MPS FLASH TALKS 2021

October 16, 2021

MPS Fall Program, "Novel Approaches to Psychiatry"

Minnesota Humanities Center, St Paul, MN - Saturday, October 16, 2021

1

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Valbenazine (Ingrezza)

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2

1. Brief Description/Background

- Class
  - Selective Vesicular Monoamine Transporter 2 (VMAT-2) Inhibitor
- Mechanisms
  - Selective and reversible inhibition of VMAT-2
- Context
  - Second generation VMAT inhibitor, selective for VMAT-2
    - The other drug in this class approved for TD is deutetrabenazine (Austedo)
  - Yields active metabolite similar to tetrabenazine (not approved for TD in the U.S.) but with little off-target activity and fewer side effects

3

2. Indication

- First FDA-approved drug for Tardive Dyskinesia (TD) in adults (2017)
  - Indicated for management of abnormal, involuntary movements associated with TD
    - Note: Improved symptoms regardless of underlying diagnosis or concurrently administered antipsychotic
  - Often monitored for efficacy using change in Abnormal Involuntary Movement (AIM) score
  - Evidence supporting tolerability and efficacy for long-term use
- Dosing
  - Start at 40mg for 1wk, then increase to 80mg (higher dose generally more effective)
  - Once-daily dosing, generally at night to mitigate possible sedation
- Noted Side Effects/Adverse Effects
  - Generally well-tolerated
  - Possible Sedation, suicidal behavior/ideation, dizziness, parkinsonian symptoms, akathisia, tremor
  - QT prolongation possible - generally not clinically significant at typical doses

4

3. Considerations

- Price
  - No generic, remains expensive
- Special Populations
  - Hepatic: Likely need to reduce dose to 40mg in pts with moderate to severe hepatic impairment
  - Cardiac: Can increase digoxin levels (monitor); avoid in patients with long QT syndrome (or other QT prolonging arrhythmia)
- Other Drugs
  - Inhibitors of CYP450 3A4 (ex. ketoconazole) & 2D5 (ex. paroxetine, fluoxetine) can INCREASE drug exposure
  - CYP450 3A4 inducers (ex. carbamazepine) can reduce drug exposure
  - Not recommended for patients taking MAOI
- Appropriate Use
  - Important to delineate symptoms of TD vs. drug-induced parkinsonism

5

Additional Information/Key Studies

- Hauser RA, Factor SA, Marder SR, Knesevich MA, Ramirez PM, Jimenez R, Burke J, Liang GS, O'Brien CF. KINECT 3: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Valbenazine for Tardive Dyskinesia. Am J Psychiatry. 2017 May 1;174(5):476-484. doi: 10.1176/appi.ajp.2017.16091037. Epub 2017 Mar 21. PMID: 28320223.
- Josiassen RC, Kane JM, Liang GS, Burke J, O'Brien CF. Long-Term Safety and Tolerability of Valbenazine (NBI-98854) in Subjects with Tardive Dyskinesia and a Diagnosis of Schizophrenia or Mood Disorder. Psychopharmacol Bull. 2017 Aug 1;47(3):61-68. PMID: 28839341; PMCID: PMC5546552.
- Marder SR, Lindenmayer JP, Shah C, Carmack T, Angelov AS, Lundt L. Onset and Resolution of Key Adverse Events in Valbenazine-Treated Patients with Tardive Dyskinesia: Pooled Analyses from Two Long-Term Clinical Trials. CNS Spectr. 2021 Apr;26(2):151. doi: 10.1017/S1092852920002394. PMID: 34127126.
- Lindenmayer JP, Verghese C, Marder SR, Burke J, Jimenez R, Siegert S, Liang GS, O'Brien CF. A long-term, open-label study of valbenazine for tardive dyskinesia. CNS Spectr. 2021 Aug;26(4):345-353. doi: 10.1017/S109285292000108X. Epub 2020 May 18. PMID: 32419679.

6