Generic Name:
Everolimus
Trade Name:
Afinitor Disperz
Company:
Novartis
Notes:

FDA approved everolimus tablets for oral suspension for adjunctive treatment of adult and pediatric patients aged 2 years and older with tuberous sclerosis complex (TSC)?associated partial-onset seizures.

Everolimus is also approved for TSC-associated subependymal giant cell astrocytoma (SEGA) and TSC-associated renal angiomyolipoma.

Approval was based on EXIST-3, a randomized, double-blind, multicenter trial in 366 patients with TSC-associated partial-onset seizures, inadequate seizure control with 2 or more sequential antiepileptic drug (AED) regimens, and a TSC diagnosis (modified Gomez criteria). In addition, eligible patients were required to have had 16 or more partial-onset seizures during the 8-week baseline phase on a stable AED regimen.

Patients were randomized (1:1.09:1) to everolimus targeting a low trough (LT, n = 117) or high trough (HT, n = 130) concentration of everolimus or placebo (n = 119). Patients initiated treatment with everolimus/matching placebo at 3?6 mg/m^2 (depending on age or further adjusted for concomitant CYP3A4/*P*-glycoprotein inducer use) orally once daily.

Subsequent doses were titrated to achieve the targeted trough concentrations as directed by an automated system to maintain the study blind. The major efficacy measure was the percentage reduction in average weekly seizures during a 12-week treatment period compared with the average weekly seizures during the 8-week baseline period.

The trial demonstrated statistically significant reductions in seizures for each of the everolimus arms (LT arm, 29.3%; HT arm, 39.6%), compared with the placebo arm (14.9%). The proportion of patients with 50% reduction in seizure frequency during the 12-week treatment period compared with baseline also was higher in the LT and HT everolimus arms (28.2% and 40%, respectively) compared with the placebo arm (15.1%).

The most common adverse reactions, occurring in at least 10% of patients, were stomatitis, diarrhea, vomiting, nasopharyngitis, upper respiratory tract infection, pyrexia, cough, and rash.

The recommended starting dose of everolimus arms for this indication is 5 mg/m^2 orally once daily with dose adjustments (in increments up to 5 mg) to achieve trough concentrations of 5?15 ng/mL.

The dose should be reduced in patients with severe hepatic impairment or in patients taking concurrent *P*-glycoprotein and moderate CYP3A4 inhibitors. The dose should be increased in patients taking concurrent *P*-glycoprotein and strong CYP3A4 inducers.

Medication Monitor Categories:
Supplemental Approvals
