

## Sirolimus Prescribing Guide

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### Indications

Definite diagnosis of LAM based on ATS/ERS Guidelines with one of the following indications: abnormal FEV1 ( $\leq 70\%$  predicted), problematic chylothous effusions, progressive disease (typically defined as FEV1 loss  $\geq 90\text{ml/year}$ ), or substantial disease burden (abnormal DLCO, air trapping or hyperinflation, supplemental oxygen requirement).

### Initiation:

1. Obtain baseline labs: Complete blood count (CBC), Comprehensive metabolic profile (CMP), Lipid profile, Urinalysis.
2. Begin drug at 1-2mg daily.

### Maintenance:

1. Instruct patients to take drug the same time every day.
2. After 14 days of treatment, perform a serum trough level. Instruct patients to wait 24 hours (20-28 hours) after taking the medication (and just prior to the next dose) prior to drawing a serum trough level.
3. Check sirolimus level, CBC, CMP, lipid profile, urinalysis every month for the first 3 months, and if ok, extend repeat testing to every 3 months.
4. Inquire about other adverse effects such as acne, oral ulcers, worsening of pulmonary symptoms (to evaluate for drug-induced pneumonitis) at every visit
5. Encourage patients to stay up to date on vaccinations against COVID-19, Varicella zoster, pneumococcal pneumonia, and influenza. Avoid live vaccines while on sirolimus.
6. Hold drug for at least 1 week before and 1 week after a surgical procedure or after an injury.

### Other useful tips:

1. **Dosing:** We typically begin at low dose sirolimus (1mg daily) for most patients, unless disease is rapidly progressive. In general, most patients respond well with stabilization of lung function with low dose sirolimus, and we should strive towards prescribing the lowest effective dose in order to minimize adverse effects, especially given the need for long-term treatment. For rapidly progressive patients, it may be better to start at 2mg per day, and titrate downward once a response is assured.
2. **Oral ulcers:** In general, oral ulcers are uncommon at low sirolimus doses. Local corticosteroid-based applications are very effective in treating sirolimus-induced oral ulcers. Swish and spit dexamethasone is most effective. For topical gels, fluocinonide or clobetasol is preferred over Kenalog.
3. **Acne:** Acne is not a common occurrence in patients taking low dose sirolimus. Over the counter medications such as benzoyl peroxide and/or salicylic acid are quite effective, and reasonable first line treatment options, in treating acne.
4. **Hyperlipidemia:** Treatment of hyperlipidemia should be undertaken as per existing guidelines, including dietary modifications and statins.
5. **Common interactions:**
  - a) OTC medications such as St John's Wort may reduce sirolimus levels.
  - b) Grapefruit juice may elevate sirolimus levels.
  - c) CYP3A4 inducers (Rifampin, Carbamazepine, Barbiturates, Phenytoin).

- d) CYP3A4 inhibitors (Ketoconazole, Voriconazole, Itraconazole, Erythromycin, Clarithromycin, etc.).

**Other Advice**

- a. Avoid direct sun exposure. Use sunscreen and hats to avoid skin cancer.
- b. Do not split tablets.
- c. Hold sirolimus for fever requiring antibiotics, or serious infections. Call your physician if you are uncertain about stopping.
- d. Hold sirolimus for any event that requires optimal wound healing, such as an accident with injuries.
- e. Spirometry should be obtained at regular intervals, every three months for those with disease progression, to every year or so for stable patients.

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