

## Safety Guidance - Clozapine on Admission to an Acute Hospital Ward

### CONTACT ACUTE PSYCHIATRY LIASION TO ENSURE THAT THE TEAM IS AWARE OF THE ADMISSION

The purpose of this safety guidance is to highlight key issues to be considered when patients who are taking clozapine are admitted to an Acute Hospital. Clozapine is a high risk drug used for the management of schizophrenia in patients who are unresponsive to, or intolerant of, conventional antipsychotic drugs. It may also be used for psychoses in patients with Parkinson’s disease. Clozapine requires regular monitoring to ensure it remains a safe and effective treatment, including monitoring to identify any constipation and to monitor the patient’s smoking status. **If safe to do so, it is important to promptly prescribe and ensure a supply of clozapine is available for administration as, if more than 2 days of treatment are missed, the patient will require re-titration.**

### FOR ALL PATIENTS ADMITTED TO AN ACUTE HOSPITAL WARD

#### ESTABLISH IF THE PATIENT IS TAKING CLOZAPINE

- Clozapine treatment may not be immediately obvious on admission. Ask the patient if they receive any treatment from other hospitals or clinics other than their GP. **Note - clozapine may not be on the patient’s GP medication list as it will be prescribed by their mental health trust.**
- Clozapine may also be known as **Clozaril®**, **Denzapine®** or **Zaponex®**. The preferred brand in Tees Esk & Wear Valley (TEWV) patients is Clozaril®. If the patient has difficulty swallowing tablets they will be prescribed Denzapine® liquid or Zaponex® orodispersible tablets. Please discuss with TEWV before switching formulation.

### FOR PATIENTS ADMITTED TO AN ACUTE HOSPITAL WARD TAKING CLOZAPINE BEFORE ADMISSION

#### STOP – CHECK COMPLIANCE

- **Check patient compliance with Clozapine.** If a patient has missed clozapine for more than 48 hours they will require re-titration and **MUST NOT** be prescribed clozapine at their previous dose.
- **DO NOT re-commence clozapine after a treatment break of 48 hours or more without specialist advice and guidance from TEWV.**

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**ACT - CONTACT TEWV**

- **Contact TEWV immediately** to inform them of the patient’s admission and again prior to discharge. Details of patient’s compliance and whether they have taken a supply into hospital with them will be needed by TEWV. The patient will need to have their next blood test arranged and communicated prior to discharge.
- For patients outside TEWV contact the patient’s local mental health trust for information.
- TEWV will confirm the dose, whether bloods are needed immediately prior to any supply, and how that supply can be arranged (details of how to contact TEWV are listed at the end of the document).
- **Clozapine is NOT usually stocked in Acute Hospitals** – the patient’s own drug should be used. TEWV will be able to provide further supplies if appropriate. If the patient transfers to a different ward, please ensure that the clozapine supply moves with them. In an unplanned admission if the patient does not bring in a supply contact TEWV immediately for advice.
- There are processes in place (Memorandum of understanding) to allow dispensing of clozapine by an alternative Trust -usually in the case of patients on holiday. TEWV pharmacy can advise if this is thought applicable

**CHECK - FULL BLOOD COUNT (FBC) AND SMOKING STATUS**

- **Check full blood count (FBC)** - especially white blood cell (WBC) and neutrophils (ANC) as clozapine can cause agranulocytosis as a significant side effect. This result may be needed to allow TEWV to dispense clozapine. If at any point during admission WBC count is found to be less than  $3.0 \times 10^9/L$  and neutrophils less than  $1.5 \times 10^9/L$  contact TEWV immediately for advice.
- Check if patient is a current smoker – **stopping smoking can increase clozapine serum levels significantly.**
- If the patient is a smoker request advice from TEWV as to whether their dose should be lowered. **DO NOT amend dose without advice from TEWV. See additional information below regarding monitoring.**

**PRESCRIBING AND DOCUMENTING**

**Prescribe**

- Clozapine does not require a consultant signature for prescribing within an Acute Hospital, however it should be treated as a high risk medication.
- For patients who are undergoing surgery please refer to local guidelines for information on the management of clozapine before and after surgery.

**Documentation**

Information specifying the dose, brand and formulation must be:

- Recorded in the patient’s notes and prescribed on ePMA/paper kardex for in-patient administration. This information must also be included in the discharge letter.
- Included in the medicines reconciliation / medication history section of the medical notes.

**MONITOR – FOR CONSTIPATION**

- Monitor via bowel chart and treat (where appropriate) for constipation. Clozapine has been known to cause problems with the bowel ranging from constipation (which is very common), to intestinal obstruction, faecal impaction, and paralytic ileus (which are very rare but significant). On a few occasions, cases have been fatal [MHRA 2017](#).

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## ADDITIONAL INFORMATION

### Monitoring of clozapine levels

- Clozapine levels are not routinely monitored by non-specialist centres and there is no evidence to support an annual blood level check.
- Monitoring blood clozapine levels for toxicity is advised (MHRA 2020) in certain clinical situations such as:
  - ✓ A patient stops smoking or switches to an e-cigarette.
  - ✓ Concomitant medicines may interact to increase blood clozapine levels.
  - ✓ A patient has pneumonia or other serious infection.
  - ✓ Poor (reduced) clozapine metabolism is suspected.
  - ✓ Toxicity is suspected.

Maintain regular contact with TEWV. TEWV will provide the assay sample kit via the appropriate liaison team. The clozapine monitoring services provide TEWV with the kits. The main brand prescribed is Clozaril but there are some patients on other brands. The brand determines the laboratory used. Details below for reference. The acute trust would not normally be required to contact the labs.

Clozaril – Kings Path

Denzapine – ASI - St Georges – Red envelope

Zaponex – Magna labs – Herefordshire

Samples should be taken in the morning immediately BEFORE the morning dose of clozapine (if clozapine is taken morning and night) or 10-12 hours post dose (if taken once a day) as the timing of the sample is important. Blood should be taken in a standard EDTA tube and the sample posted to the external laboratory. Please note the timing of the sample after the last dose. Samples are only accurate if a patient has been taking a dose for 2-3 days minimum. Results may take up to a week to be reported and a notification is sent to nominated staff in TEWV alongside the clinician recorded on the clozapine database as being the patient's usual responsible clinician.

### Interactions with other medicine products

- Review any drugs that increase the serum concentration of clozapine or drugs that may cause/contribute to agranulocytosis. **Severe interactions noted with** - carbamazepine, ciprofloxacin, combined hormonal contraceptives, erythromycin, fluvoxamine, levodopa, rifampicin and ritonavir.

**Note: this list is not exhaustive; please see current BNF via [www.medicinescomplete.com](http://www.medicinescomplete.com) for a full list of clozapine interactions. Further information may be found on [www.medicines.org.uk](http://www.medicines.org.uk).**

## REMEMBER

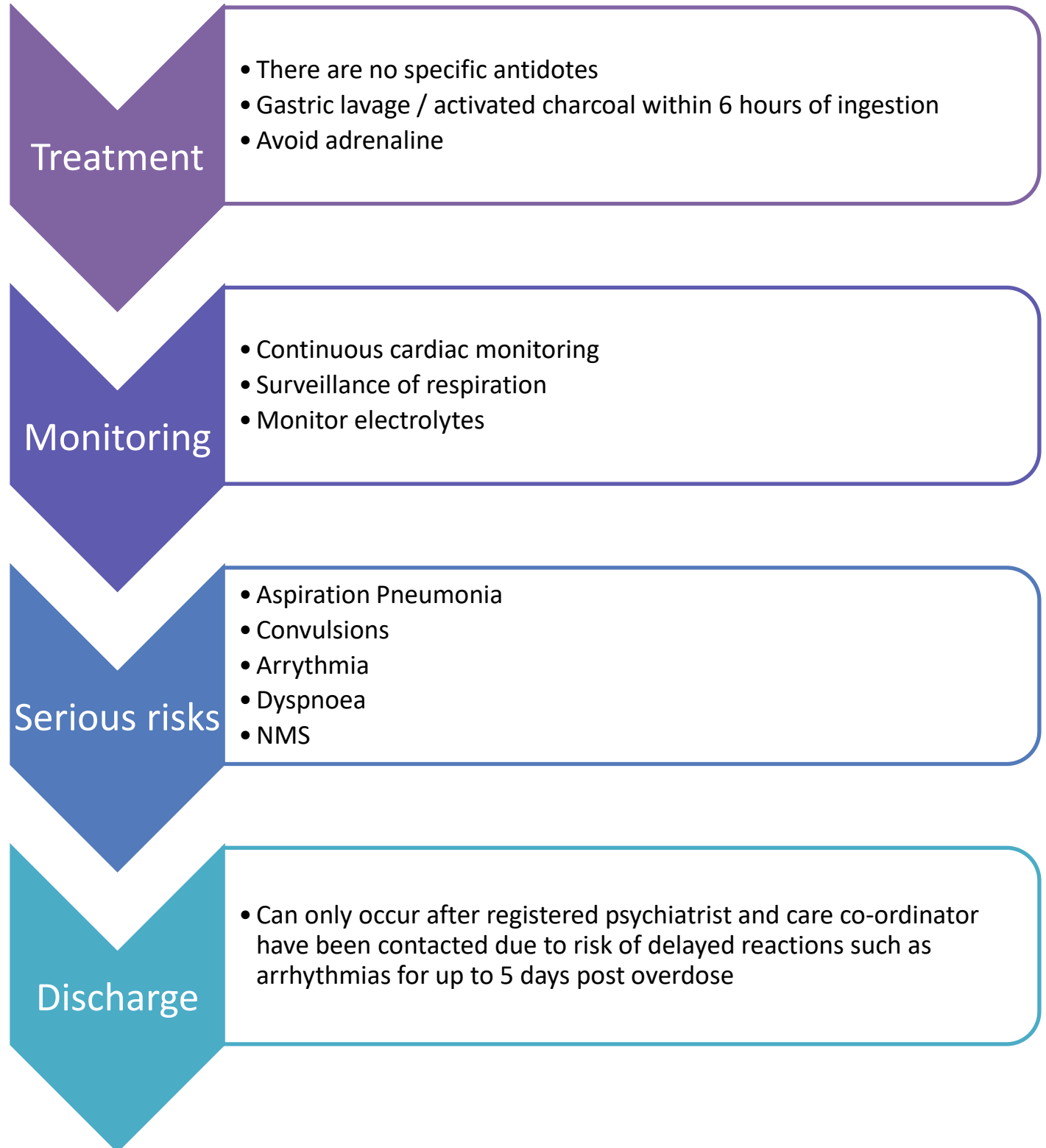
**CONTACT TEWV IMMEDIATELY IF A PATIENT IS IDENTIFIED AS BEING PRESCRIBED CLOZAPINE AND AGAIN AT DISCHARGE.** Durham pharmacy office – 0191 4415775, Darlington pharmacy office – 01325 552105, Roseberry Park pharmacy office – 01642 838360, York pharmacy office - 0190 4717790. For other areas, acute hospital liaison can be contacted via the Trust Switchboard. The TEWV on call pharmacist can be contacted via the hospital switchboard out of hours.

**TEWV Switchboard: 01642 838050.**

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## Appendix 1: Managing Clozapine Overdose

The information below is not intended to be a definitive treatment strategy, but a suggested approach for clinicians. It is based on previous successful experience. Each case should, of course, be considered individually. This information is provided for healthcare professionals and should not be used as a patient information leaflet. If notified of a potential overdose in the community, the importance of attending A and E should be reiterated and followed up to ensure the patient has been reviewed.



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Clozapine overdose	Signs and Symptoms	Treatment
<p><i>The Summary of Product Characteristics (SmPC) for clozapine<sup>1</sup> states:</i></p> <p><i>In cases of acute intentional or accidental clozapine overdose for which information on the outcome is available, mortality to date is about 12%. Most of the fatalities were associated with cardiac failure or pneumonia caused by aspiration and occurred at doses above 2000 mg.</i></p> <p>Seizures have been reported to occur in patients with plasma clozapine levels above 1mg/L following overdose.<sup>4</sup></p>	<p>All of the side-effects associated with clozapine at therapeutic dose may be seen following overdose except those seen with long-term therapy only, e.g. constipation, weight gain and agranulocytosis<sup>3</sup>. In addition, altered respiratory function and aspiration may be observed and these are seldom seen at therapeutic doses. Pulmonary oedema is not a recognised side-effect but has occurred following overdose<sup>3</sup></p> <p>Drowsiness, lethargy, areflexia, coma, confusion, hallucinations, agitation, delirium, extrapyramidal symptoms, hyperreflexia, convulsions; hypersalivation, mydriasis, blurred vision, thermolability; hypotension, collapse, tachycardia, cardiac arrhythmias; aspiration pneumonia, dyspnoea, respiratory depression or failure.</p> <p>There is a risk of neuroleptic malignant syndrome.<sup>5</sup></p> <p><b>Due to the high risk of cardiac arrhythmias (including late occurrence or recurrence), consider seeking advice from cardiology specialists if clinically indicated.</b></p>	<ul style="list-style-type: none"> <li>• Consult Toxbase.</li> <li>• There are no specific antidotes for clozapine.</li> <li>• Gastric lavage and/or administration of activated charcoal within the first 6 hours after the ingestion of the drug. Peritoneal dialysis and haemodialysis are unlikely to be effective. Symptomatic treatment under continuous cardiac monitoring, surveillance of respiration, monitoring of electrolytes and acid-base balance.</li> <li>• The use of adrenaline should be avoided in the treatment of hypotension because of the possibility of a 'reverse adrenaline' effect.</li> <li>• <b>Close medical supervision is necessary for at least 5 days because of the possibility of delayed reactions, such as cardiac arrhythmias.</b></li> <li>• <b>Any decision to discharge from medical care before this should be carried out by a consultant.</b></li> <li>• <b>Work with the liaison psychiatry team and care co-ordinator prior to discharge for help and advice, and to arrange ongoing treatment and follow up.</b></li> </ul>

**References**

1. Clozapine Summary of Product Characteristics <https://www.medicines.org.uk/emc/product/4411>
  2. Dev VJ, Krupp P. Adverse Event Profile and Safety of Clozapine. Rev Contemp Pharmacother 1995; 6: 197-208.
  3. Le Blaye I et al. Acute Overdosage with Clozapine: a Review of the Available Clinical Experience. Pharm Med 1992; 6: 169-78.
  4. Taylor D and Duncan D. The Use of Clozapine Plasma Levels in Optimising therapy. Psych Bulletin 1995; 19: 753-5.
- This information was developed from the 2018 Mylan information leaflet CLZ-2018-0126
5. Toxbase- clozapine. [www.toxbase.org](http://www.toxbase.org) accessed 30 Sept 2022

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