ERIC W. LEPPINK
UOFM

Valbenazine (Ingrezza)
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

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
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

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**Additional Information/Key Studies**


- 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.
