Characteristics and Antipsychotic Treatment Pathways of Patients With Schizophrenia Who Received Once-Every-6-Months Paliperidone Palmitate Within the First 2 Years of Approval

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Introduction

- Schizophrenia is a chronic and severe mental illness affecting between 0.25% and 1.1% of adults in the United States for which long-term adherence to treatment is important to reduce symptoms and the likelihood of relapse[1-4]
- Among patients with schizophrenia, long-acting injectable (LAI) antipsychotic (AP) medications have shown improved clinical outcomes relative to oral antipsychotics (OAP),[5,6] with some evidence suggesting advantages for formulations with longer injection intervals[7]
- In a pivotal, randomized, double-blind, phase 3 clinical trial, the efficacy of once-every-6-months paliperidone palmitate (PP6M) was found to be noninferior to that of once-every-3-months paliperidone palmitate (PP3M) in preventing relapse among patients with schizophrenia.[8] A subsequent 2-year open-label extension of the clinical trial demonstrated long-term safety and efficacy of PP6M, with a low rate of patient relapse[9]
- The US Food and Drug Administration (FDA) approved the PP6M Prescribing Information on August 30, 2021[10]
- Currently, there is limited real-world evidence on the performance of PP6M and understanding of patients with schizophrenia initiated on PP6M

Objective

- To describe the characteristics and AP treatment pathways of US patients with schizophrenia who were initiated on PP6M within the first 2 years of FDA approval

Methods

Data source

- Closed insurance claims from Komodo Research Data (KRD) from January 1, 2016, to June 30, 2023, were used
- KRD captures a US census-level representation of ages, incomes, and ethnicities to characterize a diverse patient cohort; data were de-identified and were compliant with the Health Insurance Portability and Accountability Act

Study design

- A retrospective cohort study design was used
- The index date was the date of PP6M initiation

Sample selection

- Patients were included in the study based on the criteria shown in **Figure 1**

Study measures and statistical analyses

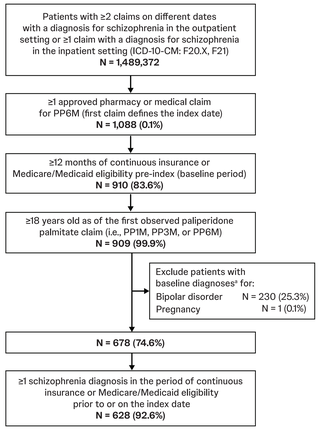
- Demographic characteristics were evaluated at the index date while clinical characteristics were evaluated over the 12-month baseline period before the index date; AP treatment pathways were evaluated any time in the period of continuous insurance eligibility or Medicaid/Medicare eligibility preceding the index date
- Baseline comorbidities were evaluated based on the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5) and Elixhauser algorithm definitions[11,12]
- Patients were categorized as transitioning to PP6M from either once-monthly paliperidone palmitate (PP1M) or PP3M based on the most recent observed claim for PP1M or PP3M directly before PP6M initiation
- The dose strength at PP6M initiation was reported based on the strength associated with the first observed PP6M claim (i.e., 1,092 mg or 1,560 mg)
- Outcomes were described using means and standard deviations for continuous variables and frequencies and proportions for categorical variables

Results

Study sample

- A total of 628 patients initiating PP6M were selected (**Figure 1**)

FIGURE 1. Sample selection



ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; PPIM, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate; PP6M, once-every-6-months paliperidone palmitate.
[a]Bipolar disorder is identified by ICD-10-CM: F31, and pregnancy is identified by ICD-10-CM: Z33, Z34, Z36, Z37, Z3A, Z64.0, and O00-O9A.

Baseline characteristics

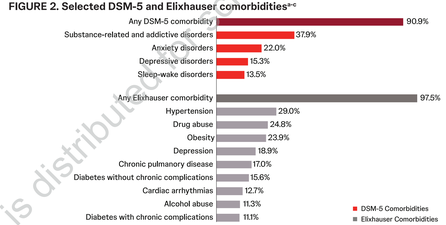
- Of the patients selected, three-quarters of patients were male (75.2%), and the mean age was 41.1 years (**Table 1**)
- Patients were racially and ethnically diverse (32.8% White, 25.0% Black, 17.7% Hispanic), and nearly all patients were covered by Medicaid (74.8%) or Medicare (18.5%)
- Nearly two-thirds of patients used antidepressants (62.4%) and one-third used mood stabilizers (34.6%) before initiating PP6M
- During the 12-month baseline period, patients had 2.3 unique mental health diagnoses on average, per the DSM-5 definitions; specifically, 37.9% of patients had substance-related and addictive disorders, 22.0% had anxiety disorders, and 15.3% had depressive disorders (**Figure 2**)

TABLE 1. Baseline demographic and clinical characteristics[a]

Length of pre-index observation period (months), mean ± SD [median]	55.3 ± 23.3 [57.3]
Age at index date (years), mean ± SD [median]	41.1 ± 12.6 [39.0]
Age at first observed schizophrenia diagnosis (years), mean ± SD [median][b]	37.4 ± 12.3 [35.0]
Female, n (%)	156 (24.8)
Race and ethnicity, n (%)	
White	206 (32.8)
Black or African American	157 (25.0)
Hispanic	111 (17.7)
Asian or Pacific Islander	33 (5.3)
Other	90 (14.3)
Unknown	31 (4.9)
Payer type, n (%)	
Medicaid	470 (74.8)
Medicare Advantage	116 (18.5)
Commercial	37 (5.9)
Missing	5 (0.8)
Dual Medicaid/Medicare coverage	5 (0.8)
Year of index date, n (%)	
2021[c]	48 (7.6)
2022	389 (61.9)
2023	191 (30.4)
Quan-CCI, mean ± SD [median]	0.6 ± 1.2 [0.0]
Number of unique DSM-5 mental health diagnoses, mean ± SD [median]	2.3 ± 1.7 [2.0]
Other mental health–related medications,[d] n (%)	
Antidepressants	392 (62.4)
Mood stabilizers	217 (34.6)
Anxiolytics	175 (27.9)

DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; FDA, Food and Drug Administration; PP6M, once-every-6-months paliperidone palmitate; Quan-CCI: Quan-Charlson Comorbidity Index; SD, standard deviation.
[a]Demographic characteristics were evaluated at the index date while clinical characteristics (i.e., Quan-CCI and number of DSM-5 diagnoses) were evaluated in the 12-month baseline period preceding the index date. [b]Age at first schizophrenia diagnosis was evaluated in the period of continuous insurance eligibility or Medicare/Medicaid eligibility anytime up to and including the index date. [c]Incomplete years of data included 2021 and 2023, given that PP6M was approved by the FDA on September 1, 2021, and the end of data was June 30, 2023. [d]Mental health medication use was evaluated any time in the period of continuous insurance eligibility or Medicare/Medicaid eligibility preceding the index date.

FIGURE 2. Selected DSM-5 and Elixhauser comorbidities[a–c]

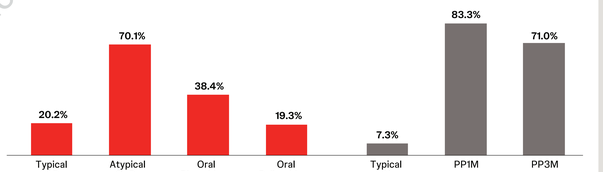


DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.
[a]DSM-5 and Elixhauser comorbidities with a prevalence of ≥10% were reported.
[b]Comorbidities were evaluated in the 12-month baseline period preceding the index date.
[c]Categories are not mutually exclusive; diagnosis codes used to report comorbidities based on DSM-5 and Elixhauser definitions overlap, and a patient may have been diagnosed with multiple comorbidities simultaneously.

Antipsychotic treatment pathways

- On average, patients were observed for 4.6 years before initiating PP6M, during which almost three-quarters of patients (70.1%) used an atypical OAP, and few patients (7.3%) used a typical LAI (**Figure 3**)
- The majority of patients were observed as having pre-index PP1M use (83.3%) or PP3M use (71.0%), with average durations of 21.9 months and 27.8 months, respectively

FIGURE 3. AP use prior to PP6M initiation[a]

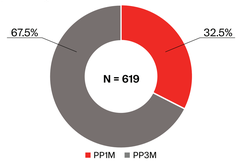


Duration of use, months	Typical OAPs	Atypical OAPs	Oral Risperidone	Oral Paliperidone	Typical LAIs	PP1M	PP3M
Mean	17.4	30.2	19.2	12.5	16.8	21.9	27.8
SD	20.1	25.1	21.1	18.3	18.8	21.2	21.5
Median	8.1	24.9	11.0	4.2	12.9	13.5	21.3

AP, antipsychotic; LAI, long-acting injectable; PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate; PP6M, once-every-6-months paliperidone palmitate; SD, standard deviation.
[a]AP use was evaluated over the entire period of continuous insurance eligibility or Medicaid/Medicare eligibility preceding the index date. The average (mean ± SD [median]) length of pre-index observation period was 55.3 ± 23.3 [57.3] months.

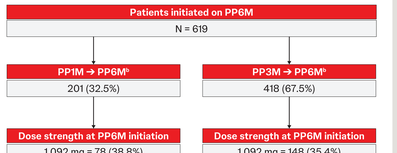
- Nearly all patients (98.6%) had observed use of PP1M or PP3M before initiating PP6M, of whom approximately two-thirds (67.5%) transitioned to PP6M from PP3M and approximately one-third (32.5%) transitioned from PP1M (**Figure 4**)
- Approximately two-thirds of patients transitioning to PP6M from PP1M (61.2%) and PP3M (64.6%) each initiated PP6M at the higher dose strength of 1,560 mg (**Figure 5**)

FIGURE 4. PP1M and PP3M use directly preceding PP6M initiation[a,b]



PP1M, once-monthly paliperidone palmitate; PP3M, once-every-3-months paliperidone palmitate; PP6M, once-every-6-months paliperidone palmitate.
[a]Based on available data, utilization of PP1M and PP3M was not observed in 9 patients before PP6M initiation.
[b]Patients were categorized as transitioning to PP6M from either PP1M or PP3M based on the most recent observed claim for PP1M or PP3M directly before PP6M initiation. Patients with a claim for PP1M and PP3M on the same day were included in the PP3M cohort.

FIGURE 5. Disposition of initiation of PP6M[a]



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[a]Based on available data, utilization of PP1M and PP3M was not observed in 9 patients before PP6M initiation. [b]Patients were categorized as transitioning to PP6M from either PP1M or PP3M based on the most recent observed claim for PP1M or PP3M directly before PP6M initiation. Patients with a claim for PP1M and PP3M on the same day were included in the PP3M cohort.

Limitations

- Data analyzed in this study were obtained from administrative claims data sources, which may be subject to inaccuracies and omissions, and were not constructed or designed to answer specific questions on patients' clinical profiles
- As with all studies utilizing administrative claims data, prescription fills do not account for whether the medication dispensed was taken as prescribed, potentially overestimating AP treatment utilization
- Given that a baseline period of only 12 months was required before the index date, this may have limited the ability to observe all pre-index AP treatment use

Conclusions

- This real-world study of patients with schizophrenia initiated on PP6M characterized a racially and ethnically diverse cohort, the majority of whom transitioned from PP3M to PP6M
- Utilization of PP1M and PP3M before initiation of PP6M was high, with a vast majority of patients observed using PP1M or PP3M for an average of approximately 2 years
- Most patients initiated PP6M at the higher dose strength of 1,560 mg, regardless of whether they transitioned from PP1M or PP3M
- These findings give valuable insights into the characteristics and AP treatment pathways of patients who initiate PP6M in real-world clinical practice within the first 2 years of approval

Disclosures
CP and CB are employees of Janssen Scientific Affairs, LLC, a Johnson & Johnson company. DP, LM, AV, LD, and MHL are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC, a Johnson & Johnson company, which funded the development and conduct of this study. LC reports personal consulting fees from AbbVie/Allergan, Acadia, Adamas, Alkermes, Angelini, Astellas, Avanir, Axsome, Biogen, BioXcel, Boehringer Ingelheim, Cadent Therapeutics, Cerevel, Clinilabs, COMPASS, Delpor, Eisai, Enterin BioPharma, HLS Therapeutics, Idorsia, INmune Bio, Impel, Intra-Cellular Therapies, Janssen, Karuna, Lundbeck, Luye, Lyndra, MapLight, Marvin, Medavante-ProPhase, Merck, Mitsubishi-Tanabe Pharma, Neumora, Neurocrine, Neurelis, Noema, Novartis, Noven, Otsuka, Ovid, Praxis, Recordati, Relmada, Reviva, Sage, Sumitomo/Sunovion, Supernus, Teva, University of Arizona, Vanda, Wells Fargo, and one-off ad hoc consulting for individuals/entities conducting marketing, commercial, or scientific scoping research; Speakers Bureau for AbbVie/Allergan, Acadia, Alkermes, Angelini, Axsome, BioXcel, Eisai, Idorsia, Intra-Cellular Therapies, Janssen, Lundbeck, Neurocrine, Noven, Otsuka, Recordati, Sage, Sunovion, Takeda, and Teva. LC was involved in CME activities organized by medical education companies such as Medscape, NACCME, NEI, Vindico and Universities and Professional Organizations/Societies. LC has stock options in Bristol-Myers Squibb, Eli Lilly, J & J, Merck, and Pfizer purchased >10 years ago, stock options in Reviva, and has royalties/publishing income from Taylor & Francis, Wiley, UpToDate, and Springer Healthcare.

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