Second-Generation Antipsychotics (SGAs): Monitoring Panel

💊 Comprehensive Monitoring Protocol

Parameter	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Clinical Considerations
🔄 **Metabolic Parameters**							
Weight/BMI	✓	✓	✓	✓	✓	✓	• Early weight gain (first 4 weeks) predicts long term gain • Consider intervention if >5% increase from baseline • Risk: olanzapine, clozapine > quetiapine, risperidone > aripiprazole, ziprasidone, lurasidone
Waist Circumference	✓	—	—	✓	✓	✓	• Better predictor of metabolic risk than BMI alone • High risk: >40 inches (men), >35 inches (women) • Consider metformin for significant increases
Blood Pressure	✓	✓	✓	✓	✓	✓	• Monitor closely with clozapine (orthostatic changes) • Risperidone may cause orthostatic hypotension • QTc prolongation risk with ziprasidone

							if hypokalemia present

Fasting Glucose ✓ — — ✓ ✓ ✓

• Consider more frequent monitoring

with high-risk agents

Parameter	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Clinical Considerations
							• Diabetes risk: 1.3-1.8× higher than general population • Monitor for polyuria, polydipsia, unexplained weight loss
HbA1c	✓	—	—	✓	—	✓	• Better for long-term glucose monitoring • Consider if baseline glucose abnormal • Target <7.0% for most patients • Diagnostic if ≥6.5%
Fasting Lipid Panel	✓	—	—	✓	—	✓	• HDL, LDL, total cholesterol, triglycerides • Consider more frequent monitoring with olanzapine/ clozapine • Hypertriglyceridemia often precedes other lipid abnormalities
Hematological Parameters							

Complete Blood Count	✓	—	—	—	—	✓	• Baseline for all SGAs • More frequent monitoring with specific agents (see below) • Monitor for signs of infection with neutropenia
Absolute Neutrophil Count	✓	*	*	*	*	*	• *Required for clozapine per REMS protocol • Weekly for 6 months, biweekly for 6 months, then monthly • ANC <1000/mm³: interrupt treatment and consult protocol (GlobalRPH, 2024)

Platelets ✓ * * * * *• *Monitor with clozapine (risk of

Parameter	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Clinical Considerations
							thrombocytopenia) • Consider with valproate co prescription • Discontinue if <50,000/mm³
❤️ **Cardiac Parameters**							
ECG	✓	†	†	†	†	✓	• Baseline for all patients >40 years or with cardiac risk factors • †Repeat if dose increases or symptoms develop • QTc monitoring critical with ziprasidone, iloperidone • Discontinue if QTc >500ms or increase >60ms from

							baseline(Edinoff et al., 2022)
Troponin/CRP	—	‡	‡	—	—	—	• ‡Consider with clozapine in first 4 months • Monitor for myocarditis/ cardiomyopathy symptoms • Chest pain, unexplained tachycardia, fever, dyspnea
🔬 **Hepatic Parameters**							
Liver Function Tests	✓	—	—	—	—	✓	• Baseline for all SGAs • More frequent monitoring with hepatic disease • ALT/AST >3× ULN: consider dose reduction/ discontinuation • Monitor for jaundice, malaise, right upper quadrant pain

Parameter	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Clinical Considerations
🧪 **Prolactin Levels**							

Prolactin	✓	§	§	§	—	§	• §Check if symptomatic (sexual dysfunction, galactorrhea, amenorrhea) • Highest risk: risperidone, paliperidone • Lowest risk: aripiprazole, brexpiprazole, cariprazine • Consider prolactin sparing agent if symptomatic
🧠 **Neurological Monitoring**							
AIMS/SAS/BARS	✓	✓	✓	✓	✓	✓	• AIMS: Abnormal Involuntary Movement Scale (TD) • SAS: Simpson-Angus Scale (parkinsonism) • BARS: Barnes Akathisia Rating Scale • Higher risk with high potency agents and elderly
📋 **Other Parameters**							
Medication Adherence	✓	✓	✓	✓	✓	✓	• Assess at each visit • Consider levels if adherence questionable • Discuss LAI options for partial/non-adherence • Identify and address adherence barriers
Therapeutic							• PANSS, BPRS, or CGI scales if possible • Document target

Response	✓	✓	✓	✓	✓	✓	symptoms and response

Parameter	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Clinical Considerations
							• Consider TDM for clozapine (target: 350-450 ng/mL) • Adequate trial: 4-6 weeks at therapeutic dose
Side Effect Assessment	✓	✓	✓	✓	✓	✓	• Systematic assessment (e.g., GASS, LUNSERS) • Document side effects and management strategies • Consider quality of life impact • Assess sexual side effects specifically (often underreported)

💊 Agent-Specific Monitoring Considerations

🔴 Clozapine

Required Monitoring (REMS Program):
- ANC monitoring schedule:
- Weekly for first 6 months
- Every 2 weeks for second 6 months
- Monthly after 12 months of treatment (if stable)
- ANC thresholds:
- Normal: ≥1500/mm³ (≥1000/mm³ for BEN)
- Mild neutropenia: 1000-1499/mm³ (500-999/mm³ for BEN)
- Moderate: 500-999/mm³ (≤500/mm³ for BEN)
- Severe: <500/mm³

Additional Recommended Monitoring:
- Myocarditis/cardiomyopathy surveillance:
- Highest risk in first 8 weeks
- Consider troponin, CRP, BNP at baseline and weekly for first 4-8 weeks
- ECG at baseline and as clinically indicated
- Seizure risk monitoring:

- EEG if history of seizures or at doses >600mg/day
- Consider prophylactic valproate if dose >600mg/day
- Constipation assessment:
- Active questioning at each visit (can be life-threatening)

- Prophylactic bowel regimen often necessary
- Sialorrhea assessment:
- Consider anticholinergic treatment if severe
- Sedation assessment:
- Consider divided dosing to minimize daytime sedation
- Metabolic parameters:
- More frequent monitoring recommended (highest risk agent)
- Plasma levels:
- Consider monitoring if:
- Suspected non-adherence
- Limited/no response despite adequate dose
- Adverse effects at standard doses
- Drug interactions present
- Therapeutic range: 350-450 ng/mL
- Toxic effects more common >600-700 ng/mL

🟠 Olanzapine

Metabolic Monitoring:
- Weight/BMI: Most significant risk of all SGAs
- Consider more frequent metabolic monitoring:
- Monthly weight for first 3 months
- Glucose/lipids at 3 months, then quarterly for first year
- Consider metformin 500-1000mg BID for significant weight gain (Fitzgerald et al., 2021) - Monitor for rapid weight gain in first 4-6 weeks (predictor of long-term gain)

Other Considerations:
- Sedation assessment:
- Common side effect, especially at higher doses
- Consider bedtime dosing
- Anticholinergic effects:
- Monitor for constipation, urinary retention, dry mouth, cognitive effects
- Prolactin:
- Moderate elevation possible
- Check if symptomatic

🟡 Risperidone/Paliperidone

Prolactin Monitoring:
- Highest prolactin elevation of all SGAs

- Consider baseline and follow-up levels even if asymptomatic
- Monitor for:
- Females: Amenorrhea, galactorrhea, sexual dysfunction, osteoporosis risk
- Males: Gynecomastia, sexual dysfunction, decreased bone density - Consider switching to prolactin-sparing agent if symptomatic

- Dose-dependent EPS:

Other Considerations:

- Higher risk >6mg/day risperidone or >6mg/day paliperidone - Regular AIMS/SAS/BARS assessment
- QTc interval:
- Modest prolongation possible
- Baseline ECG recommended
- Orthostatic hypotension:
- More common during initiation
- Monitor BP sitting/standing
- Renal function:
- Paliperidone requires dose adjustment with renal impairment - Monitor renal function if concerns

🟢 Quetiapine

Metabolic/Cardiovascular Monitoring:
- Moderate metabolic risk:
- Regular weight/metabolic monitoring
- Orthostatic hypotension:
- Common during initiation and dose increases
- Monitor BP sitting/standing
- Slow titration reduces risk
- Sedation assessment:
- Significant sedation common
- Consider divided dosing or predominant evening dosing - Assess for daytime somnolence and driving safety

Other Considerations:
- Cataracts:
- Baseline eye exam recommended
- Annual eye exam for long-term use
- QTc interval:
- Modest prolongation possible
- Baseline ECG recommended with cardiac risk factors - Anticholinergic effects:
- Moderate anticholinergic burden
- Monitor in elderly patients

🔵 Aripiprazole/Brexpiprazole/Cariprazine

Akathisia Monitoring:
- Higher risk of akathisia than other adverse effects - BARS at baseline and follow-up visits
- Typically emerges in first 2 weeks
- Consider dose reduction, divided dosing, or beta-blocker if severe 7

- Metabolic parameters:

Other Considerations:

- Lower risk than other SGAs but not zero
- Standard metabolic monitoring still applies
- Activation/insomnia:
- More common than sedation
- Consider morning dosing
- Monitor sleep quality
- Prolactin:
- May reduce prolactin levels (partial D2 agonism)
- Potential treatment for antipsychotic-induced hyperprolactinemia - Cariprazine specific:
- Long half-life (1-3 weeks)
- Delayed adverse effects possible
- Slower dose adjustments recommended

🟣 Ziprasidone/Lurasidone

Cardiovascular Monitoring:
- QTc prolongation (ziprasidone):
- Baseline ECG required
- Follow-up ECG with dose increases
- Avoid in congenital long QT syndrome
- Caution with other QT-prolonging medications
- Minimal orthostatic effects

Administration Considerations:
- Food requirements:
- Lurasidone: Requires 350+ calorie meal for proper absorption (Drugs.com, 2024) - Ziprasidone: Requires food for optimal absorption - Document adherence to food requirements
- Consider alternative if meal adherence problematic

Other Considerations:
- Metabolic parameters:
- Lower risk than other SGAs

- Standard monitoring still applies
- Akathisia:
- Monitor with BARS
- More common with lurasidone than some other SGAs 8

Special Population Considerations

Elderly Patients

Modified Monitoring Protocol:
- Start with lower doses (25-50% of adult dose)
- More frequent monitoring of:
- Orthostatic vital signs (fall risk)
- Cognitive function (anticholinergic burden)
- Electrolytes (risk of hyponatremia)
- QTc interval (higher risk of prolongation)
- AIMS/SAS/BARS at each visit (increased EPS sensitivity)
- Consider ECG monitoring with each dose increase -
Monitor for atypical presentations of adverse effects

Specific Concerns:
- Cerebrovascular events:
- Increased risk with antipsychotics in dementia
- Monitor neurological status
- Document risk-benefit assessment
- Mortality risk:
- Black box warning for elderly with dementia
- Document informed consent discussion
- Regular reassessment of continued need
- Anticholinergic burden:
- Higher sensitivity to cognitive effects
- Avoid high anticholinergic agents (clozapine, olanzapine)
- Monitor for delirium

Children and Adolescents

Modified Monitoring Protocol:
- More frequent metabolic monitoring:
- Weight/BMI monthly for first 3 months

- Height measurements to track growth
- Fasting glucose/lipids at baseline, 3 months, and quarterly
- Prolactin monitoring:
- Baseline and at 3 months
- Monitor growth and sexual development
- Cardiovascular:
- Baseline ECG recommended for all
- BP monitoring at each visit

Specific Concerns:
- Growth effects:
- Monitor height velocity

- Plot on growth charts

- Consider endocrine consultation for concerns - Metabolic effects:
- Greater sensitivity to weight gain
- Lower threshold for intervention
- Consider metformin earlier
- Neurological effects:
- Lower threshold for EPS
- Monitor for academic/cognitive impacts
- Assess for sedation effects on learning

Pregnancy and Postpartum

Modified Monitoring Protocol:
- Preconception planning when possible
- Baseline assessment:
- Comprehensive metabolic panel
- Thyroid function
- Folate levels
- Pregnancy test
- Ongoing monitoring:
- Coordinate with obstetrics
- Monthly weight/BMI
- Glucose tolerance testing
- Fetal growth ultrasounds

Specific Concerns:
- Gestational diabetes:
- Higher risk with SGAs
- Early glucose tolerance testing
- Consider alternatives to high-risk agents
- Neonatal complications:
- Monitor for extrapyramidal symptoms in neonate - Monitor for withdrawal symptoms
- NICU consultation for delivery planning

- Breastfeeding considerations:
- Document risk-benefit discussion
- Monitor infant for sedation, feeding issues
- Consider agents with lower milk transfer (e.g., olanzapine) 10

Intervention Thresholds and Management Strategies

Metabolic Abnormalities

Parameter	Threshold for Intervention	Management Strategies
Weight Gain	• >5% from baseline • BMI increase to next category • Crossing into overweight/ obese	• Nutritional counseling • Exercise program • Consider metformin 500-1000mg BID • Consider switching to lower-risk agent • Endocrinology consultation if severe
Glucose	• Fasting glucose 100-125 mg/dL • HbA1c 5.7-6.4% • Fasting glucose ≥126 mg/dL • HbA1c ≥6.5%	• Prediabetes: Lifestyle intervention, metformin • Diabetes: Endocrinology referral • Consider antipsychotic switch • More frequent monitoring • Diabetes education
Lipids	• LDL >130 mg/dL • Triglycerides >150 mg/dL • HDL <40 mg/dL (men) • HDL <50 mg/dL (women)	• Dietary intervention • Exercise counseling • Consider statin therapy based on ASCVD risk • Consider omega-3 fatty acids for hypertriglyceridemia • Consider switching to lower-risk agent
Blood Pressure	• >130/80 mmHg • >140/90 mmHg	• Lifestyle modifications • Antihypertensive therapy per guidelines • Consider switching from clozapine if orthostatic • Cardiology consultation if severe/resistant

Hematological Abnormalities

Parameter	Threshold for Intervention	Management Strategies

Neutropenia (Clozapine)	• ANC 1000-1499/mm^3 • ANC 500-999/mm^3 • ANC <500/mm^3	• Mild: Continue with increased monitoring • Moderate: Interrupt treatment, daily monitoring • Severe: Discontinue, hematology consultation • Follow REMS protocol • Consider G-CSF for rechallenge in consultation with hematology
Agranulocytosis	• ANC <500/mm^3 with infection	• Immediate hospitalization • Broad-spectrum antibiotics • Hematology consultation • G-CSF consideration • Permanent discontinuation of causative agent

Thrombocytopenia • Mild: Increased monitoring • Moderate/Severe: Consider discontinuation

Parameter	Threshold for Intervention	Management Strategies
	• Platelets <100,000/mm^3 • Platelets <50,000/mm^3	• Hematology consultation • Monitor for bleeding signs

Cardiac Abnormalities

Parameter	Threshold for Intervention	Management Strategies
QTc Prolongation	• QTc >470ms (women) • QTc >450ms (men) • QTc >500ms • Increase >60ms from Baseline **(McClelland & Mathys, 2016)**	• Moderate: Consider dose reduction • Severe: Discontinue high-risk agent • Check electrolytes, correct abnormalities • Review/discontinue other QT-prolonging medications • Cardiology consultation • Consider switch to lower-risk agent
Orthostatic Hypotension	• Systolic drop >20 mmHg • Diastolic drop >10 mmHg • Symptomatic orthostasis	• Slow titration • Divided dosing • Adequate hydration • Salt loading if appropriate • Compression stockings • Fludrocortisone if severe (0.1-0.2mg daily)**(Rahman & Anjum, 2023)**
Myocarditis/ Cardiomyopathy	• Elevated troponin/CRP • New-onset heart failure symptoms • ECG abnormalities	• Immediate discontinuation of clozapine • Cardiology consultation • Echocardiogram • Supportive management • Consider permanent contraindication

Neurological Abnormalities

Parameter	Threshold for Intervention	Management Strategies
Akathisia	• BARS score ≥2 • Subjective distress **(Poyurovsky, 2010)**	• Dose reduction • Beta-blocker (propranolol 20-40mg TID) • Benzodiazepine (short-term) • Anticholinergic (less effective) • Consider switching agents
Parkinsonism	• SAS score ≥3 • Functional impairment **(Elbe et al., 2015)**	• Dose reduction • Anticholinergic (benztropine 1-2mg BID) • Amantadine (100mg BID-TID) • Consider switching to lower EPS risk agent
Tardive Dyskinesia	• AIMS score ≥2 in any category • New-onset abnormal movements	• Document baseline and follow-up AIMS • Consider VMAT2 inhibitor (valbenazine, deutetrabenazine) • Consider antipsychotic dose reduction if clinically feasible • Consider switching to clozapine • Neurology consultation
Seizures	• Any seizure activity	• Neurology consultation • EEG • Consider dose reduction • Consider anticonvulsant (valproate, lamotrigine) • Consider switching from high-risk agent (clozapine)

Prolactin Abnormalities

Parameter	Threshold for Intervention	Management Strategies
Asymptomatic Elevation	• >Upper limit of normal • No symptoms	• Routine monitoring • Document level • Consider baseline DEXA in long-term therapy

Symptomatic Elevation	• Amenorrhea • Galactorrhea • Sexual dysfunction • Gynecomastia	• Consider switching to prolactin-sparing agent • Consider aripiprazole augmentation (2.5-5mg) • Consider dopamine agonist (cabergoline) in consultation with endocrinology • DEXA scan if long-term elevation

Documentation and Quality Measures

Essential Documentation Elements

1. **Assessment: Baseline**
   - Comprehensive metabolic panel
   - Lipid panel
   - Fasting glucose/HbA1c
   - Weight/BMI/waist circumference
   - Blood pressure
   - ECG (if indicated)
   - AIMS/SAS/BARS
   - Pregnancy test (if applicable)
2. **Monitoring Plan:**
   - Individualized schedule based on agent and risk factors - Documentation of planned intervals
   - Assignment of responsibility for follow-up 13
3. **Informed Consent:**
   - Discussion of metabolic risks -
   Discussion of neurological risks
   - Discussion of cardiac risks
   - Documentation of risk-benefit assessment
   - Patient education provided
4. **Documentation: Follow-up**
   - Adherence to monitoring schedule
   - Results of monitoring tests
   - Interventions for abnormalities
   - Reassessment of risk-benefit ratio -
   Consideration of agent switches if indicated

Quality Improvement Metrics

1. **Measures:**

Process

- Percentage of patients with baseline metabolic screening - Percentage of patients with follow-up metabolic screening at 12 weeks - Percentage of patients on clozapine with appropriate ANC monitoring - Percentage of patients with documented AIMS at baseline and follow-up

2. **Outcome Measures:**

- Percentage of patients developing metabolic syndrome
- Percentage of patients with significant weight gain (>7%)
- Percentage of patients developing new-onset diabetes
- Percentage of patients developing tardive dyskinesia

3. **Balancing Measures:**

- Medication adherence rates
- Psychiatric hospitalization rates
- Quality of life measures
- Functional outcome measures

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