

R-5000 Rapamycin, >99%

[RAPA] [Rapamune] [Sirolimus] [AY-22989] [NSC-226080]

M.W. 914.19

 $C_{51}H_{79}NO_{13}$

[53123-88-9] RTECS: VE6250000 M.I. 12: 8288

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Immunosuppressant, related to FK-506, but without calcineurin inhibitory activity even when complexed to FK-506 binding protein. Selectively blocks signalling that leads to p70 S6 kinase activation (IC50 = 50 pM). Terada, N. et al. "Failure of rapamycin to block proliferation once resting cells have entered the cell cycle despite inactivation of p70 S6 kinase." J. Biol. Chem. 268: 12062 (1993). Fingar, D.C. et al. "Dissociation of pp70 ribosomal protein S6 kinase from insulin-stimulated glucose transport in 3T3-L1 adipocytes." J. Biol. Chem. 268: 3005 (1993). Price, D.J. et al. "Rapamycin-induced inhibition of the 70-kilodalton S6 protein kinase." Science 257: 973 (1992). Chung, J. et al. "Rapamycin-FKBP specifically blocks growth-dependent activation of and signaling by the 70 kd S6 protein kinases." Cell 69: 1227 (1992).
- Lymphokine-induced cell proliferation at the G1 phase is inhibited and apoptosis in a murine B cell line is induced by rapamycin. Rapamycin arrests the Saccharomyces cerevisiae cell cycle irreversibly in the G1 phase. Morice, W.G. et al. "Rapamycin-induced inhibition of p34cdc2 kinase activation is associated with G1/S-phase growth arrest in T lymphocytes." J. Biol. Chem. 268: 3734 (1993). Kay, J.E. et al. "Inhibition of T and B lymphocyte proliferation by rapamycin." Immunology 72: 544 (1991). Heitman, J. et al. "Targets for cell cycle arrest by the immunosuppressant rapamycin in yeast." Science 253: 905 (1991).
- Due to a different mechanism of action than cyclosporin and FK506, rapamycin may prove to be important in organ transplant patient therapy. Fewer side effects than the standard anti-rejection treatments have been observed. Proliferation of activated T cells is blocked by rapamycin, but not apoptosis. The induction of rejection-causing T cell apoptosis reduces the tendency towards transplant rejection. Schwarz, C. and Oberbauer, R. "The future role of target of rapamycin inhibitors in renal transplantation." *Curr Opin Urol.* 12: 109 (2002). Wells, A.D. *et al.* "Requirement for T-cell apoptosis in the induction of peripheral transplantation tolerance." *Nat Med.* 5: 1303 (1999). Li, Y. *et al.* "Blocking both signal 1 and signal 2 of T-cell activation prevents apoptosis of alloreactive T cells and induction of peripheral allograft tolerance." *Nat. Med.* 5: 1298 (1999).
- See also our other standard immunosuppressant products:



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