FDA Approves Iwilfin for High-Risk Neuroblastoma

Eflornithine is the first FDA-approved therapy to reduce the risk of relapse in children with high-risk neuroblastoma.

December 18, 2023 By Food and Drug Administration (FDA)

On December 13, 2023, the Food and Drug Administration approved eflornithine (Iwilfin, USWM, LLC) to reduce the risk of relapse in adult and pediatric patients with high-risk neuroblastoma (HRNB) who have demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy.

This represents the first FDA approval of a therapy intended to reduce the risk of relapse in pediatric patients with HRNB.

View full prescribing information for Iwilfin.

Efficacy was evaluated in an externally controlled trial comparing outcomes from Study 3b (investigational arm) and Study ANBL0032 (clinical trial-derived external control arm). Study 3b (NCT02395666) was a multi-center, open label, non-randomized trial with two cohorts. A total of 105 eligible patients with HRNB from one cohort (Stratum 1) received eflornithine orally, twice daily at a dosage based on body surface area (BSA) until disease progression, unacceptable toxicity, or for a maximum of 2 years. Study 3b was prospectively designed to compare outcomes to the historical benchmark event free survival (EFS) rate from Study ANBL0032 reported in published literature.

The external control arm was derived from 1,241 patients on the experimental arm of Study ANBL0032, a multi-center, open-label, randomized trial of dinutuximab, granulocyte-macrophage colony-stimulating factor, interleukin-2, and cis-retinoic acid compared to cis-retinoic acid alone in pediatric patients with HRNB.

Patients who met the criteria for the comparative analysis of Study 3b and ANBL0032, with complete data for specified clinical covariates, were matched (1:3) using propensity scores; the matched efficacy populations for the primary analysis included 90 patients treated with Iwilfin and 270 control patients from Study ANBL0032.

The major efficacy outcome measure was event free survival (EFS), defined as disease progression, relapse, secondary cancer, or death due to any cause. An additional efficacy outcome

measure was overall survival (OS), defined as death due to any cause. In the protocol-specified primary analysis, the EFS hazard ratio (HR) was 0.48 (95% CI: 0.27, 0.85) and OS HR was 0.32 (95% CI: 0.15, 0.70). Given the uncertainty in treatment effect estimation associated with the externally controlled study design, supplementary analyses in subpopulations or using alternative statistical methods were performed. In these analyses, the EFS HR ranged from 0.43 (95% CI: 0.23, 0.79) to 0.59 (95% CI: 0.28, 1.27), and the OS HR ranged from 0.29 (95% CI: 0.11, 0.72) to 0.45 (95% CI: 0.21, 0.98).

The most common adverse reactions (≥5%) in Study 3b, including laboratory abnormalities, were otitis media, diarrhea, cough, sinusitis, pneumonia, upper respiratory tract infection, conjunctivitis, vomiting, pyrexia, allergic rhinitis, decreased neutrophils, increased ALT, increased AST, hearing loss, skin infection, and urinary tract infection.

The recommended dose is based on BSA. See the prescribing information for more information.

This review used the Real-Time Oncology Review (RTOR) pilot program, which streamlined data submission prior to the filing of the entire clinical application, and the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

This application was granted priority review, breakthrough designation, and orphan drug designation. FDA expedited programs are described in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

This announcement was published by the Food and Drug Administration/ on December 14, 2023.
