Real-World Clinical Outcomes of Patients Switching to Treatment With Auvelity® (Dextromethorphan-Bupropion)

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Objective

To assess the real-world outcomes in adult patients initiating dextromethorphan-bupropion, including improvements over time in anxiety symptoms on the GAD-2 scale, improvements over time in depressive symptoms on the CGI-I and PHQ-9 scales, and changes in body weight

Introduction

- Major depressive disorder (MDD) is a chronic condition affecting more than 20% of adults in the United States (US) during their lifetime[1]
- Challenges in the pharmacological treatment of patients with MDD can include delayed treatment response and suboptimal clinical outcomes such as residual anhedonia and anxiety symptoms, as well as tolerability issues and adverse effects such as weight gain[2-6]
- Dextromethorphan-bupropion (45 mg/105 mg) (Auvelity®) is an oral N-methyl-d-aspartate (NMDA) receptor antagonist and sigma-1 agonist that has been approved in the US since 2022 for the treatment of adults with MDD[7]
- The aim of this study was to examine real-world patient-reported and clinician-rated outcomes in patients initiating dextromethorphan-bupropion treatment in the US

Methods

Study Design

- Adults who initiated dextromethorphan-bupropion (first prescription = index date) were identified using electronic health record (EHR) data collected from the Rochester Center for Behavioral Medicine (RCBM) – an outpatient behavioral health clinic in Michigan – between August 2022 and March 2025
- Included patients were required to have valid baseline data for ≥1 clinical outcome of Generalized Anxiety Disorder 2-item (GAD-2), Clinical Global Impression–Improvement (CGI-I), Patient Health Questionnaire-9 (PHQ-9), and body weight within the pre-dextromethorphan-bupropion initiation window (Day -13 to Day 0)

Outcomes

- Patient demographics, other medical conditions, and MDD-related medication use prior to or at index
- Outcomes of GAD-2, CGI-I, PHQ-9, PHQ-9 item 1 ("little interest or pleasure in doing things" [anhedonia]), and body weight over follow-up (Week 1, Week 2, Week 6, and Month 3)

Analysis

- Descriptive statistics were reported as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables
- Outcomes were evaluated over time; pairwise comparisons were made between baseline and each follow-up timepoint
  - Analyzed patients were required to have continuous dextromethorphan-bupropion treatment (≤ 60-day gap permitted) from initiation through each respective timepoint
  - Statistical significance ($P < 0.05$) was determined using the Wilcoxon signed-rank test, paired t-test, McNemar's test, or McNemar–Bowker test, as appropriate

References

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Disclosures
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C Zeni, S Alter, and **Y Zhao** are employees of Axsome Therapeutics, Inc. **Z Zheng** and **Q Qin** are employees of KMK Consulting, Inc.

Results

Patient Characteristics

Table 1: Demographic and Clinical Characteristics

	Overall cohort N = 217
Age, years, mean (SD)	42.6 (13.9)
Age category, years	
18–44	133 (61.3%)
45–64	67 (30.9%)
65+	17 (7.8%)
Female	126 (58.1%)
Race	
White	208 (95.9%)
Patients with depressive disorders	196 (90.3%)
Severity of depression[a]	
PHQ-9 score, mean (SD)	11.5 (6.1)
PHQ-9 category	
0–4: No/minimal depression	21 (11.2%)
5–9: Mild depression	58 (30.9%)
10–14: Moderate depression	50 (26.6%)
15–19: Moderately severe depression	37 (19.7%)
20–27: Severe depression	22 (11.7%)

Patient characteristics measured prior to or at index. Data are n (%) unless otherwise stated.
[a]Evaluated in 188 (86.6%) patients with completed PHQ-9.
PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

- Among 217 patients initiating dextromethorphan-bupropion, the mean age was 42.6 years, 58.1% were female, and almost all (95.9%) were White
- 58.0% of patients had moderate-to-severe depressive symptoms
- The mean PHQ-9 score at baseline was 11.5

Table 2: Other Medical Conditions

	Overall cohort N = 217
Mental health disorders	217 (100.0%)
Anxiety disorders	192 (88.5%)
ADHD[a]	172 (79.3%)
Eating disorders	33 (15.2%)
Bipolar disorder	32 (14.7%)
Post-traumatic stress disorder	25 (11.5%)
Sleep disorders	111 (51.2%)
Insomnia	92 (42.4%)
Sleep apnea	24 (11.1%)
Metabolic disorders	72 (33.2%)
Obesity	23 (10.6%)
Diabetes/prediabetes	16 (7.4%)
Hyperlipidemia	15 (6.9%)
Hypothyroidism	14 (6.5%)
Musculoskeletal/pain disorders	56 (25.8%)
Migraine/chronic headache	33 (15.2%)
Cardiovascular diseases	41 (18.9%)
Hypertension	19 (8.8%)
Substance use disorders	19 (8.8%)

Other medical conditions measured prior to index. Data are n (%) unless otherwise stated.
[a]ADHD, conduct disorders, hyperkinetic syndrome.
ADHD, attention-deficit/hyperactivity disorder; SD, standard deviation.

- Prior to index, many patients had documented anxiety (88.5%) and/or ADHD (79.3%) 51.2% had sleep disorders, 33.2% had metabolic disorders, and 25.8% had musculoskeletal/pain disorders

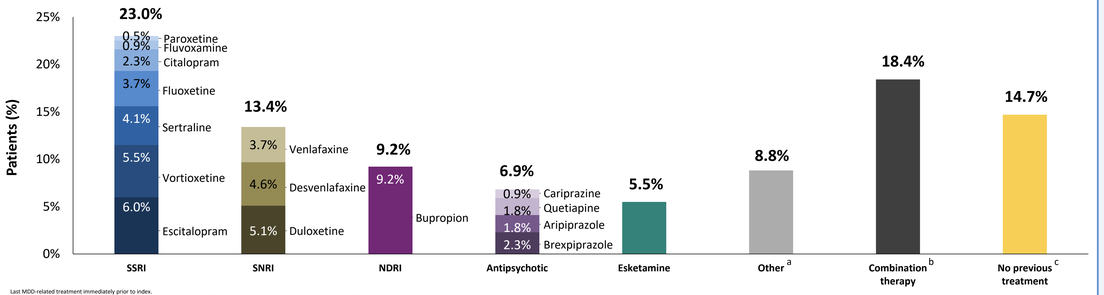
Treatment Use

Table 3: Prior MDD-related Treatment Use

	Overall cohort N = 217
Prior MDD-related treatment use	185 (85.3%)
Any SSRI/SNRI/NDRI[a]	173 (79.7%)
SSRI	117 (53.9%)
Vortioxetine	37 (17.1%)
Sertraline	27 (12.4%)
Escitalopram	24 (11.1%)
Fluoxetine	24 (11.1%)
Other[b]	21 (9.7%)
NDRI[c]	79 (36.4%)
SNRI	66 (30.4%)
Desvenlafaxine	25 (11.5%)
Venlafaxine	23 (10.6%)
Duloxetine	22 (10.1%)
Antipsychotics	69 (31.8%)
Aripiprazole	33 (15.2%)
Other[d]	46 (21.2%)
SARI[e]	41 (18.9%)
Ketamine[f]	17 (7.8%)
TeCA[g]	12 (5.5%)
TCA[h]	8 (3.7%)

MDD-related treatment use measured prior to index. Data are n (%) unless otherwise stated.
[a]Use as monotherapy or combination therapy. [b]Citalopram, vilazodone, fluvoxamine, paroxetine. [c]Bupropion. [d]Quetiapine, brexpiprazole, cariprazine, olanzapine. [e]Trazodone. [f]Esketamine. [g]Mirtazapine. [h]Nortriptyline, doxepin, amitriptyline, desipramine.
MDD, major depressive disorder; NDRI, norepinephrine-dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant.

Figure 1: Last MDD-related Treatment Pre-index

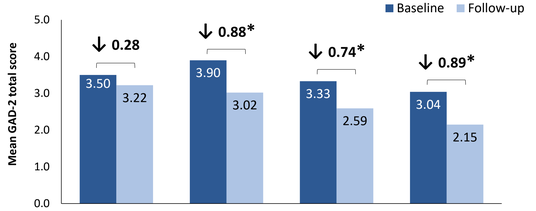


Last MDD-related treatment immediately prior to index.
[a]Other includes SARI, TCA, TeCA. [b]Combination therapy includes the use of ≥1 MDD-related medication. [c]Patients who did not receive MDD-related treatment pre-index.
MDD, major depressive disorder; NDRI, norepinephrine-dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant.

- Most patients (85.3%) had used other MDD-related treatments before initiating dextromethorphan-bupropion, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and/or norepinephrine-dopamine reuptake inhibitors (NDRIs) in 79.7% of patients, and antipsychotics in 31.8%
- The last MDD-related treatment before dextromethorphan-bupropion initiation was most commonly an SSRI (23.0%), combination therapy (18.4%), SNRI (13.4%), or NDRI (9.2%)
- Dextromethorphan-bupropion was initiated as monotherapy in 71.9% of patients

GAD-2

Figure 2: Change in GAD-2 Total Score Over Time

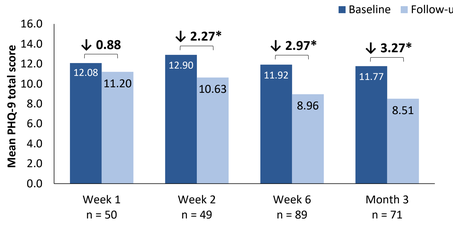


*P < 0.05. Pairwise comparison between each follow-up timepoint and the corresponding baseline for that timepoint.
GAD-2, Generalized Anxiety Disorder 2-item.

- Improvements in the GAD-2 total score were significant ($P < 0.05$) at Week 2, Week 6, and Month 3

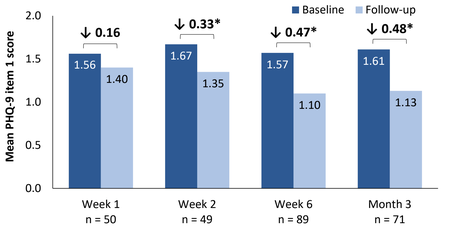
PHQ-9

Figure 3A: Change in PHQ-9 Total Score Over Time



*P < 0.05. Pairwise comparison between each follow-up timepoint and the corresponding baseline for that timepoint.
PHQ-9, Patient Health Questionnaire-9.

Figure 3B: Change in Interest or Pleasure (Anhedonia) Over Time



*P < 0.05. Pairwise comparison between each follow-up timepoint and the corresponding baseline for that timepoint. PHQ-9 item 1 evaluates agreement with the statement of "little interest or pleasure in doing things".
PHQ-9, Patient Health Questionnaire-9.

- Improvements in the PHQ-9 total score and the PHQ-9 Item 1 score were significant ($P < 0.05$) at Week 2, Week 6, and Month 3

CGI-I ≤ 3

- Most patients achieved CGI-I scores ≤ 3 ("very much improved," "much improved," or "minimally improved") at all timepoints, with improvement rates increasing from Week 1 (72.7%) through Week 2 (78.0%), Week 6 (82.5%), and Month 3 (83.9%)

Body Weight

- Body weight remained stable over time, with mean changes of -1.83 lbs at Week 1, +3.23 lbs at Week 2, +0.63 lbs at Week 6, and +0.07 lbs at Month 3 relative to baseline

Limitations

- This study was an EHR analysis based on a single US clinic; general limitations of studies derived from EHR data include potential information bias related to the availability and quality of data contained within a patient's structured and unstructured medical information
- Information was unavailable on certain factors such as the duration of MDD or disease severity
- Results from this study may not be generalizable to other patient populations

Conclusions

- In this real-world, retrospective EHR analysis of adults in the US initiating dextromethorphan-bupropion, most patients had moderate-to-severe depressive symptoms
- The majority of patients also had documented anxiety and/or ADHD, and most had prior MDD treatment exposure
- Dextromethorphan-bupropion was initiated as monotherapy in >70% of patients
- Treatment initiation with dextromethorphan-bupropion was associated with rapid and sustained improvements in both patient-reported and clinician-rated measures of anxiety and depressive symptoms over 3 months (GAD-2, CGI-I, PHQ-9, and PHQ-9 item 1 [anhedonia] scales); improvements were observed as early as Week 1, with statistically significant improvements beginning at Week 2
- Body weight remained stable following dextromethorphan-bupropion initiation