

MEDICATION NAME:	SIROLIMUS BRAND: RAPAMUNE/RAPAMYCIN
HOW IS IT GIVEN:	Oral tablet or liquid solution.
HOW DOES IT WORK:	Interferes with the function of lymphocytes involved in (auto)immune responses.
COMMON DOSING REGIMENS:	Maintenance dose: 1-2.5 mg/m ² /day. Dosing monitored by trough levels (lowest concentration of the drug in patient's system before next dose). Requires slow taper. Very young children (<2 years of age) may require twice daily dosing.
COMMON SIDE EFFECTS:	Susceptibility to infection, hypertension (high blood pressure), angioedema (swelling to the lips), peripheral edema (swelling to the arms and legs), impaired wound healing, hyperlipidemia, impaired renal function with proteinuria.
RARE BUT SERIOUS SIDE EFFECTS:	There is a 'black box' warning for infections in both liver and lung transplant patients. Possible increased risk of lymphoma or other malignancies.
TYPICAL TIME TO RESPONSE:	2-4 weeks.
LIKELIHOOD OF INITIAL RESPONSE:	Estimated 25-75%.
LIKELIHOOD OF LONG-TERM RESPONSE (3-5 YEARS):	The prevalence of sustained response off treatment has not been established.
OTHER CONSIDERATIONS:	Monitor cholesterol and triglycerides; management may be required. Monitor potassium, AST, ALT, eGFR and proteinuria. Not advised to use during pregnancy. <u>Drug Interactions:</u> Grapefruit juice may increase blood levels due to inhibition of CYP3A4.

References:

1. Bride, K.L., Vincent, T., Smith-Whitley, K., Lambert, M., Blessing, J.J., Seif, A.E., Manno, C.S., Casper, J., Grupp, S.A., and Teachey, D.T. (2016). Sirolimus is effective in relapsed/refractory autoimmune cytopenias: results of a prospective multi-institutional trial. *Blood*. 127(1): 17-28.
2. Gao, L., et. al. (2017). Sirolimus Is Effective in Refractory Immune Thrombocytopenia: Results of an Open-Label Prospective Multicenter Trial in China. *Blood*, 130(Suppl 1), 4728.
3. Jasinski, S., Weinblatt, M.E., and Glasser, C.L. (2017). Sirolimus as an effective agent in the treatment of immune thrombocytopenia (ITP) and Evans syndrome (ES): A single institution's experience. *Journal of Pediatric Hematology and Oncology*. Aug 39(6): 420-424.
4. Li, J., Wang, Z., Dai, L., Cao, L., Su, J., Zhou, M., Yu, Z., Bai, X., and Ruan, C. (2013). Effects of Rapamycin combined with low dose prednisone in patients with chronic immune thrombocytopenia. *Clinical and Developmental Immunology*. Hindawi Publishing Corporation. Vol 2013 Article ID 548085