# Real-World Auvelity® (AXS-05) Patient Characteristics in Major Depressive Disorder

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## Objective

- To examine how Auvelity is used in the real-world setting for patients with MDD in the US

## Conclusions

- Using a large claims database in the US, this initial real-world assessment of Auvelity identified 22,288 patients diagnosed with MDD who began Auvelity treatment within one year of its introduction
- Approximately 10% of patients were treatment-naïve during the 12-month pre-index period
- Nearly 29% of all patients and 98% of treatment-naïve patients initiated Auvelity as monotherapy
- PCPs, NPs, and PAs played a significant role in MDD management, accounting for 27% of initial Auvelity prescriptions
- The majority of patients presented with mental health-related comorbidities and had previously attempted various treatments for MDD, emphasizing the necessity for alternative therapeutic approaches

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## Disclosures

**A Muzyk** and **FZ Syed** report no conflict of interest relevant to this poster
**H Zhou** and **J Cong** are employees of KMK Consulting, LLC.
**H Tabuteau**, and **Y Zhao** are employees of Axsome Therapeutics Inc.

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## Introduction

- Major depressive disorder (MDD) is a prevalent and chronic disorder associated with decreased quality of life, increased functional impairment, morbidity, and mortality[1-4]
- MDD treatment varies due to differences in presentation, patient demographics, and clinical characteristics, often leading to inadequate patient response to monoamine-targeted therapies[5,6]
- Despite several approved treatment classes, patients often struggle to achieve remission, highlighting the need for new options[6,7]
- N-methyl-D-aspartate (NMDA) receptor antagonism, exemplified by esketamine and now Auvelity (45-mg dextromethorphan/105-mg bupropion), offers novel therapeutic pathways for MDD[8]
- Auvelity, an oral, NMDA receptor antagonist, sigma-1 receptor agonist, and aminoketone CYP2D6 inhibitor, was approved in Aug 2022 for the treatment of MDD in adults[9]
  - The dextromethorphan component of Auvelity is an antagonist of the NMDA receptor, an ionotropic glutamate receptor, and a sigma-1 receptor agonist which modulates glutamatergic neurotransmission
  - The bupropion component of Auvelity is an aminoketone that is a CYP2D6 inhibitor that increases the bioavailability of dextromethorphan, and is a weak norepinephrine and dopamine reuptake inhibitor

## METHODS

### Study design

- Adult patients initiating Auvelity in the Symphony IDV® claims databases between Aug 2017-Sep 2023 were identified with the first Auvelity claim as the index date
- Eligible patients had ≥1 active claim over the 12-month pre-index period, and ≥1 MDD diagnosis (ICD-10-CM codes: F32.*, F33.*) over the 5-year pre-index period

### Outcomes

- Patient demographics and clinical characteristics (comorbidities and prior MDD-related medication use) during the 12-month pre-index period
- Initiation status of Auvelity: monotherapy or add-on therapy
  - Therapies that Auvelity was added on to
- Specialty of the prescriber for the initial Auvelity claim
- Characteristics of patients who did not receive any MDD-related treatment during the 12-month pre-index period ("treatment-naïve patients") and their Auvelity initiation status

## RESULTS

### Patient characteristics

- Overall, 22,288 patients with MDD treated with Auvelity (mean age 45.1 years; 68.1% women) were included (**Figure 1** and **Table 1**)
- The largest proportion of patients were aged 35-44 years (22.6%), lived in the South (40.0%), and were covered by commercial insurance (58.5%)
- Around 70% of patients obtained their initial Auvelity prescription from psychiatrists/mental health specialists, with primary care physicians (PCPs) and nurse practitioners/physician's assistants (NPs/PAs) each accounting for 13.6% of prescriptions
- The most common comorbidities in the 12-month pre-index period were mental health disorders (53.5%; 47.6% had anxiety disorders), followed by metabolic (26.4%) and musculoskeletal/pain (22.6%) (**Table 2**)

**Figure 1. Patient Attrition Diagram**




[a]ICD-10-CM codes: F32.*, F33.*

**Table 1. Patient Demographics**

| Parameter | All Auvelity Patients (N=22,288) | Treatment-naïve Patients Prior to Auvelity Initiation[a] (n=2,254) |
|---|---|---|
| **Age, mean (SD), years** | 45.1 (14.7) | 44.0 (14.5) |
| **Age groups, n (%)** | | |
| 18 to 34 years | 6,089 (27.3) | 686 (30.4) |
| 35 to 54 years | 9,894 (44.4) | 988 (43.8) |
| 55 to 64 years | 4,005 (18.0) | 358 (15.9) |
| ≥65 years old | 2,300 (10.3) | 222 (9.8) |
| **Female, n (%)** | 15,188 (68.1) | 1,451 (64.4) |
| **U.S. Region, n (%)** | | |
| South | 8,915 (40.0) | 1,042 (46.2) |
| Midwest | 6,860 (30.8) | 586 (26.0) |
| Northeast | 3,748 (16.8) | 314 (13.9) |
| West | 2,650 (11.9) | 295 (13.1) |
| **Health insurance, n (%)** | | |
| Commercial | 13,035 (58.5) | 1,318 (58.5) |
| Medicaid | 3,991 (17.9) | 374 (16.6) |
| Medicare | 3,443 (15.4) | 284 (12.6) |
| **Initiating healthcare provider specialty, n (%)** | | |
| Psychiatry and mental health | 15,562 (69.8) | 1,427 (63.3) |
| PCP | 3,032 (13.6) | 394 (17.5) |
| NP/PA | 3,041 (13.6) | 338 (15.0) |

[a]Patients who did not receive treatment during the 12-month pre-index period.
NP, nurse practitioner; PA, physician's assistant; PCP, primary care provider.

**Table 2. Patient Comorbidities**

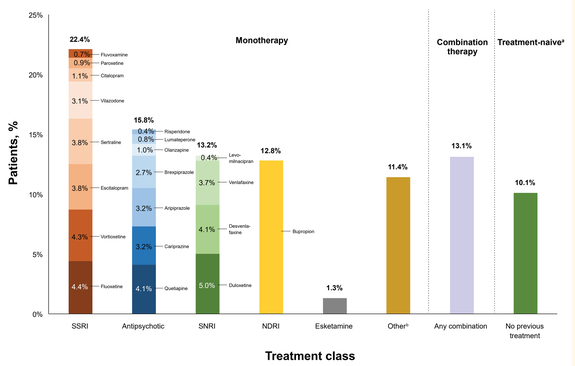
| Parameter | All Auvelity Patients (N=22,288) | Treatment-naïve Patients Prior to Auvelity Initiation[a] (n=2,254) |
|---|---|---|
| **Comorbidities, n (%)[b]** | | |
| **Mental health disorder** | **11,933 (53.5)** | **1,074 (47.6)** |
| Anxiety | 10,606 (47.6) | 946 (42.0) |
| ADHD, conduct disorders, and hyperkinetic syndrome | 3,132 (14.1) | 283 (12.6) |
| Bipolar disorder | 2,682 (12.0) | 187 (8.3) |
| PTSD | 2,548 (11.4) | 181 (8.0) |
| **Metabolic** | **5,890 (26.4)** | **539 (23.9)** |
| Hyperlipidemia | 3,409 (15.3) | 316 (14.0) |
| Obesity | 3,154 (14.2) | 287 (12.7) |
| Diabetes/prediabetes | 2,091 (9.4) | 181 (8.0) |
| **Musculoskeletal/pain** | **5,029 (22.6)** | **446 (19.8)** |
| Low back pain | 2,559 (11.5) | 224 (9.9) |
| Rheumatoid arthritis/osteoarthritis | 2,475 (11.1) | 208 (9.2) |
| Migraine and chronic headache | 1,657 (7.4) | 134 (5.9) |
| **Cardiovascular disease** | **4,227 (19.0)** | **382 (16.9)** |
| Hypertension | 3,789 (17.0) | 347 (15.4) |
| **Sleep disorders** | **4,097 (18.4)** | **347 (15.4)** |
| Sleep apnea | 2,620 (11.8) | 223 (9.9) |
| Insomnia | 1,810 (8.1) | 145 (6.4) |
| **Substance use disorder** | **1,965 (8.8)** | **155 (6.9)** |

[a]Patients who did not receive treatment during the 12-month pre-index period. [b]Additional medical conditions included: Mental health - eating disorder, obsessive compulsive disorder, personality disorders, schizoaffective disorder, schizophrenia; Musculoskeletal/pain - arthritis, osteoporosis with or without pathologic fracture; Cardiovascular - heart failure, ischemic heart disease, myocardial infarction, peripheral vascular disease, stroke/transient ischemic attack; Sleep disorders - narcolepsy; Substance use disorder - alcohol use disorder, drug use disorder.
ADHD, attention deficit disorder; PTSD, post-traumatic stress disorder.

### MDD treatments prior to Auvelity initiation

- The last MDD-related treatment that was used prior to Auvelity initiation comprised SSRI (22.4%), SNRI (13.2%), and NDRI (12.8%) monotherapies; only 1.3% of patients were treated with esketamine (**Figure 2**)
- A total of 2,254 (10.1%) patients initiated Auvelity without any MDD-related treatment in the 12-month pre-index period

**Figure 2. Last MDD-Related Treatment Prior to Auvelity Initiation**




[a]Patients who did not receive treatment during the 12-month pre-index period. [b]Other includes MAOI, SARI, TCA, TeCA.
MAOI, monoamine oxidate inhibitor; MDD, major depressive disorder; NDRI, norepinephrine and dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant.

### MDD treatment during the 12-month pre-index period

- 20,034 (89.9%) patients received any MDD-related treatment and 18,665 (83.7%) patients had received treatment with any SSRI/SNRI/NDRI (**Table 3**)
- Overall, 2.9% of patients utilized esketamine treatment

**Table 3. MDD-Related Treatment During the 12-Month Pre-Index Period**

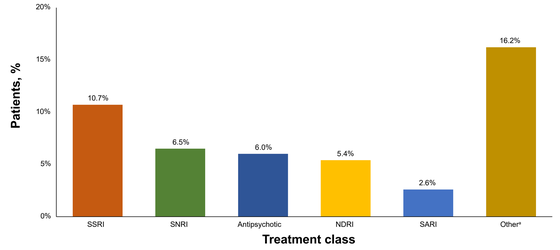
| Treatment, n (%) | All Auvelity Patients (N=22,288) |
|---|---|
| **Any MDD-related treatment** | **20,034 (89.9)** |
| **Any SSRI/NDRI/SNRI** | **18,665 (83.7)** |
| **Any SSRI** | **12,234 (54.9)** |
| Fluoxetine | 3,071 (13.8) |
| Vortioxetine | 2,902 (13.0) |
| Escitalopram | 2,849 (12.8) |
| Sertraline | 2,775 (12.5) |
| Vilazodone | 1,948 (8.7) |
| Citalopram | 815 (3.7) |
| Paroxetine | 665 (3.0) |
| Fluvoxamine | 529 (2.4) |
| **NDRI (bupropion only)** | **9,015 (40.4)** |
| **Any SNRI** | **8,002 (35.9)** |
| Duloxetine | 3,306 (14.8) |
| Desvenlafaxine | 2,683 (12.0) |
| Venlafaxine | 2,608 (11.7) |
| Levomilnacipran | 371 (1.7) |
| **Any antipsychotic** | **10,182 (45.7)** |
| Aripiprazole | 3,656 (16.4) |
| Quetiapine | 3,214 (14.4) |
| Cariprazine | 2,422 (10.9) |
| Brexpiprazole | 2,378 (10.7) |
| Olanzapine | 1,186 (5.3) |
| Lumateperone | 700 (3.1) |
| Risperidone | 530 (2.4) |
| **Any SARI** | **5,205 (23.4)** |
| **Any TCA** | **2,523 (11.3)** |
| **TeCA (mirtazapine only)** | **2,150 (9.6)** |
| **Ketamine** | **660 (2.9)** |
| Esketamine | 654 (2.9) |
| Ketamine | 8 (0.0) |
| **Any MAOI** | **202 (0.9)** |

MAOI, monoamine oxidate inhibitor; MDD, major depressive disorder; NDRI, norepinephrine and dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant.

### Auvelity initiation

- Auvelity was initiated as monotherapy in 6,418 (28.8%) patients and as an add-on therapy in 15,870 (71.2%) patients, most frequently to an SSRI (10.7%) alone or SNRI (6.5%) alone (**Figure 3**)

**Figure 3. Initiation of Auvelity as an Add-On Therapy (Frequency ≥2%)**




[a]Other includes antipsychotics + SSRI, NDRI + SSRI, antipsychotics + SNRI, NDRI + SNRI, and SARI + SSRI.
MDD, major depressive disorder; NDRI, norepinephrine and dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

### Treatment-naïve patients

- Demographics of the 2,254 (10.1%) treatment-naïve patients resembled the overall Auvelity population (mean age 44.0 years; 64.4% women) (**Table 1**)
- The largest proportion of treatment-naïve patients lived in the South (46.2%), had commercial insurance (58.5%), and received their initial Auvelity prescriptions from their psychiatrist/mental health provider (63.3%)
- PCPs and NPs/PAs accounted for a higher proportion of Auvelity prescriptions in treatment-naïve patients than the overall population (32.5% vs 27.2%)
- The prevalence of comorbidities was lower in treatment-naïve patients than the overall Auvelity population (**Table 2**)
- Overall, 2,200 (97.6%) of the treatment-naïve patients initiated Auvelity treatment as monotherapy