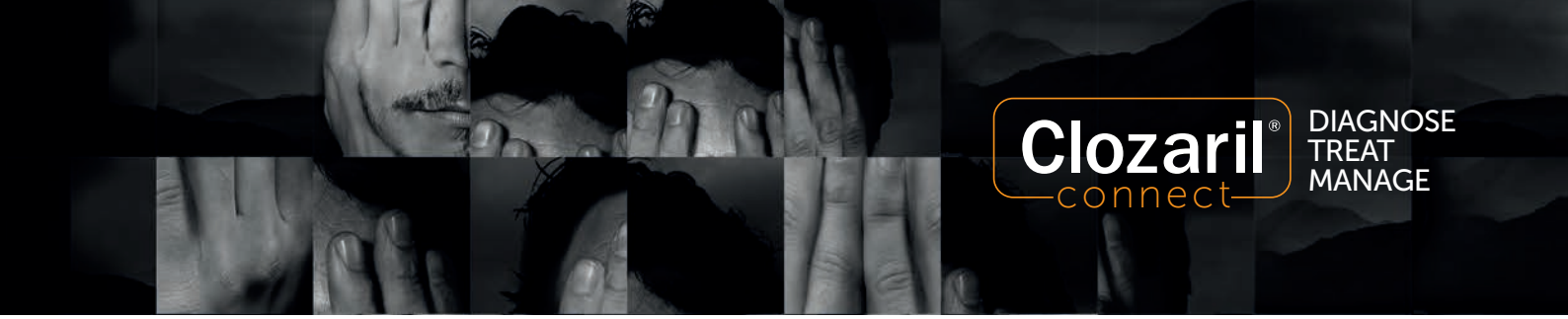



# Discontinuing clozapine treatment

**The information in this document is not intended as a definitive treatment strategy, but as 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.**

The Summary of Product Characteristics (SmPC) for Clozaril® (clozapine)[1,2] states:

In the event of planned termination of Clozaril® therapy, a gradual reduction in dose over a 1 to 2-week period is recommended. If abrupt discontinuation is necessary, the patient should be carefully observed for the occurrence of withdrawal reactions.

In patients with Parkinson's Disease a gradual reduction in dose by steps of 12.5mg over a period of at least one week (preferably two) is recommended.

Treatment must be discontinued immediately in the event of neutropenia or agranulocytosis. In this situation, careful psychiatric monitoring of the patient is essential since symptoms may recur quickly.

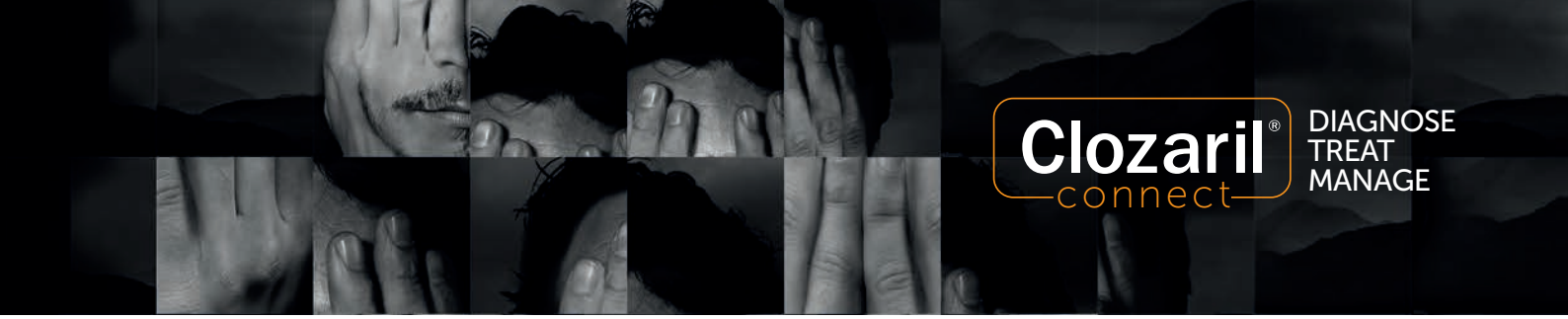
Before discontinuing clozapine treatment, it may be worth considering whether the following points are relevant:

- Inadequate treatment duration – some patients take up to 12 months to respond[3]
- Inadequate dose – some patients require 900mg/day. Plasma clozapine concentrations provide guidance on required dose – a threshold of 0.35mg/L is generally accepted for good therapeutic response[4]
- Poor compliance – with medication or blood tests
- Side-effects – many side-effects can be managed successfully, please contact your local clinical pharmacist for advice

## How to discontinue Clozaril®

- Clozapine should be discontinued if the patient has:
  - blood dyscrasias
  - intolerable or serious side-effects (for example, myocarditis)
  - true failure to respond
- Discontinuation of clozapine for reasons other than a red alert or other serious side-effect should be done gradually, over at least a 1-2 week period, to minimise the risk of withdrawal effects[1,2]
- In patients with Parkinson's Disease a gradual reduction in dose by steps of 12.5 mg over a period of at least one week (preferably two) is recommended[1,2]
- The CPMS should be notified
- Follow-up samples should be taken for 4 weeks after stopping clozapine at the frequency at which they are currently being monitored, for example, if weekly monitored, sample every week for 4 weeks after stopping clozapine; if 4-weekly monitored, sample once more 4 weeks after stopping.

In patients who stop clozapine due to a red alert, blood monitoring will be continued until haematological recovery occurs. CPMS will advise on this.



Clozaril® connect

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## Breaks in treatment

Patients who have been on Clozaril® for more than 18 weeks and have had their treatment interrupted for more than 3 days but less than 4 weeks should have their white blood cell (WBC) count and absolute neutrophil count (ANC) monitored weekly for an additional 6 weeks. Provided that the blood count remains stable the patient can return to their normal monitoring frequency at the end of this period. If Clozaril® treatment has been interrupted for 4 weeks or longer, weekly monitoring is required for the next 18 weeks of treatment. Any patient who has a break in treatment of more than 48 hours will require retitration.

Please contact CPMS for further information regarding breaks in treatment.

## Sudden discontinuation of Clozaril®

When a patient has a red alert or other serious side-effect it is essential to stop clozapine immediately.

This sudden cessation of treatment can lead to physical and mental withdrawal effects which may occur within 2-3 days and usually within the first 2 weeks.[5] Patients may experience a rapid deterioration in their mental state with rebound psychosis.[6] In addition, abrupt withdrawal of clozapine has been associated with symptoms such as nausea, vomiting, diarrhoea, headache and agitation[6] and it has been suggested that these are a result of cholinergic rebound since clozapine has strong anticholinergic action.[5]

If abrupt discontinuation is necessary the patient should be observed carefully for return of psychotic symptoms, which may recur quickly and withdrawal symptoms related to cholinergic rebound.

The SPC for Clozaril® lists cholinergic syndrome (after abrupt withdrawal of Clozaril®) as an adverse reaction which has a frequency of 'not known'.

In cases where clozapine has been stopped for a confirmed red alert, the patient must not be re-exposed to clozapine. Prescribers are encouraged to keep a record of all patients' blood results and to take any steps necessary to prevent the patient being accidentally rechallenged in the future.[1,2]


**References**

1. Clozaril (clozapine) Summary of Product Characteristics (online). Mylan Products Ltd. <http://www.medicines.org.uk/emc/> (Accessed on 09/05/2018).
2. Clozaril (clozapine) Summary of Product Characteristics (online). BGP Products Ireland Limited. <http://www.medicines.ie/> (Accessed on 09/05/2018).
3. Meltzer HY. Dimensions of Outcome with Clozapine. *Br J Psychiatry* 1992; **160**: 46-53.
4. Taylor D and Duncan D. The use of clozapine plasma levels in optimising therapy. *Psychiatric Bulletin* 1995; **19**: 753-5.
5. Verghese C *et al.* Clozapine Withdrawal Effects and Receptor Profiles of Typical and Atypical Neuroleptics. *Biological Psychiatry* 1996; **39**: 135-138.
6. Shiovitz TM *et al.* Cholinergic Rebound and Rapid Onset Psychosis Following Abrupt Clozapine Withdrawal. *Schizophr Bull* 1996; **22**: 591-5.




Clozaril® (clozapine)

CLOZARIL® Clozapine PATIENT MONITORING SERVICE


NON 2018 0776 Date of preparation: May 2018


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