Clinical Pearls

Real-World Implementation of Xanomeline-Trospium in Schizophrenia: A Consensus Panel Report

Methods

Consensus Panel: On July 13, 2025, an expert panel was convened to discuss the real world clinical implementation of xanomeline-trospium (XT) for the treatment of adult patients with schizophrenia. The published article reflects the panel's consensus findings. The panel was chaired by Ilan Melnick, MD with participants Erin C. Crown, MHS, PA-C, Manish Zinzuvadia, MD, and Michael M. Halassa, MD, PhD.

Xanomeline-Trospium Clinical Fit

Early Intervention

Consider xanomeline-trospium (XT) early (including first-episode psychosis/early-stage illness) for symptom control without cumulative D2-blockade burden, and potentially to support functional recovery/cognitive preservation.

Rapid Benefit, Negative & Cognitive Symptom Improvement

In real-world experience, the panel reported relatively rapid benefit—often within ~1 week, particularly noted for negative symptoms and cognition/thought organization (anecdotal but practical for counseling and follow-up planning).

Switch or Combination Option

Consider XT as a switch or combination option when the limiting factor is antipsychotic side effects (metabolic/EPS/prolactin) or persistent symptoms despite adherence. XT was noted to be antipsychotic dose-sparing.

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Initiation and Titration

Available Fixed-Dose Combinations for Xanomeline-Trospium Chloride

Starting Dose:
50 mg/20 mg BID

Maintenance Dose(s):
100 mg/20 mg or 125 mg/30 mg BID

Outpatient Initiation

1. Start 50/20 BID for 1–2 weeks → assess efficacy + tolerability at first follow-up (ideally in person early in treatment course).
2. If tolerated → increase to 100/20 BID; follow-up interval individualized (the report notes typical duration of 2–12 weeks, depending on plan).
3. If needed and tolerated → increase to 125/30 BID.

Real-world observation: Panel noted many stabilize on 100/20–125/30 BID, though some younger or early-stage patients may do well on 50/20 BID.

Operational pearl: Panel recommends patients fill the prescription immediately so first dose can begin the same evening, minimizing drop-off between visit and start.

Inpatient Initiation

XT may provide rapid stabilization, including improvements in negative symptoms after a few doses. Gradual titration is often impractical for acutely decompensated inpatients. Based on personal experience, the panel recommends:

1. Start 50/20 BID for 1-2 days
2. Escalate to 100/20–125/30 by hospital day 2-3 (strategy similar to trials)

Operational pearl: Set up success post-discharge by teaching fasting requirement and side effect recognition, and ensure psychiatry follow-up is scheduled before discharge.

Tolerability and Monitoring

Take on “empty stomach” to mitigate nausea/vomiting

The panel emphasizes XT should be taken on an empty stomach because trospium absorption is reduced with food, and GI AEs (nausea/vomiting) can be worse if taken after eating.

Co-prescribe 4 mg ondansetron at initiation to limit N/V

Panel recommendations co-prescribing 4 mg ondansetron at initiation to reduce early nausea/vomiting and prevent discontinuation. Re-dose after 30 min if needed.

Expect early AEs; commonly fade

Common events in trials/extension: dry mouth, constipation, dyspepsia (anticholinergic) and nausea, vomiting, diarrhea (procholinergic), typically within first ~2 weeks and usually self-limited.

Manage anticholinergic burden proactively

Perform a full medication reconciliation (Rx/OTC/supplements) with explicit attention to anticholinergic load because trospium is a potent peripheral anticholinergic. Many patients use diphenhydramine for sleep; the panel recommends discontinuing it in favor of a non-anticholinergic alternative. Monitor and address urinary retention, constipation, dry mouth; minimize additive anticholinergic burden.

Caution noted: XT may be less appropriate in men >50 with BPH history or other patients with high urinary retention risk. Use caution and medical judgment.

Cross-Titration and Combination Strategies

Even though XT is approved as monotherapy, the panel expects cross-titration to be common. Start XT 50/20 BID the same evening you see the patient, while tapering the existing antipsychotic based on class. See Table 4 in publication for more detail.

Taper Speed by Antipsychotic Class

"-dones"

High potency D2 antagonists

- Taper over 2-5 days
- Initiate XT at 50/20 BID concurrently

"-pines"

Agents with strong histaminergic/ anticholinergic effects

- Taper slowly, 1–3 weeks
- Start XT at 50/20 BID; maintain until ~50% taper
- Add XT PM dose once "pine" reduced to low dose

"-azoles"

D2 partial agonists

- May discontinue rapidly due to long half-lives
- Initiate XT at 50/20 BID without overlap

Safety guidance: If the patient decompensates during the switch, reintroduce the antipsychotic and reassess.

Combination Strategy

- XT can be antipsychotic dose-sparing—often allowing lower doses of dopamine blockers while maintaining symptom control, potentially reducing long-term metabolic/motor risks.
- Panel noted real-world success with XT 100/20–125/30 BID + a low-dose atypical antipsychotic when needed.

Patients on LAIs

- Panel suggests a tailored approach: in some patients on maintenance LAIs, clinicians can initiate XT concomitantly, stabilize on an XT maintenance dose, then consider LAI down-titration via shared decision-making if symptoms improve.
- They estimated "possibly as many as 50%" of patients may be well managed with XT 100/20 + low-dose atypical (context: personal clinical experience).