

ALAMEDA COUNTY BEHAVIORAL HEALTH CARE SERVICES

Clozapine Monitoring Committee Guidelines

Table 1 – Drug Interactions (see Section II.E.6.)

Class	Examples	Interaction
Bone marrow suppressants	Carbamazepine, sulfonamides, propylthiouracil, zidovudine, chemotherapeutic agents	Additive risk of myelosuppression
Antihypertensive agents	Hydrochlorothiazide, atenolol, metoprolol, verapamil, diltiazem, lisinopril, enalapril, prazosin, terazosin	Additive risk of orthostasis, hypotension
CNS depressants	Benzodiazepines, lithium, other very sedating agents	Additive risks of sedation, respiratory depression, loss of consciousness
Highly protein bound drugs	Warfarin, divalproex Na, phenytoin, digoxin	Clozapine may displace or be displaced from protein binding sites by these agents. Monitor closely for adverse effects.
Substrates/inhibitors/inducers of CYP 1A2, 2D6, and 3A4	Erythromycin, ketoconazole, SSRIs can increase clozapine levels Cigarette smoking, carbamazepine may decrease clozapine levels	Potential for drug-drug interactions. Monitor for loss/reduction of drug efficacy or for increased toxicity.

Table 2: Frequency of Monitoring based on Stage of Therapy or Results from WBC Count and ANC Monitoring Tests

Situation	Hematological Values for Monitoring	Frequency of WBC and ANC Monitoring
Initiation of therapy	WBC = 3500/mm ³ ANC = 2000/mm ³ Note: Do not initiate in patients with 1) history of myeloproliferative disorder or 2) Clozaril® (clozapine) induced agranulocytosis or granulocytopenia	Weekly for 6 months
6 months – 12 months of therapy	All results for WBC = 3500/mm ³ and ANC = 2000/mm ³	Every 2 weeks for 6 months
12 months of therapy	All results for WBC = 3500/mm ³ and ANC = 2000/mm ³	Every 4 weeks ad infinitum
Immature forms present	N/A	Repeat WBC and ANC
Discontinuation of Therapy	N/A	Weekly for at least 4 weeks from day of discontinuation or until WBC = 3500/mm ³ and ANC > 2000/mm ³
Substantial drop in WBC or ANC	Single Drop or cumulative drop within 3 weeks of WBC = 3000/mm ³ or ANC = 1500/mm ³	1. Repeat WBC and ANC 2. If repeat values are 3000/mm ³ = WBC ≤ 3500/mm ³ and ANC > 2000/mm ³ , then monitor twice weekly
Mild Leukopenia	3500/mm ³ > WBC ≥ 3000/mm ³ and/or	Twice-weekly until WBC > 3500/mm ³ and ANC > 2000/mm ³ then return to previous monitoring frequency
Mild Granulocytopenia	2000/mm ³ > ANC ≥ 1500/mm ³	
Moderate Leukopenia	3000/mm ³ > WBC = 2000/mm ³ and/or	1. Interrupt therapy 2. Daily until WBC > 3000/mm ³ and ANC > 1500/mm ³ 3. Twice-weekly until WBC > 3500/mm ³ and ANC > 2000/mm ³ 4. May rechallenge when WBC > 3500/mm ³ and ANC > 2000/mm ³ 5. If rechallenged, monitor weekly for 1 year before returning to the usual monitoring schedule of every 2 weeks for 6 months and then every 4 weeks ad infinitum
Moderate Granulocytopenia	1500/mm ³ > ANC ≥ 1000/mm ³	
Severe Leukopenia Severe Granulocytopenia	WBC < 2000/mm ³ and/or ANC < 1000/mm ³	1. Discontinue treatment and do not rechallenge patient 2. Monitor until normal and for at least four weeks from day of discontinuation as follows: • Daily until WBC > 3000/mm ³ and ANC > 1500/mm ³ • Twice weekly until WBC > 3500/mm ³ and ANC > 2000/mm ³ • Weekly after WBC > 3500/mm ³
Agranulocytosis	ANC ≤ 500/mm ³	1. Discontinue treatment and do not rechallenge patient 2. Monitor until normal and for at least four weeks from day of discontinuation as follows: • Daily until WBC > 3000/mm ³ and ANC > 1500/mm ³ • Twice weekly until WBC > 3500/mm ³ and ANC > 2000/mm ³ • Weekly after WBC > 3500/mm ³