

Drug	Interactions	Comments
Bone marrow suppressants (e.g. carbamazepine, chloramphenicol), sulphonamides (e.g. co-trimoxazole), pyrazolone analgesics (e.g. phenylbutazone), penicillamine, cytotoxic agents and long-acting depot injections of antipsychotics	Interact to increase the risk and/or severity of bone marrow suppression.	Clozapine must not be used concomitantly with other agents having a well known potential to suppress bone marrow function.
Benzodiazepines	Concomitant use may increase risk of circulatory collapse, which may lead to cardiac and/or respiratory arrest.	Caution advised if using together. Respiratory depression and collapse more likely to occur at start of this combination or when clozapine is added to an established benzodiazepine regimen.
Anticholinergics	Clozapine potentiates action of these agents through additive anticholinergic activity.	Observe patients for anticholinergic side-effects, e.g. constipation, especially when using to help control hypersalivation.
Antihypertensive agents	Clozapine can potentiate hypotensive effects of these agents due to sympathomimetic antagonistic effects.	Caution is advised. Patients should be advised of the risk of hypotension, especially during the period of initial dose titration.
Alcohol, MAOIs, CNS depressants, including narcotics and benzodiazepines	Enhanced central effects. Additive CNS depression and cognitive and motor performance interference when used in combination with these substances.	Caution is advised if clozapine is used concomitantly with other CNS active agents. Advise patients of the possible additive sedative effects and caution them not to drive or operate machinery.
Highly protein bound substances (e.g. warfarin and digoxin)	Clozapine may cause increase in plasma concentration of these substances due to displacement from plasma proteins.	Patients should be monitored for the occurrence of side effects associated with these substances, and doses of the protein bound substance adjusted, if necessary.
Antibiotics such as erythromycin and ciprofloxacin	Can elevate clozapine levels	Avoid combination if possible. Consider closer monitoring involving FBCs
Phenytoin	Addition of phenytoin to clozapine regimen may cause a decrease in the clozapine plasma concentrations.	If phenytoin must be used, the patient should be monitored closely for a worsening or recurrence of psychotic symptoms. Consider measuring serum clozapine to ensure therapeutic levels are maintained.
Lithium	Concomitant use can increase the risk of development of neuroleptic malignant syndrome (NMS).	Observe for signs and symptoms of NMS.
CYP1A2 inhibiting substances (e.g. fluvoxamine, caffeine, ciprofloxacin)	Concomitant use may increase clozapine levels	Potential for increase in adverse effects. Care is also required upon cessation of concomitant CYP1A2 inhibiting medications as there will be a decrease in clozapine levels.
CYP1A2 inducing substances (e.g. omeprazole)	Concomitant use may decrease clozapine levels	Potential for reduced efficacy of clozapine should be considered.

## Important information about clozapine and potentially fatal side effects

making a

difference

together

## Two potentially serious side effects of clozapine that are sometimes overlooked are constipation and bowel obstruction (occasionally fatal).

The patient named in the attached letter is to be started on **clozapine** at home under the supervision of the mental health team.

All patients initiated on clozapine will be given information about following a high fibre diet and advised to seek help from their GP or pharmacist if they become constipated.

If the patient presents to you with symptoms of constipation please ensure:

- Regular laxatives are prescribed. A bulk forming laxative (Fybogel) and, if necessary a stimulant laxative (senna) are advised.
- The mental health team is informed if constipation persists.
- Prescribing of any other medication that may cause constipation as a side effect, (e.g. antimuscarinic medicines) is avoided.

Certain medicines are contra-indicated with the use of clozapine; a table of those more commonly prescribed can be found on the reverse of this leaflet.

The manufacturer's Summary of Product Characteristics for clozapine at [www.medicines.org.uk](http://www.medicines.org.uk) should be referred to for a full list of contraindicated medication and additional cautions.

If this patient either starts smoking or decides to stop, please inform the mental health team. When smoking status changes, this can significantly affect plasma levels of clozapine and clozapine plasma level monitoring may be needed to determine if any changes to the dose are required. Dose increases for smokers of up to 70% are sometimes needed, whilst the average patient who stops smoking needs to reduce their dose by at least one quarter to avoid serious side-effects developing.

Whilst clozapine is being titrated the patient will be supervised closely at home. They have been given an emergency number to contact out-of-hours and at weekends if they have any side-effects or feel unwell.

Please update your records, including the prescribing system, to indicate that this patient has started clozapine and to monitor for constipation, even though secondary care will do all the prescribing.

We will keep you informed of their progress.

*Adapted from Sussex Partnership NHSFT GP clozapine letter*