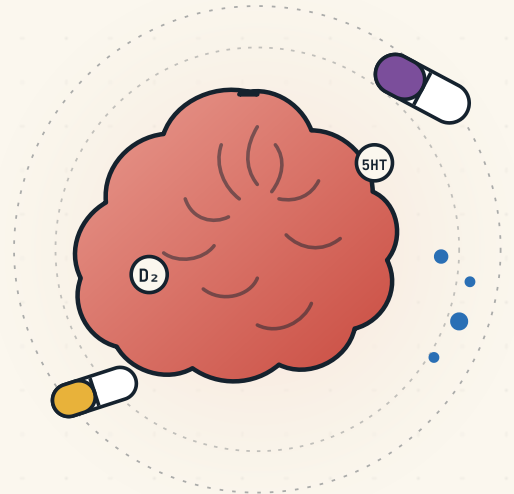


SYSTEM: PSYCHIATRIC / CNS · CLASS: ATYPICAL ANTIPSYCHOTICS

Second-Generation Antipsychotics (Atypicals)

Dopamine + serotonin blockers that treat schizophrenia, bipolar mania, and treatment-resistant depression — **less EPS** than first-gen, but **higher metabolic risk**. Know the labs. Know the red flags.



1

OVERVIEW

Definition — what they are & why they matter



01

USED FOR

Psychosis & mood

Schizophrenia (1st-line), bipolar mania, treatment-resistant depression, severe agitation, Tourette's.

02

WHY PREFERRED

Treats BOTH symptom types

Positive sx (hallucinations, delusions) + **Negative** sx (flat affect, social withdrawal, anhedonia).

03

TRADE-OFF

Less EPS, more metabolic

Lower risk of dystonia/TD than 1st-gen — but **weight gain, diabetes, dyslipidemia** are serious.

2

PATHOPHYSIOLOGY — SIMPLIFIED

Mechanism: how atypicals re-balance the brain



STEP 1

Excess dopamine
Overactive D₂ in mesolimbic pathway drives psychosis



STEP 2

Drug blocks D₂
Loosely (unlike 1st-gen), so fewer EPS effects



STEP 3

Also blocks 5-HT_{2A}
Serotonin blockade treats **negative sx**



STEP 4

Balance restored
↓ hallucinations, ↑ mood, ↑ social engagement



STEP 5

Off-target hits
H₁, α₁, M₁ receptors → sedation, ↓ BP, weight gain

Key distinction: 1st-gen = tight D₂ block → high EPS. 2nd-gen = loose D₂ + 5-HT_{2A} block → wider coverage, fewer movement side effects.

Onset: Agitation/insomnia improves in days. Hallucinations/delusions take **2-6 weeks**. Negative sx can take **months**. Teach patience.

Early vs Late — know the red flags



EARLY / MILD (FIRST DAYS–WEEKS)

- Sedation, drowsiness, dizziness
- Orthostatic hypotension (α_1 block)
- Dry mouth, blurred vision, constipation
- Mild weight gain begins
- GI upset, nausea
- Mild tremor, restlessness (akathisia)

LATE / SEVERE **REPORT IMMEDIATELY**

Neuroleptic Malignant Syndrome (NMS): fever, muscle rigidity, $\uparrow$ BP/HR, $\downarrow$ LOC, $\uparrow$ CK — **stop drug, cool patient**

Agranulocytosis (esp. CLOZAPINE): sore throat, fever, flu-like sx → check ANC

Metabolic syndrome: weight gain, $\uparrow$ glucose, $\uparrow$ lipids, new-onset T2DM

Tardive dyskinesia (TD): involuntary lip-smacking, tongue thrust — often irreversible

QT prolongation (esp. ziprasidone) → torsades risk

Seizures (dose-related, clozapine)

NCLEX RED FLAG

HYPERTHERMIA + MUSCLE RIGIDITY + AMS = NMS UNTIL PROVEN OTHERWISE. STOP THE DRUG. THIS IS A MEDICAL EMERGENCY.

ABCs • Safety • Monitor • Teach



A AIRWAY
(SEDATION,
ASPIRATION)

B BREATHING

C CIRCULATION
($\downarrow$ BP, QT)

D DISABILITY
(LOC, NMS)

S SAFETY
(FALLS,
SUICIDE)

PRIORITY 1

ASSESS Baseline & vitals

- VS, orthostatic BP, weight, BMI, waist circumference
- Baseline ECG (QT), fasting glucose, lipid panel
- CBC w/ ANC — **mandatory pre-clozapine**
- Suicide risk screen; AIMS test for TD

PRIORITY 2

MONITOR Red-flag reactions

- Temp + rigidity → rule out NMS
- Sore throat / fever → rule out agranulocytosis
- Orthostasis & fall risk — $\uparrow$ in elderly
- QT interval if ziprasidone / high doses

PRIORITY 3

ADMINISTER Safely

- Ziprasidone & lurasidone — **give with food** (≥ 350 –500 kcal)
- Clozapine — only dispense if **ANC ≥ 1500** (REMS)
- Never stop abruptly → rebound psychosis; taper
- Give at bedtime if sedating (quetiapine)

PRIORITY 4

PROTECT Safety & dignity

- Fall precautions; sit up slowly
- Seizure precautions (clozapine, high dose)
- Suicide precautions — $\uparrow$ risk as energy returns
- Therapeutic communication: calm, consistent, brief

The atypicals you'll be tested on

Clozapine

(Clozaril)

HIGH ALERT • REMS

USE	Treatment-resistant schizophrenia · ↓ suicide risk
MECH	Weak D ₂ , strong 5-HT ₂ A blockade
△ S/E	Agranulocytosis, myocarditis, seizures , weight gain, drooling
NURSING	ANC weekly × 6 mo , then q2wk × 6 mo, then monthly. Hold if ANC < 1500.

Olanzapine

(Zyprexa)

METABOLIC RISK

USE	Schizophrenia, bipolar mania, agitation
MECH	D ₂ & 5-HT ₂ A antagonist
△ S/E	Highest weight gain , hyperglycemia, dyslipidemia, sedation
NURSING	Weight, A1C, lipids q3mo. Diet/exercise teaching.

Risperidone

(Risperdal)

EPS AT HIGH DOSE

USE	Schizophrenia, bipolar, autism-associated irritability
MECH	Potent D ₂ & 5-HT ₂ A block
△ S/E	Hyperprolactinemia (galactorrhea, amenorrhea, ED), EPS at >6 mg/day
NURSING	Report breast changes, sexual dysfunction. LAI (Consta) q2wk.

Quetiapine

(Seroquel)

SEDATING

USE	Schizophrenia, bipolar, MDD adjunct
MECH	D ₂ , 5-HT ₂ A, H ₁ blockade
△ S/E	Sedation, orthostasis , weight gain, cataracts (rare)
NURSING	Dose at bedtime. Eye exams q6mo. Fall precautions.

Aripiprazole

(Abilify)

PARTIAL AGONIST

USE	Schizophrenia, bipolar, MDD augmentation
MECH	Partial D₂ agonist — dopamine stabilizer
△ S/E	Akathisia , insomnia, nausea; low metabolic risk
NURSING	Morning dose (activating). Report restlessness.

Ziprasidone

(Geodon)

QT PROLONGATION

USE	Schizophrenia, acute mania, IM for agitation
MECH	D ₂ , 5-HT ₂ A blockade
△ S/E	QT prolongation → torsades , rash, sedation
NURSING	Take with ≥500 kcal meal (↑absorption 2×). Baseline ECG.

Lurasidone

(Latuda)

LOW METABOLIC

USE	Schizophrenia, bipolar depression
MECH	D ₂ , 5-HT ₂ A, 5-HT ₇ block
△ S/E	Akathisia, somnolence, nausea; weight-neutral
NURSING	Take with ≥350 kcal meal . Avoid grapefruit juice (CYP3A4).

Paliperidone

(Invega)

LAI OPTION

USE	Schizophrenia, schizoaffective disorder
MECH	Active metabolite of risperidone
△ S/E	Hyperprolactinemia, EPS, QT, weight gain
NURSING	LAI monthly/q3mo → ↑ adherence. Swallow whole (ER).

6

■ NCLEX TEST TRAPS

What students miss · priority vs non-priority



1

NMS ≠ Serotonin Syndrome. Both have fever + AMS, but NMS = **rigidity + bradyreflexia**; SS = **hyperreflexia + clonus + diarrhea**.

Priority → STOP drug, cool, support airway, give dantrolene (NMS) or cyproheptadine (SS).

2

Agranulocytosis = ANC, not just WBC. A sore throat is the earliest red flag in a clozapine patient.

Priority → Hold dose, draw ANC, assess for infection.

3

2nd-gen has LESS EPS, but still has EPS. Akathisia & TD still happen — especially risperidone at high dose.

Priority → Use AIMS tool; treat acute EPS with benztropine or diphenhydramine.

4

Weight gain is the #1 reason for non-adherence, not sedation. Don't dismiss the patient's concern about weight.

Priority → Teach diet, activity, and routine A1C/lipid checks.

5

Ziprasidone & lurasidone MUST be taken with food. Without food, blood levels drop below therapeutic.

Priority → Ziprasidone ≥ 500 kcal · Lurasidone ≥ 350 kcal.

6

"I'm feeling better, can I stop?" — Never. Abrupt discontinuation → relapse and cholinergic rebound.

Priority → Teach: continue as prescribed; taper only with MD.

7

■ PATIENT & FAMILY EDUCATION

What to teach before discharge

**Take with food when required**

Ziprasidone & lurasidone need a substantial meal. Others: with or without food; consistent timing helps.

**Rise slowly**

Orthostatic hypotension is real — sit on edge of bed 30 seconds before standing. Prevent falls.

**Patience with onset**

Full effect takes 2–6 weeks. Negative sx may improve over months. Keep appointments.

**No alcohol / CNS depressants**

Additive sedation → respiratory depression risk. Avoid driving until sedation resolves.

**Report red-flag symptoms**

Fever, sore throat, muscle stiffness, confusion, irregular heartbeat, new abnormal movements — call provider.

**Weight & labs matter**

Weekly weights at home, yearly A1C + lipids, protect teeth (dry mouth), sunscreen (photosensitivity).



★ NMS → remember "FEVER"

F **E** **V** **E** **R**

Fever (hyperthermia) · Encephalopathy (AMS) · Vitals unstable (autonomic) · Enzymes elevated (↑CK) · Rigidity (lead-pipe)

★ Metabolic side effects "The 4 W's"

W **W** **W** **W**

Weight gain · Waist expansion · Wonky sugar (hyperglycemia) · Wonky lipids (dyslipidemia).
Screen at baseline, 3 months, then yearly.

💡 "-pine / -done / -peridone" endings = usually atypical (olanzaPINE, risperiDONE, paliperiDONE).

💡 Clozapine = "Counting cells" — always think ANC, REMS, weekly labs.

💡 Ziprasidone = Z for Zap (QT prolongation, ECG baseline).

💡 Olanzapine = "Olanza-PIE" — the fattening one (biggest weight gain).

💡 Aripiprazole = "A-1 balanced" — partial agonist, activating, morning dose.

💡 Quetiapine = "Quiet-iapine" — sedating, bedtime dose.