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**Everolimus, an Oral mTOR Inhibitor, for the Treatment Of Renal Angiomyolipoma (AML)
Associated With Tuberous Sclerosis Complex (TSC) or
Sporadic Lymphangiomyomatosis (sLAM): Adverse Event (AE) Management Strategies**

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EXIST-2 (NCT00790400), a double-blind phase 3 trial, demonstrated efficacy and safety of everolimus in reducing renal AML volume compared with placebo ($P < .0001$). As use of everolimus in this patient population increases, it is important to be aware of the onset of AEs and how best to manage them. Patients ≥ 18 years of age with ≥ 1 renal AML ≥ 3 cm were randomized 2:1 to receive everolimus 10 mg/d ($n=79$) or placebo ($n=39$). All AEs related to study drug were consistent with the known safety profile of everolimus in the TSC setting and mostly grade 1/2. Clinically notable AEs in the everolimus vs placebo groups, respectively, included stomatitis/oral mucositis/ulcers (79% vs 23%), rash (11% vs 0%), infections and infestations (65% vs 72%), noninfectious pneumonitis (1% vs 0%), and cytopenia (23% vs 21%). Metabolic events such as hypercholesterolemia and hyperglycemia are identified risks with everolimus treatment. Stomatitis management consists of temporary dose interruption and/or topical analgesic mouth treatments +/- topical corticosteroids. Treatment of severe or bothersome skin rash depends on the type of rash and consists of topical agents, including steroids and anti-infectives. If the AE persists everolimus dosing adjustments or treatment interruptions can lead to resolution. Advise patients on the risk of developing noninfectious pneumonitis and to promptly report new or worsening respiratory symptoms (shortness of breath, cough, fever). Periodically monitor for hematological and metabolic abnormalities. Awareness and vigilant monitoring for AEs is critical for maximizing patient tolerability and therapeutic efficacy. Management of AEs should be individualized and strategies include concomitant medication and temporary dose reduction or interruption.

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