Welcome

Clozapine & LAI Virtual Forum

April 3, 2024 | 4:00 – 4:45 pm ET

The Clozapine & LAI Virtual Forum is a peer-to-peer, interactive dialogue between psychiatrists, nurse practitioners, and other prescribing clinicians. It is informal, no registration required — just join our Zoom call and share your challenges and questions on the month's trending topic around either clozapine or LAIs.

TODAY'S TOPIC:
Long-Acting Injectable Antipsychotic Medications (LAIs) & VMAT2 Inhibitors

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Moderators

Donna Rolin, PhD, APRN, PMHCNS-BC, PMHNP-BC

SMI Adviser Nursing Expert; University of Texas, Austin

Dr. Donna Rolin is Clinical Associate Professor and the Director of the Psychiatric Mental Health Nurse Practitioner program at the University of Texas with 23 years of experience in psychiatric nursing, including inpatient, community, forensic, and older adult settings.

Megan Ehret, PharmD, MS, BCPP

SMI Adviser Pharmacist Expert; University of Maryland, Baltimore

Dr. Megan Ehret is a Professor at University of Maryland School of Pharmacy in the Department of Practice, Sciences, and Health Outcomes Research and is Co-Director of the Mental Health Program. She is a Past-President of the American Association of Psychiatric Pharmacists. Her current interests include psychotropic medication adherence and the incorporation of the psychiatric pharmacist in practice.

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Discussion Questions

- How often are your patients with SMI on LAIs generally assessed for TD with a structured instrument?
- What is your experience in utilizing VMAT2 inhibitors with your patients?
  - Any pearls of wisdom to share?
  - Have you seen TD symptoms improve? If so, on what scale?
- What tolerability issues have you seen?

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VMAT2 MEDICATIONS FOR TARDIVE DYSKINESIA

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14. APA *recommends* (1B) that patients who have moderate to severe or disabling tardive dyskinesia associated with antipsychotic therapy be treated with a reversible inhibitor of the vesicular monoamine transporter 2 (VMAT2).

SUPPORTING EVIDENCE

- Based on information from a good-quality systematic review (Solmi et al. 2018) on deutetrabenazine and valbenazine treatment and less robust clinical trials on tetrabenazine
- Clinical assessment of akathisia, dystonia, parkinsonism, and other abnormal involuntary movements, including tardive dyskinesia, at each visit.
  - Assessment with a structured instruments (e.g. AIMS, DISCUS) at a minimum of every 6 months in patients at high risk of TD and at least every 12 months in other patients as well as in new onset or exacerbation of pre-existing movements is detected at any visit

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American Academy of Neurology (AAN): Recommendations for Treatment of Tardive Syndrome

Level A	Level B	Level C	Level U
must *be recommended as treatment*	***should*** *be considered as treatment*	***might*** *be considered as treatment*	*insufficient evidence to support or refute*
• Deutetrabenazine • Valbenazine	• Clonazepam • Ginkgo biloba	• Amantadine • Tetrabenazine • Pallidal deep brain stimulation (intractable TD)	• Withdrawing causative agents • Switching from typical to atypical DRBA

Bhidayasiri R et al. J Neurol Sci. 2018;389:67-75.

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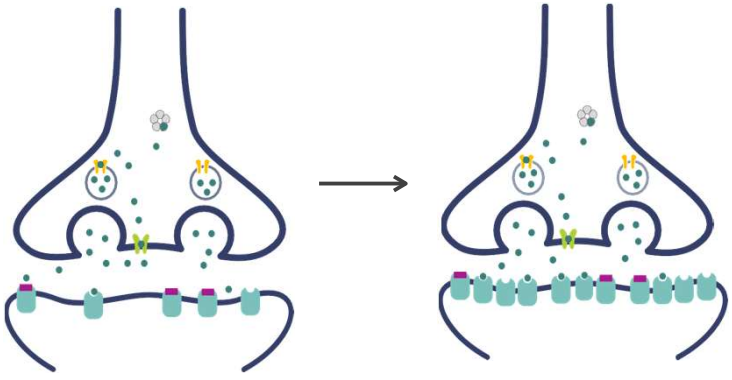
Consequences of Chronic D2 Blockade

Acute treatment with D2 receptor blocking drugs

Chronic treatment with D2 receptor blocking drugs



APs counteract excess DA signaling by blocking D2 receptors

- Attenuates mesolimbic DA signaling → Reduces positive symptoms
- Long-term DA receptor blockade in the nigrostriatal pathway causes upregulation of DA receptors → Leads to drug-induced movement disorders

More inhibition of stop signaling → more 'go' signaling = tardive dyskinesia

D2 = dopamine D2 receptors, APs = antipsychotic drugs, DA = dopamine

Adapted from: Stahl SM, Mignon L. Multifunctionality of Antipsychotics. In: *Stahl's Illustrated Antipsychotics: Treating Psychosis, Mania, and Depression*. 2nd ed. New York, NY: Cambridge University Press; 2010: 34-38.

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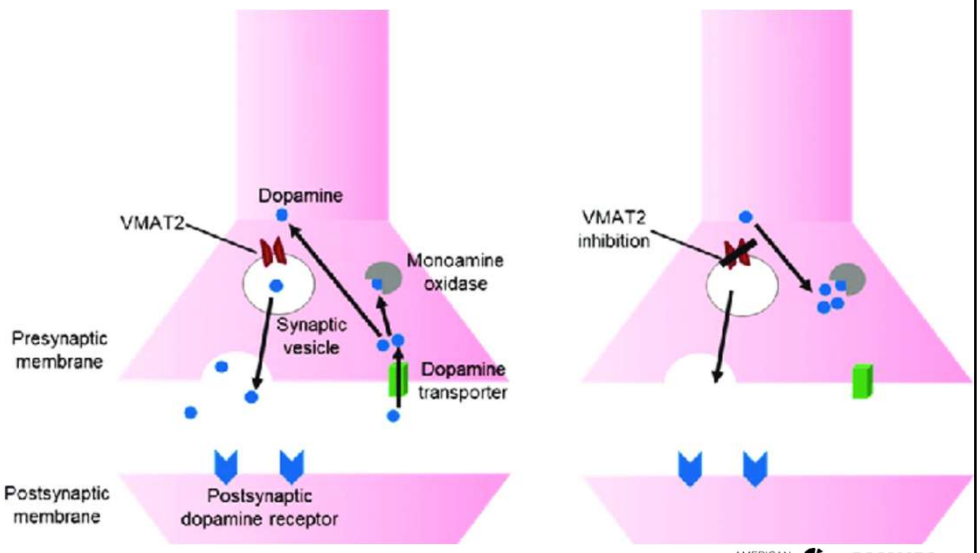
VMAT2 Inhibitior

(Vesicular Monoamine Transporter 2)



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	Tetrabenazine (Xenazine®)	Valbenazine (Ingrezza®)	Deutetrabenazine (Austedo®)
Approved by FDA	Huntington's Disease	TD	TD
Mechanism	Reversibly binds VMAT2	Reversibly and selectively binds VMAT2	Reversibly binds VMAT2
Formulation; dose,mg	Tablets; 12.5, 25	Capsule; 40, 80	Tablets; 6,9,12 XR: tablets; 6, 12, 24
Initial Dose	12.5	40	12 XR: 12
Titration	12.5 mg/d per week, based on TD improvement and tolerability	Increase 80 mg/d after 1 week on 40 mg/d	6 mg/d per week, based on TD improvement and tolerability XR: 6 mg/d per weeks, based on TD improvement and tolerability
Dosing Frequency	3 times daily	Once daily	2 times daily XR: once daily
Metabolism	Hepatic; CYP2D6	Hepatic; CYP3A4, CYP2D6	Hepatic; CYP2D6
Contraindications	Active suicidality or depression; hepatic impairment; taking MAOIs or other VMAT2	None	Hepatic impairment; taking MAOIs or other VMAT2
Hepatic Impairment	Contraindicated	Dose 40 mg/d in moderate to severe hepatic impairment	Contraindicated

Virameteekul S, et a. Emerging Treatments for Tardive Syndrome. Practical Neurology;2023

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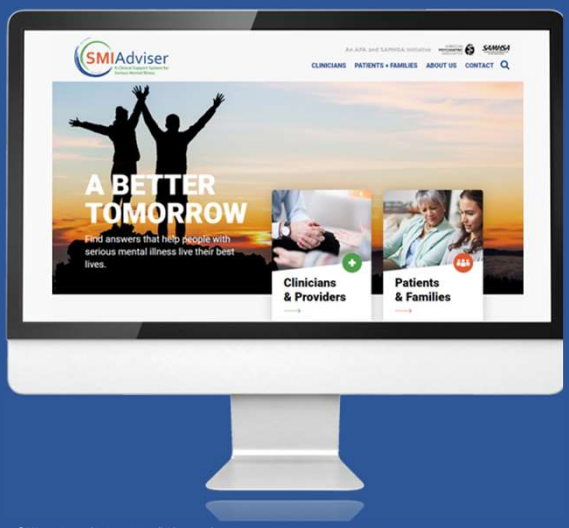
FEEDBACK

Please help us improve the Clozapine & LAI Virtual Forum by completing this survey:
http://smiadviser.org/forumfeedback



Pre-submit Cases

www.smiadviser.org/vfcases

- **[TBD: Clozapine Topic]**
- June 5, 2024 @4-4:45pm ET

- For additional questions and resources – join the Clozapine and LAI Centers of Excellence Exchange Community
  - www.smiadviser.org/cloz_lai_signup

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