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Novel ADHD Therapy Is More Tolerable, Less Effective Than Current Treatment Options: Centanafadine is a serotonin-norepinephrine-dopamine reuptake inhibitor.

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Date: July-August 2023
From: Drug Topics(Vol. 167, Issue 7)
Publisher: Intellisphere, LLC
Document Type: Article
Length: 470 words
Lexile Measure: 1400L

Full Text:
Although centanafadine has a better safety profile and demonstrates more favorable tolerability, this novel attention-deficit/hyperactivity disorder (ADHD) therapy is less effective than lisdexamfetamine dimesylate (Vyvanse) for adults with ADHD, according to research presented at the American Society of Health-System Pharmacists 2023 Summer Meetings and Exhibition.

Recent phase 3 clinical trials have demonstrated significant reductions in ADHD symptoms vs placebo in adults treated with centanafadine, a serotonin-norepinephrine-dopamine reuptake inhibitor--a novel therapy for ADHD. Although centanafadine appears to be well tolerated, investigators conducted a matching-adjusted indirect comparison of safety and efficacy outcomes between centanafadine and the stimulant lisdexamfetamine and the nonstimulants atomoxetine (Strattera) and viloxazine extended-release (ER) capsules (Qelbree).

Patient-level data were pooled from 2 centanafadine trials (NCT03605680 and NCT03605836) and 3 comparator trials: NCT00334880 for lisdexamfetamine, NCT00190736 for atomoxetine, and NCT04016779 for viloxazine ER. Propensity-score weighting was used to match baseline characteristics, including age, sex, race, Adult ADHD Investigator Symptom Rating Scale score, Clinical Global Impression-Severity of Illness Scale score, and--for centanafadine and viloxazine ER--body mass index. Estimated risk diferences "representing the incremental risk of each adverse event" with centanafadine vs placebo compared with comparator vs placebo were also reported. (1)

After matching, baseline characteristics were the same across all trials. Adverse outcomes, including dry mouth, insomnia, anxiety, nausea, lack of appetite, and fatigue, were evaluated. The risk diference between centanafadine and lisdexamfetamine was -23.43% for lack of appetite, -19.27% for dry mouth, and -15.35% for insomnia; between centanafadine and atomoxetine, it was -18.64% for nausea and -17.44% for dry mouth; and between centanafadine and viloxazine ER, it was -11.07% for fatigue and -10.67% for insomnia.

Additionally, investigators evaluated the reduction from baseline in ADHD Investigator Symptom Rating Scale (AISRS)/ADHD Rating Scale score. Adults with ADHD treated with lisdexamfetamine experienced a 6.58 points greater reduction from baseline scores vs those treated with centanafadine. No statistically significant changes were noted in the AISRS score from baseline between centanafadine and atomoxetine or viloxazine ER (2.02 and 0.90 points, respectively).

"Centanafadine showed a better safety/tolerability profile than lisdexamfetamine, atomoxetine, and viloxazine ER, as evidenced by a significantly lower incidence of several adverse... effects," the researchers noted. "Efficacy was lower than lisdexamfetamine and nondiferent compared [with] atomoxetine and viloxazine ER.

"This study provides important insights on the relative efficacy and safety of common treatment options for adults with ADHD to help inform treatment decisions," the researchers concluded.

The investigators also noted that future studies are warranted to "better understand how the trade-of between safety/tolerability and efficacy affects management in clinical practice" as well as patient treatment preferences.

REFERENCE

(1.) Schein J. Assessment of centanafadine in adultswithADHD:a matching adjusted indirect comparison vs lisdexamfetaminedimesylate, atomoxetine, and viloxazine ER. Presented at:American Society of Health-System Pharmacists 2023 Summer Meetings and Exhibition; June 10-14, 2023; Baltimore, MD.

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Source Citation (MLA 9th Edition)
Biscaldi, Lauren. "Novel ADHD Therapy Is More Tolerable, Less Effective Than Current Treatment Options: Centanafadine is a serotonin-norepinephrine-dopamine reuptake inhibitor." *Drug Topics*, vol. 167, no. 7, July-Aug. 2023, p. 39. *Gale Academic OneFile*, link.gale.com/apps/doc/A762026125/AONE?u=nysl_oweb&sid=googleScholar&xid=a7871930. Accessed 20 Dec. 2023.
Gale Document Number: GALE|A762026125