Management of Parkinson’s Disease Psychosis

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#ASCP50

Management of Parkinson’s Disease Psychosis

To enter the Q&A and polling questions for this activity, go to ascp.com/qa and click on the title of this activity, as seen below.

Management of Parkinson’s Disease Psychosis
8:00am - 9:00am
Jack J. Chen
Disclosure

• Dr. Chen has no relevant conflicts of interest to disclose.

• Off-label Discussion:
  • Antipsychotics, acetylcholinesterase inhibitors

Learning Objectives

1. Define the provisional diagnostic criteria for Parkinson’s disease psychosis (PDP).
2. Examine the role of serotonin in the pathophysiology of PDP.
3. Discuss the clinical evidence for pharmacologic agents used in the management of PDP.
Turn and talk to an individual next to you and introduce yourself, describe your professional role / job.

Parkinson’s Disease Psychosis (PDP): Symptom Spectrum

- Severity of symptoms increase over time
- Clinical profile distinct from other psychotic conditions
  - Hallucinations: visual > voices
    - Visual: 20 - 70%
    - Somatic / Tactile: 10 - 15%
    - Auditory: ≤ 20%
    - Gustatory: 5%
    - Olfactory: 10 - 15%
  - Delusions (≤ 15%): paranoia / jealousy > thought control

References:
Parkinson’s Disease Psychosis (PDP): Common and Under-recognized\(^1-4\)

- Approx. 50% of patients with PD will develop persistent psychotic symptoms
  - 2.5 times greater risk of nursing home placement

- Under-recognized and under-treated due to:
  - mistakenly considered “benign”
  - greater emphasis on motor symptoms
  - under-reporting/under-recognition by patients / caregivers
  - prior lack of effective or tolerated treatment options

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**NINDS-NIMH Provisional Diagnostic Criteria for Parkinson’s Disease Psychosis (PDP)**

1. Occurs in patients with established diagnosis of PD
2. Onset \(\geq 1\) year after PD diagnosis
   - exclude Dementia with Lewy bodies (DLB)
3. At least 1 symptom of: hallucinations, illusions, false sense of presence, delusions
4. Symptoms present for at least 1 month
5. May occur with or without: dementia, insight, PD drugs

Differential diagnoses: Psychosis due to delirium, depression, dementias, schizophrenia, other psychiatric disorders

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## Antipsychotic Evidence-Based Pharmacology

<table>
<thead>
<tr>
<th></th>
<th>D₂</th>
<th>5HT₂A</th>
<th>Alpha₁</th>
<th>Muscarinic₁-₄</th>
<th>Histaminic₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>++++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Clozapine</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Risperidone</td>
<td>++++</td>
<td>+++++</td>
<td>+++</td>
<td>--</td>
<td>++</td>
</tr>
<tr>
<td>Pimavanserin</td>
<td>--</td>
<td>+++++</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Effects</th>
<th>Antipsych, EPS</th>
<th>Antipsychotic</th>
<th>Hypotension</th>
<th>Anticholinergic</th>
<th>Sedation, weight gain</th>
</tr>
</thead>
</table>

D₂=Dopamine type 2; EPS=Extrapyramidal symptoms; 5HT₂A=Serotonin type 2A

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## PDP: Increased 5-HT2A receptor binding

![Brain Diagram](http://thebrain.mcgill.ca/flash/capsules/celli_journey02.html)

Ventral visual pathway (including Brodmann areas 19, 20, 37).
Also BA 9, 10, 46, 11.

PET imaging setoperone F 18 ligand.
N = 7 patients with PD + VHS matched to N = 7 patients with PD no VHS
PDP: Risk Factors and Mimics\textsuperscript{1-3}

• Risk factors (pre-existing conditions):
  • Advanced age, cognitive impairment, depression, PD severity, longer duration of PD, REM sleep behavior disorder, visual perception disorders

• Mimics:
  • Delirium, dementia or depression with psychotic features

\begin{itemize}
\item Thomsen TR et al. J Neurol Neurosurg Psychiatry. 2008;79:1413-5.
\item Chen JJ. Neurol Clin 2004;22(3 Suppl 1):S83-90.
\item Brandt NJ, Chen JJ, Manza M. Consultant Pharmacist 2016;32(suppl A):4-13.
\end{itemize}

PDP: Triggers\textsuperscript{1-3}

• Triggers:
  • 40% by meds: amantadine, anticholinergics, MAO-B inhibitors, dopamine agonists, levodopa; CNS sedatives, muscle relaxants

  • 20% by: Infection, fluid/electrolyte/metabolic disturbance, CNS lesion

\begin{itemize}
\item Thomsen TR et al. J Neurol Neurosurg Psychiatry. 2008;79:1413-5.
\item Chen JJ. Neurol Clin 2004;22(3 Suppl 1):S83-90.
\item Brandt NJ, Chen JJ, Manza M. Consultant Pharmacist 2016;32(suppl A):4-13.
\end{itemize}
# PDP: Initial Management Approach (Part I)\(^1\-^3\)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Response rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Address 2° causes: fluid / electrolyte / metabolic disturbances, infection, brain lesion</td>
<td>20(^1)%</td>
</tr>
<tr>
<td>2. Re-assess and de-prescribe contributory non-PD meds (e.g., anticholinergics, benzos, bladder antispasmodics, muscle relaxants, sedatives, TCAs)</td>
<td></td>
</tr>
<tr>
<td>3. Re-assess medical necessity and sequentially de-prescribe contributory PD meds (in suggested order):(^2)</td>
<td></td>
</tr>
<tr>
<td>a. Anticholinergics, MAO-B inhibitors, amantadine, dopamine agonist, COMT-inhibitor</td>
<td></td>
</tr>
<tr>
<td>b. Lastly: carbidopa/levodopa</td>
<td>40(^1)%</td>
</tr>
</tbody>
</table>

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# PDP: Antipsychotic Recommendations (Part II)\(^1\-^6\)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Responder Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. If symptoms persist and MMSE ≥ 20: Add an atypical antipsychotic:</td>
<td></td>
</tr>
<tr>
<td>a. Pimavanserin 34 mg qd</td>
<td>49(^1)%</td>
</tr>
<tr>
<td>b. Quetiapine 25 mg at qhs; increase 25 mg weekly until improvement / AEs</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>c. Clozapine 12.5 mg at qhs; increase 12.5 mg weekly until improvement / AEs</td>
<td>48(^2)%</td>
</tr>
<tr>
<td>5. If MMSE &lt;20: Consider acetylcholinesterase inhibitor</td>
<td></td>
</tr>
</tbody>
</table>

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5. Seppi K et al. Mov Disord. 2019;34:180-198
## Conclusions From 2019 MDS Evidence-Based Review

<table>
<thead>
<tr>
<th>Drug</th>
<th>Efficacy</th>
<th>Safety</th>
<th>Practice Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>Efficacious</td>
<td>Acceptable risk with specialized monitoring</td>
<td>Clinically useful</td>
</tr>
<tr>
<td>Pimavanserin</td>
<td>Efficacious</td>
<td>Acceptable risk without specialized monitoring</td>
<td>Clinically Useful</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Insufficient evidence</td>
<td>Acceptable risk without specialized monitoring</td>
<td>Possibly useful</td>
</tr>
</tbody>
</table>

1. MDS = Movement Disorder Society

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## Antipsychotics That Are Not Recommended

- The following ARE NOT recommended for PDP due to lack of efficacy and/or unacceptable risk of motor deterioration (harmful):
  - Traditional antipsychotics¹ (EFNS/MDS-ES)
  - Aripiprazole¹ (EFNS/MDS-ES)
  - Olanzapine¹-³ (AAN, EFNS/MDS-ES; MDS)
  - Risperidone¹ (EFNS/MDS-ES)

³. Seppi K et al. Mov Disord. 2019;34:180-198
### Use of Antipsychotics for PD Psychosis In U.S. Long-Term Care Residents (Oct 2010 – June 2016)¹

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>LTC Database 1</th>
<th>LTC Database 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>8.6%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Clozapine</td>
<td>1.7%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>6.4%</td>
<td>20%</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>11%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>51.7%</td>
<td>57%</td>
</tr>
<tr>
<td>Pimavanserin</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Risperidone</td>
<td>17.4%</td>
<td>24.6%</td>
</tr>
</tbody>
</table>

¹ Pimavanserin not commercially available during study time frame


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### Pimavanserin: 5-HT₂A Inverse Agonist & Antagonist

- **Full agonist**: "Promotes receptor activity"
- **Partial agonist**: "Partially promotes receptor activity"
- **Neutral antagonist**: "Blocks receptor"
- **Inverse agonist**: "Downregulates receptor activity"

**Activation by saturating endogenous ligand**

**Constitutive activity of receptor in absence of ligand**

**Response**

**[Drug]**
Pimavanserin PDP: Dosage and Adverse Effects\textsuperscript{1,2}

Note: pimavanserin access via specialty pharmaceutical channels

- Initial and Maintenance Dose: 34 mg once daily (no titration)
- Clinical benefits at 4 weeks
  - Does not impair motor function
- Common AEs: Confusion (6%), peripheral edema (7%)
- Drug interactions: See Table
- Rare & serious AEs: QT\textsubscript{c} interval prolongation

\textsuperscript{2} Nuplazid (pimavanserin) package insert. San Diego, CA: ACADIA Pharmaceuticals; 2019

\*incidence \(\geq 5\%\) and at least twice the rate of placebo
Clozapine: PDP Efficacious vs placebo\textsuperscript{1-6}

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Antipsychotic Mean (SD)</th>
<th>Placebo Mean (SD)</th>
<th>VMO (fixed) 95% CI</th>
<th>Weight %</th>
<th>VMO (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Clozapine vs. placebo</td>
<td>-1.80 (1.50)</td>
<td>-0.60 (1.10)</td>
<td>4.07</td>
<td>-1.20 (-1.86, -0.54)</td>
<td></td>
</tr>
<tr>
<td>FCPSG 1999</td>
<td>32</td>
<td>28</td>
<td>95.93</td>
<td>-1.10 (-1.24, -0.96)</td>
<td></td>
</tr>
<tr>
<td>PSYCLOPS 1999</td>
<td>27</td>
<td>27</td>
<td>100.00</td>
<td>-1.10 (-1.24, -0.97)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95%) CI</td>
<td>59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Exclusion: MMSE <20

- CGI responders: 48% clozapine vs 11% placebo\textsuperscript{6}

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Clozapine for PDP: Dosage and Adverse Effects\textsuperscript{1-5}

Note: Treatment access granted via Clozapine REMS Program

- Initial dose: 12.5 mg at bedtime; titrate up weekly
- Usual effective dose: 50+ mg /day
- Benefits within Week 2 (dependent on titration schedule)
  - Does not impair motor function
  - Common AEs: Somnolence (50%), orthostatic hypotension (17%), sialorrhea (14%), weight gain (9%), mild neutropenia (5%)
- Drug interactions: See Table
- Rare & serious AEs: ANC < 500 µg/L, myocarditis, seizures

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### Quetiapine: PDP Efficacy Not Supported by Evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>N</th>
<th>Duration</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fernandez et al, 2009</td>
<td>Quetiapine vs placebo</td>
<td>16</td>
<td>4 weeks</td>
<td>Quetiapine effective. CGI improvement &gt; placebo. Mean dose 58.3 mg/day.</td>
</tr>
<tr>
<td>Shotbolt et al, 2009</td>
<td>Quetiapine vs placebo</td>
<td>24</td>
<td>12 weeks</td>
<td>No different vs placebo in time to drop out due to lack of efficacy. Mean dose 73 mg/day.</td>
</tr>
<tr>
<td>Kurlan et al, 2007</td>
<td>Quetiapine vs placebo</td>
<td>40</td>
<td>10 weeks</td>
<td>No different vs placebo on change in total BPRS. Mean dose 120 mg/day.</td>
</tr>
<tr>
<td>Rabey et al, 2007</td>
<td>Quetiapine vs placebo</td>
<td>58</td>
<td>12 weeks</td>
<td>No different vs placebo on change in total BPRS. Mean dose 119 mg/day.</td>
</tr>
<tr>
<td>Ondo et al, 2004</td>
<td>Quetiapine vs placebo</td>
<td>31</td>
<td>12 weeks</td>
<td>No different vs placebo on change in total BPRS or Baylor PD Hallucination Questionnaire.</td>
</tr>
<tr>
<td>Merims et al, 2007</td>
<td>Quetiapine vs clozapine</td>
<td>27</td>
<td>22 weeks</td>
<td>Both similarly improved CGI. Mean doses: quetiapine 91 mg/day; clozapine 13 mg/day.</td>
</tr>
<tr>
<td>Morgante et al, 2004</td>
<td>Quetiapine vs clozapine</td>
<td>27</td>
<td>12 weeks</td>
<td>Both similarly improved BPRS and CGI. Mean doses: quetiapine 91 mg/day; clozapine 26 mg/day.</td>
</tr>
</tbody>
</table>

### Quetiapine for PDP: Dosage and Adverse Effects

- **Initial dose**: 25 mg at bedtime; titrate up weekly
- **Usual effective dose**: 50 - 200 mg /day
- **Benefits within Week 2** (dependent on titration schedule)
  - Potential for modest worsening of motor function
  - Common AEs: Somnolence (40%), orthostatic hypotension (25%)
- **Drug interactions**: See Table
- **Rare & serious AEs**: QTc prolongation

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Drug Interactions

<table>
<thead>
<tr>
<th>CYP450 1A2 Inhibitors</th>
<th>CYP450 2D6 Inhibitors</th>
<th>CYP450 3A4 Inducers</th>
<th>CYP450 3A4 Inhibitors</th>
<th>Concomitant Drugs that Prolong QT Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine¹</td>
<td>Reduce CLOZ by one third</td>
<td>Monitor for AEs</td>
<td>Avoid; if inducer necessary: monitor of efficacy</td>
<td>Monitor for AEs</td>
</tr>
<tr>
<td>Pimavanserin²</td>
<td>NA</td>
<td>NA</td>
<td>Avoid; if inducer necessary: monitor of efficacy</td>
<td>Reduce PIMA to 10 mg daily</td>
</tr>
<tr>
<td>Quetiapine³</td>
<td>NA</td>
<td>NA</td>
<td>Increase quetiapine dose up to 5 fold</td>
<td>Reduce QUE dose to one sixth</td>
</tr>
</tbody>
</table>


CYP450 1A2 inhibitors: e.g., ciprofloxacin, enoxacin, fluvoxamine
CYP450 2D6 inhibitors: e.g., quinidine, paroxetine, fluoxetine, bupropion
CYP450 3A4 inducers: e.g., carbamazepine, rifampin
CYP450 3A4 inhibitors: e.g., azole antifungals, HIV and HCV protease inhibitors, nefazodone, divalproex sodium

Summary Evidence Table: Mean Difference vs Placebo

<table>
<thead>
<tr>
<th></th>
<th>N*</th>
<th>CGI (95% CI) (% improvement)</th>
<th>SAPS (% improvement)</th>
<th>UPDRS motor (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(95% CI)</td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td>Clozapine¹,²</td>
<td>114</td>
<td>-1.1 (-1.24, -0.97) (25%)</td>
<td>-8**† (37%)</td>
<td>-1.44 (-1.24, -0.97)</td>
</tr>
<tr>
<td>Pimavanserin³</td>
<td>185</td>
<td>-0.58 (-0.92, -0.25) (14%)</td>
<td>-3.06† (SAPS-PD) (20%)</td>
<td>-0.06 (-2.22, 0.6)</td>
</tr>
<tr>
<td>Quetiapine⁴</td>
<td>11</td>
<td>-1.09 (SD 1.01)‡</td>
<td>Not reported</td>
<td>-2.91</td>
</tr>
</tbody>
</table>

*Total evaluable subjects from treatment and placebo groups
**SAPS data from PSG study (n=54)¹ †p<0.015 $p=0.03

CGI = Clinical Global Impression of Severity
SAPS = Scale for the Assessment of Positive Symptoms
UPDRS = Unified Parkinson’s Disease Rating Scale

Share your current knowledge of mortality in patients with PD psychosis.

### Post-marketing Mortality Rates: PD & PD Psychosis

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Mortality Rate per 100 Patient-Years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Medicare Data (Jan 2012 to Dec 2015)&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Parkinson’s disease (n=106,893)</td>
<td>7.31 (7.15 – 7.47)</td>
</tr>
<tr>
<td>PD psychosis (n=68,821)</td>
<td>28.18 (27.53 – 28.8)</td>
</tr>
<tr>
<td>Clozapine (April 1995 to February 1997)&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Patients with PD psychosis</td>
<td>~ 12</td>
</tr>
<tr>
<td>Pimavanserin (April 2016 to April 2018)&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Patients with PD psychosis</td>
<td>12.8 (12.0 – 13.7)</td>
</tr>
<tr>
<td>U.S. Veterans Administration (June 1999 – July 2010)&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Patients with PD taking antipsychotics (n=7877)</td>
<td>Quetiapine 18.6 (16.9 – 20.3)</td>
</tr>
<tr>
<td></td>
<td>Olanzapine 29.3 (24.1 – 35.2)</td>
</tr>
<tr>
<td></td>
<td>Risperidone 31 (26.4 – 36.1)</td>
</tr>
<tr>
<td></td>
<td>Haloperidol 49 (37.4 – 63)</td>
</tr>
</tbody>
</table>

---

# Pimavanserin and Quetiapine: Mortality

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pimavanserin</th>
<th>Quetiapine</th>
<th>Pimavanserin + Quetiapine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>113</td>
<td>505</td>
<td>58</td>
</tr>
<tr>
<td>% Female</td>
<td>38.1</td>
<td>42</td>
<td>37.9</td>
</tr>
<tr>
<td>Total Deaths (2 year period)</td>
<td>8</td>
<td>58</td>
<td>7</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>7.1</td>
<td>11.5</td>
<td>12.1</td>
</tr>
<tr>
<td>Mean Age of Deceased (SD)</td>
<td>81.4 (7.4)</td>
<td>79.6 (8.7)</td>
<td>82 (8)</td>
</tr>
<tr>
<td>Odds Ratio (95% CI)*</td>
<td>1.23 (0.57–2.68)</td>
<td>1.74 (1.15–2.62)</td>
<td>2.16 (0.93–5.01)</td>
</tr>
</tbody>
</table>

*April 2016 to April 2018; Compared to age-matched PD cohort mortality of 5.9%*  

Mean Changes in QTc Interval with Selected Psychotropics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Mean Increase in QTc Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziprasidone</td>
<td>160 mg x 10 days</td>
<td>15.9 msec¹</td>
</tr>
<tr>
<td>Citalopram</td>
<td>40 mg</td>
<td>12.6 msec²</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>100 mg</td>
<td>10.2 msec³</td>
</tr>
<tr>
<td>ICH E14 Threshold ΔΔQTc</td>
<td>Drug vs. placebo</td>
<td>10 msec⁴</td>
</tr>
<tr>
<td>Citalopram</td>
<td>20 mg</td>
<td>8.5 msec²</td>
</tr>
<tr>
<td>Pimavanserin</td>
<td>34 mg daily x8 days</td>
<td>6.9 msec⁵</td>
</tr>
<tr>
<td>Clozapine</td>
<td>NA</td>
<td>NA (case reports)⁶</td>
</tr>
</tbody>
</table>

- Follow institutional protocol. If QTc >500 msec or > 60 msec from baseline, D/C drug
- Risk factors: age > 65 yrs, female, underlying medical condition, clinical chemistries (low K+, low Mg++), co-prescribed medications

Case

- 65-year-old man with PD. Lives with spouse in 55+ community.
- Pt. with visual hallucinations, paranoid delusions. Initially infrequent; however, escalating frequency and severity of past 6 months
- Hallucinations of 4 men who loiter in his patio; believes these “patio people” conspiring with neighbors and “spying” on him. Wife admits increasing concern for her safety
- Given the escalation of behavior, “rapid” symptomatic treatment with antipsychotic is desired. Discuss treatment approach and recommendation for outpatient management
Tips for Switching from Quetiapine to Pimavanserin

• Quetiapine a short-erm “bridge” therapy to pimavanserin
• If quetiapine suboptimal efficacy or not tolerated

1. Add pimavanserin 34 mg once daily to regimen
   • Overlap both drugs x 4 weeks
2. Then reduce quetiapine dose by 25 mg weekly until discontinued

Tips for Switching from Clozapine to Pimavanserin\textsuperscript{1,2}

• If clozapine suboptimal efficacy or not tolerated
1. Add pimavanserin 34 mg once daily to regimen
   • Overlap both drugs x 4 weeks
2. Then discontinue clozapine over 1 to 2 weeks (e.g., 12.5 to 25 mg weekly) until discontinued
3. Maintain in clozapine REMSs program until pimavanserin efficacy and tolerability established

\textsuperscript{1} Clozaril (clozapine) package insert. Rosemont, PA: HLS Therapeutics; 2015
Tips for Switching from Pimavanserin to Clozapine or Quetiapine

• If pimavanserin suboptimal efficacy or not tolerated
• Note: Pimavanserin $T_{1/2}$ is 57 hours

1. Overnight switch
   a. Discontinue pimavanserin
   b. Next day: start new agent at initiation dose and titrate up as per protocol / standard of practice

Self-Assessment Question 1

Pharmacologically significant binding affinity to which of the following receptors is shared by all antipsychotics (traditional and atypical)?

A. Dopamine$_2$
B. Histaminic$_1$
C. Muscarinic$_{1-5}$
D. Serotonin$_{2A}$
Poll: Pharmacologically significant binding affinity to which of the following receptors is shared by all antipsychotics (traditional and atypical)?

To access the polling questions, go to this link: ascp.com/qa and select the “Management of Parkinson’s Disease Psychosis” activity, as seen below.

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A. Dopamine$_2$
B. Histaminic$_1$
C. Muscarinic$_{1-5}$
D. Serotonin$_{2A}$
Self-Assessment Question 2

Fill in the blank. In the treatment of PD psychosis, ______ does NOT require gradual dose titration for efficacy.

A. Clozapine
B. Pimavanserin
C. Quetiapine
D. All the above
Self-Assessment Question 2

Fill in the blank. In the treatment of PD psychosis, _______ does NOT require gradual dose titration for efficacy.

A. Clozapine
B. Pimavanserin
C. Quetiapine
D. All the above

Self-Assessment Question 3 Case

A patient with PD psychosis requires treatment with an antipsychotic. Patient has a history of insomnia, nighttime arousals with hallucinations. Given the available information, which of the following would be most clinically useful as initial therapy?

A. Clozapine
B. Pimavanserin
C. Olanzapine
D. Quetiapine
Poll: A patient with PD psychosis requires treatment with an antipsychotic. Patient has a history of insomnia, nighttime arousals with hallucinations. Given the available information, which of the following would be most clinically useful as initial therapy?

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Self-Assessment Question 3 Case

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D. Quetiapine
Self-Assessment Question 4

For patients with PD, which of the following statements is shared by clozapine and pimavanserin?

A. Associated with increased mortality
B. Worsening of motor function is common
C. Results from RCTs support efficacy in PD psychosis
D. Common adverse effects include orthostatic hypotension, somnolence, and weight gain

Poll: For patients with PD, which of the following statements is shared by clozapine and pimavanserin?
Self-Assessment Question 4

For patients with PD, which of the following statements is shared by clozapine, pimavanserin, and quetiapine?

A. Associated with increased mortality
B. Worsening of motor function is common
C. **Results from RCTs support efficacy in PD psychosis**
D. Common adverse effects include orthostatic hypotension, somnolence, and weight gain

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PD Psychosis Summary 1

- Interview patients, caregivers, staff to better identify symptoms; assess urgency and impact
- **First:** treat systemic illness; remove triggers; assess meds for deprescribing
- **Second:** consider clozapine, pimavanserin, or quetiapine for enduring therapy
- **Third:** Avoid traditional or atypical antipsychotics (i.e., aripiprazole, olanzapine, risperidone) due to lack of efficacy and/or adverse safety risk
PD Psychosis Summary 2

**Patient-specific choices for pharmacotherapy include:**

- First consideration: **Pimavanserin**
  - Utility may be reduced by time to onset of benefit
  - Quetiapine as “bridge” therapy
- If no access to pimavanserin: **Clozapine**
  - Utility may be reduced by REMS for neutropenia
- If no access to pimavanserin or clozapine: **Quetiapine**

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**Live Content Slide**

*When playing as a slideshow, this slide will display live content*

**Social Q&A**

To access Q&A, go to this link: ascp.com/qa and select the “Management of Parkinson’s Disease Psychosis” activity, as seen below.
Thank You!