Clozapine and consumers who resume or might resume smoking

- Consumers might return to smoking on discharge or when going on leave from a smoke-free facility.
- Consumers who take clozapine need higher doses if they smoke.
- If a consumer has been smoke-free while an inpatient their dosage may have been reduced.
- Resumption of smoking may cause clozapine blood levels to drop; symptoms should be closely monitored.

**NOTE:** It is the TAR in cigarettes which affects clozapine metabolism NOT the nicotine. NRT use does not affect clozapine levels.

### ON DISCHARGE
1. Assess clinically.
2. Record current clozapine dosage in notes.
3. Record other medications and dosage in notes.
4. Take blood clozapine level and record in notes. Ensure results are copied to the consumer’s GP.
5. Ask the consumer about their intended smoking behaviour outside the facility and record in the notes and discharge notes.
6. Discuss the impact of smoking on clozapine levels with the consumer.
7. Discuss the consumer’s intended smoking behaviour and its impact on clozapine dosage with their GP, carer and family.

**NOTES:**
Blood levels of clozapine will begin to drop within days of resuming smoking. Blood results will come back after discharge so it is important to ensure a copy is sent to the consumer’s GP.

### GOING ON LEAVE
1. Assess clinically.
2. Record current clozapine dosage in notes.
3. Record other medications and dosage in notes.
4. Ask the consumer about their intended smoking behaviour outside the facility and record in notes.
5. Strongly discourage them from smoking while on leave.
6. Discuss the impact of smoking on clozapine levels with the consumer.
7. Review or offer NRT if appropriate.

**NOTE:**
Blood levels of clozapine will begin to drop within days of resuming smoking.

### ON RETURN FROM LEAVE
1. Ask the consumer if they smoked while on leave.
2. Assess clinically.
3. Monitor and record clozapine levels. Monitor for side effects.
4. Adjust dosage as appropriate.

**NOTE:**
Blood levels of clozapine will start to rise within 24 hours of smoking cessation.

At all times, clinical assessment overrides suggestions made in this guide.
Background

- Clozapine has a narrow therapeutic index and significant toxic side effects.
- Clozapine is metabolised in the liver by the cytochrome P450 system.
- The tar in cigarettes induces P450 1A2 activity which affects the metabolism of clozapine.
- Other drugs are also affected, including olanzapine, fluvoxamine and haloperidol. Caffeine and non-psychiatric drugs such as warfarin and insulin are affected by smoking through a different mechanism.
- Clozapine concentrations do not correlate well with efficacy or toxicity and are simply a marker to allow for dose adjustment (1, 2). There is no ‘right’ dose or blood level of clozapine; the aim is symptom control without toxicity.
- Higher blood levels of clozapine can cause sedation, hypotension and increased risk of neurological adverse effects including seizures. Other toxic effects of clozapine, including agranulocytosis, are not dose related.

Smoking and clozapine

- To have equivalent blood levels smokers need higher doses of clozapine (up to 50% higher) (1, 4).
- Many factors can affect blood levels of clozapine eg, age, gender and other medications. There is significant individual variation (4, 5).
- The tar in cigarettes induces P450 1A2 activity.
- Five cigarettes a day may be enough for enzyme system induction (1).

Smoking cessation and clozapine levels

- Smoking cessation leads to a rapid exponential decrease in cytochrome P450 activity. A new steady state is reached in about 1 week (4, 5).
- When smokers taking clozapine quit smoking their blood levels can rise and toxic effects can occur (1, 4, 6–9). It is not clear how common this is but it appears to be uncommon†.

Monitoring clozapine dosage in smoking cessation

- There is no research examining what happens to the clozapine blood levels of people who resume smoking after a period of abstinence.
- It is expected that clozapine blood levels will be affected by resumption of smoking.
- Therapeutic drug monitoring should occur to account for individual variation (5, 6).
- Blood and clinical monitoring should continue for up to six months.
- Consumers who restart smoking after discharge or who smoke while on leave need ongoing monitoring.


† A literature search done in August 2011 of Embase + Medline and PsycInfo found 4 case reports of clozapine related adverse events associated with smoking cessation published between 2000 and 2011.