ECHO IDAHO

Behavioral Health in Primary Care

New Psychiatric Medications

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Disclosures

- Consultant for Alkermes
- Consultant & Speakers Bureau for BMS
- Consultant for Genomind
- Consultant for Janssen
- Consultant for Lundbeck
- Consultant & Speakers Bureau Otsuka

Learning Objectives

- Describe the efficacy and safety data of the emerging (Phase 3) and recently approved mental health and neurologic medications
- Explain appropriate monitoring requirements, patient education points, and provider education for these agents where known
- Discuss the clinical use of these new and emerging medications and where they may fit into current clinical practice

Key Points

- ✓ The Cheapest Drug May Not be the Cheapest Treatment
- ✓ Many New Psychotropics are Now Available
- ✓ Many New Digital Therapeutics are Now Available
- ✓ New LAIs are Available and Remain Greatly Underused
- ✓ After 70 Years, the Treatment of Schizophrenia has a New Mechanism of Action
- ✓ Psychedelics are Nearing the Market

Global Cost Effectiveness of Medications

FDA Psychiatric & Neurologic Treatment Chronological Approvals in 2024–2025

Risvan (Risperidone LAI) Discontinued in US	Rejoyn (Digital Therapeutic)	Mama Lift Plus (Digital Therapeutic)	Rezenopy (High Dose Naloxone Nasal Spray)	Fanapt (Iloperidone)
Ingrezza Sprinkles (Valbenazine)	Modius Stress (Transdermal Neurostimulation)	Onyda XR (Clonidine ER Suspension)	Austedo XR (Deutetrabenazine XR)	EndeavorOTC (Video-based Digital Therapeutic)
Kisunla (Donanemab-azbt)	Erzofri (Paliperidone Palmitate LAI)	Zunveyl (Benzgalantamine)	Zurnai (Nalmefene Auto-injector)	Crexont (Carbidopa + Levodopa IR & ER)
DaylightRx (Digital Therapeutic)	Vyalev (Foscarbidopa + Foslevodopa)	Lumryz (Sodium Oxybate Oral Suspension)	Journeaux (Suzetrigine)	Leqembi (Lecanemab-irmb)

Drugs@FDA: FDA-Approved Drugs; Individual Product Names Linked to Product Labels

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FDA Psychiatric & Neurologic Treatment Chronological Approvals in 2024–2025

Brand (Generic)	Indication	Comment
Risvan (Risperidone LAI)	Schizophrenia	✓ No Loading or Initiation Dose; 75–100 mg/month ✓ Suspension: 100 pushes & pulls to mix! ✓ Never Launched Due to Low Anticipated Sales
Ingrezza Sprinkle (Valbenazine)	Tardive Dyskinesia or Huntington's Disease with Difficulty Swallowing	"Sprinkle on Applesauce" Compared to "Oral Fasting" ✓ 1 hr Longer to Peak ✓ 31% Lower Peak ✓ 13% Less Absorbed "Sprinkle with High Fat Meal" is Similar to "Oral with High Fat Meal"
Austedo XR (Deutetrabenazine XR)	Tardive Dyskinesia or Huntington's Disease	No Differences in Pharmacokinetics in XR from IR when Fasting When Fed IR C_{max} Increased 50%; XR is Unchanged
Erzofri (Paliperidone Palmitate LAI)	Schizophrenia & Schizoaffective Disorder	✓ Initial Dose = 351 mg ✓ Then 39–234 mg/month

Ingrezza Product Label CP-VBZ-US-3860v2, Neurocrine, San Diego, CA 02/2025

Comparison of Paliperidone Palmitate LAI Dosing Recommendations

Erzofi Product Label 5516264, Luye, Yantai, Shandong Province, China, 01/2025
https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/216352s001lbl.pdf

Comparison of Paliperidone Palmitate LAI Missed Dose Recommendations

No Differences

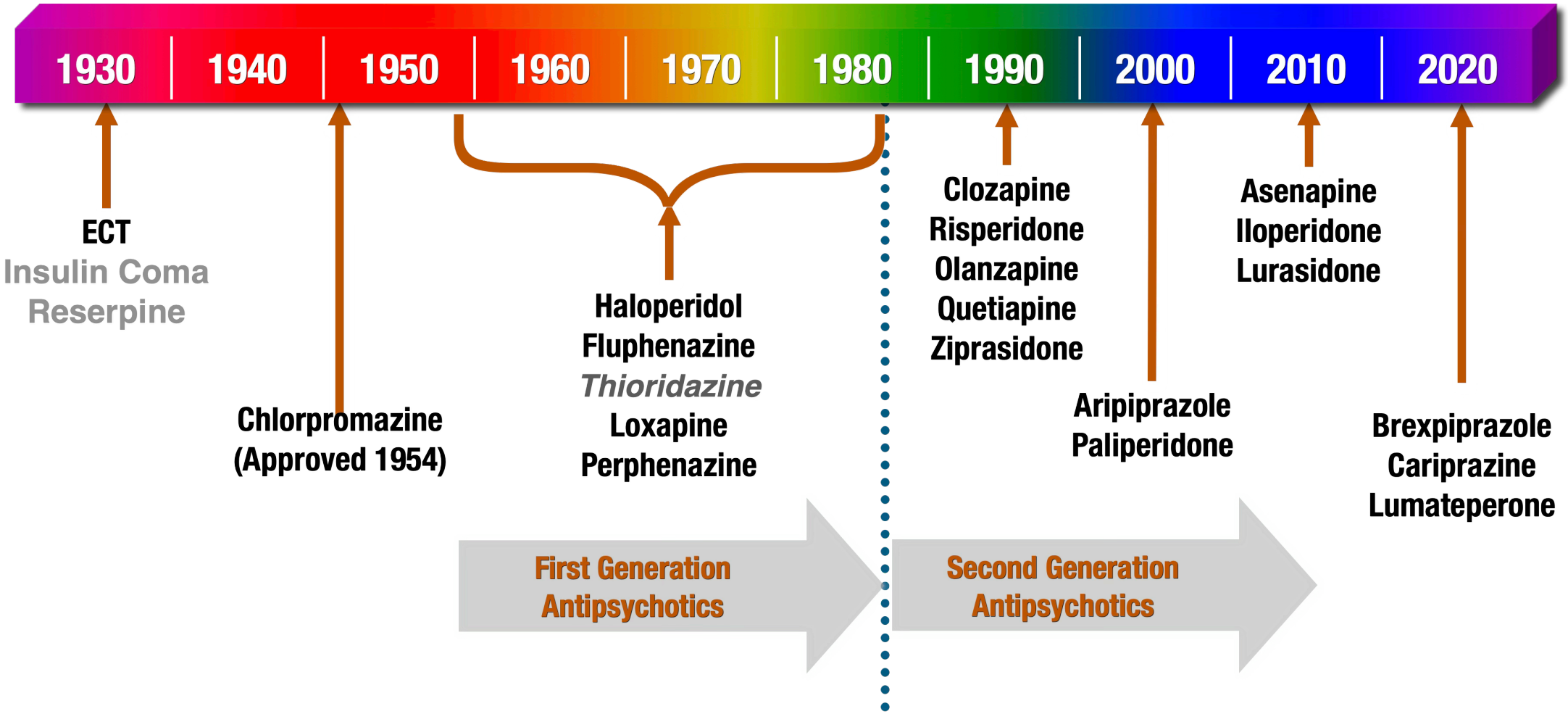
Erzofi Product Label 5516264, Luye, Yantai, Shandong Province, China, 01/2025
Invega Sustenna Product Label cp-64086v15, Janssen, Titusville, NJ, 01/2025

Augmentation for Schizophrenia has Some Benefits

- ✓Na Benzoate & Memantine for Persistent Positive Symptoms: ES Small to Moderate
- ✓Risperidone, Tropisetron, Pioglitazone, Minocycline & Memantine for Reducing Negative Symptoms: ES Moderate to Large
- ✓Clozapine + Antipsychotics for Reducing Negative Symptoms: ES Small to Moderate
- ✓Clozapine with Added Duloxetine for Reducing Negative Symptoms: ES Large

Key: NSA-16 = Negative Symptom Assessment-16. ES = Effect Size. Etchecopar-Etchart D, et al. Comprehensive evaluation of 45 augmentation drugs for schizophrenia: a network meta-analysis. Lancet 2024;69:1–13. https://doi.org/10.1016/j.eclinm.2024.102473. Also see Carr, et al. https://www.nature.com/articles/s41380-025-03255-y.pdf

Timeline of FDA Approved Medications for Schizophrenia



Key: Light Shading = No Longer Used; Italic = Brand Withdrawn, Generic Avaliable. For FDA Approved Agents see Drug@FDA
https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm
Also see List of Antipsychotics https://en.wikipedia.org/wiki/List_of_antipsychotics

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Xanomeline + Trospium (X+T) is the First in a *New FDA Category* of Medications

"Antipsychotic" Does Not Appear in the Product Label Even Once

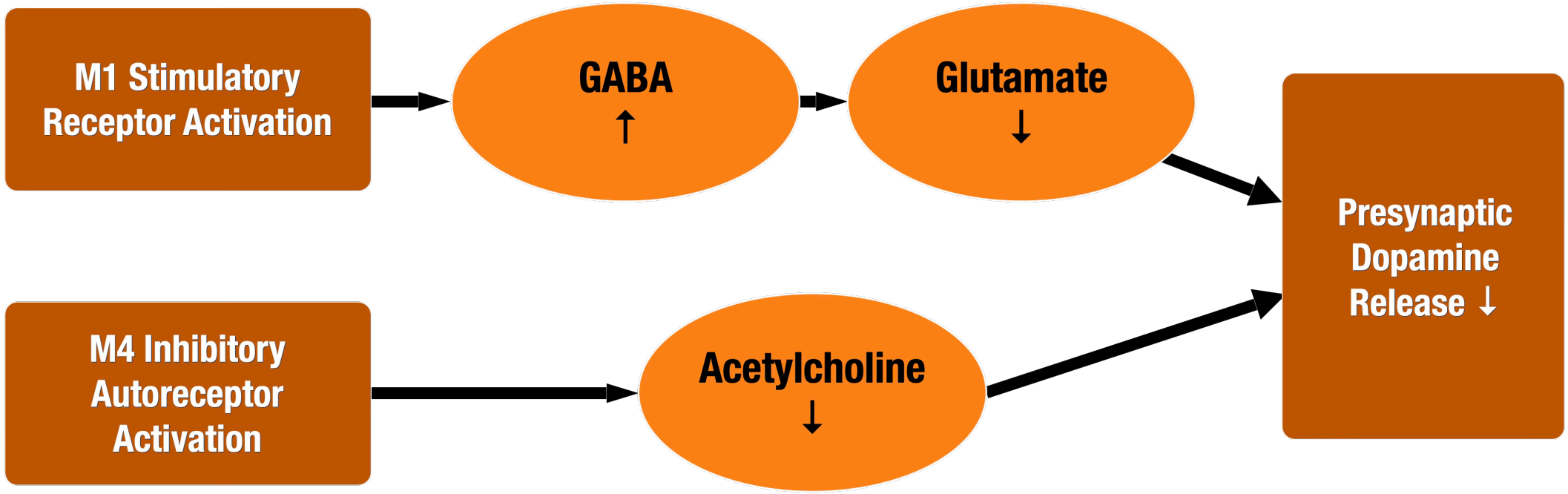
The FDA Approved Product Label Describes X+T as:

"…a Combination of Xanomeline, a Muscarinic Agonist, and Trospium Chloride, a Muscarinic Antagonist, Indicated for the Treatment of Schizophrenia in Adults"

X+T is not a dopamine receptor blocker

Cobenfy Product Label 1629-US-2400371, Karuna, BMS, Princeton, NJ 08543 09/2024

Cholinergic Modulation is a Presynaptic Mechanism & Schizophrenia is a Predominately Presynaptic Disorder



Post-synaptic Dopamine Receptors are Not Bound or Have Their Binding Ability Modulated

Paul SM, et al. Am J Psychiatry 2022;179(9):611–627. https://doi.org/10.1176/appi.ajp.21101083. Picciotto MR, et al. Neuron. 2012;76(1):116-129. http://dx.doi.org/10.1016/j.neuron.2012.08.036. Yohn SE, et al. Muscarinic acetylcholine receptors for psychotic disorders: bench-side to clinic. Trends in Pharmaceutical Sciences. 2022;43(12):1098–1112. https://doi.org/10.1016/j.tips.2022.09.006

The Muscarinic Agonists Are Indicated for the "Treatment of Schizophrenia"

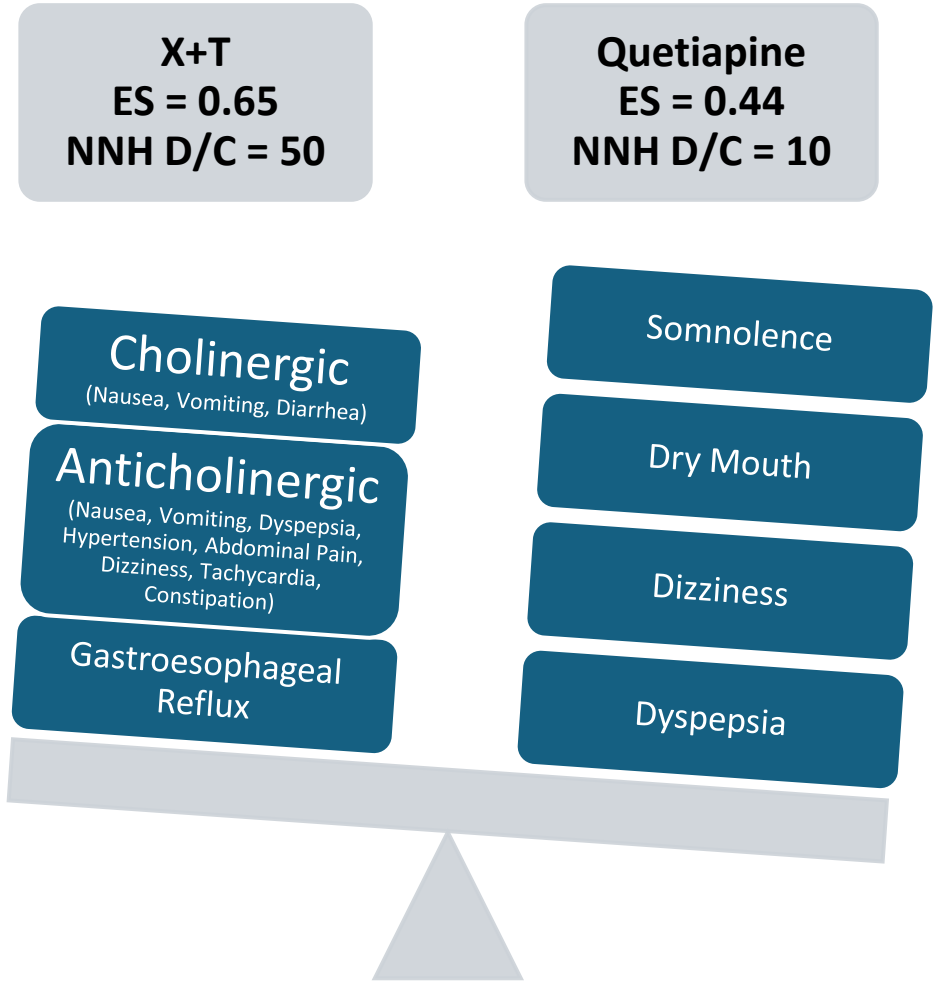
X+T is Similar to Olanzapine PANSS Total Score vs Placebo

Agent and Original Registration Trials	PANSS Total Score Improvement from Baseline (Active Drug)	PANSS Total Score Improvement from Baseline (Placebo)	Difference (95% CI)	Effect Size for Improvement (Cohen's d; 95% CI)	Responders (≥30% Change from Baseline)	Number Needed to Treat
Xanomeline + Trospium (3 R DB PC 5 Week Trials)	17.4 ± 1.8 (N = 314)	5.9 ± 1.7 (N = 326)	9.6 (12.4 to 7.3)	**0.65**	41.4%	4.9
Olanzapine (Meta-analysis; mostly 6 Week Trials)				**0·59 (0·65 to 0·53)**		

Z+T is Highly Effective in Schizophrenic Adults in 5 Weeks

Kaul I, et al. Schizophrenia (2024)10:102 ; https://doi.org/10.1038/s41537-024-00525-6
Leucht S, et al. Lancet 2013; 382: 951–62. https://doi.org/10.1016/S0140-6736(13)60733-3

Muscarinic Agents have *Much Different Adverse Effects* than Dopamine Receptor Agents



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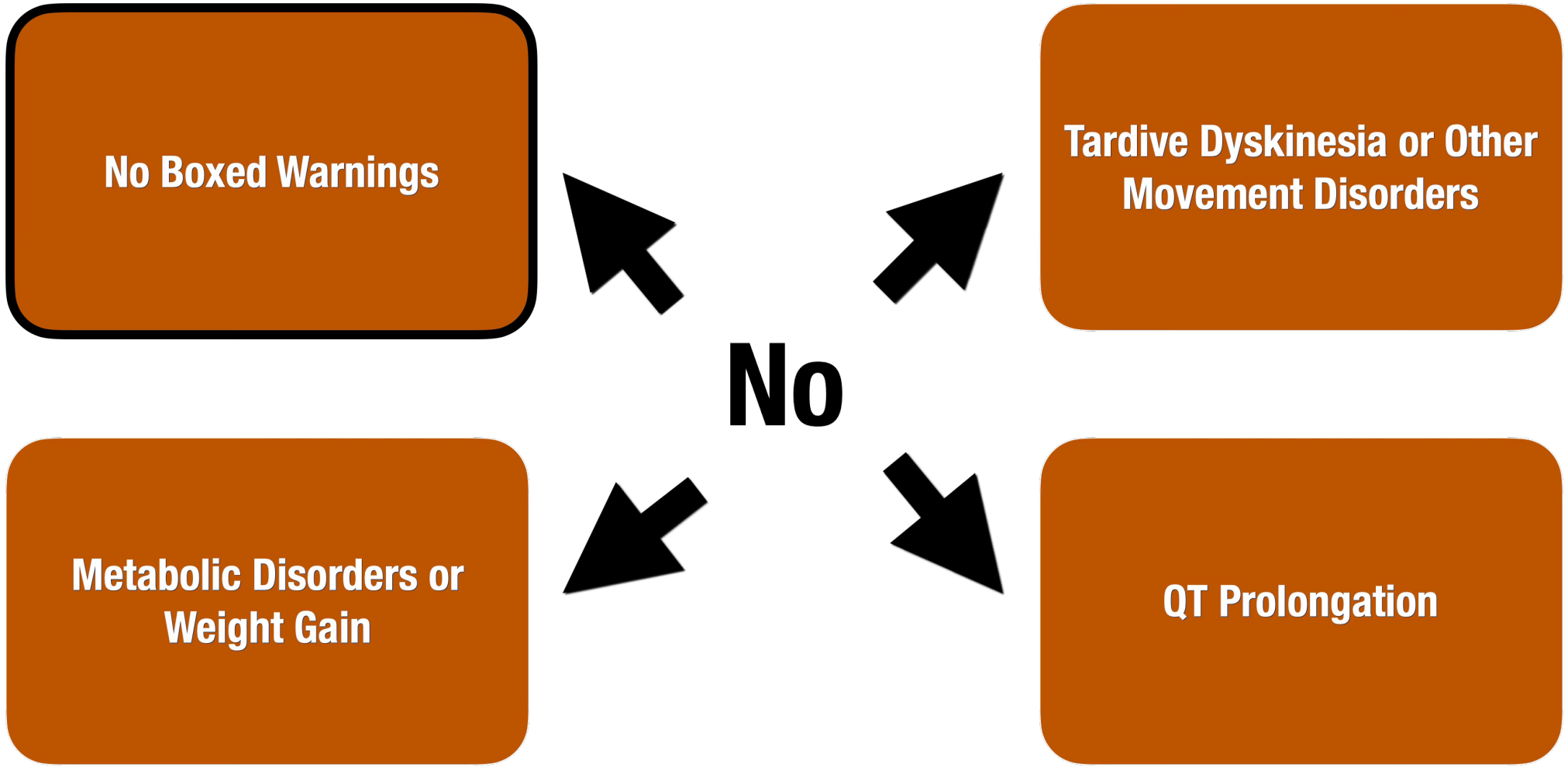
X+T Warnings & Precautions

- Urinary Retention
- Decreased Gastrointestinal Motility
- Increases Heart Rate
- Hepatic Impairment
- Angioedema
- Anticholinergic Adverse Reactions with Renal Impairment
- Biliary Disease
- Narrow Angle Glaucoma
- Central Nervous System

Data from Cobenfy Product Label 1629-US-2400371, 09/2024, Bristol Myers Squibb, Princeton, NJ 08543

Dopamine Receptor Blockers Class Warnings & Precautions that are Absent



Psychedelic Medications are Approaching Clinical Use

Psychedelics In Phase 2 or 3 Clinical Trials

Agent Name / Code	Indication(s)	Phase	References
Psilocybin (COMP360)	Treatment-resistant depression	3	1-2
Psilocybin	Major depressive disorder	2, 3	1-3
Psilocybin	Cancer-related anxiety	2	3
Psilocybin	Alcohol use disorder	2	2-3
Psilocybin	Tobacco use disorder	2	2-3
MDMA (MAPS MDMA)	PTSD	3	1, 3-5
MDMA	Social anxiety	2	3
MDMA	Alcohol use disorder	2	3
LSD	Generalized anxiety disorder	2	1, 3, 6
LSD	Major depressive disorder	2	3, 7-8
LSD	Severe somatic disorders	2	7
DMT (SPL026)	Major depressive disorder	2	2, 7, 9
5-MeO-DMT (GH001)	Major depressive disorder	2	7, 9
5-MeO-DMT	Anxiety	2	7, 9
Ketamine	Major depressive disorder	2, 3	8
Ketamine	Treatment-resistant depression	2, 4	8
Ketamine	PTSD	2	8
Ibogaine HCl (IBG)	Substance use disorder	2	1, 5, 7
Ibogaine HCl	Alcohol use disorder	2	5, 7
Ayahuasca	Major depressive disorder	2	7, 93
Ayahuasca	PTSD	2	7
Salvia divinorum	Major depressive disorder	2	7, 9
Salvia divinorum	PTSD	2	7
Esmethadone	Major depressive disorder	2	6
Esmethadone	Treatment-resistant depression	2	6

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3. Hosein MM, et al. Considerations and Cautions for the Integration of Psilocybin Into Routine Clinical Care: A Consensus Statement From the US National Network of Depression Centers' Task Group on Psychedelics and Related Compounds. Eclinical Medicine. 2025;89:103517. https://doi.org/10.1016/j.eclinm.2025.103517.
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