**sirolimus** *(sih-roh-lim-us)*

**Classification:** Immunomodulators

**Pregnancy Category:** C

### Indications
- Prevention of organ rejection in allogenic kidney transplantation (with corticosteroids and cyclosporine). Sirolimus is also utilized from the Cypher coronary stent in angioplasty procedures.

### Action
- Inhibits T-lymphocyte activation/proliferation, which occurs as a response to antigen and cytokine stimulation; antibody production is also inhibited.

### Therapeutic Effects
- Decreased incidence and severity of organ rejection.

### Contraindications/Precautions
- Hypersensitivity; Alcohol intolerance/sensitivity (solution contains ethanol); Concurrent ketoconazole, voriconazole, itraconazole, erythromycin, telithromycin, clarithromycin, rifampin, rifabutin, or grapefruit juice; Severe hepatic impairment; OB, Lactation: Women with childbearing potential.

### Interactions
- **Drug-Disease:** Hepatitis, lymphoma, interstitial lung disease, PML, dermatitis, interstitial pneumonitis; **Drug-LFQ:** Rifampin, phenobarbital, phenytoin, carbamazepine, rifapentine, verapamil, leomycin, metoclopramide, danazol, protease inhibitors, rifabutin, and fluconazole; **Drug-Adverse:** Echinacea, grapefruit juice; **Drug-Cy:** Echinacea.

### Adverse Reactions/Side Effects
- **CNS:** Headache; **CV:** Hypotension, pericardial effusion; **GI:** Nausea, vomiting; **GU:** Amnionitis, nephrotoxicity, increased serum creatinine, renal impairment; **Hemat:** Anemia, thrombocytopenia; **MS:** Rash; **Resp:** Interstitial pneumonitis; **Skin:** Rash, pruritus; **Other:** Decreased lymphocytes.

### Pharmacokinetics
- **Route ONSET PEAK DURATION**
  - PO rapid 1–2 hr 24 hr

- **Half-life:** 62 hr.

- **Metabolism and Excretion:** Extensively metabolized (some metabolism by CYP3A4 system); 91% excreted in feces.

- **Protein Binding:** 92%.

- **Distribution:** Concentrates in erythrocytes; distributes to heart, intestines, kidneys, liver, lungs, muscle, spleen, and testes in high concentrations.

- **Absorption:** Rapidly absorbed following oral administration (14% bioavailability).

- **Primary Pathway:** Over the liver by way of the P450 3A4 system.

### Use Cautiously:
- In: Mild to moderate hepatic impairment; OB: Women with childbearing potential. **Ped:** Children <15 yr (safety not established).

### Therapeutic Classification
- **Rapamune** *(sirolimus)*
- **Classification:** Immunomodulators
- **Chemical Name:** *N*-[(4-hydroxy-2-(2H-1,2,4-triazol-3-yl)phenyl)amino]-1-piperazineethanesulfonic acid (racemic and levorotatory form).
Route/Dosage
PO (Adults and Children 13 yr): 6-mg loading dose, followed by 2 mg/day maintenance dose. Dosing following cyclosporine withdrawal—Patients at low to moderate risk for rejection after transplantation may be withdrawn from cyclosporine over 4–8 wk beginning 2–4 mo after transplant. Thereafter, sirolimus dose should be titrated upward to maintain a whole blood trough level of 12–14 ng/mL. Clinical assessment should also be used to gauge dose. Dose changes can be made at 1–6 wk intervals. The following formula may also be used: sirolimus maintenance dose = current dose x (target concentration/current concentration). If a large q is needed, a loading dose may be given and blood levels reassessed 3–4 days later. Loading dose may be calculated by the following formula: sirolimus loading dose = 3 (new maintenance dose-current maintenance dose) Loading dose = 40 mg should be spread over 2 days.
PO (Adults and Children 13 yr and 40 kg): 3 mg/m² loading dose, followed by 1 mg/m²/day maintenance dose. See adjustments above for doses following cyclosporine withdrawal.
Hepatic Impairment
PO (Adults and Children 13 yr and 40 kg): decrease maintenance dose by 33%; loading dose is unchanged.

NURSING IMPLICATIONS
Assessment
● Monitor BP closely during therapy. Hypertension is a common complication of sirolimus therapy and should be treated.
● Assess for any new signs or symptoms that may be suggestive of PML, an opportunistic infection of the brain that leads to death or severe disability; withhold dose and notify health care professional promptly. Symptoms of PML may include hemiparesis, apathy, confusion, cognitive deficiencies, and ataxia. Consider decreasing the amount of immunosuppression in these patients.
● Lab Test Considerations: Monitor sirolimus blood levels when dose forms are changed and in patients likely to have altered drug metabolism, patients 13 yr who weigh <40 kg, patients with hepatic impairment, and during concurrent administration of drugs that may interact with sirolimus. Trough concentrations of 15 ng/mL are associated with an 1% adverse effects.
● Monitor patients for hyperlipidemia. May require additional interventions to treat hyperlipidemia.
● Monitor for anemia, leukopenia, thrombocytopenia, and hypokalemia.
● Monitor for AST, ALT, and hyperphosphatemia, and hyperglycemia.

Potential Nursing Diagnoses
Build for infections (Adverse Reactions)
Implementation
● Therapy with sirolimus should be started as soon as possible post-transplant. Concurrent therapy with cyclosporine and corticosteroids is recommended. Sirolimus should be initiated in all cyclosporine (NEORAL/Sandimmune) patients.
● Sirolimus should be ordered by physicians skilled in immunosuppressive therapy, with the staff and facilities to manage renal transplant patients.
● Antimicrobial prophylaxis for Pneumocystis jirovecii pneumonia for 1 year and for cytomegalovirus prophylaxis for 3 mo post-transplant are recommended.
● PO: Administer consistently with or without food. Swallow tablet whole; do not crush, break, or chew. Do not administer with or mix with grapefruit juice.
● To dilute from bottle, use amber oral dose syringe to withdraw prescribed amount. Empty syringe from syringe into a glass or plastic container holding at least 2 oz (60 mL) of water or orange juice; do not use other liquids. Stir vigorously and drink at once. Reconstitute with at least 4 oz of additional liquid, stir thoroughly, and drink at once.
● If using the pouch, empty entire contents of pouch into at least 2 oz of water or orange juice; do not use other liquids. Stir vigorously and drink at once. Reconstitute with at least 4 oz of additional liquid, stir thoroughly, and drink at once.
● Store bottles and pouches in refrigerator. Protect from light. Solution may develop a slight haze when refrigerated; allow to stand at room temperature and shake gently until haze disappears. Sirolimus may remain in syringe at room temperature or refrigerated for up to 24 hr. Discard syringe after one use. Oral solution must be used within 1 min of opening bottle.
Patient/Family Teaching
● Instruct patient to take medication at the same time each day, as directed. Advise patient to avoid taking with or diluting with grapefruit juice. Do not skip or double up on missed doses. Do not discontinue medication without advice of health care professional.
● Advise patients to avoid grapefruit and grapefruit juice during therapy.
sirolimus

- Reinforce the need for lifelong therapy to prevent transplant rejection. Review symptoms of rejection for transplanted organ and stress need to notify health care professional immediately if they occur.
- Advise patient to notify health care professional if swelling of your face, eyes, or mouth; trouble breathing or wheezing; throat tightness; chest pain or tightness; feeling dizzy or faint; rash or peeling of skin; swelling of hands or feet; or symptoms of PML occur.
- Advise patient to wear sunscreen and protective clothing and limit time in sunlight and UVA light due to increased risk of skin cancer.
- Caution patient to notify health care professional if signs of infection occur.
- Advise patient to avoid vaccinations with live virus during therapy.
- Advise patient of the risk of taking sirolimus during pregnancy. Caution women of childbearing age to use effective contraception prior to, during, and for 12 wk following therapy.
- Emphasize the importance of repeated lab tests during sirolimus therapy.

Evaluation/Desired Outcomes
- Prevention of transplant organ rejection.

Why was this drug prescribed for your patient?