Mindful Medicine: Updates and Insights in Psychiatric Pharmacy

Ashleigh Barrickman, PharmD, BCACP, CTTS

WestVirginiaUniversity.
School of Pharmacy

Disclosure

I have nothing to disclose concerning possible financial relationships with ineligible companies that may have a direct or indirect interest in the subject matter of this presentation.

Objectives

1) Discuss clinical treatment guidelines for psychiatric disorders
2) Review long-acting injectable options for antipsychotic medications
3) Recognize warning signs of suicidality in patients with and without diagnosed psychiatric conditions
4) Apply guidelines and recommendations to patient cases

Schizophrenia

Clinical Presentation
Medications
Clinical Practice Guidelines

Clinical Presentation

Positive Symptoms: (psychotic) symptoms that are present, but should not be

- Delusions*
- Hallucinations*
- Disorganized speech*
- Illogical thoughts and speech
- Disorganized behavior

Negative Symptoms: symptoms that are not present, but should be

- Impoverished speech and thinking
- Lack of social drive
- Apathy
- Flatness of emotional expression

Cognitive symptoms and additional limitations, including possible substance abuse

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

2020 APA Guidelines for Treatment of Schizophrenia

American Psychiatric Association recommends that:

- **Patients with schizophrenia be treated with an antipsychotic medication and monitored for efficacy and side effects**
  - Person-centered treatment
- **Treatment-resistant patients, patients with substantial aggressive behavior or multiple suicide attempts should be treated with clozapine**
- **LAIs should be used in patients who have histories of poor adherence**
- **Dystonias and parkinsonism should be treated with anticholinergic medications**
- **Akathisia should be treated with a beta-blocker**
- **Tardive dyskinesia should be treatment with VMAT2 inhibitor**
- **Psychosocial interventions should be implemented, including CBT, psychoeducation, supported employment services and social skills training**

American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

2020 APA Guidelines for Treatment of Schizophrenia

- **Evidence indicates little difference in efficacy between FGAs and SGAs (except clozapine).**
- **Factors that should influence selection of antipsychotic:**
  - Past treatment response
  - Affordability
  - Comorbidities
  - Side effects
  - Patient preference
  - Route of administration
  - Concomitant medications
  - Adherence
  - Treatment resistance

American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

Comparative Meta-Analysis of FGAs and SGAs

Minimal differences in efficacy:

- Overall change in symptoms
  - Clozapine, olanzapine, risperidone
- Positive symptoms
  - Haloperidol, olanzapine, paliperidone, risperidone
- Negative symptoms
  - Clozapine, olanzapine, risperidone
- Depressive symptoms
  - Clozapine, olanzapine
- Social functioning
  - Brexpiprazole, lurasidone, olanzapine, paliperidone

Differences in tolerability were more significant, suggesting that safety should be the primary driver in antipsychotic selection

Huhn, M. *et al.* (2019) 'Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: A systematic review and network meta-analysis', *The Lancet*, 394(10202), pp. 939–951. doi:10.1016/s0140-6736(19)31135-3.

Application Case

KM is a 25-year old female who presents to your clinic with her mother. KM has just been released from the hospital and has been diagnosed with schizophrenia. Her mother explains that for the past 8 months, KM has been experiencing auditory and visual hallucinations of “spirits,” and having delusions about constantly being followed by members of an alien task force. Her mother also states that over the last 8 months, she has noticed signs of extreme social withdrawal, flat emotional expression, difficulty concentrating, difficulty sleeping, and illogical thoughts and speech in KM.

Application Case (continued)

Which of the following medications would be an appropriate first line treatment for KM based on the APA guidelines?

A. Haloperidol
B. Aripiprazole
C. Chlorpromazine
D. Clozapine
E. Fluphenazine

Second Generation Antipsychotics (SGAs)

Aripiprazole (Abilify®)
Asenapine (Saphris®)
Brexpiprazole (Rexulti®)
Cariprazine (Vraylar®)
Clozapine (Clozaril®)
Iloperidone (Fanapt®)
Lumateperone (Caplyta®)
Lurasidone (Latuda®)
Olanzapine (Zyprexa®)
Paliperidone (Invega®)
Quetiapine (Seroquel®)
Risperidone (Risperdal®)
Ziprasidone (Geodon®)

- "Atypical" antipsychotics
- **Less affinity for D_2 receptors**
- **Higher affinity for 5-HT receptors**
- Work on ***both positive and negative*** symptoms
  - $5\text{-}HT_{2A}$ antagonism in combination with D_2 blockade → release of dopamine in prefrontal cortex → improvement in negative symptoms
- First line therapy*

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

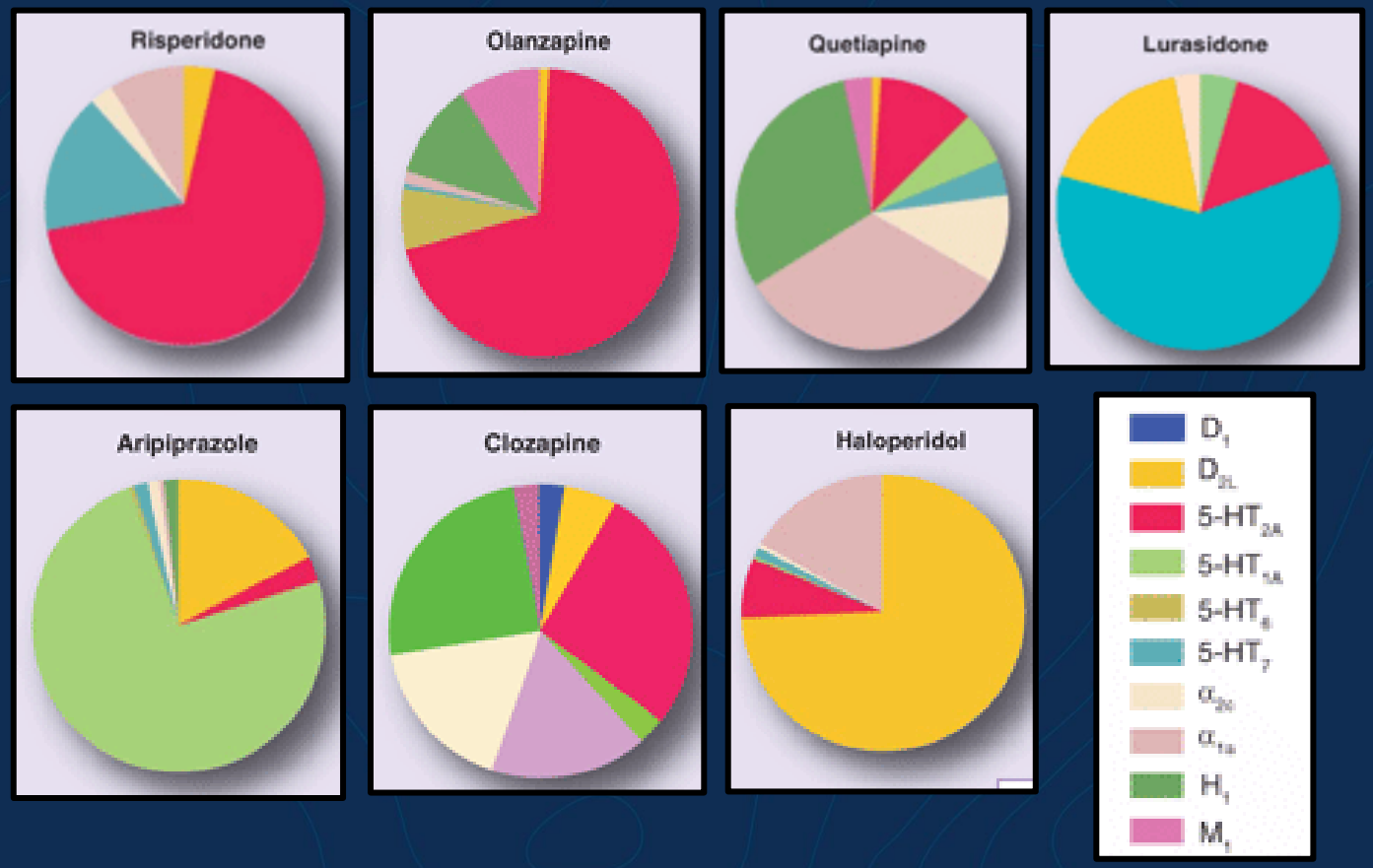
Common Adverse Effects - SGAs

- **Weight gain**
- **Glucose dysregulation**
- **Lipid abnormalities**
- **Anticholinergic effects**
- **Orthostatic hypotension**
- **Hyperprolactinemia**
- **QT_c prolongation**
- **Sedation**
- **Seizures**

- ↓ Extrapyramidal effects:
  - Akathisia: motor restlessness
  - Dystonia: muscle spasms
  - Pseudoparkinsonism: akinesia, tremor, bradykinesia, rigidity
  - Tardive Dyskinesia: abnormal, rigid, irregular, and spontaneous movements

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Heterogeneity of SGAs



https://www.medscape.com/viewarticle/584586_1

Application Case

KM takes aripiprazole 15 mg QD for 12 weeks, with no significant improvement in her symptoms. She comes to clinic today with her mother, and the physician asks you to develop a new treatment plan for her. Her updated labs are as follows:

A1c: 6.5% LDL: 170 mg/dL HDL: 25 mg/dL TG: 170 mg/dL

Wt: 215 lbs Ht: 5'4" QT Interval: 410ms

Which of the following antipsychotics would be most appropriate to initiate in KM at this time?

A. Clozapine
B. Ziprasidone
C. Olanzapine
D. Fluphenazine

Application Case

KM takes aripiprazole 15 mg QD for 12 weeks, with no significant improvement in her symptoms. She comes to clinic today with her mother, and the physician asks you to develop a new treatment plan for her. Her updated labs are as follows:

A1c: 6.5% LDL: 170 mg/dL HDL: 25 mg/dL TG: 170 mg/dL
Wt: 215 lbs Ht: 5'4" QT Interval: 410ms

Which of the following antipsychotics would be most appropriate to initiate in KM at this time?

A. Clozapine
B. Ziprasidone
C. Olanzapine
D. Fluphenazine

Adverse Effect Profiles of Second Generation Antipsychotics

	Anti-Ach	EPS	↓ BP	↑Prolactin	QTc	Sedation	Metabolic	Seizures
Associated Receptor:	Muscarinic	D2	Alpha	D2	KiR	H_1	H_1 + $5HT_{2A}$	---
Aripiprazole	±	+	±	0	±	+	±	±
Asenapine	+	+	+	±	+	+	+	±
Brexpiprazole	±	+	±	0	±	+	±	±
Cariprazine	±	+	±	0	±	+	±	±
Clozapine	+++	+	+++	0	+	+++	+++	+++
Iloperidone	±	+	++	+	+	++	±	±
Lurasidone	±	+	+	±	+	±	±	±
Lumateperone	±	+	±	0	±	++	+	±
Olanzapine	++	±	+	+	±	+	+++	±
Paliperidone	±	++	++	+++	±	+	++	±
Quetiapine	+	±	++	±	+	++	++	±
Risperidone	±	++	++	+++	±	+	++	±
Ziprasidone	±	±	+	+	+	+	±	±

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Application Case

KM has been taking ziprasidone for 6 weeks when she returns to clinic for a follow-up appointment. KM and her mother tell you that they have not noticed much improvement in KM's symptoms since starting the ziprasidone.

What would you want to ask the patient/caregiver before making medication changes?

Patient Education

Medication-Specific Patient Education Points:

- Asenapine
  - Sublingual tablet (Saphris®)
  - Transdermal patch (Secuado®)
- Lurasidone (Latuda®), Ziprasidone (Geodon®) and Lumateperone (Caplyta®)
  - Absorption is increased with food
- Paliperidone (Invega®)
  - Ghost tablet

Asenapine. Lexi-Drugs [database online]. Lexi-Comp, Inc; October 2, 2024.
Lueasidone. Lexi-Drugs [database online]. Lexi-Comp, Inc; October 2, 2024.
Ziprasidone. Lexi-Drugs [database online]. Lexi-Comp, Inc; October 2, 2024.
Lumateperone. Lexi-Drugs [database online]. Lexi-Comp, Inc; October 2, 2024.
Paliperidone. Lexi-Drugs [database online]. Lexi-Comp, Inc; October 2, 2024.

Application Case

KM starts taking the ziprasidone with food for 12 weeks, and notices some improvement in symptoms, but is still experiencing visual and auditory hallucinations and a lack of social drive. At her appointment today, her mother states concerns about suicidal thoughts and KM reports that the voices have been command in nature and have been telling her that she should harm herself. Based on this information, which of the following medications would be best to initiate in KM today?

A. Clozapine
B. Quetiapine
C. Paliperidone
D. Aripiprazole

Clozapine

1st SGA released on market

Only medication with proven and superior efficacy in treatment-resistant patients

- Additional FDA approval for treatment of suicidal behavior in people with psychosis
- Recommended for patients displaying aggressive behaviors

Use is limited due to adverse effects

American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

Application Case

What counseling points would be important to discuss with KM and her mother prior to recommending clozapine?

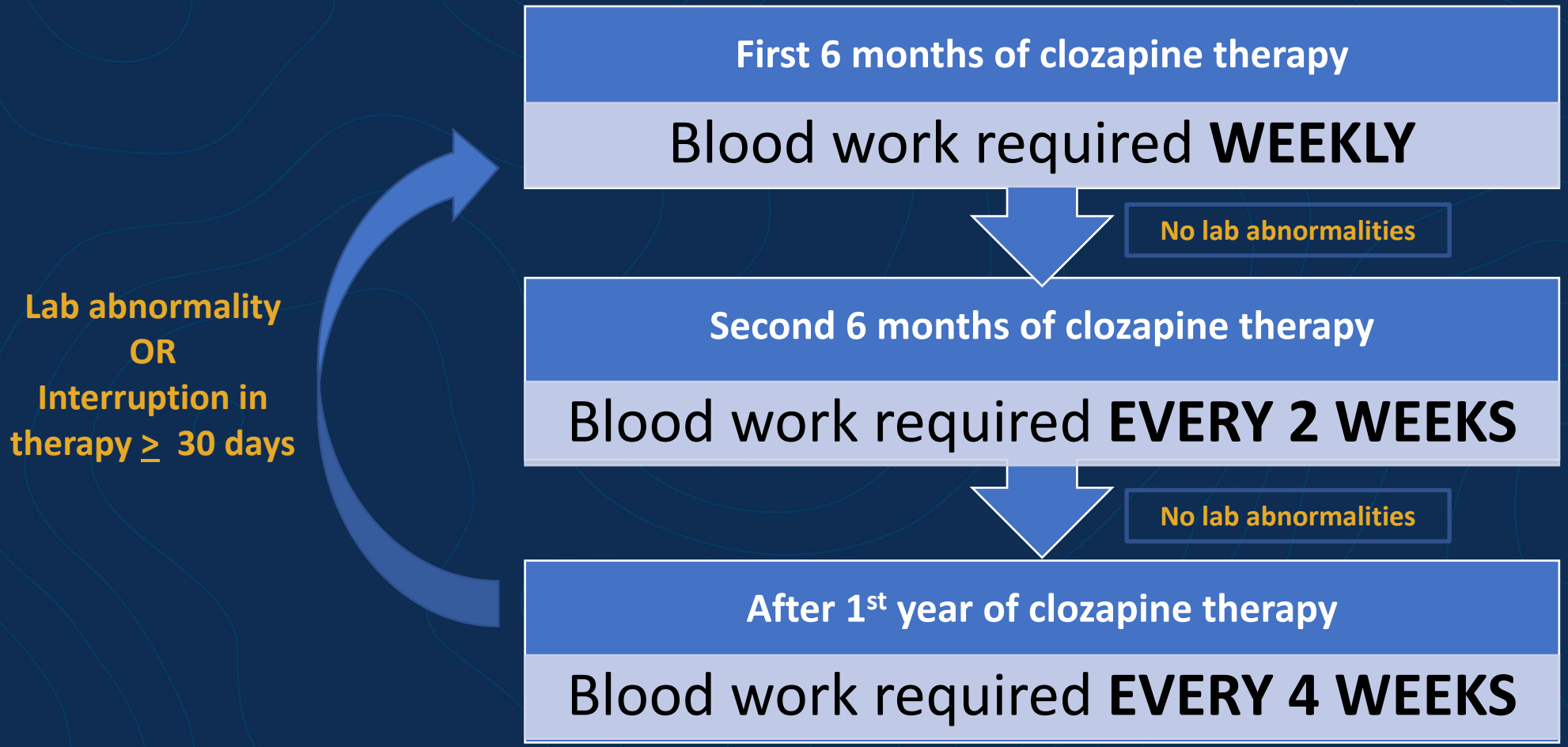
Clozapine

Adverse Effects:

- Seizures
- Anticholinergic effects
- Hypersalivation
- Sedation
- Weight gain
- Agranulocytosis*

American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

Clozapine Monitoring - Toxicity



American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

CLOZAPINE REMS

The Single Shared System for Clozapine

No Blood, No Drug™

Recommended Monitoring Frequency and Clinical Decisions by ANC Level

ANC Level	Treatment Recommendation	ANC Monitoring
Normal Range for a New Patient • General Population (ANC ≥ 1500/µL)	• Initiate treatment • If treatment interrupted: - < 30 days, continue monitoring as before - ≥ 30 days, monitor as if new patient	• Weekly from initiation to 6 months • Every 2 weeks from 6 to 12 months • Monthly after 12 months
BEN POPULATION • BEN Population (ANC ≥ 1,000/µL) • Obtain at least two baseline ANC levels before initiating treatment	• Discontinuation for reasons other than neutropenia	• See Section 2.4 of the full Prescribing Information
Mild Neutropenia (1000 to 1499/µL)*	**GENERAL POPULATION** • Continue treatment	**GENERAL POPULATION** • Three times weekly until ANC ≥ 1500/µL • Once ANC ≥ 1500/µL, return to patient's last "Normal Range" ANC monitoring interval**

https://www.clozapinerems.com/CpmgClozapineUI/rems/pdf/resources/ANC_Table.pdf

CLOZAPINE REMS

The Single Shared System for Clozapine

No Blood, No Drug™

Moderate Neutropenia (500 to 999/μL)*	**GENERAL POPULATION** • Recommend hematology consultation • Interrupt treatment for suspected clozapine induced neutropenia • Resume treatment once ANC normalizes to ≥ 1000/μL	**GENERAL POPULATION** • Daily until ANC ≥ 1000/μL, then • Three times weekly until ANC ≥ 1500/μL • Once ANC ≥ 1500/μL, check ANC weekly for 4 weeks, then return to patient's last "Normal Range" ANC monitoring interval**
	BEN POPULATION • Recommend hematology consultation • Continue treatment	**BEN POPULATION** • Three times weekly until ANC ≥ 1000/μL or ≥ patient's known baseline. • Once ANC ≥ 1000/μL or patient's known baseline, then check ANC weekly for 4 weeks, then return to patient's last "Normal BEN Range" ANC monitoring interval**
Severe Neutropenia (less than 500/μL)*	**GENERAL POPULATION** • Recommend hematology consultation • Interrupt treatment for suspected clozapine induced neutropenia • Do not rechallenge unless prescriber determines benefits outweigh risks	**GENERAL POPULATION** • Daily until ANC ≥ 1000/μL • Three times weekly until ANC ≥ 1500/μL • If patient rechallenged, resume treatment as a new patient under "Normal Range" monitoring once ANC ≥ 1500/μL
	BEN POPULATION • Recommend hematology consultation • Interrupt treatment for suspected clozapine induced neutropenia • Do not rechallenge unless prescriber determines benefits outweigh risks	**BEN POPULATION** • Daily until ANC ≥ 500/μL • Three times weekly until ANC ≥ patients established baseline • If patient rechallenged, resume treatment as a new patient under "Normal Range" monitoring once ANC ≥1000/μL or at patient's baseline

https://www.clozapinerems.com/CpmgClozapineUI/rems/pdf/resources/ANC_Table.pdf

Clozapine Monitoring

Stage of Neutropenia	ANC Range (cells/mm^3)	Clozapine Action and Monitoring Required
Mild	1000-1500	**Continue clozapine**; monitor 3x weekly until resolved (ANC>1500)
Moderate	500-999	**Interrupt therapy**; monitor daily until ANC >1000 then 3x weekly until resolved, then check weekly x 4 weeks (may restart clozapine)
Severe	<500	Discontinue therapy*; Monitor daily until ANC >1000 then 3x weekly until ANC >1500 If patient is re-challenged – resume treatment as new patient

May restart clozapine ONLY if prescriber determines benefits outweigh risks

https://www.clozapinerems.com/CpmgClozapineUI/rems/pdf/resources/ANC_Table.pdf

ClozapineREMS

Pharmacist Responsibilities:

- Register at clozapinerems.com
- Can no longer enroll patients
- Prior to Dispensing: Check REMS website and obtain Pre-Dispense Authorization (PDA)
  - Will not generate if ANC is not on file
  - Will not generate if ANC indicates moderate-severe neutropenia unless Treatment Rationale has been provided by prescriber
- Inpatient pharmacists: must verify patient enrollment prior to dispensing clozapine

https://www.clozapinerems.com/CpmgClozapineUI/rems/pdf/resources/ANC_Table.pdf

Application Case (continued)

KM comes to a follow-up appointment 4 weeks after starting clozapine. She tells you that she has noticed an improvement in her visual and auditory hallucinations, but still has no motivation to hang out with her friends. Her mother tells you that she has noticed a drastic improvement in KM's mood, but she has not been sleeping well because she is drooling so much on her pillow at night that it is waking her up. She also reports only having 2-3 bowel movements per week, as opposed to 1x/day prior to starting clozapine.

What would you recommend for KM?

Managing Antipsychotic-Induced Adverse Effects

Constipation

Hypersalivation

Extrapyramidal effects

- Akathisia
- Bradykinesia
- Tardive dyskinesia

Sexual dysfunction

Managing Antipsychotic-Induced Adverse Effects

Constipation:

- Prevention is critical (especially with clozapine)
  - Adequate hydration
  - Stool softeners
- Treatment:
  - 1st line:
    - Osmotic laxatives (PEG, lactulose)
    - Stimulant laxatives (senna, bisacodyl)
  - Bulk-forming, fiber-based laxatives not recommended

Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry 2018;17:341-356.

Managing Antipsychotic-Induced ADEs

Hypersalivation:

- Non-Pharmacologic: sugar-free gum, chewing on ice chips
- Pharmacologic:
  - 1st line:
    - Ipratropium nasal spray: 1-2 sprays sublingually every 6 hours prn
    - Atropine ophthalmic drops: 1-2 drops sublingually QHS
  - 2nd line:
    - Terazosin 2mg PO QHS
    - Benztropine 1-2 mg PO BID
    - Glycopyrrolate 1-2mg PO QD-BID
    - Amitriptyline 100 mg PO QHS
    - Clonidine 0.1 mg PO QD

Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry 2018;17:341-356.

Managing Antipsychotic-Induced Adverse Effects

Sexual Dysfunction:

- Multiple possible mechanisms
- May present as reduced libido, anorgasmia or erectile dysfunction
- Management:
  - ↓ dose
  - PDE5 inhibitors in males
  - Switch to different antipsychotic
  - Add aripiprazole

John J, Thomas RP, Paul S, EK J, Job K. Antipsychotic induced sexual dysfunction. J Psychiatry 2018,21:1.
Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry 2018;17:341-356.

Sexual Dysfunction: Adverse Effect Profiles of Second Generation Antipsychotics

	Anti-Ach	EPS	↓ BP	↑Prolactin	QTc	Sedation	Metabolic	Seizures
Aripiprazole	±	+	±	0	±	+	±	±
Asenapine	+	+	+	±	+	+	+	±
Clozapine	+++	+	+++	0	+	+++	+++	+++
Iloperidone	±	+	++	+	+	++	±	±
Lumateperone	±	+	±	0	±	++	+	±
Lurasidone	±	+	+	±	+	+	±	±
Olanzapine	++	±	+	+	±	+	+++	±
Paliperidone	±	++	++	+++	±	+	++	±
Quetiapine	+	±	++	±	+	++	++	±
Risperidone	±	++	++	+++	±	+	++	±
Ziprasidone	±	±	+	+	+	+	±	±

SGAs with ↓ incidence of sexual dysfunction:

- **Aripiprazole, brexpiprazole, cariprazine**
- **Lumateperone**
- **Lurasidone**
- **Asenapine**

Information compiled from: Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Managing Antipsychotic-Induced Adverse Effects

Extrapyramidal Side Effects:

- **Akinesia, bradykinesia, muscle rigidity:**
  - Benztropine 1-2mg PO BID
  - Trihexyphenidyl 1-3mg PO TID
  - Diphenhydramine 25-50mg PO BID

- **Akathisia or Tremors:**
  - Propranolol 30-120mg PO QD
  - Mirtazapine 15-45 mg PO QD

Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. World Psychiatry 2018;17:341-356.

American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

WestVirginiaUniversity.
School of Pharmacy

Managing Antipsychotic-Induced Tardive Dyskinesia

Valbenazine (Ingrezza®):

- VMAT2 inhibitor
- Dosing: 40 mg PO QD x 1 week, then increase to 80 mg QD
  - ↓dose in CYP2D6 poor metabolizers
  - Avoid use with strong CYP3A4 inducers
  - ↓dose to 40 mg QD with strong strong CYP3A4 inhibitors
- Administration: take without food
- ADEs:
  - Somnolence
  - QT prolongation
  - Anticholinergic effects
  - Headache
- Cost: ~$7000 per month

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209241lbl.pdf

American Psychiatric Association. (2020). *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. American Psychiatric Association Publishing. https://doi.org/10.1176/appi.books.9780890424841

Managing Antipsychotic-Induced Tardive Dyskinesia

Deutetrabenazine (Austedo®):

- VMAT2 inhibitor
- Dosing: 12mg/day initially (48mg/day maximum)
  - Administer doses >12mg per day in divided doses
  - Baseline EKG with doses >24 mg/day
  - Avoid doses >36mg/day (18mg/dose) with CYP2D6 inhibitors or poor CYP2D6 metabolizers
- Administration: take with food
- ADEs:
  - Nasopharyngitis,
  - Insomnia
  - Depression
  - Agitation/restlessness
- Cost: ~$6000 per month

https://www.austedo.com/globalassets/austedo/prescribing-information.pdf

Managing Antipsychotic-Induced Tardive Dyskinesia

Clinical Considerations:

- AIMS prior to treatment and after to show efficacy

Facial and Oral Movements					
1. Muscles of Facial Expression e.g., movements of forehead, eyebrows, periorbital area, cheeks; Include frowning, blinking, smiling, grimacing	0	1	2	3	4
2. Lips and Perioral Area e.g., puckering, pouting, smacking	0	1	2	3	4
3. Jaw e.g., biting, clenching, chewing, mouth opening, lateral movement	0	1	2	3	4
4. Tongue Rate only increases in movement both in and out of mouth, NOT inability to sustain movement	0	1	2	3	4
Extremity Movements					
5. Upper (arms, wrists, hands, fingers) Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT include tremor (i.e., repetitive, regular, rhythmic).	0	1	2	3	4
6. Lower (legs, knees, ankles, toes) e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0	1	2	3	4
Trunk Movements					
7. Neck, shoulders, hips e.g., rocking, twisting, squirming, pelvic gyrations	0	1	2	3	4
Global Judgments					
8. Severity of abnormal movements	0	1	2	3	4
9. Incapacitation due to abnormal movements	0	1	2	3	4
10. Patient's awareness of abnormal movements (rate only patient's report) 0 = not aware; 1 = aware, no distress; 2 = aware, mild distress; 3 = aware, moderate distress; 4 = aware, severe distress	0	1	2	3	4
Dental Status					
11. Current problems with teeth and/or dentures?	No	Yes			

https://www.aacap.org/App_Themes/AACAP/docs/member_resources/toolbox_for_clinical_practice_and_outcomes/monitoring/AIMS.pdf

Antipsychotic PK Parameters

Antipsychotic	Major CYP Enzymes	Other CYP Enzymes
Aripiprazole	3A4	2D6
Asenapine	1A2	3A4, 2D6
Brexpiprazole	2D6, 3A4	
Cariprazine	3A4	2D6
Clozapine	1A2	3A4, 2D6, 2C19
Haloperidol	2D6, 3A4	
Iloperidone	2D6, 3A4	
Lurasidone	3A4	
Olanzapine	1A2	2D6
Paliperidone	2D6, 3A4	
Perphenazine	2D6	
Quetiapine	3A4	2D6
Risperidone	2D6	3A4
Ziprasidone	3A4	

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

CYP2D6

Metabolism of >25% of all prescription drugs

Polymorphic gene

- 4-7%: slow-metabolizers
- 3%: ultra-rapid metabolizers

Ultra-rapid metabolizers → possible link to increased risk of suicide

Genetic testing opportunity

Stephens DB, de Leon J. CYP2D6 ultra-rapid metabolizer phenotype not associated with attempted suicide in a large sample of psychiatric inpatients. Pharmacogenomics 2016;17(12):2016-2086.
Ma MK, Woo MH, Mcleod HL. Genetic Basis of Drug Metabolism. Am J Health Syst Pharm. 2002;59(21).

Tobacco Use

>70% of patients with schizophrenia smoke

↑ smoking rates in other psychiatric disorders as well

Meta-analysis: Abstinence Rates for Medications Compared to Placebo	
Medication	**Estimated Abstinence Rates (95% CI)**
Placebo	13.8
Nicotine Patch + ad lib gum or lozenge	36.5 (28.6-45.3)
Varenicline (1 mg BID)	33.2 (28.9-37.8)
Nicotine Patch + Bupropion SR	28.9 (23.5-35.3)
Bupropion SR (150mg BID)	24.2 (22.2-26.4)

https://bphc.hrsa.gov/buckets/treatingtobacco.pdf

Application Case

KM returns to clinic 6 months later and states that she was “doing great” with her medications and her symptoms were well-controlled until 2 weeks ago when her hallucinations worsened. She tells you that she has been under more stress at work, and she noticed that her symptoms worsened around that time. Her current dose of clozapine is 400 mg PO QHS.

KM’s mother tells you that she has also noticed an increase in KM’s symptoms and is concerned about KM’s constant smoking because of the increased stress at work.

What do you recommend for KM?

Effect of Smoking on Drug Metabolism

Smoking induces CYP1A2

↑ or ↓ in smoking can alter levels of antipsychotics

- Clozapine, olanzapine, asenapine

Monitor patients for changes in efficacy and ADEs

Antipsychotic	Major CYP Enzymes	Other CYP Enzymes
Asenapine	1A2	3A4, 2D6
Clozapine	1A2	3A4, 2D6, 2C19
Olanzapine	1A2	2D6

Andrade, Chittarangan. Schizophrenia and Smoking. J Clin Psychiatry; 2012 73:6.

Application Case

After discussing the negative health effects of smoking, KM decides that she is ready to quit. She is currently smoking 1 ppd, and she has tried to quit cold turkey multiple times but was unsuccessful. Which of the following products would be appropriate for KM?

A. Varenicline
B. Bupropion
C. Nicotine patches + nicotine lozenges prn
D. She is not a candidate for pharmacologic therapy for cessation because of her psychiatric illness

Application Case

After discussing the negative health effects of smoking, KM decides that she is ready to quit. She is currently smoking 1 ppd, and she has tried to quit cold turkey multiple times but was unsuccessful. Which of the following products would be appropriate for KM?

A. Varenicline

B. Bupropion

C. Nicotine patches + nicotine lozenges prn

D. She is not a candidate for pharmacologic therapy for cessation because of her psychiatric illness

EAGLES Trial

Multinational, multicenter, randomized, double-blind, placebo and active-controlled trial

8144 patients with *stable* psychiatric conditions randomized to:

- Nicotine patch
- Varenicline
- Bupropion
- Placebo

12-week treatment phase and 12 week non-treatment phase

Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double blind, randomized, placebo-controlled trial. Lancet 2016;387:2507-20.

EAGLES Trial

	Non-psychiatric cohort* (n=3984)				Psychiatric cohort* (n=4074)			
	Varenicline (n=990)	Bupropion (n=989)	Nicotine patch (n=1006)	Placebo (n=999)	Varenicline (n=1026)	Bupropion (n=1017)	Nicotine patch (n=1016)	Placebo (n=1015)
Primary composite neuropsychiatric endpoint	13 (1·3%)	22 (2·2%)	25 (2·5%)	24 (2·4%)	67 (6·5%)	68 (6·7%)	53 (5·2%)†	50 (4·9%)
Estimated primary composite neuropsychiatric adverse events (% [95% CI])	1·25% (0·60 to 1·90)	2·44% (1·52 to 3·36)	2·31% (1·37 to 3·25)	2·52% (1·58 to 3·46)	6·42% (4·91 to 7·93)	6·62% (5·09 to 8·15)	5·20% (3·84 to 6·56)	4·83% (3·51 to 6·16)
Difference in risk of composite primary endpoint (RD% [95% CI])								
Versus placebo	−1·28 (−2·40 to −0·15)	−0·08 (−1·37 to 1·21)	−0·21 (−1·54 to 1·12)	..	1·59 (−0·42 to 3·59)	1·78 (−0·24 to 3·81)	0·37 (−1·53 to 2·26)	..
Versus nicotine patch	−1·07 (−2·21 to 0·08)	0·13 (−1·19 to 1·45)	..	..	1·22 (−0·81 to 3·25)	1·42 (−0·63 to 3·46)	..	..
Versus bupropion	−1·19 (−2·30 to −0·09)	..	..	..	−0·20 (−2·34 to 1·95)	..	..	..

	Non-psychiatric cohort* (n=3984)				Psychiatric cohort* (n=4074)			
	Varenicline (n=990)	Bupropion (n=989)	Nicotine patch (n=1006)	Placebo (n=999)	Varenicline (n=1026)	Bupropion (n=1017)	Nicotine patch (n=1016)	Placebo (n=1015)
(Continued from previous page)								
Primary composite neuropsychiatric endpoint (severe intensity only)	1 (0·1%)	4 (0·4%)	3 (0·3%)	5 (0·5%)	14 (1·4%)	14 (1·4%)	14 (1·4%)	13 (1·3%)

Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double blind, randomized, placebo-controlled trial. Lancet 2016;387:2507-20.

EAGLES Trial

	Non-psychiatric cohort*(n=3984)				Psychiatric cohort* (n=4074)			
	Varenicline (n=990)	Bupropion (n=989)	Nicotine patch (n=1006)	Placebo (n=999)	Varenicline (n=1026)	Bupropion (n=1017)	Nicotine patch (n=1016)	Placebo (n=1015)
During treatment and ≤30 days after last dose								
Assessed	988	983	996	995	1017	1012	1006	1006
Suicidal behaviour and/or ideation	7 (1%)	4 (<1%)	3 (<1%)	7 (1%)	27 (3%)	15 (1%)	20 (2%)	25 (2%)
Suicidal behaviour†‡	0	0	1 (<1%)	1 (<1%)§	0	1 (<1%)	0	2 (<1%)
Suicidal ideation	7 (1%)	4 (<1%)	3 (<1%)	6 (1%)	27 (3%)	15 (1%)	20 (2%)	25 (2%)
During follow-up (>30 days after last treatment dose and through end of study)								
Assessed	807	816	800	805	833	836	824	791
Suicidal behaviour and/or ideation	3 (<1%)	2 (<1%)	3 (<1%)	4 (<1%)	14 (2%)	4 (<1%)	9 (1%)	11 (1%)
Suicidal behaviour†¶	0	1 (<1%)	0	0	1 (<1%)	0	1 (<1%)	1 (<1%)
Suicidal ideation	3 (<1%)	2 (<1%)	3 (<1%)	4 (<1%)	14 (2%)	4 (<1%)	9 (1%)	11 (1%)

Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double blind, randomized, placebo-controlled trial. Lancet 2016;387:2507-20.

EAGLES Trial

Abstinence Rates:

- Varenicline (highest) → nicotine patch → bupropion → placebo

Most Common ADEs:

- Varenicline: nausea
- Bupropion: insomnia
- Nicotine patch: abnormal dreams
- Placebo: headache

Conclusion: No significant increase in neuropsychiatric effects attributable to varenicline or bupropion compared to nicotine patch or placebo

Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double blind, randomized, placebo-controlled trial. Lancet 2016;387:2507-20.

Application Case (continued)

The medical team has discussed smoking cessation options with KM, and she has decided to try nicotine patches and lozenges. Which of the following is the most appropriate recommendation that you should make to the medical resident regarding the plan for smoking cessation?

A. Monitor closely for ↑ in ADEs of clozapine
B. Monitor closely for ↓ in efficacy of clozapine and possible ↑ in symptoms
C. Monitor for serotonin syndrome
D. Monitor for hypertensive crisis

Application Case (continued)

The medical team has discussed smoking cessation options with KM, and she has decided to try nicotine patches and lozenges. Which of the following is the most appropriate recommendation that you should make to the medical resident regarding the plan for smoking cessation?

A. **Monitor closely for ↑ in ADEs of clozapine**
B. Monitor closely for ↓ in efficacy of clozapine and possible ↑ in symptoms
C. Monitor for serotonin syndrome
D. Monitor for hypertensive crisis

Long-Acting Antipsychotics

CATIE Trial

Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)

Medication	Overall Discontinuation (D/C) Rate	D/C Rate for Lack of Efficacy	D/C Rate for Intolerable Side Effects
Olanzapine	64%	15%	18%
Perphenazine	75%	25%	16%
Quetiapine	82%	28%	15%
Risperidone	74%	27%	10%
Ziprasidone	79%	24%	15%

Liebereman J, Stroup T, McEvoy J, et al. Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. New England Journal of Medicine, 2005; 353;12:1209- 1223.

LAI Administration in WV

- **Scope of practice for pharmacists in WV:**
  - §30-5-10(a)(3)
  - A licensed pharmacist may "provide drug administration."
    "Administer" is defined in §30-5-4 as the direct application of a drug to the body of a patient or research subject by injection, inhalation, ingestion, or any other means.

- **Pharmacists may administer medications, but are not authorized to order or prescribe them**
  - Authority is only granted to pharmacists (cannot be delegated)
  - Must ensure that proper training and education has been completed

Suggested Training:

American Association of Psychiatric Pharmacists (AAPP) - Psychotropic Long-Acting Injectable Training Program

https://code.wvlegislature.gov/30-5-10/

https://aapp.org/ed/lai

Application Case (continued)

KM returns to clinic 12 weeks later and was successful in her quit attempt. She feels like her symptoms are fairly well-controlled, but her auditory hallucinations are still interfering with her ability to concentrate at work. She is hesitant about increasing her clozapine dose because she has experienced an increase in side effects with each dose increase, and she does not want to have to take another pill every day.

What do you recommend for KM?

Depot Formulations of Antipsychotics

Medication	Maintenance Dosing	Frequency
Aripiprazole monohydrate (Abilify Maintena®)	300-400 mg	Every 4 weeks
Aripiprazole lauroxil (Aristada®)	441 mg	Every 4 weeks
	882 mg	Every 6 weeks
	1064 mg	Every 8 weeks
Haloperidol (Haldol deconate®)	100-450 mg	Every 4 weeks
Olanzapine (Zyprexa Relprevv®)	150–210 mg	Every 2 weeks
	300–405 mg	Every 4 weeks
Paliperidone (Invega Sustenna®)	39–234 mg	Every 4 weeks
Paliperidone (Invega Trinza®)	273-819 mg	Every 12 weeks
Paliperidone (Invega Hafyera	1560mg	Every 6 months
Risperidone (Risperdal Consta®)	25–50 mg	Every 2 weeks
Risperidone (Perseris®)*	90-120 mg	Every 4 weeks (**SQ**)
Risperidone (Uzedy®)	50-250 mg	Every 4-8 weeks (**SQ**)

Riboldi I, Cavaleri D, Capogrosso CA, Crocamo C, Bartoli F, Carrà G. Practical Guidance for the Use of Long-Acting Injectable Antipsychotics in the Treatment of Schizophrenia. Psychol Res Behav Manag. 2022 Dec 30;15:3915-3929. doi: 10.2147/PRBM.S371991. PMID: 36605176; PMCID: PMC9809355.

LAIs - SGAs

Medication	Conversions
Aripiprazole (Abilify Maintena®)	10mg/day PO → 300 mg IM Qmonth 15mg/day PO → 400 mg IM Qmonth ≥20mg/day PO → 600 mg IM Qmonth
Aripiprazole (Aristada®)	Maintena Dose → Aristada Dose 300mg Qmonth → 441mg Qmonth 400mg Qmonth → 662mg Qmonth 600mg Qmonth → 882mg-1064mg Q4-8 weeks
Olanzapine (Zyprexa Relprevv®)	10mg/day PO → 150mg Q2wks OR 300mg Q4wks 15mg/day PO → 210mg Q2wks OR 405mg Q4wks 20mg/day PO → 300mg Q2wks

https://www.pbm.va.gov/PBM/clinicalguidance/drugmonographs/Aripiprazole_Long_acting_IM_Monograph_Updated_March_2016.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022173s027lbl.pdf

LAIs - SGAs

Medication	Conversions
Paliperidone (Invega Sustenna®)	Initial Dosing: 234mg IM on Day 1 & 156mg IM on Day 8 Maintenance Dosing: 3mg PO/day → 39-78mg IM Qmonth 6mg PO/day → 117mg IM Qmonth 9mg PO/day → 156mg IM Qmonth 12mg PO/day → 234mg IM Qmonth
Paliperidone (Invega Trinza®)	Sustenna Dose → Trinza Dose 78mg/month → 273mg Q3months 117mg/month → 410mg Q3months 156mg/month → 546mg Q3months 234mg/month → 819mg Q3months
Risperidone (Risperdal Consta®)	Initial dosing: 25mg Q2wks >4mg/day PO → 37.5mg-50mg Q2wks

http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/RISPERDAL+CONSTA-pi.pdf

https://www.invegasustennahcp.com/dosing/transitioning
https://www.invegatrinzahcp.com/dosing/treatment-transition

Bipolar Disorder

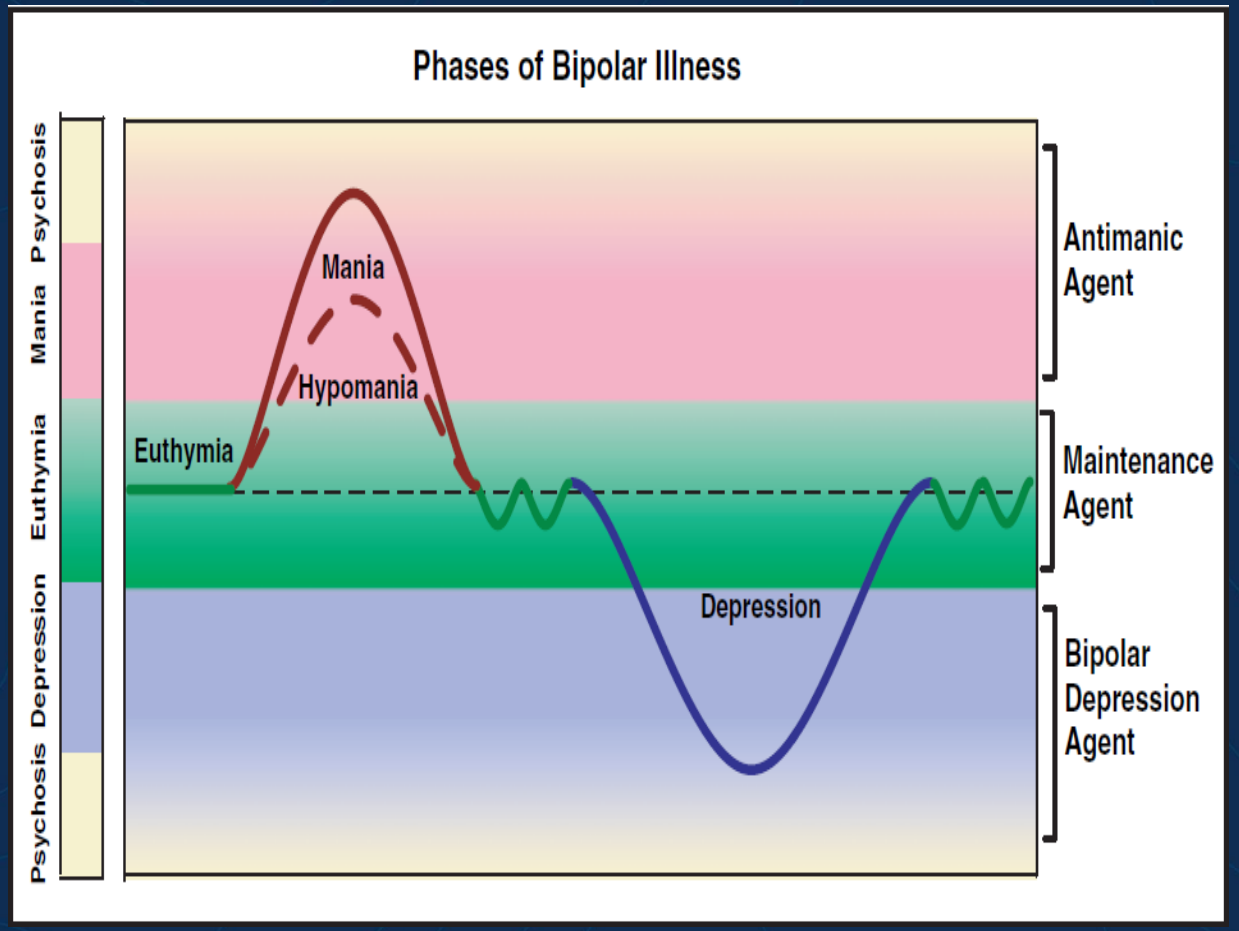
Clinical Presentation
Medications
Clinical Practice Guidelines

Application Case (continued)

KM's schizophrenia symptoms have been managed with clozapine (400 mg PO QHS) and aripiprazole LAI for the last 3 years. She comes to clinic today with her mother, who is concerned because for the last 3 months, KM had been "very down" and had lost interest in daily activities. Her PCP prescribed sertraline 50 mg PO daily 4 weeks ago. Her mother tells you that for the past 5 days, KM has been talking rapidly, not sleeping more than 2 hours per day, experiencing racing thoughts and is easily distracted.

What is KM experiencing? What is the likely cause of these symptoms?

Bipolar disorder



https://www.bipolarpsychologist.com.au/understanding-bipolar/

Phases of bipolar disorder:

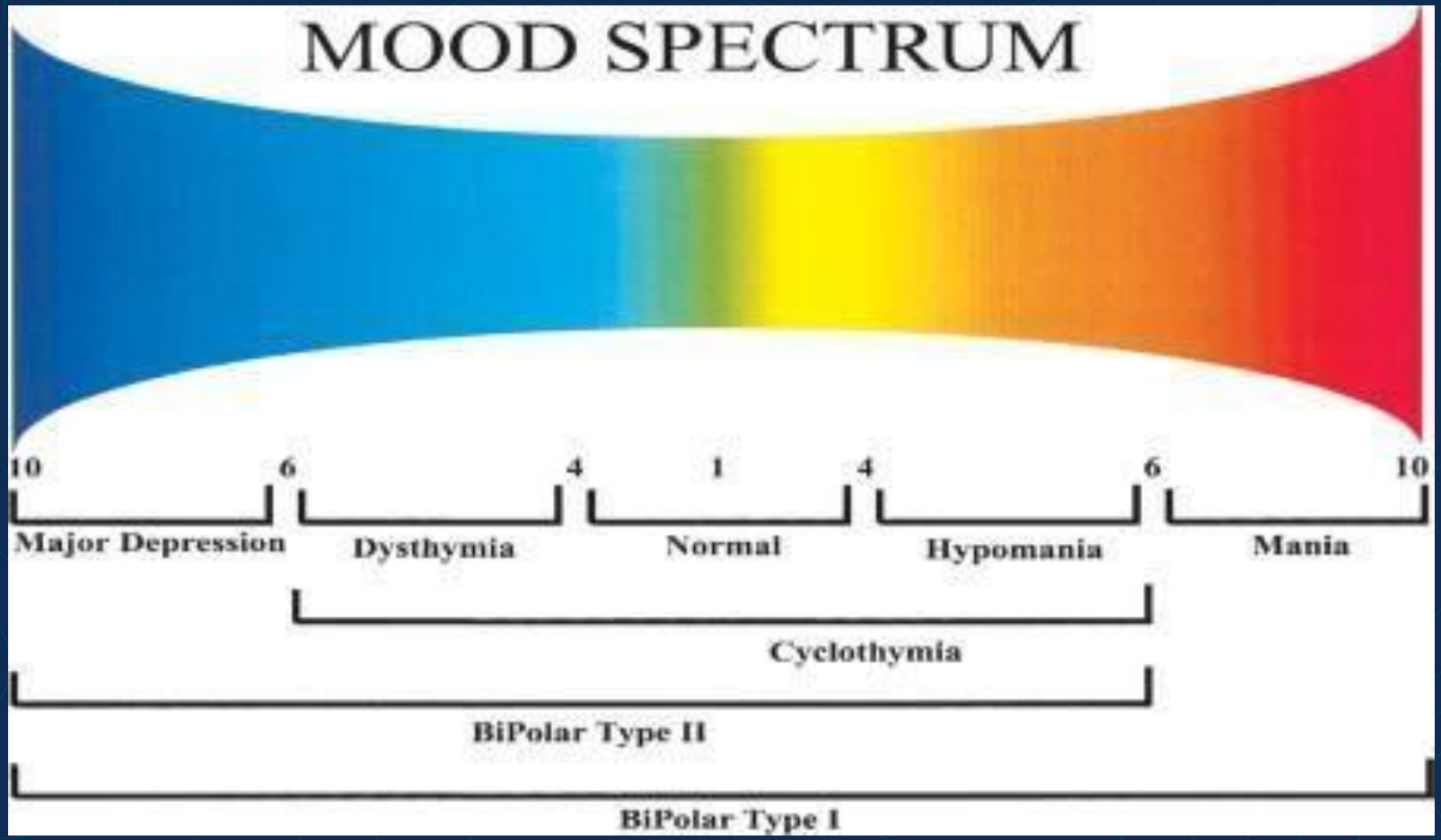
- Euthymia
- Depression
- Mania or hypomania

Types of bipolar disorder:

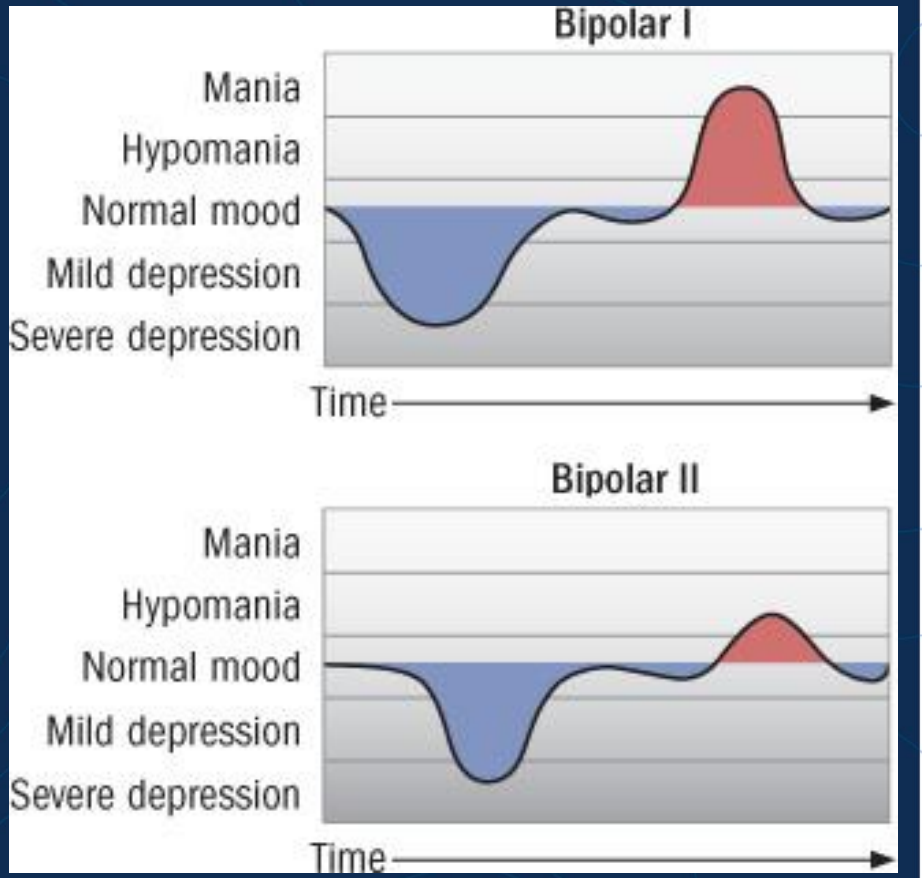
- Bipolar I Disorder: Depression + **Mania**
- Bipolar II Disorder: Depression + **Hypomania**
- Cyclothymia: Depressive Episodes + Hypomania

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Bipolar disorder



https://www.bipolarpsychologist.com.au/understanding-bipolar/



https://www.health.harvard.edu/newsletter_article/Bipolar_disorder

Clinical presentation - Mania

Mania:

- **1 week** of elevated mood and energy with at **least 3** of the following:
  - Inflated self-esteem (grandiosity)
  - Decreased need for sleep
  - Increased talking
  - Racing thoughts
  - Distractibility
  - Increased goal-directed activity
  - Excessive involvement of high-risk activities
- **Entails impairment of functioning or need for hospitalization**

Mania vs. Hypomania:

Hypomania occurs for at least 4 days and does not entail need for hospitalization

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Manic/Hypomanic Symptoms

Affective	Behavioral	Cognitive	Social
Euphoria	Pressured Speech	Grandiosity	Suicidal
Elated	Hyperactive	Poor Insight	Irritable
Boisterous	Speeded Up	Distractible	Suspicious
Labile	Restless	Flight of Ideas	Violent
Anger/Rage	Hyposomnia	Ideas of Reference	Impulsive
Irritability	Overconfident	Loose Associations	Seductive
Dissatisfaction	Fearless	Disorganized	Overconfident
Rapid Fluctuations	Reckless	Delusions	Controlling
Panic	Poor Judgment	Hallucinations	Conflict

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Depressive Symptoms

Table 39–1

Evaluation and Diagnosis of Mood Episodes

Diagnosis Episode	Impairment of Functioning or Need for Hospitalization[a]	*DSM-5* Criteria[b]
Major depressive	Yes	At least 2-week period of either depressed mood or loss of interest or pleasure in normal activities, associated with at least five of the following symptoms: • Depressed, sad mood (adults); can be irritable mood in children • Decreased interest and pleasure in normal activities • Decreased or increased appetite, weight loss or weight gain • Insomnia or hypersomnia • Psychomotor retardation or agitation • Decreased energy or fatigue • Feelings of excessive guilt or worthlessness • Impaired concentration or indecisiveness • Recurrent thoughts of death, suicidal thoughts or attempts

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

APA Guidelines – Bipolar Disorder (2002)

Acute Mania - First Line	**Severe Mania**	Lithium + Antipsychotic Valproate + Antipsychotic
	Less Ill Patients	Lithium, valproate or antipsychotic
Acute Depression - First Line:	**Severe depression**	Lithium + Antidepressant* ECT (if suicidal or psychotic)
	Less ill Patients	Lithium or lamotrigine
Maintenance - First Line:	**Monotherapy**	Lithium, VPA or lamotrigine Antipsychotics should be reassessed and tapered if initiated during mania**

*Limited data
**First generation antipsychotics

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

CANMAT Guidelines – Bipolar Disorder

Acute Mania - First Line	**Monotherapy**	Lithium, divalproex, SGAs
	Adjunctive Therapy	WITH lithium or divalproex: SGAs
Acute Depression - First Line:	**Monotherapy**	Lithium, lamotrigine, quetiapine
	Combination Therapy	Lithium or divalproex and SSRI, olanzapine and SSRI, lithium and divalproex, lithium or divalproex and bupropion
Maintenance - First Line:	**Monotherapy**	Lithium, SGA, VPA or lamotrigine
	Combination	Mood stabilizer + SGA or lamotrigine

Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, Sharma V, Goldstein BI, Rej S, Beaulieu S, Alda M, MacQueen G, Milev RV, Ravindran A, O'Donovan C, McIntosh D, Lam RW, Vazquez G, Kapczinski F, McIntyre RS, Kozicky J, Kanba S, Lafer B, Suppes T, Calabrese JR, Vieta E, Malhi G, Post RM, Berk M. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018 Mar;20(2):97-170. doi: 10.1111/bdi.12609. Epub 2018 Mar 14. PMID: 29536616; PMCID: PMC5947163.

Medications for Bipolar Disorder

- Lithium
- Valproic acid (divalproex)
- SGAs
- Lamotrigine

Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Application Case (continued)

KM is diagnosed with schizoaffective disorder in clinic. Which of the following medications would be most appropriate to manage KM's acute manic episode?

A. Valproic acid/valproate
B. Carbamazapine
C. Lamotrigine
D. Quetiapine

Valproic acid (VPA)

Acute mania, mixed episodes, maintenance

ADEs:

- GI complaints
- Weight gain
- Fine hand tremors
- Sedation
- Alopecia

Drug-drug interactions: common (LTG, warfarin, CNS depressants)

Sprinkle formulation available

Should be avoided in pregnancy

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Lithium

1st line for acute mania, acute depression and maintenance

ADEs:

- GI upset
- Tremors
- Polyuria (nephrogenic diabetes insipidus)
- Rash
- Alopecia
- Akathisia
- Hypothyroidism
- Weight gain
- Leukocytosis

- Benefit in suicidal patients
- Interactions:
  - No CYP interactions
  - Several drug-drug interactions
- Renally eliminated
- Narrow therapeutic index
  - 0.8-1.2 mEq/L
  - Monitor trough levels

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Lithium toxicity

Blood levels >1.5 mEq/L

- >1.5 mEq/L → ataxia, tremor, vomiting, diarrhea, confusion
- >2.5 mEq/L → CNS depression, arrhythmia, seizure, coma

↑ Risk of Lithium Toxicity:

- Sodium restriction
- Dehydration
- Vomiting/Diarrhea
- Age > 50 years
- Heart failure
- Cirrhosis
- Drug interactions

- Management of Lithium Toxicity:
  - Discontinue lithium
  - ER management
    - IV fluids
  - Monitor:
    - Renal and electrolyte status
    - Fluid balance
    - Neurologic changes
  - Dialysis if lithium [] >4 mEq/L

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Management of Lithium-Induced Side Effects

Adverse Drug Effect	Management
Dermatologic (rash, worsening psoriasis)	Discontinue
Tremor	↓ dose, add propranolol
CNS (agitation, confusion, ↓ concentration)	↓ dose
GI	↓ dose, use XR formulation
Hypothyroidism	Add levothyroxine
Polydipsia/Polyuria	↓ dose, add amiloride, dose QHS or ↑ fluid intake
Nephrotoxicity	Use lowest effective dose; discontinue
Teratogenicity	Avoid during 1st trimester

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Lithium Drug-Drug Interactions

↑ Lithium Levels:

- Thiazides
- NSAIDs
- ACEi/ARBs
- Renal dysfunction
- Dehydration
- Salt restriction

↓ Lithium Levels:

- Theophylline

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

SGAs

Efficacy in acute mania has been well documented

- Fairly rapid time to symptom improvement

May be especially beneficial for anxiety symptoms during manic episode

ADEs:

- Metabolic effects
  - High: olanzapine, quetiapine
  - Moderate: risperidone, asenapine, brexpiprazole,
  - Low: Ziprasidone, aripiprazole, cariprazine, lurasidone, lumateperone
- EPS, sedation, orthostatic hypotension, Ach effects, QTc prolongation

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Lamotrigine

Less effective for mania; used for depression or maintenance

ADEs:

- Maculopapular rash
- Dizziness
- Drowsiness
- Headache
- Blurred vision
- Nausea

Slower onset due to slow titration

Drug-drug interactions: common

- LTG + VPA → severe interaction → reduce LTG dose by 50%
- LTG + CBZ → increase LTG dose

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Guidelines: CANMAT (Mania)

First Line	**Monotherapy**	Lithium, divalproex, olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone, asenapine, paliperidone
	Adjunctive Therapy	WITH lithium or divalproex: risperidone, quetiapine, olanzapine, aripiprazole, asenapine
Second Line	**Monotherapy**	Carbamazepine, ECT, haloperidol
	Combination Therapy	Lithium and divalproex
Not Recommended	**Monotherapy**	Gabapentin, topiramate, lamotrigine, verapamil, tiagabine
	Combination therapy	Risperidone and carbamazepine, olanzapine and carbamazepine

Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, Sharma V, Goldstein BI, Rej S, Beaulieu S, Alda M, MacQueen G, Milev RV, Ravindran A, O'Donovan C, McIntosh D, Lam RW, Vazquez G, Kapczinski F, McIntyre RS, Kozicky J, Kanba S, Lafer B, Suppes T, Calabrese JR, Vieta E, Malhi G, Post RM, Berk M. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018 Mar;20(2):97-170. doi: 10.1111/bdi.12609. Epub 2018 Mar 14. PMID: 29536616; PMCID: PMC5947163.

ACUTE MANIA

D/C antidepressants
D/C caffeine
Psychotherapy

Not on 1st line Medication

Initiate lithium, VPA, SGA or 2-drug combo

On 1st line Medication

Lithium or VPA → Add or switch to SGA

SGA → Add or switch to Lithium or VPA

2-drug combo → Replace 1 or both with other 1st line agents

Replace 1 or both with other 1st line agents

Consider CBZ or clozapine or ECT

Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, Sharma V, Goldstein BI, Rej S, Beaulieu S, Alda M, MacQueen G, Milev RV, Ravindran A, O'Donovan C, McIntosh D, Lam RW, Vazquez G, Kapczinski F, McIntyre RS, Kozicky J, Kanba S, Lafer B, Suppes T, Calabrese JR, Vieta E, Malhi G, Post RM, Berk M. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018 Mar;20(2):97-170. doi: 10.1111/bdi.12609. Epub 2018 Mar 14. PMID: 29536616; PMCID: PMC5947163.

Pharmacologic treatment – Acute depression

Assess for secondary causes

Taper off benzos, sedative-hypnotics

Mild – Moderate → Lithium, SGA, VPA, LTG

Severe → 2-3 drug combination

- Mood stabilizer (VPA or Lithium) + SGA ± LTG

Clinical Pearl: Only use antidepressants in combination with a mood stabilizer in patients with bipolar disorder

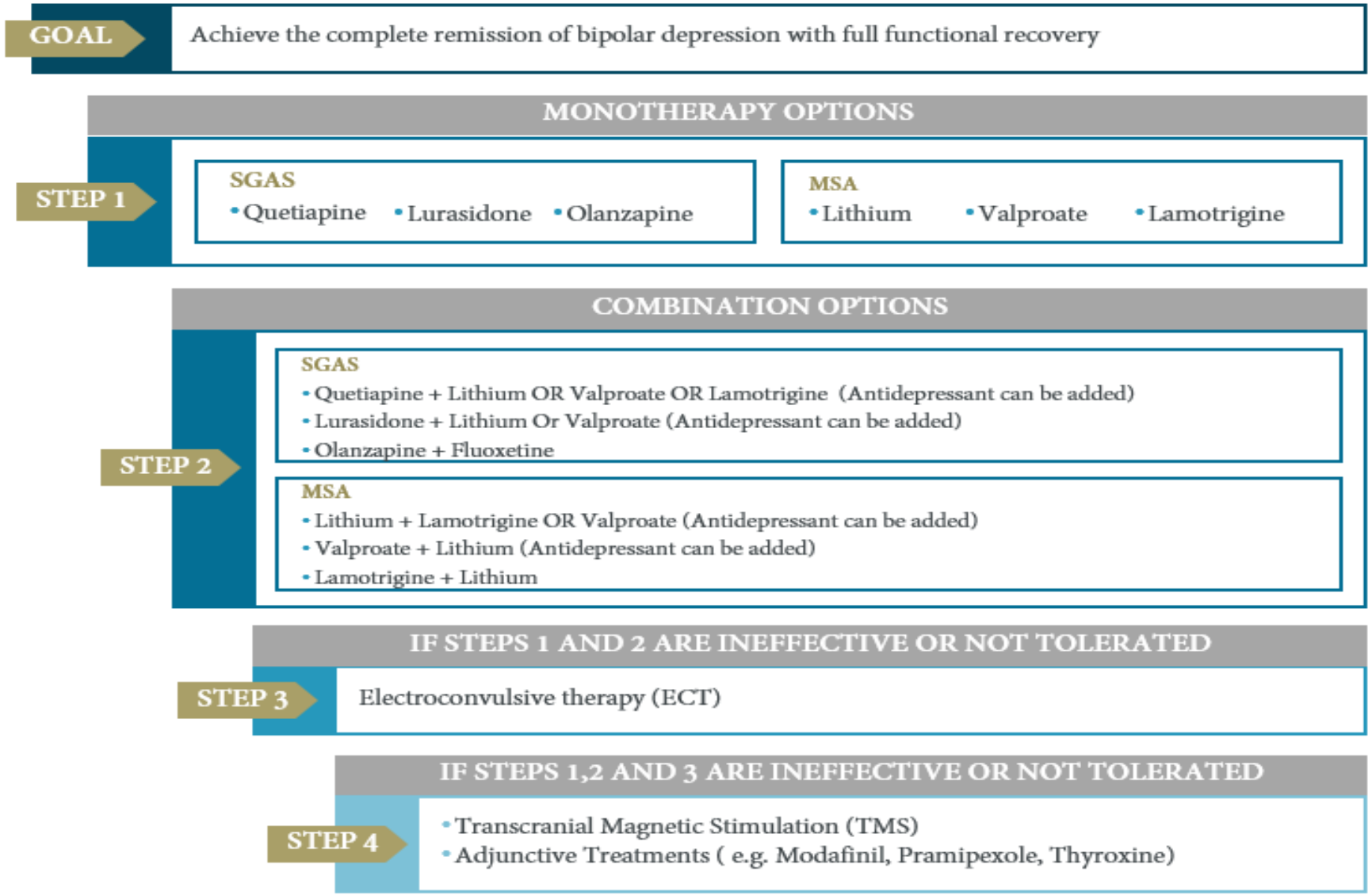
Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Guidelines: CANMAT (Depression)

First Line	**Monotherapy**	Lithium, lamotrigine, quetiapine
	Combination Therapy	Lithium or divalproex and SSRI, olanzapine and SSRI, lithium and divalproex, lithium or divalproex and bupropion
Second Line	**Monotherapy**	Divalproex, lurasidone
	Combination Therapy	Quetiapine and SSRI, adjunctive modafinil, lithium or divalproex and lamotrigine, lithium or divalproex and lurasidone
Third Line	**Monotherapy**	Carbamazepine, olanzapine, ECT
Not Recommended	**Monotherapy**	Gabapentin, aripiprazole, ziprasidone
	Combination therapy	Adjunctive ziprasidone, adjunctive levetiracetam

Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, Sharma V, Goldstein BI, Rej S, Beaulieu S, Alda M, MacQueen G, Milev RV, Ravindran A, O'Donovan C, McIntosh D, Lam RW, Vazquez G, Kapczinski F, McIntyre RS, Kozicky J, Kanba S, Lafer B, Suppes T, Calabrese JR, Vieta E, Malhi G, Post RM, Berk M. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018 Mar;20(2):97-170. doi: 10.1111/bdi.12609. Epub 2018 Mar 14. PMID: 29536616; PMCID: PMC5947163.

TREATMENT OF ACUTE BIPOLAR DEPRESSION.



Malhi, G. S., et al. (2015). Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. *Australian & New Zealand Journal of Psychiatry, 49*(12), 1087-1206.

psych scene EXCELLENCE IN PSYCHIATRY

WestVirginiaUniversity. School of Pharmacy

Application Case (continued)

KM's acute hypomanic episode resolves, and the medical resident wants to know what changes should be made to her medication regimen for maintenance of her schizoaffective disorder. Which of the following is the most appropriate recommendation?

A. Discontinue clozapine and continue the valproic acid
B. Continue the clozapine and valproic acid
C. Discontinue the valproic acid and continue the clozapine
D. Discontinue clozapine and valproic acid and initiate lamotrigine

Pharmacologic treatment - Maintenance

1st line: SGA, lithium, VPA or lamotrigine

2nd line: CBZ

Goal: monotherapy if possible

Based on clinical scenario:

- Depressive-dominant → Lamotrigine may be preferred
- Manic-dominant → SGA or lithium may be preferred

Polytherapy:

- Mood Stabilizer (VPA or Lithium) + SGA or Lamotrigine

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Pharmacologic Therapy Overview

Medication	Acute Mania	Acute Depression	Maintenance
Lithium	+	+	+
VPA	+	+	+
Lamotrigine		+	+
Aripiprazole	+		+
Olanzapine	+	w/fluoxetine	+
Ziprasidone	+		+
Lurasidone	+	+	+
Risperidone	+		+
Quetiapine	+	+	+
CBZ/OXC	+		+
Lumateperone		+	

Information in table complied from: Chisholm-Burns MA, Wells BG, Schwinghammer TL, Malone PM, Kolesar JM, DiPiro JT (eds). Pharmacotherapy Principles & Practice, 6th ed. New York: McGraw-Hill, 2021

Therapeutic Drug Monitoring

Therapeutic Drug Levels:

- Monitor **troughs** weekly during titration → monitor monthly once stabilized
  - Monitor more frequently with interacting agents
- Lithium:
  - 0.8-1.2 mEq/L
- VPA:
  - 50-125 mcg/mL
- CMZ:
  - 4-12 mcg/mL

Hirschfeld, R. M. A., Bowden, C. L., Gitlin, M. J., Keck, P. E., Suppes, T., Thase, M. E., & Perlis, R. H. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. In N. C. Numerous Contributors (Ed.), *American Psychiatric Association practice guidelines for the treatment of psychiatric disorders: Compendium 2002* (pp. 547–634). American Psychiatric Association.

Application Case (continued)

KM comes to clinic for a follow-up appointment and states that she is not having any issues with her medications, but has been having increasing suicidal thoughts and is having difficulty using coping mechanisms to manage them.

What questions would you want to ask KM to determine next steps in your treatment plan?

Suicidality – Warning Signs and Red Flags

Suicidality

Suicide rate: up to 30x higher in patients with schizophrenia and bipolar disorder than general population

Suicidal thoughts may be mediated by the hippocampus

Changes in prefrontal cortical metabolism has also been linked to suicidal behavior

Dome P, Rihmer Z, Gonda X. Suicide Risk in Bipolar Disorder: A Brief Review. Medicina (Kaunas). 2019 Jul 24;55(8):403. doi: 10.3390/medicina55080403. PMID: 31344941; PMCID: PMC6723289.

Suicidality

Risk Factors

Health Disorders

Environmental

- Access to lethal means
- Prolonged stress
- Stressful life events
- Exposure to another person's suicide

Historical

- Prior suicide attempt(s)
- Family history of suicide
- Childhood abuse, neglect or trauma

Protective Factors

- Access to mental health care
- Feeling connected to family and community support
- Problem-solving and coping skills
- Limited access to lethal means
- Beliefs that encourage connecting and help-seeking and/or discourage suicidal behaviors

Dome P, Rihmer Z, Gonda X. Suicide Risk in Bipolar Disorder: A Brief Review. Medicina (Kaunas). 2019 Jul 24;55(8):403. doi: 10.3390/medicina55080403. PMID: 31344941; PMCID: PMC6723289.

Suicidality

National Suicide Hotline: (800)-283-8255

Watch for changes in behavior or presence of new behaviors

Warning Signs: Talk

- Hopelessness
- Having no reason to live
- Being a burden to others
- Feeling trapped
- Unbearable pain

Warning Signs: Mood

- Depressed
- Anxious
- Irritable
- Humiliated/Shamed
- Angry

Warning Signs: Behavior

- Increased use of alcohol or drugs
- Investigating methods of suicide
- Withdrawing from activities
- Isolating from family and friends
- Changes in sleep patterns
- Saying goodbye to people
- Giving away possessions
- Aggression

Dome P, Rihmer Z, Gonda X. Suicide Risk in Bipolar Disorder: A Brief Review. Medicina (Kaunas). 2019 Jul 24;55(8):403. doi: 10.3390/medicina55080403. PMID: 31344941; PMCID: PMC6723289.

Providing Comprehensive Care to Patients with Schizophrenia and Bipolar Disorder

WestVirginiaUniversity.
School of Pharmacy

Comprehensive Care

- Monitoring for efficacy and side effects
  - PANSS
  - AIMS
  - Suicidal ideations
  - Metabolic labs (A1c, lipids)
- Patient and caregiver education
- Cognitive behavioral therapy
- Miscellaneous
  - Nutrition counseling, financial resources, transportation
  - Vaccines

Useful Resources for Clinicians

Resources for Clinicians

American Psychiatric Association
- Pocket guides
- Guideline summaries

American Association of Psychiatric Pharmacists
- Training programs
- Updates

SMI Adviser
- LAI dosing and conversions
- Clozapine resources

Medications on the Horizon

Therapeutic Targets for New Schizophrenia Medications

- Noradrenergic alpha2-receptor modulators
- $5HT_{2C}$ receptor agonists
- Cholinergic receptor modulators
- Glutamate receptor modulators
- GABA receptor agonists
- NMDARs Stimulants

https://www.empr.com/home/news/drugs-in-the-pipeline/disappointing-results-for-ulotaront-in-two-phase-3-schizophrenia-trials/

Medication Update

Xanomeline and trospium (KarXT®)

- Xanomeline: M1 and M4 agonist
- Trospium: peripherally acting muscarinic antagonist → goal is to ameliorate xanomeline-related adverse effects in peripheral muscarinic receptors

- **No activity on D_2 receptors**

- **EMERGENT-2 Trial:**
  - Randomized, double-blind, placebo-controlled 5-week phase 3 trial for adults 18-65 years of age with schizophrenia diagnosis and PANSS score of ≥80
- **EMERGENT-4 and EMERGENT-5 : 52-week open-label trials showed similar results**

- **FDA currently reviewing; regulatory decision expected by end of September**

https://www.labiotech.eu/in-depth/new-treatments-schizophrenia/#:~:text=that%20you%20need.%E2%80%9D-,KarXT%3A%20muscarinic%20agonist%20offers%20promising%20advances%20in%20the%20long%2Dterm,of%20drugs%20called%20muscarinic%20agonists.

EMERGENT-2 Results

	KarXT (n=117)	Placebo (n=119)	Difference (95% CI)	Cohen's *d*	p value
Primary endpoint					
PANSS total score*	−21·2 (1·7)	−11·6 (1·6)	−9·6 (−13·9 to −5·2)	0·61	<0·0001
Secondary outcome measures					
PANSS positive symptom subscale score†	−6·8 (0·5)	−3·9 (0·5)	−2·9 (−4·3 to −1·5)	0·59	<0·0001
PANSS negative symptom subscale score‡	−3·4 (0·5)	−1·6 (0·5)	−1·8 (−3·1 to −0·5)	0·40	0·0055
PANSS Marder negative factor score§	−4·2 (0·5)	−2·0 (0·5)	−2·2 (−3·6 to −0·8)	0·44	0·0022
CGI-S scale score¶	−1·2 (0·1)	−0·7 (0·1)	−0·6 (−0·9 to −0·3)	0·58	<0·0001
PANSS responders (≥30% reduction from baseline in PANSS total score)‖	51/93 (55%)	28/99 (28%)	27% (13 to 39)	NA	<0·0001

Data are LSM change (SE) from baseline or n/N (%). CGI-S=Clinical Global Impression–Severity. mITT=modified intent-to-treat. NA=not applicable. PANSS=Positive and Negative Syndrome Scale. KarXT=xanomeline–trospium. *PANSS total score range, 30–120 (higher score reflects greater severity). †PANSS positive symptoms subscale score range, 7–49 (higher score reflects greater severity). ‡PANSS negative symptoms subscale score range, 7–49 (higher score reflects greater severity). §PANSS Marder negative factor range, 7–49 (higher score reflects greater severity). ¶CGI-S scale range, 1–7 (1 indicating no illness and 7 indicating severe illness). ‖On the basis of the floor-adjusted total score (total score minus 30), assessed in patients with available week-5 scores.

Table 2: **Efficacy measures at week 5 (mITT population)**

Kaul I, Sawchak S, Correll C, et al. Efficacy and safety of the muscarinic receptor agonist KarXT (xanomeline–trospium) in schizophrenia (EMERGENT-2) in the USA: results from a randomised, double-blind, placebo-controlled, flexible-dose phase 3 trial. The Lancet, 2024. 403 (10422): 160-170. https://doi.org/10.1016/S0140-6736(23)02190-6.

EMERGENT-2 Results

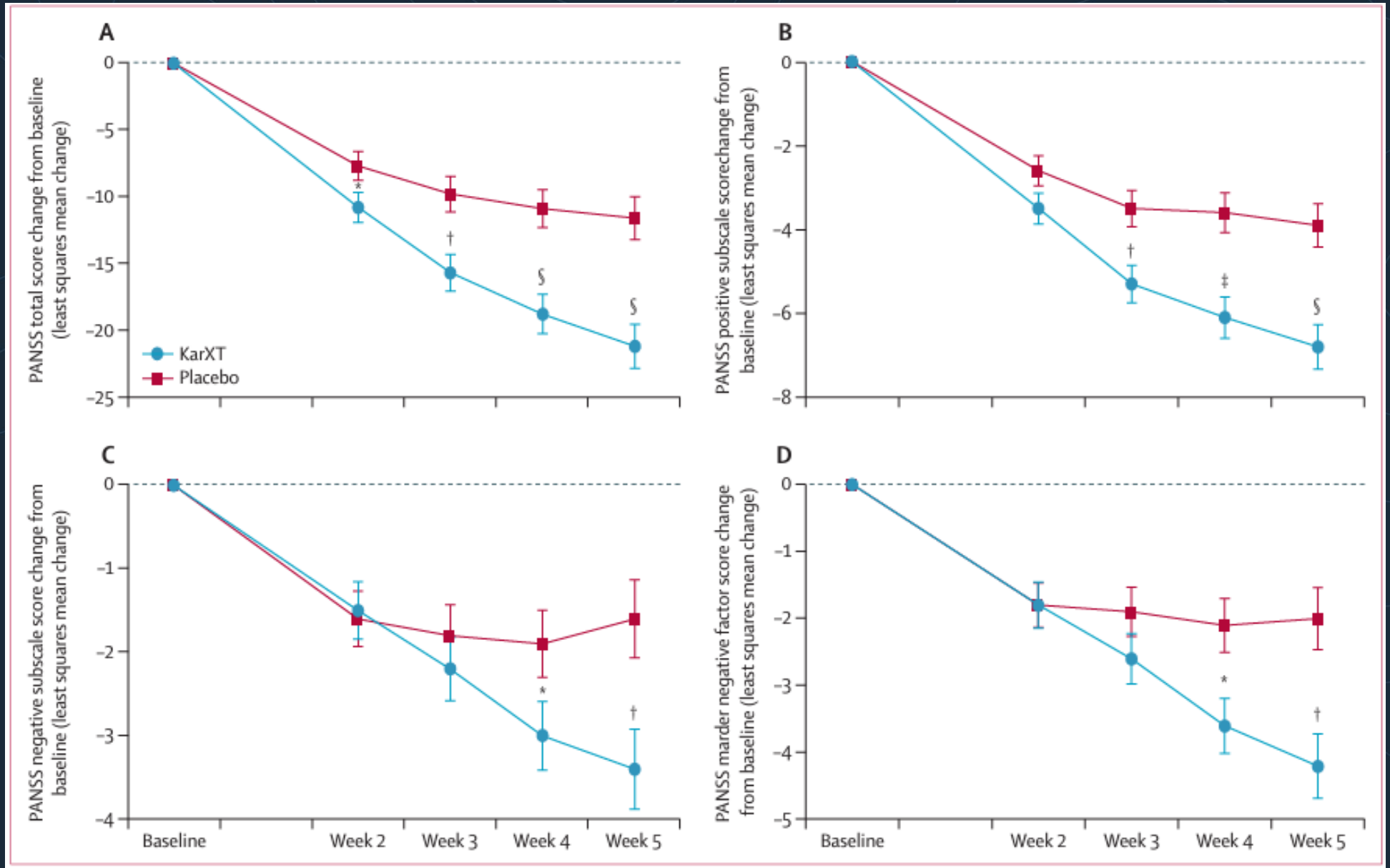


Figure 2: **Mean change from baseline in PANSS total score (A), PANSS positive subscale score (B), PANSS negative subscale score (C), and PANSS Marder negative factor score (D)**

Error bars indicate SEM. KarXT=xanomeline–trospium. PANSS=Positive and Negative Syndrome Scale. *p<0·05. †p<0·01. ‡p<0·001. §p<0·0001.

Kaul I, Sawchak S, Correll C, et al. Efficacy and safety of the muscarinic receptor agonist KarXT (xanomeline–trospium) in schizophrenia (EMERGENT-2) in the USA: results from a randomised, double-blind, placebo-controlled, flexible-dose phase 3 trial. The Lancet, 2024. 403 (10422): 160-170. https://doi.org/10.1016/S0140-6736(23)02190-6.

EMERGENT-2 Results

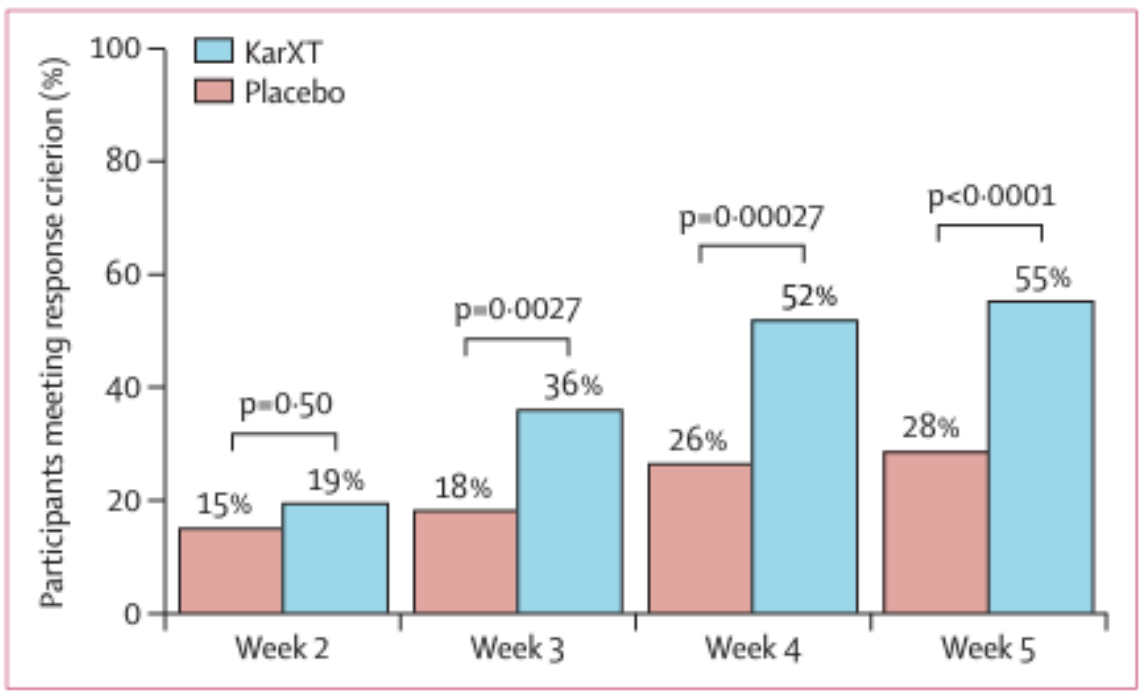


***Figure 4*: Percentage of participants with ≥30% reduction from baseline in PANSS total score by trial week**

Based on floor-adjusted total score (total score minus 30). PANSS=Positive and Negative Syndrome Scale. KarXT=xanomeline–trospium.

Kaul I, Sawchak S, Correll C, et al. Efficacy and safety of the muscarinic receptor agonist KarXT (xanomeline–trospium) in schizophrenia (EMERGENT-2) in the USA: results from a randomised, double-blind, placebo-controlled, flexible-dose phase 3 trial. The Lancet, 2024. 403 (10422): 160-170. https://doi.org/10.1016/S0140-6736(23)02190-6.

EMERGENT-2 Results

	KarXT (n=126)	Placebo (n=125)
Any TEAE	95 (75%)	73 (58%)
Serious TEAE	2 (2%)	2 (2%)
Severe TEAE	2 (2%)	4 (3%)
TEAE leading to discontinuation	9 (7%)	7 (6%)
TEAE occurring in ≥5% of participants in the KarXT group		
Constipation	27 (21%)	13 (10%)
Dyspepsia	24 (19%)	10 (8%)
Headache	17 (14%)	15 (12%)
Nausea	24 (19%)	7 (6%)
Vomiting	18 (14%)	1 (1%)
Hypertension	12 (10%)	1 (1%)
Dizziness	11 (9%)	4 (3%)
Gastro-oesophageal reflux disease	8 (6%)	0
Diarrhoea	7 (6%)	4 (3%)

	KarXT (n=126)	Placebo (n=125)
Change from baseline to week 5*		
Body weight, kg	1·4 (3·31)	2·5 (6·92)
Prolactin, mg/L	1·0 (9·27)	0·8 (9·59)
Simpson-Angus Scale score	0 (0·61)	−0·1 (0·70)
Barnes Akathisia Rating Scale score	−0·1 (1·09)	−0·2 (0·98)
Abnormal Involuntary Movement Scale score	0·0 (0·28)	0·0 (0·10)

Data are n (%) or mean (SD). TEAE=treatment-emergent adverse event. KarXT=xanomeline–trospium. *Number of participants in the KarXT and placebo groups for which data were available at week 5: for body weight in KarXT, n=94, and in placebo, n=100; for prolactin in KarXT, n=75, and in placebo, n=85; for the Simpson-Angus Scale in KarXT, n=92, and in placebo, n=99; for the Barnes Akathisia Rating Scale in KarXT, n=92, and in placebo, n=99; and for the Abnormal Involuntary Movement Scale in KarXT, n=92, and in placebo, n=99.

Table 3: **TEAEs and safety during the 5-week treatment period (safety population)**

Kaul I, Sawchak S, Correll C, et al. Efficacy and safety of the muscarinic receptor agonist KarXT (xanomeline–trospium) in schizophrenia (EMERGENT-2) in the USA: results from a randomised, double-blind, placebo-controlled, flexible-dose phase 3 trial. The Lancet, 2024. 403 (10422): 160-170. https://doi.org/10.1016/S0140-6736(23)02190-6.

New Drug Update - Novel Treatment (Ulotaront)

May 2019: FDA granted Breakthrough Therapy designation to SEP-363856 for treatment of schizophrenia

MOA: trace amine-associated receptor (TAAR1) activator and $5HT_{1A}$ activator

- **No D_2 or $5HT_{2A}$ activity**

Preliminary results showed improvement in PANSS score compared to placebo

Phase 3 studies showed no improvements compared to placebo

DIAMOND 1 and DIAMOND 2 studies: 435 and 464 patients randomly assigned to medication or placebo → change in PANSS score was similar to placebo

https://www.empr.com/home/news/drugs-in-the-pipeline/disappointing-results-for-ulotaront-in-two-phase-3-schizophrenia-trials/

https://www.empr.com/home/news/drugs-in-the-pipeline/novel-treatment-for-schizophrenia-gets-fdas-breakthrough-therapy-designation/

Medications on the Horizon

BI 425809 (iclepertin)

- **Oral glycine transporter**
- **Phase II Trials:**
  - May improve cognitive function in patients with schizophrenia and Alzheimer's disease
- **Phase III trials underway**

Evenamide

- **Blocks glutamate and voltage-gated sodium channels**
  - Treatment-resistant schizophrenia
  - PANSS reduction of 10.2 points (compared to 7.6 points with placebo) in Phase II multicenter trial
- **ADEs: headache, vomiting, nasopharyngitis**

https://www.newron.com/news-and-media/regulatory-news/newron-announces-positive-top-line-results-potentially-pivotal-phase

Wunderlich, G., Blahova, Z., Garcia, M. *et al.* Efficacy and safety of the novel GlyT1 inhibitor BI 425809 in Alzheimer's dementia: a randomized controlled trial. *Alz Res Therapy* **15**, 24 (2023). https://doi.org/10.1186/s13195-023-01163-3

Medications on the Horizon

Brilaroxazine

- **Serotonin-dopamine modulator**
  - Partial agonist at $5HT_{1A}$, antagonist at 5HT2A and $5HT_7$
- **Phase III trials:**
  - PANSS reduction of 23.9 points (compared to 13.8 with placebo)
  - Low discontinuation rates
  - No serious adverse effects
  - No change in bodyweight, blood glucose or lipid levels compared to placebo
  - <1% of patients reported EPS
- **Expected to submit to FDA in 2025**

https://revivapharma.com/reviva-announces-positive-topline-results-from-global-pivotal-phase-3-recover-trial-of-brilaroxazine-in-schizophrenia/

Assessment Questions

Assessment Question

Which of the following medications is NOT available as a long acting injectable?

A. Clozapine
B. Risperidone
C. Paliperidone
D. Aripiprazole

Assessment Question

A patient that is experiencing medication-induced akathisia should be prescribed:

A. Benztropine
B. Propranolol
C. Levothyroxine
D. Deutetrabenazine

Assessment Question

The 2020 APA Guidelines for schizophrenia recommend ____ for treatment of tardive dyskinesia.

A. Anticholinergics
B. VMAT2 inhibitors
C. Beta-blockers
D. Stool softeners

Assessment Question

The APA Guidelines recommend clozapine for patients with:

A. Treatment resistance
B. Suicidal ideations
C. Aggressive behaviors
D. All of the above

Assessment Question

The CANMAT guidelines recommend all of the following medications as first line options for treatment of an acute manic episode except:

A. Quetiapine
B. Lamotrigine
C. Valproic acid
D. Lithium

Assessment Question

Which of the following is NOT effective at treating acute depressive episodes in a patient with bipolar disorder?

A. Quetiapine
B. Lithium
C. Aripiprazole
D. Valproic acid

Assessment Question

Name 3 risk factors for suicide in a patient with schizophrenia or bipolar disorder.

Assessment Question

Pharmacists in WV are permitted to administer long-acting injectable antipsychotics if proper training and education are completed.

A. True

B. False

Assessment Question

Which of the following will NOT cause increased lithium levels?

A. Increased sodium
B. ACE inhibitors
C. NSAIDs
D. Thiazides

Assessment Question

Which of the following medications for bipolar disorder interacts with lamotrigine?

A. Valproic acid

B. Lithium

C. Quetiapine

Assessment Question

If a patient with schizophrenia increases his smoking habits from ½ ppd to 1 ppd while taking olanzapine, which of the following is true?

A. The patient should be monitored for increased symptoms
B. The patient should be monitored for increased side effects
C. Olanzapine metabolism is not affected by changes in smoking

Questions?

ashleigh.barrickman@hsc.wvu.edu

WestVirginiaUniversity.
School of Pharmacy

CE Evaluation Access Code

******

Capital Letters, No spaces, complete by _____

Note: CE credit will be reported to NABP CPE Monitor within 4-6 weeks

Mindful Medicine: Updates and Insights in Psychiatric Pharmacy

Ashleigh Barrickman, PharmD, BCACP, CTTS

WestVirginiaUniversity.
School of Pharmacy