Local Guideline

Health
Hunter New England
Local Health District

Perioperative Management of Patients Taking Clozapine

Sites where Local Guideline applies	
This Local Guideline applies to:	John Hunter Hospital
1. Adults	Yes
2. Children up to 16 years	No
3. Neonates – less than 29 days	No
Target audience	Psychiatrists, nurses, surgeons, anaesthetists, doctors, pharmacists.
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.

Go to Guideline

Keywords	Clozapine, ClopineCentral®, psychiatry, schizophrenia, surgery, perioperative, anaesthetics, theatre.
Document registration number	
Replaces existing document?	No

Related Legislation, Australian Standard, NSW Ministry of Health Policy Directive or Guideline, National Safety and Quality Health Service Standard (NSQHSS) and/or other, HNE Health Document, Professional Guideline, Code of Practice or Ethics:

- See Reference Section on page 8

Prerequisites (if required)	Patients should be on clozapine, enrolled in the ClopineCentral® program and be booked for elective surgery at the John Hunter Hospital.
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 a senior perioperative clinician and the Consultation Liaison Psychiatry service and document the variance in the patient's health record. If this document needs to be outside of the JHH please liaise with the local Psychiatry Service to ensure the appropriateness of the information contained within the Guideline and Procedure.
Position responsible for the Local Guideline and authorised by	JHH Perioperative Service Director
Contact person	Dr Paul Healey
Contact details	(02) 49223018 Paul.Healey@health.nsw.gov.au
Date authorised	
This document contains advice on therapeutics	Yes Approval gained from Local Quality Use of Medicines Committee on (insert date)
Issue date	
Review date	Up to 3 years

Note: Over time links in this document may cease working. Where this occurs please source the document in the PPG Directory at: http://ppg.hne.health.nsw.gov.au/

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. Because of these risks and other legal requirements, it is essential that Consultation Liaison Psychiatry be involved with any patient on clozapine who is being admitted to hospital.

The perioperative period adds additional challenges such as smoking reduction, physiologic stress from surgery or illness, possible reduced enteric absorption, constipation exacerbation, and adverse medication interactions. Cessation of clozapine may result in severe, refractory, rebound psychosis and a need to restart the titration process, 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.

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.

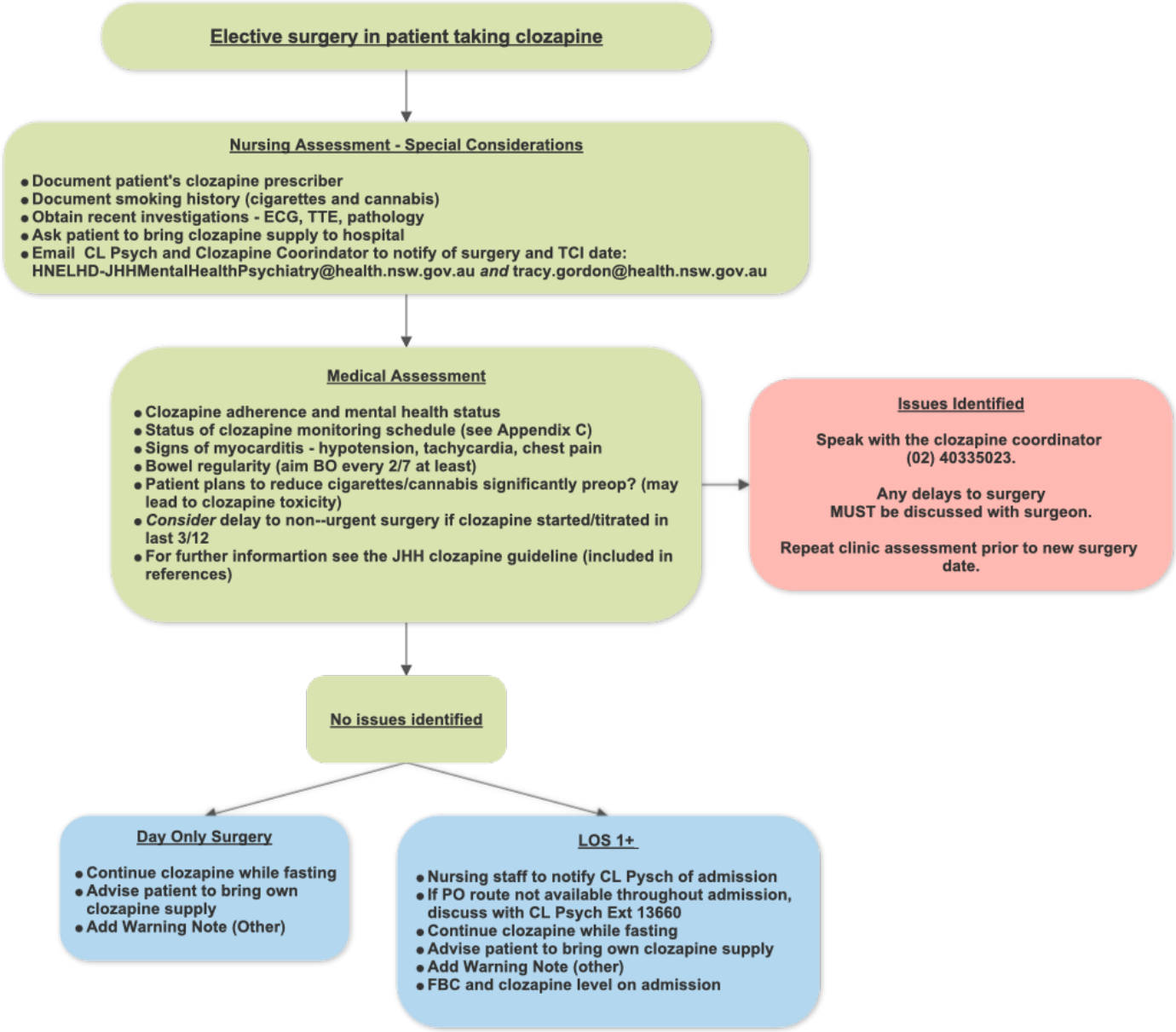
Risk Category: Clinical Care & Patient Safety

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
WCC	White cell count

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. Recommended that temperature monitoring and management be used in line with ANZCA guidance.
- *See medication interactions below.*

Postoperative phase

- **Bowel regularity is extremely important**. Aperients should be charted for all patients.
- If clozapine is withheld for several days, patient is at risk of anticholinergic rebound. Consider management.
- 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.

IMPLEMENTATION, MONITORING COMPLIANCE AND AUDIT

Clozapine Coordinator/s communicate clinical guideline requirements to relevant prescribers and clinical staff. All patients on clozapine are monitored in a database. All exceptions to the pathway are notified to the clinical staff listed on the database (e.g. if a patient misses a blood test the doctor is sent an email). ims+ reporting and monitoring via the Mental Health Quality Use of Medicines Committee is used to monitor this guideline.

The guideline will be communicated to the Perioperative Service and the Anaesthetic Department staff through our Continuing Medical Education meetings.

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)

FEEDBACK - Any feedback on this document should be sent to the Contact Officer listed on the front page.

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)

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**