WA Clozapine Initiation and Titration Chart

Version 5, 2024

Introduction

- Clozapine is a high risk medication
- It was released in early 1970s and withdrawn from market due to incidents of neutropenia, myocarditis and sudden death.
- Re-introduced for use in Australia with stringent monitoring and guidance for use in conjunction with the Clozapine Monitoring System (ClopineCENTRALTM)
- Specialised chart developed for WA Health to co-ordinate management of clozapine.
- This presentation will provide education on features.
 prompts and alerts in the chart.

General Requirements

- Chart to be completed for all in-patients initiated and re-titrated on clozapine
- The National Inpatient Medication Chart <u>MUST</u> be annotated clearly to identify when a clozapine chart is in use

Medication	chart num	berof			
Additional charts	Variable dose BGL/insulin		Other		
Palliative care	Chemotherapy	Anticoagulation	Clozapine	Chart	
Additional Cha	rts – Tick if in	use			
Blood Glucose Le	evel (BGL) monitorin	g (Subcutane	ous Insulin or	☐ Intravenous Insulin Infusion)	
Clozapine	☐ Ir	ntravenous (IV) Fluid		Chemotherapy	
Agitation & arousa	al 🗌 P	alliative care		Acute Pain	
Long acting inject	tion U	ariable dose		Other	

Chart Layout

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Week 2 to 18																							y	Park	unc				
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Front Page:

- Patient Identification
- Allergies and Adverse Drug Reactions
- Pre-commencement documentation and checklist
- Observations
 - Temperature
 - Pulse
 - Blood pressure
 - Respiratory rate
 - Level of consciousness

Chart Layout

			LICEDITAL	NUMBER			1 1000	e use ID label (ar aroun prant		
			HOSPITAL	NAME	F	Family Name:	NO	T A VALI	- 1	UMRN	SEX
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						ing to allow I					
			lozapine	Formu	lation:		с	lozapine P	atient Nun	nber:	
	Route:			Indication:				Monkle			1 1
	Pharma	acy use Day	Blood	Drae	criber	Morning	Nurse	Night	monitoring Nurse	Until: Drug	/ / Pharmacy
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	Clozapine Dose Titration Schedule													
This table Patients Titration (maximu	> 65 yea beyond	ars of ag	ge may g/day:	require	a slow	er dose	increas	se titrati	on regin	nen.				
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Morning	12.5 mg	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Evenine	$\overline{}$	$\overline{}$	$\overline{}$	25 000	25 000	E0 mm	75 ma	100 ma	100 ma	100 000	125 ma	125 ma	126 ma	160 ma

Blood	d group	He	ight	m	Smokina	status: Sm	oker Nor	Smoker
		Pre-cloza baseline		Day 7	Day 14	Day 21	Day 28	Minimum
	Intervals	Date	Results	Date:	Date:	Date:	Date:	ongoing monitoring
8	Dietician review		Performed					Annually
	Weight		kg					
doctor	Waist circumference		cm					Weekly first 18 weeks – then every 28 days
detidan detidan	BMI weight (kg) / height (m²)							, 20 00,0
To be completed by doctor / nur detician	Constipation monitoring	Daily	checks	for 4 wee	ks: Use t	owel cha	irt	Inpatients: minimum weekly Outpatients: check bowel habits at each review
	Full physical exam		Performed					Annually
	Full Blood Count		Performed	Performed	Performed	Performed	Performed	Weekly first 18 weeks - then
	White Blood Count		x101/L	x10%L	x10%L	x10%L	x109/L	every 28 days
	Neutrophils Absolute		x10%L	x10%L	x10%L	x10%L	x109L	
	Eosinophils Absolute		x10%L	x10%L	x10%L	x10%L	x109/L	
	Liver function test		Performed					6 monthly
	Urea & Electrolytes		Performed					6 monthly
podor	Fasting plasma glucose		mmol/L					
be completed by doctor	Total cholesterol (fasting)		mmol/L					At 3 months,
mplet	LDL (fasting)		mmol/L					6 months, then 6 monthly
	HDL (fasting)		mmol/L					
β	Triglycerides (fasting)		mmol/L					
	Troponin		nanograms/L	nanograms/L	nanograms/L	nanograms/L	nanograms/L	As clinically indicated
	C-Reactive Protein (CRP)		mg/L	mgL	mg/L	mg/L	mg/L	thereafter
	ECG (QT interval)							Weekly for first 4 weeks, then as clinically indicate
	Cardiac echocardiogram							At 3 months, then 1, 2, 5 yrs
	Beta HCG (female)							When needed

These are suggested guidelines only and do not replace the need for clinical discretion. Refer to the treating psychiatrist for individual monitoring requirements

		Reason For Not A	Admi	nistering (codes mu	st be	circled)	
Absent	\sim	On Leave	(L)	Refused - notify doctor	R	Vomiting – notify doctor	V
Fasting	(F)	Not Available – obtain supply and/or notify doctor, consider incident report	N	Withheld – enter reason in clinical record	w	Self-Administering – observed or claimed	<u>s</u>

Chart Layout

Clozapine Bl	ood Results Monitoring System	Recommended Action
Green Range	WBC greater than 3.5 x 10°/L AND Neutrophils greater than 2.0 x 10°/L	Continue clozapine therapy
Amber Range	WBC 3.0 - 3.5 x 10°/L AND/OR Neutrophils 1.5 - 2.0 x 10°/L	Continue clozapine therapy with twice-weekly blood tests until return to "green" range
Red Range	WBC less than 3.0 x 10°/L AND/OR Neutrophils less than 1.5 x 10°/L	Stop clozapine therapy immediately. Contact haematologist and Clozapine Monitoring Centre

Recommencing Therapy after Interruption

Dosing recommendations if clozapine dose is missed for more than 48 hours

- · Obtain psychiatric review prior to recommencing clozapine
- Recommence at 12.5 mg once or twice daily on the first day. Refer to what side effects the patient had previously
 when starting clozapine. The rate of re-titration can be adjusted to take into account emergent side effects and
 period of interruption
- · This is a guide only for further dosing options refer to treating psychiatrist.

	Blood Test I	Monitoring after Interruption of Therap	ру
Monitoring frequency	Clozapine missed for 72 hours or less	Clozapine missed for more than 72 hours up to 28 days	Clozapine missed for more than 28 days
Weekly	No change in monitoring	Monitor weekly for at least 6 weeks or for as long as necessary to achieve a total of 18 weeks of weekly monitoring	Recommence as for a new patient
Monthly]	Monitor weekly for 6 weeks then continue with monthly monitoring if no problems detected	

	monany monatoring it no p	a oblettib detected
	Associated with Clozapine Therapy	Modified from the Maudsley Prescribing Guidelines 14th ed 2021
Side effect	Signs and symptoms / Onset	Recommended Action
Neutropenia / agranulocytosis	WBC < 3.0 x 10°/L or Neutrophils < 1.5 x 10°/L. Flu-like symptoms such as sore throat & fever. (First 18 weeks – but may occur at any time)	Contact doctor. Withhold clozapine. Contact haematologist at Clozapine Monitoring Centre.
Myocarditis / cardiomyopathy	Fast or irregular heartbeat at rest with rapid breathing, dyspnoea, hypotension, raised jugular venous pressure, fatigue, infective symptoms (including gastrointestinal, urinary, and/or respiratory), chest pain or fever. Cardiomyopathy may occur at any time. Myocarditis – within 4 weeks of starting)	Withhold Clozapine. Repeat ECG and echocardiogram. Check C-Reactive Protein (CRP) and troponin. Refer to cardiologist.
Fever	> 38° C (First 4 weeks)	Contact doctor. Reduce rate of dose titration of clozapine. Check WBC, neutrophils, troponin and CRP. Physical examination for signs of infection. Consider ECG, Echocardiogram. Give paracetamol and notify doctor to ex
Seizures	Increases with high doses, rapid dose titration, concurrent use of drugs that lower seizure threshold and preexisting seizure disorders and concurrent illness. (May occur at any time)	Medical emergency, manage seizure. Withhold clozapine for one day and restart at half the dose. Consider prophylactic antiepileptic. Risk of seizures increases with higher serum clozapine levels; check serum clozapine levels.
Hypersalivation	Excessive drooling – Very troublesome at night. (First few months)	Contact doctor. Check with pharmacist for pharmacological options.
Constipation	Less frequent bowel motions, hard stools, abdominal bloating, cramping or pain, decreased appetite or fatigue. (Usually persists) Severe Clozapine Induced Gastrointestinal Hypomotility (CIGH) can be fatal.	Contact doctor. Recommend increased fluid intake and exercise. Consider pre-emptive laxatives for all patients. Review contributing medicines and consider dose reduction. Treat CIGH aggressively with laxatives and consider cessation of clozapine if treatment fails. Avoid bulk forming laxatives.
Nocturnal enuresis	Loss of bladder control, especially at night. (May occur at any time)	Contact doctor. Avoid fluids after 7pm. Check males for other causes. Continence referral. Check with pharmacist for pharmacological options.
Weight gain	This may occur early in treatment and can be significant	Dietary and lifestyle counselling before weight gain occurs. Ongoing monitoring and support.

This is not an exhaustive list of side effects. Please see product information for further advice. It is recommended that concurrent us of antipsychotic therapy be avoided where possible as this increases the patient's risk of side effects.

Back Page:

- Clozapine blood results monitoring system
- Guidelines for recommencing therapy after interruption
- Guidelines for blood test monitoring after interruption of therapy
- Side-effects associated with Clozapine therapy and recommended action

WA Health acknowledges contributions from Queensland Health Medication Management Services in the development of this chart.

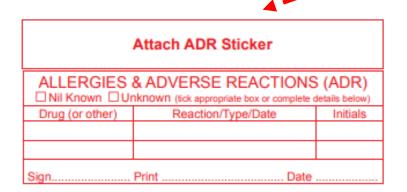
Patient Identification

Family Name:	UMRN	SEX
NOT A VALID		
Given Name(s) PRESCRIPTION UNLES	S D.O.B.:	
IDENTIFIERS PRESEN	T	
Address:		
Audicas.		

- Affix patient ID label or write information on pages 1 and 2 of chart
- If using labels: First prescriber MUST HANDWRITE (PRINT) patient name and CHECK LABELS are correct

Allergies & Adverse Reactions (ADR)

Accurate information prevents harm from known ADRs



Adverse Drug Reaction

TICK BOX if patient has 'Nil

- Known' or 'Unknown' allergies or ADRs
- If ADR exists, then <u>affix ADR</u>
 sticker to page 1 and document:
 - Drug name
 - Reaction details
 - Date of reaction
 - Sign entry

Pre-commencement Screen

	Tick the applicable box: Initiating / Recommencing after interruption Recommencing after interruption of more that Continuing titration	of 3 months or more (complete pre-comme an 48 hours up to 3 months (refer to dose and	ncement screen) d monitoring requirements on page 4)
	F	Pre-commencement Screen	
	Pre-commencement Screen is requ		
A STATE OF THE STA	Medical History:		
	Patient has chronic medical conditions	☐ No ☐ Yes Details	
	Patient has a personal or family history of	f cardiovascular disease No Yes	Details
	Patient has a history of epileptic seizures	□ No □ Yes Details	
	Clozapine registration form for new particle. PBS eligibility Continuation of supply at a registered.	clozapine centre has been considered	
8	Patient/guardian has given informed of All Pre-Clozapine Baseline Tests have	with written Medication Information and consent or second opinion obtained (# a)	pplicable) nmencement
	Consultant Name:	Signature:	Date:

Pre-commencement Screen

- A tick box to indicate if pre-commencement screen is required to be completed
- A section to ensure a medical history is obtained from the patient
- A checklist to ensure all pre-commencement clozapine requirements have been completed

Pre-commencement Screen

Tick the applicable box: Initiating / Recommencing after interruption of 3 months or more (complete pre-commencement screen) Recommencing after interruption of more than 48 hours up to 3 months (refer to dose and monitoring requirements on page 4) Continuing titration
Pre-commencement Screen
Pre-commencement Screen is required to be completed: Yes No All sections below must be completed prior to clozapine initiation or when clozapine has been discontinued for 3 months or more.
Medical History:
Patient has chronic medical conditions No Yes Details
Patient has a personal or family history of cardiovascular disease No Yes Details
Patient has a history of epileptic seizures No Yes Details
Clozapine checklist: ☐ Patient has been adequately trialled on 2 or more other antipsychotics ☐ No ☐ Yes Details
Patient/carer/family has signed the Monitoring System Privacy statement Patient/carer/family has been provided with written Medication Information and the treatment explained Patient/guardian has given informed consent or second opinion obtained (if applicable)
All Pre-Clozapine Baseline Tests have been performed before clozapine commencement Full blood picture (FBP), CRP and troponin to be performed within 10 days before clozapine commencement.
Consultant Name: Signature: Date:



Prompts to:

- return completed 'Clozapine Referral Form' to a pharmacist
- check PBS eligibility
- consider continuation of supply
- provide 'Clozapine Notification Form'; CMI and explain treatment
- obtain consent/second opinion
- perform all Pre-Clozapine Baseline Tests, prior to starting Clozapine
- perform FBP, CRP and troponin within 10 days prior to starting Clozapine

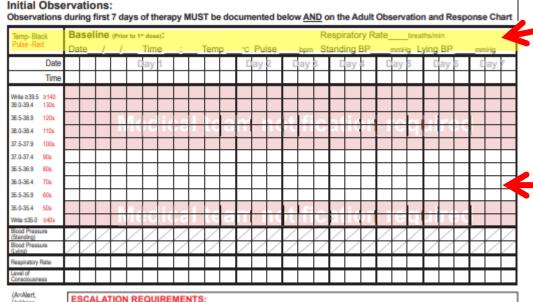
Preparation Prior to Initiation

Tick the applicable box: ☐ Initiating / Recommencing after interruption of 3 months or more (complete pre-commencement screen) ☐ Recommencing after interruption of more than 48 hours up to 3 months (refer to dose and monitoring requirements on page 4)
Continuing titration
Pre-commencement Screen
Pre-commencement Screen is required to be completed: Yes No All sections below must be completed prior to clozapine initiation or when clozapine has been discontinued for 3 months or more.
Medical History:
Patient has chronic medical conditions No Yes Details
Patient has a personal or family history of cardiovascular disease No Yes Details
Patient has a history of epileptic seizures No Yes Details
Clozapine checklist: ☐ Patient has been adequately trialled on 2 or more other antipsychotics ☐ No ☐ Yes Details ☐ Clozapine registration form for new patients has been submitted ☐ PBS eligibility
Continuation of supply at a registered clozapine centre has been considered Patient/carer/family has signed the Monitoring System Privacy statement Patient/carer/family has been provided with written Medication Information and the treatment explained Patient/guardian has given informed consent or second opinion obtained (if applicable) All Pre-Clozapine Baseline Tests have been performed before clozapine commencement Full blood picture (FBP), CRP and troponin to be performed within 10 days before clozapine commencement.
Consultant Name: Signature: Date:

✓ All sections MUST BE completed and consultant to print name, sign and date

Initial Observations

Careful observations to identify adverse events and respond appropriately



V=Voice U=Unresponsive)

Urgent medical team notification required if any of the following observed:

<u>Temperature</u> >38° C <u>Pulse</u> >100 bpm <u>Postural drop</u> >30 mmHg <u>Respiratory Rate</u> <8 or >22 breaths/minute Or patient is unresponsive

Record Baseline (Prior to 1st dose)

- Blood pressure Date
- TimeRespiratory Rate
- TempPulse

Record the first 7 days of observations here

- Temperature Black
- Pulse- Red
- Blood Pressure (standing and lying)
- Respiratory Rate
- Level of Consciousness

After 7 days, continue documentation of observations on the Adult Observation and **Response Chart.**

Initial Observations

Monitoring: Refer to hospital procedure. Where this is unavailable the following are recommended monitoring guidelines.

Day 1 Temperature, respirations, pulse and blood pressure hourly for the first six hours, then every six hours for the first 24 hours

Day 2 to 7 Temperature, respirations, pulse and blood pressure taken twice daily or more frequently if clinically required.

Week 2 to 18 Temperature, respirations, pulse and blood pressure taken daily or more frequently if required.

Initial Observations:

Observations during first 7 days of therapy MUST be documented below AND on the Adult Observation and Response Chart

Temp- Black Pulse -Red	Ва	isel	ine	(Prio	r to 1'	dose	1):										R	espi	rator	yR	ate_		brea	ths/m	in				
Pulse -Red	Da	te_	_/_	_/_	_	Tim	e	:_	_ 1	Tem	p	_°C	Pul	se		bpm	St	and	ing E	BP_		mmH	g L	ying	BP		_mm	Hg	
Date	П					ay	1						ay	2	D	ay	3	D	ay	1	D	ay	5	D	ay	6	D	ay	
Time																													
Vrte ≥39.5 ≥140																													
9.0-39.4 130s																													
8.5-38.9 120s					T.		1				0)	1					2						
8.0-38.4 110s					II.	T.		7.5		7.	C.			1	7.4	Ш	6	1	1	24		U	4	2		1,1			
7.5-37.9 100s												Г														П			П
7.0-37.4 90s	Г											Г						Г			П			Г		П			Г
6.5-36.9 80s	П			П					П		П	г		П	г		П	г		П	П		П	г		П	П	П	Г
6.0-36.4 70s	Г											Г														П			Г
5.5-35.9 60s	Г			П		Г			П		П	г		П	Г		П	г		П	П		П	г		П	П	П	Г
5.0-35.4 50s																													4
Vitte <35.0 s40s					II.	-10		00		3.5	0	Ш			Ų.	Ш	U	4	11,	Ш		G	9	3.1		Ŧ.U			Г
lood Pressure Standing)	\overline{Z}	/			7			/		\overline{Z}	$\overline{}$	7	/		7	/	7	7		\overline{Z}	\overline{Z}	7		7	7	\overline{Z}	\overline{Z}	$\overline{}$	/
lood Pressure ying)												/																	/
espiratory Rate	Г											Г						Г											Π
evel of onsciousness	Г																												,

Prompts for frequency of monitoring

Prompts to identify
when to notify a doctor
who will be able to
advise on whether to
continue treatment

#Alert, #SCALATION REQUIREMENT

U=Unresponsive)

Urgent medical team notification required if any of the following observed:

Temperature > 38° C Pulse > 100 bpm Postural drop > 30 mmHg Respiratory Rate < 8 or > 22 breaths/minut Or patient is unresponsive

Dose orders

Clozapine Dose Orders

Λ

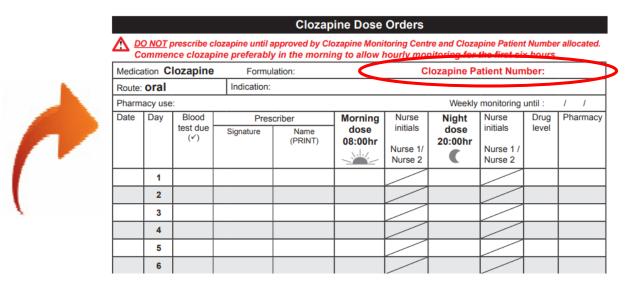
<u>DO NOT</u> prescribe clozapine until approved by Clozapine Monitoring Centre and Clozapine Patient Number allocated. Commence clozapine preferably in the morning to allow hourly monitoring for the first six hours.

Medica	tion C	lozapine	Formu	lation:		С	lozapine Pa	atient Nun	nber:	
Route:	oral		Indication:							
Pharma	acy use	:					Weekly	monitoring	until :	1 1
Date	Day	Blood	Pres	criber	Morning	Nurse	Night	Nurse	Drug	Pharmacy
		test due (✓)	Signature	Name (PRINT)	08:00hr	Nurse 1/ Nurse 2	dose 20:00hr	initials Nurse 1 / Nurse 2	level	
	1									
	2									
	3									
	4									
	5									
	6									

Document:

- Formulation (suspension / tablets)
- ✓ Clozapine Patient Number
- Indication
- ✓ Weekly monitoring until: / /

Dose orders



Doses **ONLY** to be prescribed when **approved by clozapine monitoring centre** and **clozapine patient number allocated**

Clearly document:

- Date when medication started (Chart can accommodate 28 days)
- ✓ Prescriber name (to be printed) and signature
- ✓ Dose morning (8:00) and/or night (20:00). Commence clozapine in the morning and avoid weekends
- ✓ Each nurse to double-sign each individual dose indicating dose checked and administered
- ✓ Drug level
- Pharmacy To identify medication chart has been reviewed by pharmacist

Clozapine – Dosing Regimen

Cautious titration and divided dosage are necessary to minimise adverse events (e.g. hypotension, seizures, sedation...)

Quick reference for the suggested starting regimen for clozapine based on the (Maudsley Prescribing Guidelines)

This is **ONLY** a guide and dose titration should be individualised

Clozapine Dose Titration Schedule

This table serves as a guide only and dose titration should be individualised – refer to treating psychiatrist. Patients > 65 years of age may require a slower dose increase titration regimen.

Titration beyond 200mg/day: If well tolerated, the daily dose may be increased slowly in increments of 25-50mg (maximum 100mg/week).

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Morning	12.5mg	25mg	25mg	25mg	25mg	25mg	25mg	25mg	50mg	50mg	50mg	50mg	50mg	50mg
Evening	$>\!\!<$	> <	$>\!\!<$	25mg	25mg	50mg	75mg	100mg	100mg	100mg	125mg	125mg	125mg	150mg

Monitoring Checklist

Complete all baseline measurements <u>not more than 10 days</u> of commencing clozapine. Date and document or $\overline{\square}$ tick the corresponding boxes

00	d group		ight	m	Smoking	status: Sr	noker No	n Smoker	The following pre-clozapine bas	enne measurements
	Intervals	Pre-cloza baseline	pine	Day 7	Day 14	Day 21	Day 28	Minimum ongoing monitoring	must be completed within 10 d	lays prior to commencing
		Date	Results	Date:	Date:	Date:	Date:	monitoring	•	by blief to commoneing
	Dietician review		Performed					Annually	clozapine therapy:	
	Weight		kg					Weekly first 18	17	
lician	Waist circumference		cm					weeks – then every 28 days		
de	BMI weight (kg) / height (m²)							Inpatients:	□ Blood group	□ Troponin/ CK-MB
	Constipation monitoring	Daily	checks	or 4 wee	ks: Use l	owel cha	art	minimum weekly Outpatients: check bowel	,	•
								habits at each review	□ Full physical examination	□ Echocardiogram (ECG)
	Full physical exam		Performed	_				Annually	' '	O (,
	Full Blood Count White Blood Count		Performed x10 VL	Performed x10 ¹ /L	Performed x10°/L	Performed	Performed	Weekly first 18 weeks - then every 28 days	□ Pregnancy test (if applicable)	□ Full blood Count
	Neutrophils Absolute		x10VL	x10VL	x101/L	x10%L	x10%L			
	Eosinophils Absolute		×10%L	×10%	×10º/L	×10%L	x10%L	1		
	Liver function test		Performed					6 monthly	The following pre-clozapine bas	eline measurements are also
	Urea & Electrolytes		Performed					6 monthly	The following pre clozapine bas	chile measurements are also
P. Contract	Fasting plasma glucose Total cholesterol		mmol/L						recommended:	
ened D	(fasting)		mmol/L					At 3 months, 6 months, then		
000	LDL (fasting) HDL (fasting)		Momm					6 monthly		
0	Triglycerides (fasting)		mmol/L						□ Smoking status	□ Liver Function Test
	Troponin							As clinically	U Silloking Status	- Liver i dilottori rest
	C-Reactive Protein		nanograms/L	nanograms/L	nanograms/L	nanograms/L	nanograms/L	indicated thereafter	□ Weight	□ Urea & Electrolyte
	(CRP) ECG		mg/L	mg/L	mg/L	mg/L	mg/L	Weekly for first 4		•
	(QT interval)							weeks, then as clinically indicated	□ Waist	□ Fasting plasma glucose
	Cardiac echocardiogram							At 3 months, then 1, 2, 5 yrs	⊓ BMI	. .
nesi	Beta HCG (female) e are suggested guidelines	only and do	not replace the	need for clinic	al discretion. Re	fer to the treating	ng psychiatrist f	When needed or individual	LI DIVII	□ Blood lipid
	toring requirements	, 310 00					-0		□ Dietician review	

Monitoring Checklist

Bloo	d group	Hei	ight	m	Smoking	status: Sn	noker 🗌 Nor	Smoker	
	Intervals	Pre-clozar baseline	pine	Day 7	Day 14	Day 21	Day 28	Minimum ongoing	
	Intervals	Date Results		Date:	Date:	Date:	Date:	monitoring	
m	Dietician review		Performed					Annually	
	Weight		kg						
E C	Waist circumference		cm					Weekly first 18 weeks – then every 28 days	
be completed by doctor / nurse / defician	BMI weight (kg) / height (m²)					— -		, , , , , , , ,	
о ое оошие	Constipation monitoring	Daily	checks	for 4 wee	ks: Use t	owel cha	ert	Inpatients: minimum weekly Outpatients: check bowel habits at each review	
	Full physical exam		Performed					Annually	
	Full Blood Count		Performed	Performed	Performed	Performed	Performed	Weekly first 18 weeks - then	
	White Blood Count		x10 ⁸ /L	x10 ¹ /L	x10°/L	x10°/L	x10º/L	every 28 days	
	Neutrophils Absolute		x10%L	x10VL	x10º/L	x10º/L	x10%L		
	Eosinophils Absolute		x10VL	x10VL	x10º/L	x10º/L	x10%L		
	Liver function test		Performed					6 monthly	
	Urea & Electrolytes		Performed					6 monthly	
odor	Fasting plasma glucose		mmol/L					4-	
completed by doctor	Total cholesterol (fasting)		mmoVL					At 3 months,	
mplea	LDL (fasting)		mmol/L					6 months, then 6 monthly	
8	HDL (fasting)		mmol/L						
٥	Triglycerides (fasting)		mmoVL						
	Troponin		nanograms/L	nanograms/L	nanograms/L	nanograms/L	nanograms/L	As clinically indicated	
	C-Reactive Protein (CRP)		mg/L	mg/L	mg/L	mg/L	mg/L	thereafter	
	ECG (QT interval)							Weekly for first 4 weeks, then as clinically indicate	
	Cardiac echocardiogram							At 3 months, then 1, 2, 5 yrs	
	Beta HCG (female)							When needed	

Space to document measurements for 28 days if required

Prompts for frequency of monitoring beyond first month of therapy.

Haematological Monitoring

- Regular full blood counts are required as clozapine can cause agranulocytosis
- WBC and Neutrophil counts must be performed :
 - -At least weekly for the first 18 weeks of therapy
 - -At least every four weeks (28 days) after the first 18 weeks of therapy
- Blood results are classified as green, amber or red

	Clozapine Bl	ood Results Monitoring System	Recommended Action
	Green Range	WBC greater than 3.5 x 10 ⁹ /L AND Neutrophils greater than 2.0 x 10 ⁹ /L	Continue clozapine therapy
	Amber Range	WBC 3.0 - 3.5 x 10 ⁹ /L AND/OR Neutrophils 1.5 - 2.0 x 10 ⁹ /L	Continue clozapine therapy with twice-weekly blood tests until return to "green" range
2	Red Range	WBC less than 3.0 x 10 ⁹ /L AND/OR Neutrophils less than 1.5 x 10 ⁹ /L	Stop clozapine therapy immediately. Contact haematologist and Clozapine Monitoring Centre





Haematological Monitoring

POST-THERAPY BLOOD TESTING:

WEEKLY monitoring

Patients on weekly monitoring at the time of discontinuation MUST continue to have 4 weeks of weekly monitoring

MONTHLY monitoring

Patients on monthly monitoring at the time of discontinuation MUST have one further test one month after discontinuation

Recommendations for recommencing therapy after interruption

Recommencing Therapy after Interruption

Dosing recommendations if clozapine dose is missed for > 48 hours

- · Obtain psychiatric review prior to recommencing clozapine
- Recommence at 12.5mg once or twice daily on the first day. Refer to what side effects the patient had previously
 when starting clozapine. The rate of re-titration can be adjusted to take into account emergent side effects and
 period of interruption
- This is a guide only for further dosing options refer to treating psychiatrist.

Suggested Action:

If clozapine is missed for > 48 hours, recommence at 12.5mg once or twice daily on the first day.

Refer to what side effects the patient had previously when starting clozapine. The rate of re-titration can be adjusted to take into account emergent side effects and period of interruption. For further dose options refer to the patient's treating psychiatrist.



Recommendations for Missed Doses

	Blood Test Monitoring after Interruption of Therapy								
Monitoring frequency	Clozapine missed for < 72 hours	Clozapine missed > 72 hours but less than 4 weeks	Clozapine missed > 4 weeks						
Weekly	No change in monitoring	Monitor weekly for at least 6 weeks or for as long as necessary to achieve a total of 18 weeks of weekly monitoring	Recommence as for a new patient						
Monthly		Monitor weekly for 6 weeks then continue with monthly monitoring if no problems detected							

Different monitoring frequency is required when clozapine is missed for:

- < 72 hours
- > 72 hours but less than 4 weeks
- > 4 weeks



Side-effects

Side effects	Associated with Clozapine Therapy	Modified from the Maudsley Prescribing Guidelines 14th ed 2021
Side effect	Signs and symptoms / Onset	Recommended Action
Neutropenia / agranulocytosis	WBC < 3.0 x 10°/L or Neutrophils < 1.5 x 10°/L. Flu-like symptoms such as sore throat & fever. (First 18 weeks – but may occur at any time)	Contact doctor. Withhold clozapine. Contact haematologist at Clozapine Monitoring Centre.
Myocarditis / cardiomyopathy	Fast or irregular heartbeat at rest with rapid breathing, dyspnoea, hypotension, raised jugular venous pressure, fatigue, infective symptoms (including gastrointestinal, urinary, and/or respiratory), chest pain or fever. Cardiomyopathy may occur at any time. Myocarditis – within 4 weeks of starting)	Withhold Clozapine. Repeat ECG and echocardiogram. Check C-Reactive Protein (CRP) and troponin. Refer to cardiologist.
Fever	> 38° C (First 4 weeks)	Contact doctor. Reduce rate of dose titration of clozapine. Check WBC, neutrophils, troponin and CRP. Physical examination for signs of infection. Consider ECG, Echocardiogram. Give paracetamol and notify doctor to exclude agranulocytosis / myocarditis.
Seizures	Increases with high doses, rapid dose titration, concurrent use of drugs that lower seizure threshold and preexisting seizure disorders and concurrent illness. (May occur at any time)	Medical emergency, manage seizure. Withhold clozapine for one day and restart at half the dose. Consider prophylactic antiepileptic. Risk of seizures increases with higher serum clozapine levels; check serum clozapine levels.
Hypersalivation	Excessive drooling – Very troublesome at night. (First few months)	Contact doctor. Check with pharmacist for pharmacological options.
Constipation	Less frequent bowel motions, hard stools, abdominal bloating, cramping or pain, decreased appetite or fatigue. (Usually persists) Severe Clozapine Induced Gastrointestinal Hypomotility (CIGH) can be fatal.	Contact doctor. Recommend increased fluid intake and exercise. Consider pre-emptive laxatives for al patients. Review contributing medicines and consider dose reduction. Treat CIGH aggressively with laxatives and consider cessation of clozapine if treatment fails. Avoid bulk forming laxatives.
Nocturnal enuresis	Loss of bladder control, especially at night. (May occur at any time)	Contact doctor. Avoid fluids after 7pm. Check males for other causes. Continence referral. Check with pharmacist for pharmacological options.
Weight gain	This may occur early in treatment and can be significant	Dietary and lifestyle counselling before weight gain occurs. Ongoing monitoring and support.

of antipsychotic therapy be avoided where possible as this increases the patient's risk of side effects

- This is **NOT** a complete list of clozapine related side effects
- Signs and symptoms of side effects
- To increase awareness of possible side effects
- Prompts for nurses to contact doctor if any of the side effects are present

Forms required for patient registration before initiation

- Before initiating clozapine, contact clinical pharmacist
- Forms that are still required to be completed:

»Clozapine Registration for New Patients Referral Form (For registration of patient: Contact clinical pharmacist)

»Clozapine Notification Form /Consent Form (Patient information)

Summary

- Baseline monitoring <u>MUST</u> be performed no more than
 10 days before commencing treatment
- Clozapine <u>MUST</u> only be prescribed when patient is allocated a clozapine number
- Current Clozapine Initiation Chart to be kept with other medication charts
- Commence clozapine in the morning avoid weekends (preferable to start early in the week)

Summary

- Printed resources available from pharmacy:
 - » Clozapine Registration for New Patients Referral Form
 - » Clozapine Counselling Points
 - » Clozapine Consumer Medication Information
- Please forward any comments on the Clozapine Chart to your clinical pharmacist or
 - DoH.MedicinesandTechnologyUnit@health.wa.gov.au