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NUPLAZID® (pimavanserin)

Switching From Other Antipsychotics in Patients With Parkinson's Disease Psychosis



SUMMARY

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While recommendations based on expert opinion are available in the literature, there are no controlled clinical trials that have assessed switching strategies from other antipsychotics to pimavanserin in patients with PD psychosis



Important Considerations for Switching Antipsychotics

- Drug half-life
- Time to steady state
- Time for withdrawal
- Drug-drug interaction



Three Potential Strategies for Switching Antipsychotics

- Abrupt switch
- Cross taper
- Overlap and discontinue



Optimizing Antipsychotic Transitions in PD Psychosis

- Tailoring the switch to patient's disease and current treatment
- Setting expectations with the patient or caregiver before the switch

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- For reactive use by Medical Affairs for educational and scientific purposes only. Do not copy or distribute. NUPLAZID is the only US Food and Drug Administration (FDA) approved therapy for the treatment of hallucinations and delusions associated with PD psychosis
- NUPLAZID prolongs the QT interval and should be avoided in patients with risk factors for QT prolongation or in combination with other drugs that also increase the QT interval¹
- There have been no controlled studies done to assess switching from other antipsychotics to pimavanserin, and the efficacy and safety of pimavanserin in combination with other antipsychotics has not been established and approved by the FDA. The information provided herein is to inform your clinical decision making but should not be considered an endorsement from Acadia around any particular strategy

Abbreviations and References

SUMMARY

Published Studies on Pimavanserin



Pimavanserin trials did not evaluate strategies of switching participants from other antipsychotics to pimavanserin, as concomitant antipsychotics were discontinued prior to baseline visits. In Study 020, a randomized, double-blind, placebo-controlled, multicenter, Phase 3 study of pimavanserin in 185 adult participants with PD psychosis, concomitant antipsychotics were not permitted during the study and were discontinued no less than 5 half-lives prior to the baseline visit²

Expert-Based Guidance for Initiating Pimavanserin



A panel of 14 experts in neurology and psychiatry developed guidance (2018) for switching to pimavanserin based on published data about switching antipsychotics in psychiatric disorders, PD psychosis patient-treatment experiences, and antipsychotic pharmacology. Editorial changes and corrections to this consensus were also published (2019).^{3,4}



Guidance document (2018)



Guidance document (2019)

These consensus recommendations form the basis of a quick reference document for healthcare professionals caring for patients with PD psychosis that was developed by the American Society of Consultant Pharmacists⁵



Quick reference document



A panel of 6 experts in neurology and psychiatry developed guidance on first-line and subsequent treatment strategies for PD psychosis in 2025, taking into account the treatment experience and preferences of the expert panel since their previous consensus, as well as current pathophysiology and recent clinical data⁶



Guidance document (2025)

By providing this information, Acadia is not recommending or suggesting that pimavanserin, or any other drug mentioned, should be used for conditions, purposes, or uses other than the one(s) for which the drug has been approved by the FDA

Clinical studies evaluating the optimal strategy for switching from a prior antipsychotic to pimavanserin have not been performed. Therefore, the clinical relevance of the information provided is unknown. Strategies for switching to pimavanserin should be tailored to a specific patient's disease and current treatment. Expectations should be discussed with the patient and/or caregiver prior to initiating the switch to pimavanserin

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SUMMARY

Important Considerations for Switching Antipsychotics

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PK and pharmacodynamic characteristics of the antipsychotics involved are important considerations^{2,7}
When developing the strategy for switching antipsychotics, consider^{3,7}



Half-life



Time to steady state



Time for withdrawal



Potential drug interactions

Table 1. Relevant PK parameters for switching antipsychotics

Drug	Half-life	Steady state	Major P450 metabolic enzymes
Pimavanserin ^{1,3,8}	57 hours	12 days	CYP3A4 and CYP3A5
Clozapine ⁹	12 hours (range: 4–66 hours)	2.5 hours (range: 1–6 hours)	CYP3A4, CYP1A2, and CYP2D6
Quetiapine ¹⁰	6 hours	2 days	CYP3A4



The tolerability of switching antipsychotics in patients with PD can be influenced by each medication's affinity for different receptors, especially if the withdrawal is abrupt^{3,7}

Consider affinity of different antipsychotics for

- Dopaminergic receptors
- Muscarinic receptors
- Cholinergic receptors
- Histaminergic receptors
- Adrenergic receptors

Table 2. Receptor selectivity based on the R-SAT™ platform (K_i [nM])¹¹

Receptor		Pimavanserin	Typical APD Haloperidol	Clozapine	Atypical APDs		
					Olanzapine	Quetiapine	Risperidone
Serotonergic	5-HT2A	0.4	50	7	2.5	250	0.2
	5-HT2B	nr	nr	40	80	1100	12
	5-HT2C	16	nr	40	80	nr	100
	5-HT1A	nr	nr	nr	nr	nr	nr
Histaminergic	H1	nr	nr	0.5	4	5	60
Muscarinic	M1	nr	nr	16	60	250	nr
	M2	nr	nr	nr	nr	-	nr
	M3	nr	nr	6	nr	200	nr
	M4	nr	nr	nr	40	150	nr
	M5	nr	nr	30	60	-	nr
Dopaminergic	D1	nr	100	nr	100	-	60
	D2	nr	0.1	50	4	30	0.5
	D3	nr	0.2	nr	25	9	13
Adrenergic	A1A	nr	40	8	100	nr	3
	A1D	-	nr	nr	nr	nr	50
	A2A	nr	nr	nr	nr	nr	20
	A2B	nr	nr	50	nr	nr	50
	A2C	nr	50	40	nr	nr	13

Data are K_i values in nM derived from the R-SAT™ platform

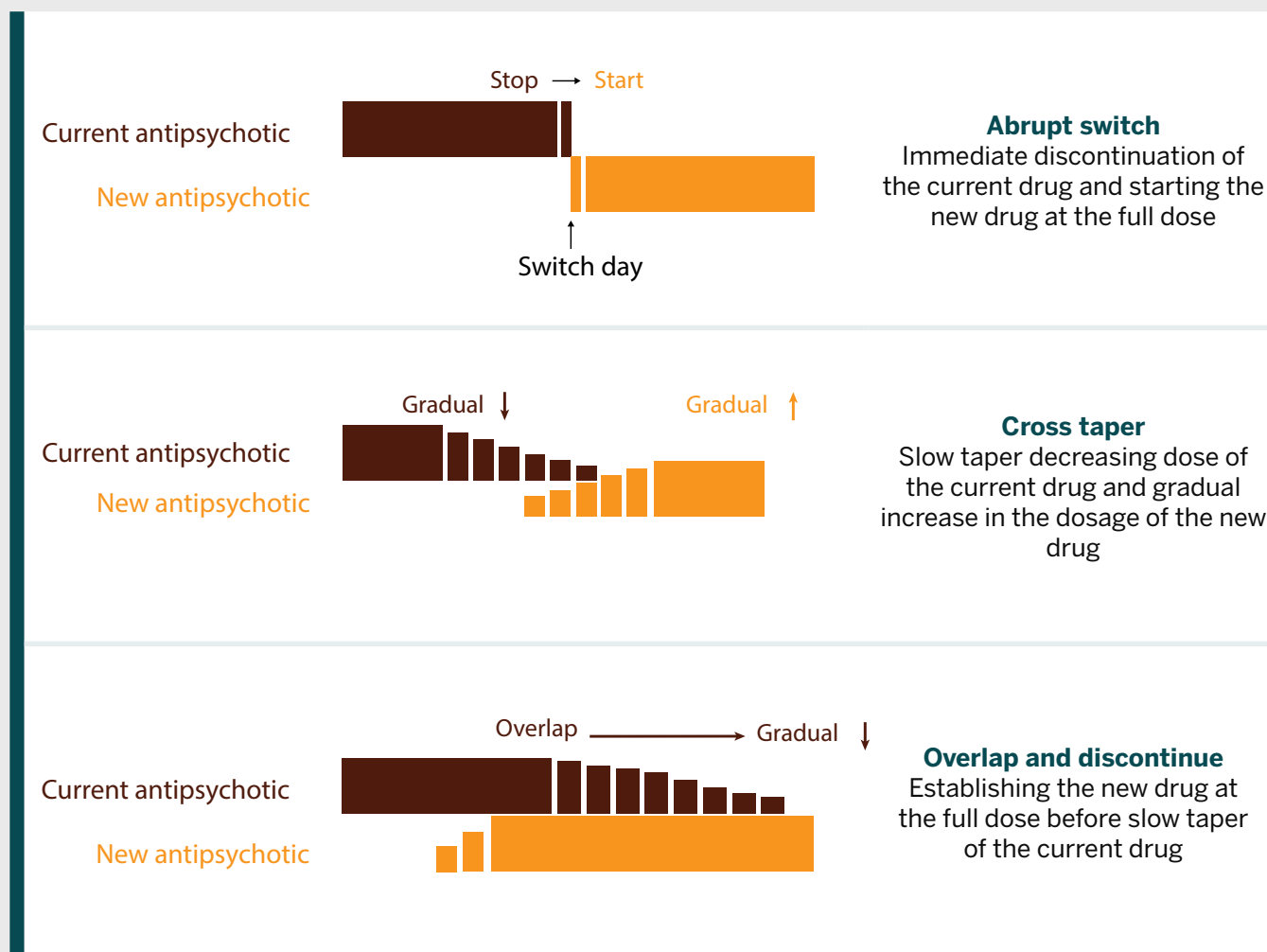
Abbreviations and References

SUMMARY

Three Potential Strategies for Switching Antipsychotics for Switching Antipsychotics

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According to medical literature, there are 3 potential strategies that could be considered for switching antipsychotics¹²



- Each strategy should be evaluated based on the efficacy-to-safety benefit and be tailored to the individual patient¹¹
- Special consideration should be made for the differences in the half-lives of clozapine, quetiapine, and pimavanserin (12 hours, 6 hours, and 57 hours, respectively)⁸⁻¹⁰

SUMMARY

Optimizing Antipsychotic Transitions in PD Psychosis

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When switching antipsychotics, there are important considerations to ensure patients attain optimal therapeutic outcomes while minimizing the risk of adverse events, including relapse⁷

Tailoring the switch to patient's disease and current treatment



Evaluate patient's condition to confirm⁷

- Indication for switching
- Feasibility of optimizing current therapy
- Risks based on health status and drug-drug interactions



If possible, maintain adjunctive therapies until the new antipsychotic switch is stabilized⁷



Tailor the approach to the patient's needs, quality-of-life considerations, and the profile of the new antipsychotic⁷

Setting expectations with the patient or caregiver before the switch



Challenges may arise during the transition period, necessitating frequent dialogue with the physician/office^{7,12}



Patients should continue the medication switch through to completion^{7,12}



Allow enough time at the full therapeutic dose to assess the impact of the new antipsychotic¹¹

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X

Abbreviations and References

Abbreviations: 5-HT = serotonin; A = alpha-adrenergic; APD = antipsychotic drug; CYP = cytochrome P; D = dopamine; FDA = Food and Drug Administration; H = histamine; K_i = inhibitory constant; M = muscarinic acetylcholine; nM = nanomole; nr = no response; PD = Parkinson's disease; PK = pharmacokinetic; R-SAT = Receptor Selection and Amplification Technology; US = United States.

References: 1. NUPLAZID® (pimavanserin) [package insert]. San Diego, CA. Acadia Pharmaceuticals Inc. [\[Link\]](#). 2. Cummings J, et al. *Lancet*. 2014;383(9916):533-540. [\[PubMed\]](#). 3. Black KJ, et al. *CNS Spectr*. 2018;23(6):402-413. [\[PubMed\]](#). 4. Black KJ, et al. *CNS Spectr*. 2019;24(5):574-575. [\[PubMed\]](#). 5. American Society of Consultant Pharmacists (ASCP). Quick Reference Document for Changing Antipsychotic Regimens for Treatment of Parkinson's Disease Psychosis. March 2024. [\[Link\]](#). 6. Isaacson SH, et al. *Expert Opin Pharmacother*. 2025;26(6):707-717. [\[PubMed\]](#). 7. Bernardo M, et al. *Rev Psiquiatr Salud Ment*. 2011;4(3):150-168. [\[PubMed\]](#). 8. Acadia Pharmaceutical Inc. NUPLAZID® Sponsor Background Information for a Meeting of the Psychopharmacologic Drugs Advisory Committee on 29 March 2016. 9. CLOZARIL® (clozapine) [package insert]. Novartis Pharmaceuticals Corporation. [\[Link\]](#). 10. SEROQUEL® (quetiapine) [package insert]. Wilmington, DE. AstraZeneca Pharmaceuticals LP. [\[Link\]](#). 11. Hacksell U, et al. *Neurochem Res*. 2014;39(10):2008-2017. [\[PubMed\]](#). 12. Weiden PJ, *J Psychopharmacol*. 2006;20(1):104-118. [\[PubMed\]](#).