



Safety Notice 017/11

Clozapine and Smoking Cessation – Potential Toxicity

6 December 2011

Distributed to:

- Chief Executives
- Directors of Clinical Governance
- Directors of Mental Health

Action required by:

- Directors of Mental Health
- Mental Health Clinical Directors

We recommend you also inform:

- Medical staff
- Nurses
- Drug and Therapeutic Committees
- Departmental Heads

Expert Reference Group

- Mental Health and Drug and Alcohol Office.
- Chief Psychiatrist, NSW
- Clinical Safety Quality and Governance Branch

Clinical Safety Quality and Governance Branch

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<http://internal.health.nsw.gov.au/quality/sabs/>

This Safety Notice highlights possible Clozapine toxicity related to smoking cessation or reduction.

Background

Case reports have described symptoms of Clozapine toxicity following smoking cessation or reduced smoking.

- Clozapine has a narrow therapeutic index and significant toxic side effects.
- Clozapine is metabolised in the liver by the cytochrome P450 system.
- Tobacco smoke induces P450 1A2 activity, affecting Clozapine metabolism.
- Smokers require higher doses of Clozapine than non-smokers.
- Smoking cessation leads to a rapid decrease in cytochrome P450 activity.
- This can lead to rapid rises in blood levels of Clozapine and toxic effects.
- There should be an immediate decrease of Clozapine dose on cessation of smoking

Note: it is the components of tobacco smoke and not nicotine that induce P450 1A2.

Signs of increased blood levels / toxic effects

- sedation
- hypotension
- hypersalivation
- akathisia
- neurological adverse effects including seizures

Note: Other toxic effects, including agranulocytosis, are not dose related.

Steps to minimise risk

- Ask about smoking status (current smoker or recently quit) and
- Current Clozapine dosage;
- Measure and record baseline Clozapine levels;
- Consider a dose reduction of 30-50% if the consumer stops smoking;
- Clinically monitor for effectiveness and toxicity; and
- Discuss the impact of smoking on Clozapine levels with the consumer; and inform other carers and GP.

Note: Clozapine levels start to rise within 24 hours of smoking cessation or reduction.

References

1. Meyer JM. Individual changes in Clozapine levels after smoking cessation: Results and a predictive model. *Journal of Clinical Psychopharmacology*. 2001;21(6):569–74.
2. Taylor D, Paton C, Kapur S. *The South London and Maudsley NHS Foundation Trust & Oxleas NHS Foundation Trust Prescribing Guidelines, 10th ed.* Taylor and Francis; 2009
3. Olivier D, Lubman DI, Fraser R. Tobacco smoking within psychiatric inpatient settings: A biospsycho-social perspective. *Australian and New Zealand Journal of Psychiatry*. 2007;41(7):572–80.
4. Schaffer SD, Yoon S, Zadezensky I. A review of smoking cessation: Potentially risky effects on prescribed medications. *Journal of Clinical Nursing*. 2009;18(11):1533–40.
5. Seppälä N et al. Clozapine Serum Concentrations are Lower in Smoking than in Non-Smoking Schizophrenic Patients. *Pharmacology & Toxicology*. 1999;85:244–6.
6. Zullino D et al. Tobacco and cannabis smoking cessation can lead to intoxication with Clozapine or olanzapine. *International Clinical Psychopharmacology*. 2002; 17(3):141–3.

Suggested Actions by Local Health Districts/Networks:

1. Ensure this safety notice is distributed to all relevant staff to ensure they are aware of the symptoms potentially associated with the consumption of Clozapine.
2. Ensure a system is in place to document actions taken.