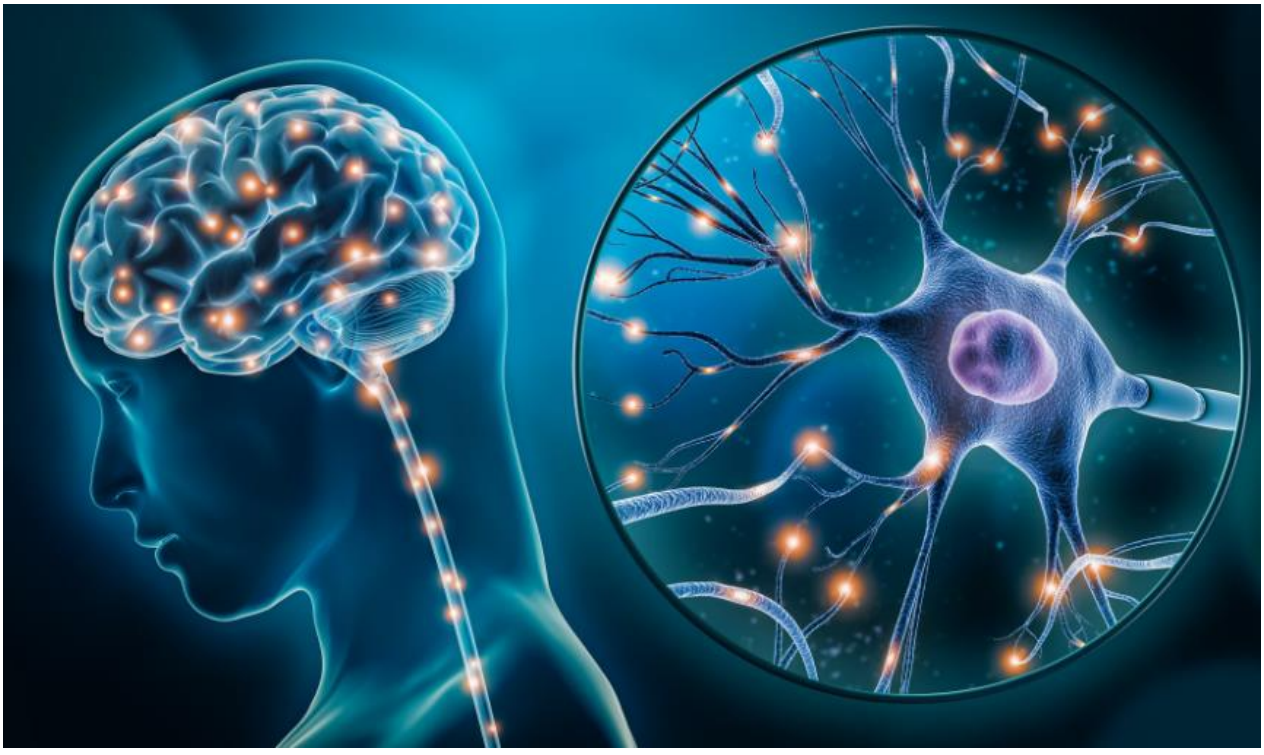
Ecopipam Significantly Reduces Risk of Relapse in Pediatric, Overall Populations With Tourette Syndrome

Key Takeaways

- Current Tourette pharmacotherapies are constrained by tolerability, with α-2 agonists linked to fatigue/hypotension and D2 modulators to weight gain and drug-induced movement disorders, driving discontinuation.
- Ecopipam, a first-in-class D1R antagonist, previously improved YGTSS-TTS by ~30% at week 12 in phase 2b and ~40% at month 12 in extension data.
- The phase 3 design used 12-week open-label treatment followed by 12-week double-blind withdrawal; responders required ≥25% YGTSS-TTS improvement at weeks 8 and 12.
- Pediatric primary endpoint showed ~50% relapse-risk reduction versus placebo (HR ~0.5; 95% CI 0.3–0.8), with placebo reaching ~50% relapse by ~5 weeks while ecopipam did not.
- Adverse events included somnolence, headache, and insomnia; anxiety and depression AEs occurred in 9.7% and 6.5%, with 2.3% reporting potential suicidal ideation, and no weight gain.

Ecopipam reduces Tourette tic relapse risk by approximately 50% with durable control and no movement-related adverse effects.

New data presented at the American Academy of Neurology 2026 Annual Meeting emphasize the potential of ecopipam (Emalex Biosciences), a novel therapeutic approach for Tourette syndrome (TS). During a presentation hosted by Kinga Tomczak, MD, PhD, a pediatric neurologist at Boston Children's Hospital, findings from a phase 3 clinical trial evaluating



ecopipam demonstrated significant reductions in relapse risk and durable treatment effects across pediatric and overall populations.[1]

For TS, treatment options include both behavioral therapy and pharmacotherapy, such as α-2 adrenergic agonists and D2 receptor (D2R) modulators (eg, antipsychotics); however, current pharmacologic approaches are often limited by adverse effects (AEs). While α-2 adrenergic

agonists are commonly associated with fatigue and hypotension, D2R modulators can lead to weight gain and drug-induced movement disorders, Tomczak explained. As a result of these tolerability concerns, discontinuation rates for existing therapies remain high.[1]

Ecopipam is a first-in-class selective D1 receptor (D1R) antagonist currently in development for TS. In clinical studies that enrolled both children and adolescents, ecopipam demonstrated meaningful improvements in tic severity as measured by the Yale Global Tic Severity Scale–Total Tic Score (YGTSS-TTS). A phase 2b randomized controlled trial showed that ecopipam resulted in a mean improvement of 30% at week 12 compared with placebo ($P = .01$), whereas an open-label extension study reported a mean improvement of approximately 40.3% at month 12 ($P < .0001$ vs baseline). The most common AEs among patients treated with ecopipam during the phase 2b trial included headache (15.8%), insomnia (13.1%), fatigue (7.9%), somnolence (7.9%), anxiety (5.3%), nausea (5.3%), and restlessness (5.3%).[1]

Tomczak explained that the objective was to evaluate the durability of efficacy, as well as the safety and tolerability of ecopipam, through a 24-week treatment duration in children, adolescents, and adults with TS. The trial was a phase 3 double-blind, placebo-controlled withdrawal that had a 28-day screening period, a 12-week open-label period, a 12-week double-blind period, and a safety follow-up period lasting 30 days. Ecopipam was titrated based on weight.[1]

"The goal weight was 1.8 mg per kg per day, and the responders were considered those who had over 25 [percent] or more improvement in tic severity, both at week 8 and week 12. So, for a whole month they had to maintain the improvement," Tomczak explained during the presentation. "[Those who maintained improvement] were [randomly assigned] to ecopipam arm or placebo, and those on placebo were tapered by 22.4 mg per day…and relapse was considered if they were losing this improvement."[1]

The primary end point of the trial was time to relapse in the pediatric population, specifically among participants aged 6 to 17 years. Relapse was defined as a 50% or greater loss of the improvement in the YGTSS-TTS observed from baseline to week 12, the initiation of additional treatment for TS, or hospitalization as a result of worsening symptoms. Ecopipam was shown to significantly reduce risk of relapse, showing an approximate 50% lower risk compared with placebo during the 12-week double-blind withdrawal period. These findings were statistically significant, with a hazard ratio of about 0.5 (95% CI, 0.3–0.8) and a p-value of .0084.

Additionally, Tomczak emphasized the durability of the effect. Although the placebo group reached an approximate 50% relapse rate nearly 5 weeks following randomization, the ecopipam group did not reach a 50% relapse rate at any point during the 12-week period.[1]

The secondary end point was also time to relapse, but this included both pediatric and adult participants. Like the primary end point, ecopipam demonstrated an approximate 50% reduced risk of relapse compared with the placebo group during the 12-week double-blind period. This

was also considered statistically significant, Tomczak noted, with a hazard ratio of about 0.5 (95% CI, 0.3–0.8) and a p-value of .0050.

Further, the ecopipam group was observed to maintain the treatment benefit significantly better than the placebo group throughout the 12-week withdrawal period. Although the analysis included adults, only 14 adult participants were enrolled in the study; however, despite the small sample size, the reduction in relapse risk observed in the adult subgroup was reported to be very similar and statistically significant.[1]

Tomczak acknowledged that there were some adverse effects (AEs), but they were considered to be mild and were similar to those observed in prior research (eg, somnolence, headaches, insomnia). In the phase 3 withdrawal trial, there were 2 potential serious AEs, and other AEs of special interests included anxiety- and depression-related AEs, of which 9.7% and 6.5% of patients, respectively, were affected in the open-label period. Additionally, 2.3% of patients were reported to have potential suicidal ideation. Notably, there were no drug-induced AEs related to movement, and no weight gain among participants.[1]

“This study shows statistically significant response in both pediatric and overall populations treated with ecopipam, and it demonstrated a 50% reduced risk of relapse versus placebo during the 12-week withdrawal period and support the maintenance and durability of treatment effect, which was very encouraging,” Tomczak concluded. “There were no clinically relevant metabolic [AEs] that were measured at all [during] these visits, and no weight gain, which is really what we were looking for.”[1]

REFERENCES

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