



## Medication Safety Series: MSS 25

# Tobacco smoking, smoking cessation & psychotropic drugs

- Patients must be advised to notify prescribers **ASAP** of any changes to smoking status.
- **Why?** A number of psychotropic drugs, and some used for physical health conditions, can be affected by changes in smoking status (See [Appendix 1](#)); the most significantly affected psychotropic drugs are **clozapine** and **olanzapine**.
- **How?** Some components of tobacco smoke (not nicotine) induce hepatic cytochrome P450 enzymes, increasing metabolism of their substrates; of these CYP1A2 is the most clinically significant, as it metabolises many drugs.
- **So what?** A change in smoking status can significantly impact on drug metabolism with the potential to reduce the therapeutic effect (if smoking more), or cause significant toxicity (if smoking less), e.g. increased sedation, muscle stiffness, tremor, dizziness, hypersalivation & constipation with clozapine
- **When?** As few as 7-12 cigarettes/day is sufficient for a full effect on CYP1A2 activity and it takes around 8 days for CYP1A2 activity to return to normal following smoking cessation
- **What do patients need to know?** Information for patients on the impact of smoking on clozapine/olanzapine are available as handy fact sheets via the [choice and medication website](#).

### Clozapine

Target level = 350-500 micrograms per litre (trough)  
But..... always treat the patient, not the level

- Plasma levels in a smoker taking a constant clozapine dose are on average 50% lower than non-smokers on the same dose
- Stopping or starting smoking suddenly can result in plasma level changes within 3-5 days.
- In patients also taking valproate, the enzyme induction effects of smoking may be stronger & the effect on plasma levels more marked on smoking cessation

#### If a patient stops smoking:

- Take a plasma level (prior to cessation where possible) and check for any adverse effects
- **At the point of stopping smoking**, reduce clozapine dose gradually over a week until around 75% of original "smoking dose" remains
- Re-check plasma level after one week
- Make further dose adjustments dependent on emerging side effects or toxicity
- Further plasma levels (2-4 weeks after stopping smoking) & dose adjustments may be necessary
- Advise patient to be alert for increased adverse effects which may indicate toxicity & report them to their HCP ASAP e.g. ↑sedation, hypersalivation, constipation & dizziness

#### If a patient restarts smoking\*:

- Take a plasma level prior to restarting (if possible)
- Increase clozapine dose to previous "smoking dose" over one week
- Re-check plasma level & adjust dose as appropriate

*\*if clozapine has been started in a smoker while an inpatient, dose increase may be required after discharge when smoking resumes*

### Olanzapine

Target level = 20-40 micrograms per litre (12 hours post-dose).  
But.... always treat the patient, not the level

- Clearance may be higher & half-life 21% shorter in smokers compared to non-smokers probably due to CYP1A2 induction
- Smoking cessation can lead to toxicity through removal of CYP1A2 induction
- Dose reduction of 30-50% may be necessary if a patient stops smoking

#### If a patient stops smoking:

- Take a plasma level (prior to cessation)
- **At the point of stopping smoking**, reduce olanzapine dose by 25%
- Re-check plasma level after one week
- Make further dose adjustments where appropriate
- Advise patient to be alert for increased adverse effects which may indicate toxicity, e.g. ↑sedation, muscle stiffness, tremor & dizziness, and report them to their HCP ASAP

#### If a patient restarts smoking\*:

- Take a plasma level prior to restarting (if possible)
- Increase olanzapine dose to previous "smoking dose" over one week
- Re-check plasma level after one week
- Make further dose adjustments where appropriate

*\*if olanzapine has been started in a smoker while an inpatient, dose increase may be required after discharge when smoking resumes*

**Please note:** Only tobacco (or cannabis) smoking induces hepatic enzymes; cannabis vaping devices may also have an effect. Nicotine replacement, nicotine vaping devices & electronic cigarettes have no effect on enzyme activity.

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|-------------------|---|--|
| Title             | MSS25: Tobacco smoking/smoking cessation & psychotropics v1 |  |
| Approved by       | Drug & Therapeutics Committee                               |  |
| Date of approval: | 27 <sup>th</sup> May 2021                                   | Review date: 1 <sup>st</sup> June 2024 |

## Appendix 1: Smoking and the effect on medicines including clozapine (From TEWV Stop Smoking Products Guidance)



The MHRA advised in October 2009 that the most important medicines to consider in those who smoke, or are trying to quit, include THEOPHYLLINE, OLANZAPINE, CLOZAPINE, CAFFEINE and WARFARIN. In 2020, the MHRA issued a reminder to prescribers of the impact of smoking/changes to smoking status on CLOZAPINE.

### Impact of Smoking on Psychotropic Drugs

| Drug                       | Effect of smoking  | Action to be taken on stopping smoking   | Action to be taken on re-starting smoking  |
|----------------------------|--|--|--|
| <b>Antipsychotics</b>      |  |  |  |
| Chlorpromazine             | Plasma levels ↓ (Varied estimates of exact effect)   | Monitor closely, consider ↓dose  | Monitor closely; consider re-starting previous smoking dose  |
| Clozapine                  | Plasma levels ↓ by up to 50%; plasma level reduction may be greater in those receiving valproate | Take plasma level before stopping; On stopping ↓ dose gradually (over 1 week) until around 75% original dose reached (i.e. 25% reduction). Repeat plasma level 1 week after stopping & anticipate further dose reductions. | Take plasma level before re-starting. Increase dose to previous smoking dose over 1 week. Repeat plasma level. |
| Fluphenazine               | Plasma levels ↓ by up to 50%   | On stopping, reduce dose by 25%. Monitor carefully over 4-8 weeks; consider further dose reductions  | On re-starting, increase dose to previous smoking dose   |
| Haloperidol                | Plasma levels ↓ by around 25-50%   | Reduce dose by around 25%. Monitor carefully. Consider further dose reductions   | On re-starting, increase dose to previous smoking dose   |
| Loxapine (Inhaled)         | Half-life ↓ from 15.7 hours to 13.6 hours  | Monitor  | Monitor  |
| Olanzapine                 | Plasma levels ↓ by up to 50%   | Take plasma level before stopping. On stopping reduce dose by 25%. After 1 week, repeat plasma level. Consider further dose reductions.  | Take plasma level before re-starting. Increase dose to previous smoking dose over 1 week. Repeat plasma level. |
| Zuclopenthixol             | Unclear, but effect probably minimal   | Monitor  | Monitor  |
| <b>Antidepressants</b>     |  |  |  |
| Agomelatine                | Plasma level ↓   | Monitor closely; may need to ↓ dose  | Consider re-introducing previous smoking dose  |
| Duloxetine                 | Plasma levels may be ↓ by up to 50%  | Monitor closely; dose may need to be reduced   | Consider re-introducing previous smoking dose  |
| Fluvoxamine                | Plasma levels ↓ by around 1/3  | Monitor closely; dose may need to be reduced   | Dose may need to be increased to previous level  |
| Mirtazapine                | Unclear, but effect probably minimal   | Monitor  | Monitor  |
| Trazodone                  | Around 25% reduction   | Monitor for increased sedation. Consider dose reduction.   | Monitor closely, consider increasing dose.   |
| Tricyclic antidepressants  | Plasma levels ↓ by 25-50%  | Monitor closely. Consider reducing dose by 10-25% over 1 week. Consider further dose reductions.   | Monitor closely, consider re-starting previous smoking dose.   |
| <b>Other Psychotropics</b> |  |  |  |
| Benzodiazepines            | Plasma level ↓ (by 0-50%; depends on drug/smoking status)  | Monitor closely, consider ↓ dose by up to 25% over 1 week  | Monitor closely; consider re-starting "normal" smoking dose  |
| Carbamazepine              | Unclear; may ↓ levels to a small extent  | Monitor for changes in severity of adverse effects   | Monitor plasma levels  |

**Note:** Only tobacco (or cannabis) smoking induces hepatic enzymes; cannabis vaping devices may also have an effect. Nicotine replacement, nicotine vaping devices & electronic cigarettes have no effect on enzyme activity

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