Local Guideline

Health
Hunter New England
Local Health District

Document number: JHH_0448

# Perioperative Management of Patients Taking Clozapine

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| **Sites where Local Guideline applies** | **John Hunter Hospital** |
| **Target audience** | Psychiatrists, nurses, surgeons, anaesthetists, doctors and pharmacists |
| **This Local Guideline applies to:** | |
| **1. Adults** | Yes |
| **Description** | This document provides guidance for nurses and doctors in the perioperative setting as to the assessment and management of patients taking clozapine who are undergoing elective surgery |
| **Keywords** | Clozapine, ClopineCentral®, psychiatry, schizophrenia, surgery, perioperative, anaesthetics, theatre. |

**Go to Guideline**

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| **Replaces existing document?** | No |

**Relevant or related Documents, Australian Standards, Guidelines etc:**

- NSW Health Policy Directive PD2017_032 Clinical Procedure Safety
- HNELHD Policy Compliance Procedure PPM Consent:PCP 3 Consent for Clinical Treatment and Care
- NSW Health Policy Directive PD 2017_013 Infection Prevention and Control Policy
- Work Health and Safety Act 2011 no. 10
- NSW Health Policy Directive PD2012_069 Health Care Records – Documentation and Management
- HNE Health Policy Compliance Procedure PD2009_060: PCP1 Clinical Handover – ISBAR
- HNELHD Policy Pol 18_03 Aseptic Technique for Level 1 to Level 2 Procedures Conducted in Clinical Settings
- Local procedure JHH_JHCH_BH_0193 Standard Aseptic Technique
- NSW Health Policy Directive 2013_049 Recognition and management of Patients who are Clinically Deteriorating
- HNE LHD Policy Compliance Procedure Recognition and Management of Patients who are Clinically Deteriorating PD2013_049:PCP 1
- HNE LHD PD2013_049 PCP2 Vital Sign Observations & Monitoring Frequency 16 Years and Over
- "See Reference Section on page 8

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| **Prerequisites (if required)** | Patients should be on clozapine, enrolled in the ClopineCentral® program and be booked for elective surgery at the John Hunter Hospital. |

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| **Local Guideline note** | This document reflects what is currently regarded as safe and appropriate practice. This guideline does not replace the need for the application of clinical judgment in respect to each individual patient. If staff believe that the guideline should not apply in a particular clinical situation they must seek advice from their unit manager/delegate and document the variance in the patient's health record.<br>If this document needs to be utilised outside of the JHH please liaise with the local Psychiatry Service to ensure the appropriateness of the information contained within the Guideline. |
| **Date initial authorisation:** | March 2022 |
| **Authorised by:** | JHH Perioperative Service Co-Director |
| **This document contains advice on therapeutics** | Yes<br>Approval gained from Local Quality Use of Medicines Committee April 2022 |
| **Contact Person:** | Dr Paul Healey |
| **Contact Details:** | (02) 49223018; Paul.Healey@health.nsw.gov.au |
| **Date Reviewed:** | March 2022 |
| **Review due date:** | March 2025 |
| **Position responsible for review:** | JHH Perioperative Service Co-Director |
| **Version:** | 1.0 26th July 2022 |

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## PURPOSE AND RISKS

Clozapine is an atypical antipsychotic which can be associated with many serious adverse effects including agranulocytosis, myocarditis, idiopathic tachycardia, severe constipation, megacolon, metabolic syndrome, lowered seizure threshold and sedation. There is a small risk of sudden death. Due to the seriousness of these risks and other legal mandates, it is essential that Consultation Liaison Psychiatry be involved with any patient on clozapine who is being admitted to hospital.

In addition to the risks with clozapine alone, the perioperative period adds additional challenges. These include:

- Smoking reduction
- Physiologic stress from surgery or illness
- Possible reduced enteric absorption
- Constipation exacerbation
- Adverse medication interactions.
- Severe, refractory, rebound psychosis due to clozapine cessation.
- A need to restart the clozapine titration process if multiple doses are withheld, with significant clinical and logistic implications for the patient.

These risks are reduced through:

1. Preoperative screening for medication adherence, smoking status, bowel status and adverse effects of clozapine.
2. Notification of planned admission to the Consultant Liaison Psychiatry team.
3. Assertive bowel management throughout their entire perioperative period.

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| While this document is intended for use in the elective surgery setting, much of it may be useful in the emergency surgery setting. Liaise with CL Psychiatry for all inpatient admissions. |
| **Risk Category*:*** Clinical Care & Patient Safety |

**GLOSSARY**

| Acronym or Term | Definition |
|---|---|
| ANZCA | Australia and New Zealand College of Anaesthetists |
| CL Psychiatry | Consultant Liaison Psychiatry |
| CNS | Central nervous system |
| PO | Per oral |

**John Hunter Hospital / Service Manager Responsibility**

- Ensure that the principles and requirements of this procedure are applied, achieved and sustained
- Ensure effective response to, and investigation, of alleged breaches of this procedure.
- Ensure all staff have completed My Health Learning online module Introduction to Safety and Quality (course number 42189807)
- Notify staff of all new and revised local procedures and guidelines through the JHH Newsletter

**Line management responsibility**

- Notify staff of new and revised policies, procedures and guidelines relevant to the workplace / unit / clinical specialty.
- Post the JHH newsletter (with policy, procedure and guideline updates) in staff rooms
- Identify high clinical risks relevant to patient population of unit/specialty and undertake audits of compliance with relevant policies, procedures or guidelines.

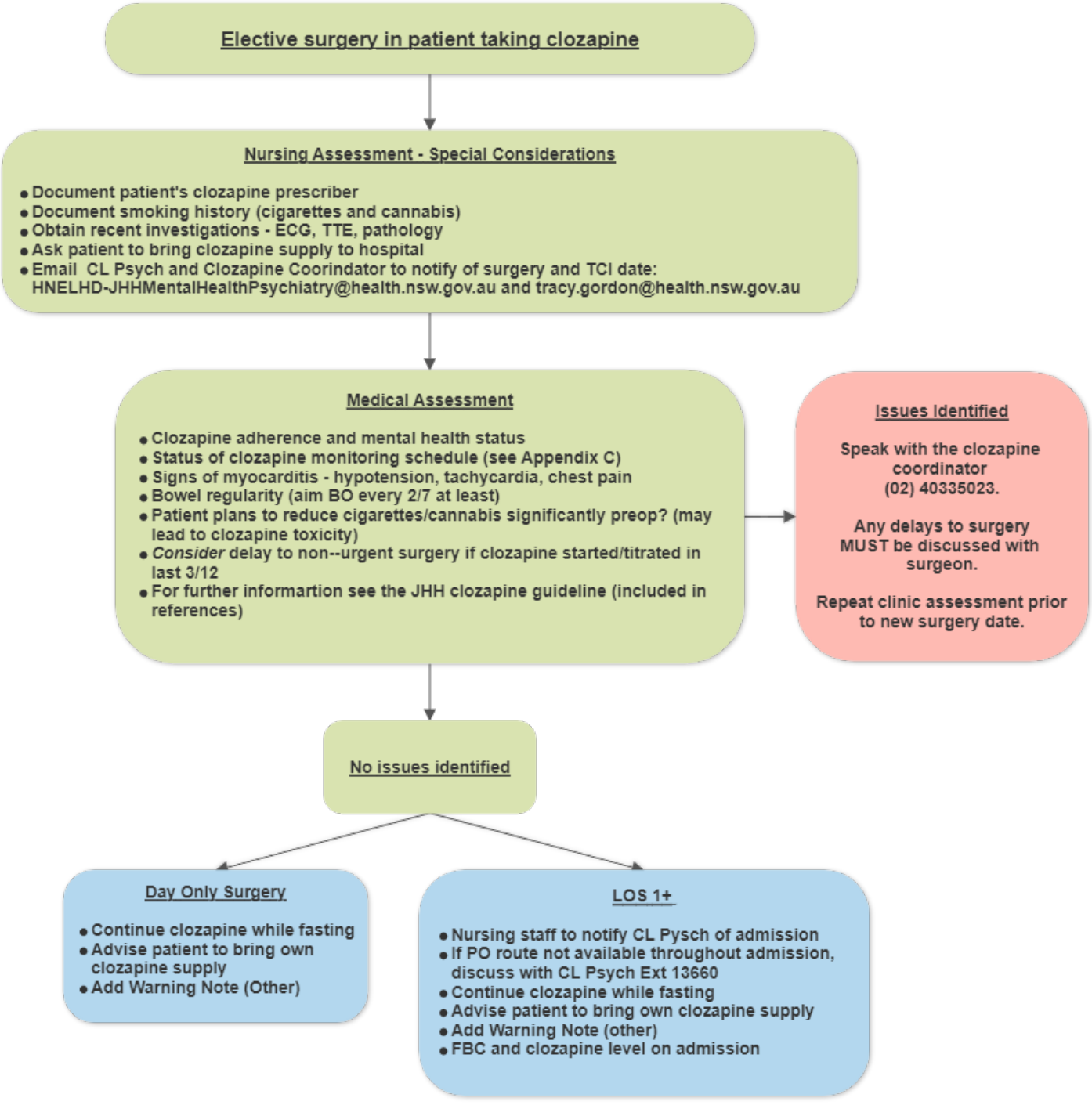
**Employee responsibility**

***Staff must:***

- Comply with policies, procedures and guidelines applying to their workplace / unit / specialty
- Report unsafe practices, equipment or environment to line manager
- Escalate any patient safety concerns to line manager, including if it is assessed that policies, procedures or guidelines do not reflect contemporary practice

## GUIDELINE

This Guideline does not replace the need for the application of clinical judgment in respect to each individual patient.




**Intraoperative phase**

- Clozapine can interfere with normal thermoregulatory mechanisms leading to hyperthermia. It is recommended that temperature monitoring be used and, where necessary, be managed in line with ANZCA guidance.
- *See medication interactions below.*

**Postoperative phase**

- **Bowel regularity is extremely important**. Aperients should be charted for all patients*, where surgically appropriate.*
- If clozapine is withheld for several days, patient is at **risk of anticholinergic rebound**. Consider management prospective management of this. E.g. alerting the treating time and documenting in the patient's notes.
- Increased risk of VTE.
- Antiemetics with lowest risk include ondansetron and droperidol (see medication interactions below)
- CL Psychiatry will chart the patient's clozapine, monitor the patient's clozapine levels, and monitor the patient for complications regarding their mental health and clozapine use. Note *only CL Psychiatry medical officers are permitted to chart clozapine.*

**Medication interactions relevant to the perioperative period**

- **Synergistic CNS depression** with all CNS depressants e.g. anaesthetic agents, benzodiazepines, opioids, phenothiazines and butyrophenones.
- **Hypotension due to alpha blockade** with anaesthetic agents, butyrophenones and phenothiazines. Increased doses of vasopressors may be required. Hypotension may be worsened by adrenaline use, due to excessive beta-2 mediated vasodilation. Vasopressin may be useful for refractory hypotension.
- **Lowering of seizure threshold** in conjunction with tramadol.
- **Additive anticholinergic effects** with other anticholingeric medications, increasing the risk of delirium, urinary retention, constipation and impaired thermoregulation.
- **Neuroleptic malignant syndrome** with butyrophenones and phenothiazines
- **QT prolongation** with ondansetron and butyrophenones (low risk with anti-emetic doses). ECG to check for baseline QTc prolongation recommended.
- **Extra-pyramidal side effects** with metoclopramide (and concurrent use of other antipsychotics). Low dose droperidol for anti-emetic purposes usually well tolerated.
- **Competition for metabolism** with local anaesthetics possibly leading to elevated plasma levels of both clozapine and local anaesthetic.

**During all phases of care**

- Document a comprehensive care plan in consultation with patient/family including patient goals and preferences, including advance care preferences.
- Ensure patient/family is aware of agreed goals and plan of care and that this is reviewed with patient/family at clinical handover.

## APPENDICES

**Appendix A – CL Psychiatry Contact Details**

**Appendix B - Monitoring for myelosuppression with WCC levels**

**Appendix C - Clozapine monitoring schedule**

## REFERENCES


- HNELHD Local Clinical Guideline JHH_015 Clozapine
- NSW Health Policy Directive PD2012_005 Clozapine-induced Myocarditis - Monitoring Protocol

- HNELHD Clinical HNELHD CG 19_41 Clozapine Initiation, Monitoring, Management and Cessation
- TGA Medicines Safety Update 1:2011 Clozapine and Severe Constipation
- NSW Health and Safety Notice 017/11 – Clozapine and Smoking Cessation – Potential Toxicity
- Huyse, F, Touw, D, Rob Strack, v. S, de Lange, J, & Slaets, J. Psychotropic drugs and the perioperative period: A proposal for a guideline in elective surgery. *Psychosomatics, 47*(1), 8-22. 2006
- Lucas C, Martin J. Smoking and drug interactions. Aust Prescr 2013;36:102–4
- ANZCA Guideline on monitoring during anaesthesia. PS18, 2017
- NSW Health Policy Directive. Prevention of Venous Thromboembolism (VTE) – Adult PD2019_057:PCP 1
- Constance LSL, Lansing MG, Khor FK, *et al* Schizophrenia and anaesthesia *BMJ Case Reports* 2017;**2017:**bcr-2017-221659.
- HNELHD CG 20_28 Mental Health: Indications for ECG monitoring in Mental Health Inpatient Units


**Useful Links**

Clozapine - UKCPA (ukcpa-periophandbook.co.uk)

## Appendix A – CL Psychiatry Contact Details

| | Contact | Charting clozapine | Latest that Consultation Liaison Psychiatry will attend to chart clozapine |
|---|---|---|---|
| **0830 -1700 Mon to Friday (*business hours)*** | Ph 13660 or call Consultation Liaison Psychiatry Registrar through switch (page 2267) | **Admitting team should not chart clozapine** – Consultation Liaison Psychiatry will attend to chart clozapine | n/a. |
| **1700 – 2230 WEEKNIGHTS** | Contact On-Call CONSULTANT Psychiatrist through switch | Admitting team able to chart stat doses **under direct order** of a psychiatry registrar or psychiatrist if they are unable to directly attend. Do not withhold, increase or decrease dose | Consultation Liaison Psychiatry or after hours psychiatry registrar to attend and chart clozapine next day – seven days per week |
| **All other times** | Contact After Hours Psychiatry Registrar through switch. | Admitting team able to chart stat doses **under direct order** of a psychiatry registrar or psychiatrist if they are unable to directly attend. Do not withhold, increase or decrease dose | Consultation Liaison Psychiatry or after hours psychiatry registrar to attend and chart clozapine next day – seven days per week. |

## Appendix B – Monitoring for myelosuppression with WCC levels

| Status | WCC and NC | Action |
|---|---|---|
| **Green** | WCC > 3.5 x $10^9$/L **&/or** NC > 2.0 x $10^9$/L | Continue treatment |
| **Amber** | WCC 3.0–3.5 x $10^9$/L **&/or** NC 1.5–2.0 x $10^9$/L | Continue treatment and commence twice weekly FBC until green. |
| **Red** | WCC < 3.0 x $10^9$/L **&/or** NC < 1.5 x $10^9$/L | Stop clozapine and immediately contact ClopineCentral® |

**Appendix C – Clozapine Monitoring Schedule**

| | Pre - treatment | * Intense monitoring at initiation / first 28 days | Every week for 18 weeks | Every 4 weeks | Every 6 months | Annually | On admission to hospital | At every medical review ( inpatient and community) | When patient reports feeling unwell after initiation |
|---|---|---|---|---|---|---|---|---|---|
| Temp (T) | □ | □ | □ | □ | □ | □ | □ | □ | □ |
| Pulse (P) | □ | □ | □ | □ | □ | □ | □ | □ | □ |
| Respiration (R ) | □ | □ | □ | □ | □ | □ | □ | □ | □ |
| Blood Pressure (BP) | □ | □ | □ | □ | □ | □ | □ | □ | □ |
| Troponin I and CRP | □ | | Note 1 | | Note 1 | | | | □ |
| Blood Group | □ | | | | | | | | |
| White Blood Cell Count | □ | | □ | □ | Note 3 | Note 3 | □ | | □ |
| Neutrophil Count | □ | | □ | □ | Note 3 | Note 3 | □ | | □ |
| Bowel Habits | □ | | □ | □ | □ | □ | □ | □ | |
| Weight | □ | | □ | □ | □ | □ | □ | □ | |
| Waist | □ | | □ | □ | □ | □ | □ | □ | |
| BMI | □ | | □ | □ | □ | □ | □ | | |
| Clozapine Plasma Levels | | | | | □ | □ | □ | Note 4 | Note 5 |
| Fasting Glucose | □ | | | | □ | □ | | | |
| Lipids (fasting cholesterol, HDL, LDL, Triglycerides | □ | | | | □ | □ | | | |
| LFTs | □ | | | | □ | □ | | | |
| EUC | □ | | | | □ | □ | | | |
| ECG | □ | | | | Note 2 | □ | | | □ |
| Echocardiogram | □ | | | | Note 2 | □ | | | Note 5 |
| CK-M8 & NT-proBNP | | | | | | | | | Note 5 |

*** After first dose of clozapine, monitor Temperature, Pulse, Respiration and Blood Pressure half hourly for the first 2 hours, hourly for the next 4 hours, then for inpatients record TPR and BP as per "Between The Flags"; for outpatients it is recommended to record TPR and BP weekly for first 4 weeks**
**Refer to Clozapine Initiation, Monitoring, Management & Cessation (HNELHD CG 13_05) & Clozapine-induced Myocarditis Monitoring Protocol (PD 2012_05)**

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| **Note 1 : Measure Troponin I and CRP** | **At weeks 1, 2, 3, 4 then week 6 and week 18 then 6 months after initiation then 6 monthly unless clinically indicated** |
| **Note 2 : ECG and Echocardiogram** | **At 6 months after initiation then annually** |
| **Note 3 : White Blood Cells / Neutrophils** | **This is completed as per routine monthly (28 days) checking** |
| **Note 4 : Clozapine Plasma Levels** | **Check levels if there are changes in smoking status, medication changes or if non-compliance is suspected** |
| **Note 5 :** | **If clinically indicated** |