May Pharmacy Newsletter

VESICULAR MONOAMINE TRANSPORTER 2 (VMAT 2) INHIBITOR IN TARDIVE DYSKINESIA

This brief summarizes the clinical evidence and appropriate role of VMAT2 inhibitors in the treatment of tardive dyskinesia (TD), with emphasis on expected benefit, functional outcomes, and patient selection. The goal is to support consistent, evidence-based prescribing and ensure these therapies are reserved for patients most likely to benefit.

Tardive dyskinesia is a persistent, involuntary movement disorder associated with exposure to dopamine-receptor blocking agents. Management begins with optimization of the causative medication (dose reduction, discontinuation when feasible, or switching agents). VMAT2 inhibitors are approved as symptomatic treatments for TD when non-pharmacologic and medication-adjustment strategies are insufficient.

Randomized controlled trials of deutetrabenazine and valbenazine demonstrate statistically significant reductions in AIMS scores, with placebo-adjusted improvements typically in the range of 2–4 points.

Key considerations:

- These changes are modest in magnitude
- Symptom reduction may be subtle and not always easily perceptible
- Response is variable across patients

Clinicians should establish realistic expectations with patients. VMAT2 inhibitors may reduce the severity of involuntary movements, but complete resolution is uncommon.

While decreases in AIMS scores meet trial endpoints, functional improvements are inconsistent. Clinical experience and trial data suggest:

- Some patients report reduced distress or improved social comfort
- Improvements in speech, swallowing, fine motor skills, and daily functioning are not uniform
- Many patients continue to have visible dyskinesias despite treatment

As a result, objective symptom reduction does not always correlate with meaningful functional benefit, underscoring the importance of individualized assessment.

TREATMENT DURATION AND MONITORING

VMAT2 inhibitors are symptomatic therapies and do not alter the underlying pathophysiology of TD.

- Symptoms frequently recur or worsen upon discontinuation
- Long-term therapy is often required once treatment is initiated
- There is no evidence of progressive benefit over time

Ongoing treatment should therefore include periodic reassessment to confirm continued clinical value. Given their benefit profile and long-term treatment implications, VMAT2 inhibitors are best reserved for patients with clear clinical need.

Appropriate candidates typically have:

- Moderate-to-severe TD
- Documented functional impairment (e.g., interference with eating, speaking, social interaction) or significant patient distress
- Inadequate response to medication optimization strategies
- Baseline objective assessment (e.g., AIMS score) with documentation of response

Use of VMAT2 inhibitors should be guided by:

- Objective severity assessment at baseline
- Clear documentation of functional impact
- Ongoing evaluation of benefit and tolerability
- Avoidance of use in mild TD without functional impairment, where benefit is unlikely to outweigh long-term treatment burden

Importantly, this approach does not intend to disrupt therapy for patients who are stable and clearly benefiting. Instead, it supports thoughtful initiation, continuation, and reassessment to promote high-value care.

References:

1. Fernandez HH, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia (ARM-TD). Neurology. 2017;88(21):2003–2010
2. Anderson KE, et al. **Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): a phase 3 randomized trial.** *Lancet Psychiatry.* 2017;4(8):595–604.
3. Factor SA, et al. **KINECT 3: A randomized, double-blind, placebo-controlled phase 3 trial of valbenazine for tardive dyskinesia.** *Movement Disorder Society Abstracts.* 2016.
4. Solmi M, et al. **Treatment of tardive dyskinesia with VMAT-2 inhibitors: A systematic review and meta-analysis of randomized controlled trials.** *Drug Design, Development and Therapy.* 2018;12:1215–1238.
5. Correll CU, et al. **Characterizing treatment effects of valbenazine for tardive dyskinesia: Additional results from the KINECT 3 study.** *Journal of Clinical Psychiatry.* 2019;80(1).
6. Correll CU, Carbon M. **A new class of VMAT-2 inhibitors for tardive dyskinesia.** *Lancet Psychiatry.* 2017;4(8):574–575.
7. Pharmacy Times Expert Panel. **Long-term outcomes with VMAT2 inhibitors.** *Pharmacy Times.* 2025.

PREFERRED DRUG LIST UPDATES CAN BE FOUND HERE:

ACC-RBHA, DD, ALTCS and DCS CHP	Behavioral Health (Non-Title 19/21)

** Drugs that are not on the formulary will require a PA (prior authorization) request to be submitted**

Reminder for quicker determinations of a Prior Authorization use the ePA link for Our Providers: Please click here to initiate an electronic prior authorization (ePA) request.

This newsletter is brought to you by the Mercy Care Pharmacy Team. For questions, please email Fanny A Musto (MustoF@mercycareaz.org), Jasmine Phillips (PhillipsJ6@aetna.com)