Antipsychotic Medications – High-Yield Cheat Sheet (PMHNP Level)

Use this as a rapid reference for first- and second-generation antipsychotics. Focus on class patterns, then memorize a few "personality traits" for each key drug.

1. Big Picture

- All antipsychotics that block D_2 receptors help reduce positive symptoms (hallucinations, delusions, disorganized thought).
- Main differences between drugs are in side effect profiles, special indications, and receptor "personality."

2. First-Generation vs Second-Generation Antipsychotics

Feature	First-Generation (Typical)	Second-Generation (Atypical)
Mechanism	Strong D_2 blockade (especially nigrostriatal and mesolimbic pathways).	5-HT_2A antagonism + moderate D_2 blockade; some are partial D_2 agonists (e.g., aripiprazole).
Positive symptoms	Improved (similar efficacy to most SGAs at equivalent D_2 occupancy).	Improved (similar efficacy; clozapine superior in treatment-resistant cases).
Negative/mood symptoms	Less benefit overall.	Often better for negative and mood symptoms (drug dependent).
EPS/TD	Higher risk of EPS and tardive dyskinesia, especially high-potency FGAs (haloperidol, fluphenazine).	Lower EPS risk overall (except at high doses or with risperidone/paliperidone).
Metabolic effects	Lower metabolic risk overall.	Higher metabolic risk, especially clozapine and olanzapine.
Examples	High-potency: haloperidol, fluphenazine. Low-potency: chlorpromazine, thioridazine.	Risperidone, paliperidone, olanzapine, quetiapine, clozapine, ziprasidone, aripiprazole, lurasidone, cariprazine, brexpiprazole.

3. Key Antipsychotics – "Personality Traits"

Haloperidol (FGA, high potency) – D_2 hammer, high EPS

- Very strong D_2 blockade → effective for acute agitation, psychosis, delirium (off-label).
- High risk of EPS (dystonia, parkinsonism, akathisia) and tardive dyskinesia with chronic use.
- Low anticholinergic and metabolic effects compared with low-potency FGAs and many SGAs.
- Available as oral, short-acting IM, and long-acting decanoate.

Chlorpromazine (FGA, low potency) – Sedating and dirty receptor profile

- Less EPS than high-potency FGAs but more anticholinergic, antihistaminic, and alpha-1 blockade.
- Common adverse effects: sedation, orthostatic hypotension, anticholinergic effects, weight gain.
- Can cause photosensitivity, rare cholestatic jaundice, and corneal deposits.

Risperidone (SGA) – Prolactin-raiser; SGA that behaves like FGA at high doses

- 5-HT_2A and D_2 antagonist; strong D_2 at higher doses.
- At low doses (1–3 mg/day): relatively low EPS; at higher doses (≥6 mg/day): EPS risk increases significantly.
- Notable for hyperprolactinemia (amenorrhea, galactorrhea, sexual dysfunction).
- Used for schizophrenia, bipolar disorder, and irritability associated with autism.

Paliperidone (SGA) – Active metabolite of risperidone

- Similar profile to risperidone (D_2 and 5-HT_2A antagonist; prolactin elevation, EPS at higher doses).
- Primarily renally excreted—dose adjust in renal impairment.
- Available as long-acting injectables (e.g., monthly, 3-monthly forms).

Olanzapine (SGA) – Very effective but very fattening

- Strong efficacy for positive symptoms and mood stabilization.
- Very high risk of weight gain, dyslipidemia, and insulin resistance (metabolic syndrome).
- Sedation and anticholinergic side effects are common.
- Used for schizophrenia, bipolar disorder, and treatment-resistant depression (with fluoxetine).

Quetiapine (SGA) – Sedating, low EPS; depends on dose

- At low doses: mainly H_1 and alpha-1 blockade (used as sedative/hypnotic off-label).
- At moderate doses: antidepressant/anxiolytic effects (bipolar depression, adjunct in MDD).
- At higher doses: antipsychotic effects via D_2 blockade.
- Low EPS risk; moderate metabolic risk; can cause orthostasis and sedation.

Clozapine (SGA) – Gold standard for treatment-resistant schizophrenia

- Superior efficacy for treatment-resistant schizophrenia and for reducing suicidality in schizophrenia/schizoaffective disorder.
- Very low EPS and TD risk; weak D_2 but strong 5-HT_2A and D_4 effects.

- Serious risks: agranulocytosis (requires ANC monitoring), myocarditis, seizures, severe constipation/ileus, sialorrhea.
- Marked metabolic risk (weight gain, lipids, glucose).

Ziprasidone (SGA) – Weight-neutral but watch the QTc

- Relatively low risk of weight gain and metabolic syndrome.
- Can prolong QTc; avoid in significant cardiac conduction disease or with other QT-prolonging agents.
- Must be taken with food to ensure adequate absorption (often ≥500 kcal).

Aripiprazole (SGA, partial D_2 agonist) – Dopamine system stabilizer; activating profile

- Partial agonist at D_2 and 5-HT_1A; antagonist at 5-HT_2A.
- Lower risk of weight gain, metabolic effects, and prolactin elevation; akathisia can be prominent.
- Often activating rather than sedating; can be helpful in depression (adjunct) and bipolar disorder.
- Used in schizophrenia, bipolar I disorder, adjunctive treatment of MDD, irritability in autism, and others.

Lurasidone (SGA) – Good for bipolar depression; weight-friendly

- D_2 and 5-HT_2A antagonist with 5-HT_7 antagonism and 5-HT_1A partial agonism.
- Indicated for schizophrenia and bipolar depression.
- Low metabolic and weight gain risk; moderate EPS risk at higher doses.
- Must be taken with food (≥350 kcal) to optimize absorption.

Cariprazine (SGA, partial D_2/D_3 agonist) – D_3-preferring; good for negative symptoms and bipolar

- Partial agonist at D_2 and D_3 receptors (D_3-preferring); some 5-HT_2A antagonism.
- Used for schizophrenia and bipolar I disorder (mania, mixed episodes, and depression).
- Relatively low metabolic risk; akathisia and insomnia can occur.

Brexpiprazole (SGA, partial D_2 agonist) – Aripiprazole's "smoother cousin"

- Partial D_2 agonist with strong 5-HT_2A antagonism; similar to aripiprazole but often less activating.
- Used for schizophrenia and as adjunctive treatment for MDD.
- Low to moderate metabolic risk; akathisia can still occur but may be less intense than with aripiprazole.

4. Classwide Adverse Effects & Monitoring (Very High Yield)

- Extrapyramidal symptoms (EPS): acute dystonia, akathisia, parkinsonism; more common with FGAs and high-dose risperidone/paliperidone.
- Tardive dyskinesia (TD): late-onset, often irreversible; risk with chronic D_2 blockade (FGAs > some SGAs).

- Neuroleptic malignant syndrome (NMS): rare but life-threatening; features hyperthermia, rigidity, autonomic instability, elevated CK—stop antipsychotic, supportive care, dantrolene/bromocriptine as indicated.
- Metabolic syndrome: especially with clozapine and olanzapine (weight, lipids, glucose); monitor BMI, waist circumference, fasting lipids, and glucose/A1C.
- Hyperprolactinemia: most common with risperidone and paliperidone (amenorrhea, galactorrhea, sexual dysfunction, decreased bone density).
- QTc prolongation: FGAs (thioridazine, high-dose IV haloperidol) and SGAs (ziprasidone, iloperidone); obtain ECG when indicated.
- Anticholinergic effects: dry mouth, constipation, urinary retention, blurred vision—more common with low-potency FGAs and some SGAs (clozapine, olanzapine).
- Orthostatic hypotension and sedation: via alpha-1 and H_1 blockade; common with chlorpromazine, quetiapine, clozapine, and olanzapine.