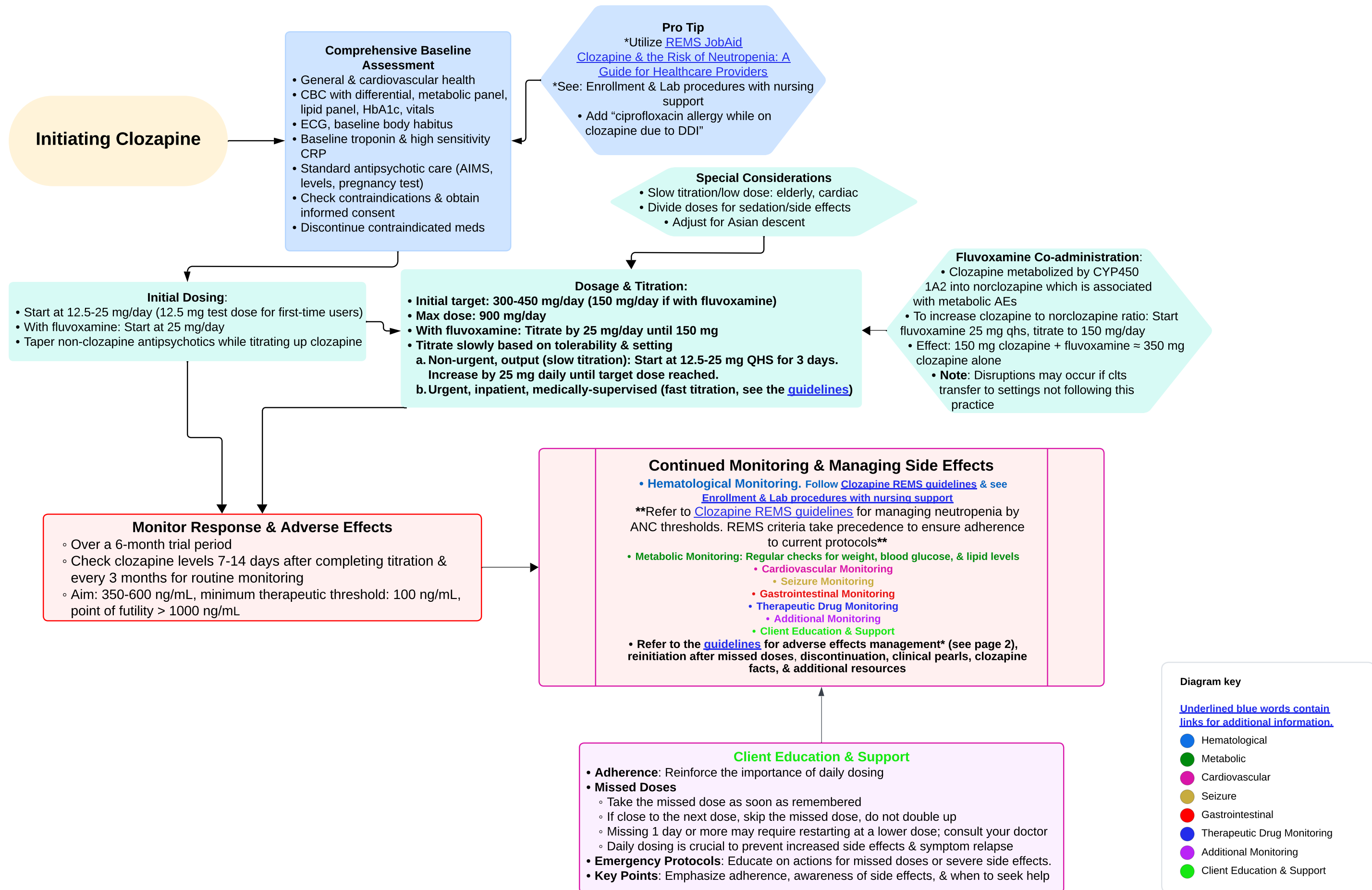


Guidelines for Prescribing & Monitoring Clozapine



Monitoring & Adverse Effects Management*

Hematological

- Frequency: Weekly (first 6 months), biweekly (second 6 months), then monthly
- Refer to ER if ANC < $0.5 \times 10^3/\mu\text{L}$
- Refer to [Clozapine REMS guidelines](#) for managing neutropenia based on ANC thresholds. REMS criteria take precedence to ensure adherence to current protocols
- Confirmatory test within 24 hours if ANC < $1.5 \times 10^3/\mu\text{L}$
- Managing Agranulocytosis: Consider filgrastim for expedited ANC recovery (impact on infection rates/mortality is unclear)
- Note: A significant portion of African Americans have Benign Ethnic Neutropenia, leading to lower ANC levels but not necessarily higher risk of severe neutropenia
- ANC Calculation: $\text{ANC} = \text{WBC count} \times (\text{percentage of segs} + \text{percentage of bands}) / 100$. WBC count is in cells/ μL ; segs & bands are percentages

Metabolic

- Weight, waist circumference, BP, fasting glucose or HbA1c, lipid panel at regular intervals
- Address abnormalities through lifestyle modifications & pharmacological interventions (e.g. metformin, topiramate, GLP-1 receptor agonists, or fluvoxamine co-administration)
- Clozapine has lower metabolic risks compared to olanzapine

Cardiovascular

- Myocarditis: Monitor particularly during first 4-8 weeks; assess symptoms & vitals at each visit
- Clinical indicators of myocarditis include fever $>38^\circ\text{C}$, chest pain, SBP <100 , HR >120 , & shortness of breath
 - Refer to ER, if myocarditis or cardiomyopathy is suspected. Diagnostic measures like echocardiogram & troponin levels should be performed in an emergency setting
- Weekly troponin I & high sensitivity CRP for 8 weeks; troponin T if I unavailable
- CRP > 100 mg/L & troponin $> 2x$ normal limit are critical indicators in symptomatic pts. Eosinophil Count may rise, but less reliable
- ECG: Baseline, annual; QTc risk. Assess ventricular & valve function if myocarditis/cardiomyopathy suspected
- Monitor for orthostatic hypotension, bradycardia, syncope

Seizure

- Inquire about seizure history, monitor for myoclonic jerking
- If Seizure Occurs: Hold clozapine for 24 hours, reduce dose by 50%, consider adding anticonvulsant
- Refer to the [Guidelines](#) for Anticonvulsant Options. Clozapine titration can be resumed after an anticonvulsant is added
- Note: 10% risk of generalized tonic-clonic seizures after 4 years; risk increases with dose (doubling at 300-600 mg/day and tripling at > 600 mg/day)

Gastrointestinal

1. Constipation

- Prevalence: 32-60% with clozapine
- Monitoring & Prophylactic Treatment
- Diet & Lifestyle: High-fiber foods, adequate fluids, exercise
- Stool Softeners: DSS 250 mg or Miralax 17g at initiation
- Laxatives: Dulcolax 10 mg or Senna 17.2 mg daily
- For Constipation: PRN lactulose; consider lubiprostone or linaclotide for non-responsive cases
- Note: Risk of paralytic ileus with fatality rate of 15-28% if untreated (vs severe neutropenia fatality rate: 2 ? 4%)

2. Hypersalivation

- Prevalence: 90% with greater severity at night
- Management: Refer to the [Guidelines](#)

Therapeutic Drug Monitoring

- Check levels during titration, poor response, or suspected non-adherence; draw in AM, 8-10 hours after the PM dose
- Check clozapine levels 7-14 days after completing titration & every 3 months for routine monitoring
- Initial monitoring is essential due to metabolic variability; ongoing monitoring though not mandated, aids adherence
- Target Range: 350-600 ng/mL; adjust based on response & side effects
- Monitor response for 2 weeks after reaching therapeutic level before further dosage increase
- Consider > 350 ng/mL for refractory symptoms; evidence of efficacy is limited

Additional Monitoring

- Smoking, caffeine intake, NMS, hepatotoxicity, PE, anticholinergic toxicity, cognitive/motor performance

Diagram key

[Underlined blue words contain links for additional information.](#)

- Hematological
- Metabolic
- Cardiovascular
- Seizure
- Gastrointestinal
- Therapeutic Drug Monitoring
- Additional Monitoring
- Client Education & Support