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

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.
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?

VMAT2 MEDICATIONS FOR TARDIVE DYSKINESIA

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

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
<th>Level C</th>
<th>Level U</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>must</strong> be recommended as treatment</td>
<td><strong>should</strong> be considered as treatment</td>
<td><strong>might</strong> be considered as treatment</td>
<td>insufficient evidence to support or refute</td>
</tr>
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- Deutetetabenazine
- Valbenazine
- Clonazepam
- Ginkgo biloba
- Amantadine
- Tetrabenazine
- Pallidal deep brain stimulation (intractable TD)
- Withdrawing causative agents
- Switching from typical to atypical DRBA

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Consequences of Chronic D2 Blockade

**Acute treatment with D2 receptor blocking drugs**

- APKs counteract excess DA signaling by blocking D2 receptors
- Attenuates mesolimbic DA signaling
- Reduces positive symptoms
- Leads to drug-induced movement disorders

**Chronic treatment with D2 receptor blocking drugs**

- Long-term DA receptor blockade in the nigrostriatal pathway causes upregulation of DA receptors
- More inhibition of stop signaling → more ‘go’ signaling = tardive dyskinesia
VMAT2 Inhibition

(Vesicular Monoamine Transporter 2)

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