| **Concordance** | *Clozapine doses are usually divided if more than 200mg per day and often divided unevenly with a larger dose at bedtime. If the patient has not taken clozapine for 48 hours the prescriber must be contacted as the dose will have to be re-titrated (doses are built up over 3 – 4 weeks).*<br>*Common dose range is 300mg to 500mg although a few patients may require doses up to a maximum of 900mg daily.*<br>*A missed dose can be taken if remembered within 4 hours otherwise it should be omitted and the next dose taken at the correct time.* ***A dose should never be doubled****.* |
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| **Is the patient taking their medicine(s) as prescribed?**<br><br>□ Yes □ No<br><br>**Does the patient know what to do if they miss a dose?**<br><br>□ Yes □ No | **Actions:**<br><br>**Ensure that the patient knows:**<br><br>• **what dose of clozapine to take**<br><br>• **when to take it**<br><br>• **what to do if a dose is missed - If more than 2 days have been missed withhold and contact key worker or Clinical Pharmacy Team**<br><br>• **Record any care issues in the patient's care plan and agree desired outcomes and actions.** |

## Interactions

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| *Smoking* | *Induction of CYP 1A2 reduces clozapine levels and higher doses may be required* |
| *Caffeine* | *Concomitant use may increase clozapine levels. Potential for increase adverse effects.* |

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| *Bone marrow suppressants (e.g.carbamazepine)*<br>*Sulphonamides (e.g. co-trimoxazole)*<br>*Pyrazolone analgesics*<br>*Penacillamine, cytotoxics and depot antipsychotics* | *Increased risk/severity of bone marrow depression.*<br>***Clozapine must not be used concomitantly with other agents known to suppress bone marrow function*** |
| *Benzodiazepines* | *Increase risk of respiratory depression and collapse at start of combination or when clozapine added to benzodiazepine* |
| *Anticholinergics* | *Observe for anticholinergic side effects e.g. constipation, especially when using to control hypersalivation* |
| *Antihypertensives* | *Patients should be advised of risk of hypotension, especially during initial dose titration* |
| *Alcohol. MAOIs, CNS depressants, including narcotics and benzodiazepines* | *Enhanced CNS effects.*<br>*Advise patients of possible sedative effects* |
| *Highly protein bound substances (e.g. warfarin, digoxin)* | *Clozapine can cause increase in concentration of substance. Monitor for side effects associated with these substances and dose of protein bound substance adjusted if necessary* |
| *Phenytoin* | *May cause decrease in clozapine level. Monitor closely for worsening or recurrence of psychotic symptoms* |
| *Lithium* | *Increase risk of NMS. Observe for signs and symptoms of NMS* |
| *CYP1A2 inducers (e.g.omperazole)* | *May decrease clozapine level. Potential for reduced efficacy* |
| *CYP1A2 inhibitors (e.g. ciprofloxacin)* | *May increase clozapine level. Potential for increased adverse effects* |

**Is the patient aware of drug interactions including those with OTC medicines?**

□ Yes □ No

**Action:**

- **Advise the patient to always check with their GP and / or pharmacist that any new medicine, including an OTC medicine, is safe to take with clozapine.**
- **Advise the patient to mention to their prescriber if their use of caffeine or smoking habits change**
- **Record any care issues in the patient's care plan and agree desired outcomes and actions.**

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| **Side Effects**<br><br>**Is the patient aware of common side effects of their medicine(s)?**<br><br>□ Yes □ No | *Side effects of clozapine include:*<br>• *Constipation, hypersalivation, nausea and vomiting*<br>• *Urinary incontinence, urinary retention*<br>• *Weight gain and hyperglycaemia*<br>• *Drowsiness, sedation, dizziness*<br>• *Blurred vision, headache, tremor, rigidity, akathisia, extrapyramidal symptoms, myoclonic jerks and seizures*<br>• *Tachycardia, hypertension, postural hypotension and thromboembolism*<br>• *Fatigue, fever, benign hyperthermia, disturbances in sweating/temperature regulation*<br>• *Cardiac disorders including myocarditis*<br>• *Hepatic disorders, including elevated liver enzymes. If jaundice develops, clozapine should be discontinued*<br>• *Neutropenia & agranulocytosis (see below under toxicity)*<br><br>**Actions:**<br><br>• **Check the patient's understanding of the side effects of clozapine**<br><br>• **Refer a patient with more severe side effects to their key worker or consultant.**<br><br>• **Record any care issues in the patient's care plan and agree desired outcomes and actions.** |
| **Toxicity**<br><br>**Is the patient aware of signs of toxicity?**<br>□ Yes □ No<br><br>**Does the patient know what to do if they experience any signs of toxicity?**<br>□ Yes □ No | *Neutropenia & agranulocytosis are rare but possible side effects of clozapine. Clozapine levels are broadly related to dose, but not routinely monitored. Monitoring can be helpful to detect or confirm toxicity. Seizures and myoclonus may occur at plasma levels above 500-600ug/L*<br><br>**Actions:**<br><br>• **Check the patient's understanding of the signs of clozapine toxicity**<br><br>• **Refer the patient to the prescriber if they are experiencing any signs of infection, such as sore throat, fever or flu-like symptoms which may be signs of toxicity**<br><br>• **Refer the patient to the prescriber if they are experiencing seizure activity e.g. jerking movements or twitching**<br><br>• **Advise the patient to report any adverse drug reactions through the MHRA Yellow Card Reporting Scheme.**<br><br>• **Record any care issues in the patient's care plan and agree desired outcomes and actions.** |

| **Monitoring** | *The Clozaril Patient Monitoring System (CPMS) is the system which is currently used in Scotland for patients who are prescribed clozapine in order to:*<br>• *record blood results*<br>• *check results for validity to dispense*<br>• *enter dispensing data*<br>*Clozaril (clozapine) may only be prescribed by a consultant or physician who is registered with CPMS.*<br>*Clozaril (clozapine) may only be dispensed to patients who are registered with CPMS.*<br>***There must always be a current, valid blood result for the patient before any Clozapine is dispensed.***<br>*Clozaril (clozapine) may only be dispensed by a pharmacist who is registered with CPMS.*<br>*Blood tests are taken weekly for the first eighteen weeks, then fortnightly up to 52 weeks, then once every four weeks after a year.*<br><br>**Actions:**<br>• **Check that there is a current, valid blood result on CPMS before dispensing clozapine – if none present contact the key worker and Mental Health Pharmacy Team**<br>• **Insert dispensing information on CPMS**<br>• **Contact the prescriber/key worker/mental health pharmacy team if patient does not present to collect prescription as expected**<br>• **Record any care issues in the patient's care plan and agree desired outcomes and actions.** |
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| **Is appropriate monitoring being carried out?**<br><br>□ Yes □ No | |
| **Summary** | **Actions:**<br>• **Any pharmaceutical care issues, desired outcomes and actions to resolve the issues should be agreed with the patient and recorded in their care plan.**<br>• **At each future dispensing:**<br>  ○ **Check for monitoring and signs of toxicity.**<br>  ○ **Review and update any outstanding care issues in the care plan if appropriate.** |
| **Please annotate any pharmaceutical care issues of note?**<br><br>□ **Concordance**<br>□ **Interactions**<br>□ **Side Effects**<br>□ **Toxicity**<br>□ **Monitoring** | |