Drug Interaction:

- Mycophenolate Sodium should not administer with Azathioprine, as Azathioprine & MPA inhibits purine synthesis
- Drugs that are eliminated by renal tubular secretion (e.g., acyclovir, ganciclovir) have the potential to inhibit the elimination of MPAG through competition for renal tubular secretion
- Antacids withmagnesium and aluminiumhydroxides decreases the absorption of mycophenolate mofetil
- Agents that interfere with enterohepatic recycling (e.g., bile acid sequestrants, antibiotics) may reduce the amount of Mycophenolic acid available for reabsorption.
- Sevelamer & other phosphate binders should not be used with mycophenolate mofetil as it reduces the absorption of Mycophenolic Acid

Adverse Reactions:

Most common mycophenolic acid adverse drug reaction

Area of Affect	Adverse Effect
Gastrointestinal	Constipation Diarrhoea Dyspepsia Nausea Vomiting Abdominal pain
General	Edema Pain Fever
Hematologic	Bone marrow suppression Anaemia Leukopenia
Infectious	Sepsis CMV infection Urinary tract infection
Nervous System Disorder	Insomnia Tremor Headache