

Supplemental Approvals

Generic Name (Trade Name) Company

April 12, 2018

Everolimus

Uses/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/m² (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

(Afinitor Disperz—Novartis)

FDA approves everolimus for tuberous sclerosis complex-associated partial-onset seizures

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/m² 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.

Source URL:

<http://aphadruinfo.com/supplemental-approvals/fda-approves-everolimus-tuberous-sclerosis-complex-associated-partial-onset>

APhA DrugInfoLine is an official publication of, and is owned and copyrighted by the American Pharmacists Association, the national professional society of pharmacists. Materials in APhA DrugInfoLine do not necessarily represent the policy, recommendations, or endorsement of APhA. The publisher, authors, editors, reviewers, and contributors have taken care to ensure that information contained in APhA DrugInfoLine is accurate and current; however, they shall have no liability to any person or entity with regard to claims, losses, or damages caused or alleged to be caused, directly or indirectly, by use of any information contained in the publication. All decisions about drug therapy must be based on the independent judgment of the clinician. Copyright © 2000–2011, American Pharmacists Association. All rights reserved.