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Clozaril® and compliance

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.

Background

Compliance may be defined as the extent to which a person's behaviour coincides with the medical advice he/she has received.[1] Non-compliance is an issue in general medicine and psychiatry and is particularly likely when the aim of treatment is to prevent symptom recurrence or illness relapse. The rate of non-compliance in schizophrenia has been estimated at 33%[2] although some studies give figures as high as 80% for non-compliance with antipsychotic medication.[3]

Compliance with medication may be total, partial, nil or erratic, and non-compliance in schizophrenia may be refusal of treatment, discontinuation of treatment or erratic taking of medication. The reasons for non-compliance in patients with schizophrenia vary and may include depression/lack of motivation, side-effects, forgetfulness, comorbid substance abuse and lack of insight or denial of illness.[4] Severity of illness may also be significant since studies have found that patients with more severe psychopathology are less likely to comply with treatment.[5]

Non-compliance can be detected by several means but it is difficult to get an accurate picture. Patient self-reporting is often unreliable since patients may deliberately give false information. Pill counting may be used but the patient may have the correct number of pills left when they have not taken the medication, and biological analysis such as plasma monitoring may also be of limited use as the patient may be compliant only in the period shortly before the blood test.[6]

For the patient, the direct consequence of non-compliance is that they may relapse and experience return of symptoms, which may in turn lead to hospital re-admission. Indirect costs of relapse include personal suffering, high morbidity, mortality and an overall reduction in quality of life for the patient and their family members.[6] From a healthcare professional's perspective, the consequences of lack of compliance may include all the costs of a patient deteriorating, for example, re-hospitalisation, additional clinic and staff resources and the cost of additional drugs.

Until all the barriers to compliance are apparent it is difficult to change the patient's behaviour. However, one of the most important positive factors is the existence of a good relationship between the patient and the healthcare professional and establishing rapport and trust is the first step to changing the patient's attitude to their medication.

Clozapine and compliance rates

It has been shown in several studies that patients stabilized on clozapine are largely content with their treatment and as a result adherence to treatment is good.[7,8]

In a survey completed by 570 patients, the majority (62.1%) rated clozapine as much better than their previous treatment, with only 2.7% rating it as slightly or much worse.[7] More importantly from a compliance perspective, 87% of patients in the same study felt that the advantages of clozapine outweighed the disadvantages and 88% of patients stated that they preferred to stay on clozapine rather than change to a different drug.

Compliance with clozapine has been shown to be better than with chlorpromazine or with haloperidol. In a comparative study with chlorpromazine, Claghorn *et al* (1987) showed that psychotic inpatients treated with clozapine had fewer discontinuations due to side-effects.[9] Rosenheck *et al* (2000) also demonstrated greater continuation with clozapine when compared with haloperidol.[10]

Use of clozapine plasma levels to detect non-compliance

Checking plasma clozapine and norclozapine levels and the clozapine:norclozapine ratio may help in detecting recent clozapine non-compliance. The assay should be a trough sample taken either immediately before a normal morning dose or in the morning after an evening dose. The clozapine:norclozapine ratio should normally be in the range of 0.5-2.5. A low clozapine level and a ratio less than 0.5 may be suggestive of non-compliance within the last 24 hours.[11]

Suggestions to improve compliance with clozapine

To improve compliance, effort should be channelled into supporting patients through the early stages of treatment until the efficacy becomes apparent, early side-effects diminish and a blood taking routine is established.

Assess the patient's attitude to therapy to establish the barriers to compliance and develop an individual care programme including an action plan to be used if symptoms start to return. Make sure that the patient knows who to contact for further advice or in case of emergency. Discuss any misconceptions that the patient may have.

Stress the benefits of treatment and check the patient is aware of the relationship between non-compliance and relapse. Relate being well to staying out of hospital. Discuss the patient's expectations and compare symptoms to those they had six months ago.

Check that the dose has been optimised and educate the patient on the expected time to response. Treat anxiety or depression where appropriate. Ensure that the current treatment regimen is simple and that explicit written instructions are provided. Use monotherapy wherever possible to reduce the complexity of treatment and reduce the likelihood of interactions. Compliance aids such as monitored dosage systems (MDS) may be useful for some patients. Other strategies include keeping the medication in a visually prominent place, or phone calls or visits to remind patients to take their medication.

Assess the clinic routine and arrangements for blood monitoring and dispensing. If distance to the clinic or waiting times are a problem, consider whether blood sampling at a GP surgery is possible.

Create a relationship where the patient feels that they can report side-effects and assess the impact on the patient. For dose-related side-effects consider reducing or splitting the dose. Check plasma levels where appropriate.

Consider the patient's level of cognitive function since cognitive impairment may reduce the ability to remember to take medication. Provide support and education at a correct level for the patient. Check the patient's support network and provide information and education for carers if necessary.

One strategy which has been effective in improving compliance is compliance therapy, where cognitive-behavioural therapy and motivational interviewing are used to demonstrate the risks and benefits of accepting antipsychotic treatment. Kemp *et al* (1996) compared this with non-specific supportive counselling and found that patients who received compliance therapy had significantly improved compliance from baseline.[12] Another study demonstrated that compliance therapy was more cost-effective than non-specific counselling.[13]

Specific factors affecting compliance with clozapine

Time to first response

Studies have shown up to 30% of patients will show a response by six weeks and 60% will have shown a response by twelve months.[14] Patients should be reassured that it may take some time for clozapine to be fully effective. Looking back with the patient over the course of treatment will enable them to appreciate improvements in functioning and motivate them to carry on until they experience a full effect. The Summary of Product Characteristics (SmPC) for Clozaril® (clozapine) recommends that treatment should be continued for at least six months.[15,16]

Blood monitoring

Patients on clozapine require regular blood monitoring and for the majority of them this will require frequent attendance at an outpatient clinic. Although the primary objective of blood monitoring is to detect neutropenia, it also assures regular contact between the therapy team and the patient, which offers frequent opportunity to assess progress and to allay concerns the patient may have. It also provides an ongoing general health check, helps in the management of side-effects, and enables early detection of patients who may be defaulting from treatment.

Studies have shown that patients generally understand the need for blood monitoring. In a survey of patients taking clozapine, 80% knew why blood tests were needed and 64% felt they were a necessary part of treatment. Less than 2% of patients wanted to stop their therapy due to the blood monitoring.[7] Other studies have found that although patients may object to blood monitoring at the outset, this diminishes over time as they experience the benefits of treatment.[8]

Patients who do not accept the need for blood monitoring easily at the outset may benefit from early referral to the local clozapine clinic, which may help to allay any concerns the patient has and also help the patient to gain confidence from meeting patients established on clozapine.

Side-effects

Clozapine can cause a range of side-effects, many of which diminish over time. The most common side-effects are drowsiness/sedation, dizziness, tachycardia, constipation and hypersalivation. Please refer to the SmPC for Clozaril® for a full list of potential side effects.[15,16] It is suggested to follow a few basic principles to minimise these effects:

- Tailoring therapy – many side-effects, such as hypotension and tachycardia, are dose-related. By starting with a low dose and titrating the dose slowly the effects of these dose-related side-effects can be reduced. In the case of hypotension, giving the largest part of the dose at night can reduce the effect on blood pressure.
- Proactive approach – it is necessary to take a proactive approach if side-effects, such as weight gain and constipation, are to be avoided. Constipation can be a potentially serious side-effect if left untreated and must be taken seriously. Patients should be counselled prior to commencement and given advice on diet, fluid intake and the importance of seeking advice from their doctor if they become constipated. Similarly, by counselling patients on the importance of a healthy diet and exercise, weight gain may be reduced.
- Monitoring – although the only mandatory requirements are monitoring of the white cell and neutrophil counts, many units conduct baseline and routine monitoring of other parameters such as pulse, BP, ECG, U&Es and LFTs. This can facilitate the early detection of adverse events and provides a baseline should problems arise later in therapy.

For further information regarding side-effect management please contact your local clinical pharmacist or CPMS.

Restarting clozapine following a break in therapy

In patients in whom the interval since the last dose of Clozaril® exceeds 2 days, treatment should be re-initiated with 12.5mg given once or twice on the first day. If this dose is well tolerated, it may be possible to titrate the dose to the therapeutic level more quickly than is recommended for initial treatment.[15,16]

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.[15,16]

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Clozaril® (clozapine)

CLOZARIL® Clozapine PATIENT MONITORING SERVICE

VIATRIS

PRESCRIBING INFORMATION
CLOZARIL 25 mg Tablets
CLOZARIL 100 mg Tablets

Please see Summary of Product Characteristics (SmPC) for full information before prescribing Clozaril.
The use of Clozaril is restricted to patients, physicians and nominated pharmacists registered with the Clozaril Patient Monitoring Service (CPMS).
In the UK a white cell count with differential count must be monitored:

- At least weekly for the first 18 weeks of treatment
- At least at 2-week intervals between weeks 18 and 52
- After 1 year of treatment with stable neutrophil counts, patients may be monitored at least at 4 week intervals

Monitoring must continue throughout treatment and for at least 4 weeks after discontinuation.
Blood clozapine level monitoring is advised in situations such as a patient ceases smoking or switches to e-cigarettes, when concomitant medicines may interact to increase clozapine blood levels, where poor clozapine metabolism is suspected, when a patient has pneumonia or other serious infection and in the event of onset of symptoms suggestive of toxicity.
Clozaril is associated with an increased risk of myocarditis and cardiomyopathy. If suspected Clozaril must be stopped immediately and the patient referred to a cardiologist and not re-exposed to Clozaril.

Presentations
Clozaril 25 mg Tablets containing 25 mg clozapine. Clozaril 100 mg Tablets containing 100 mg clozapine.

Indications
Treatment-resistant schizophrenic patients and in schizophrenia patients with severe, untreatable neurological adverse reactions to other antipsychotic agents, including an atypical antipsychotic agent prescribed for adequate duration. Psychotic disorders occurring during the course of Parkinson's disease, where standard treatment has failed.

Dosage and Administration
Treatment-resistant schizophrenic patients
12.5 mg once or twice on the first day, followed by 25 mg tablets once or twice on the second day. Increase dose slowly, by increments (see SmPC). In most patients, antipsychotic efficacy can be expected with 200 to 450 mg/day given in divided doses. If dose does not exceed 200 mg/day, it can be given as a single administration in the evening. Once control is achieved, a lower maintenance dose may be effective. Treatment should be maintained for at least 6 months. Doses up to 900 mg/day can be used but the possibility of increased adverse reactions (especially seizures) occurring at doses over 450 mg/day must be considered.
See SmPC for details on re-starting therapy, ending treatment or switching from another antipsychotic.
Psychotic disorders occurring during the course of Parkinson's disease in cases where standard treatment has failed
The starting dose must not exceed 12.5 mg/day taken in the evening. Increase dose by 12.5 mg increments, with a maximum of two increments a week up to a maximum of 50 mg, preferably given as a single dose in the evening. The mean effective dose is usually between 25 and 37.5 mg/day.
The maximum dose of 100 mg/day must never be exceeded. Dose increases should be limited or deferred if orthostatic hypotension, excessive sedation or confusion occurs. Blood pressure should be monitored during the first weeks of treatment. When there has been complete remission of psychotic symptoms for at least two weeks, an increase in anti-parkinsonian medication is possible on the basis of motor status. Cautious titration and a divided dosage schedule are necessary to minimise the risks of hypotension, seizure and sedation.

Method of administration
Clozaril is administered orally.
Switching from a previous antipsychotic therapy to Clozaril
It is generally recommended that Clozaril should not be used in combination with other antipsychotics. When Clozaril therapy is to be initiated in a patient undergoing oral antipsychotic therapy, it is recommended that the other antipsychotic should first be discontinued by tapering the dosage downwards.
Special populations: Hepatic impairment Patients with hepatic impairment should receive Clozaril with caution along with regular monitoring of liver function tests (see section 4.4 of SmPC).
Paediatric population No paediatric studies have been performed. The safety and efficacy of Clozaril in children and adolescents under the age of 16 years have not yet been established. Clozaril should not be used in this group until further data becomes available.

Patients 60 years of age and older Initiation of treatment is recommended at a particularly low dose (12.5 mg given once on the first day), with subsequent dose increments restricted to 25 mg/day.
See SmPC for information on ending therapy.

Contraindications
Hypersensitivity to the active substance or to any of the excipients. Patients unable to undergo regular blood tests. History of toxic or idiosyncratic granulocytopenia /agranulocytosis (with the exception of granulocytopenia /agranulocytosis from previous chemotherapy). History of Clozaril induced agranulocytosis. Concurrent treatment with substances known to have a substantial potential for causing agranulocytosis; concomitant use of depot antipsychotics is discouraged.
Impaired bone marrow function. Uncontrolled epilepsy. Alcoholic and other toxic psychoses, drug intoxication, comatose conditions. Circulatory collapse and/or CNS depression of any cause. Severe renal or cardiac disorders (e.g. myocarditis). Active liver disease associated with nausea, anorexia or jaundice; progressive liver disease, hepatic failure. Paralytic ileus.

Warnings and Precautions
Agranulocytosis: Before initiating clozapine therapy, patients should have a blood test and a history and physical examination. Clozaril can cause agranulocytosis, so is restricted to patients who have initially normal leukocyte findings (White Blood Cell (WBC) count > 3.5x 10^9/l and Absolute Neutrophil Count (ANC) > 2.0x 10^9l), and in whom regular WBC counts and ANC can be performed within 10 days prior to starting Clozaril, weekly for first 18 weeks, thereafter at 4 week intervals throughout treatment and for 4 weeks after complete discontinuation.
Patients with history of cardiac illness or abnormal cardiac findings on physical examination prior to treatment should be referred to a specialist for other examinations that might include an ECG, and the patient treated only if the expected benefits clearly outweigh the risks. The treating physician should consider performing a pre-treatment ECG.
QT interval prolongation: As with other antipsychotics, caution is advised in patients with known cardiovascular disease or family history of QT prolongation. As with other antipsychotics, caution should be exercised when clozapine is prescribed with medicines known to increase QTc interval.
Cerebrovascular adverse events: Clozapine should be used with caution in patients with risk factors for stroke. Risk of thromboembolism: Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. If the diagnosis of NMS is confirmed, Clozaril should be discontinued immediately and appropriate medical measures should be administered. Metabolic changes: Atypical antipsychotic drugs, including Clozaril, have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. Hyperglycaemia: Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Hepatic impairment: Patients with stable pre-existing liver disorders may receive Clozaril, but need regular liver function tests. Liver function tests should be performed in patients in whom symptoms of possible liver dysfunction, such as nausea, vomiting and/or anorexia, develop during Clozaril therapy.

Prior to treatment initiation, physicians must ensure that the patient has not experienced an adverse haematological reaction to clozapine that necessitated discontinuation.
Immediate discontinuation of Clozaril is mandatory if either the WBC count is less than 3.0x10^9 /l or the ANC is less than 1.5x10^9 /l at any time during Clozaril treatment. Patients in whom Clozaril has been discontinued as a result of either WBC or ANC deficiencies must not be re-exposed to Clozaril. Following discontinuation of Clozaril, haematological evaluation is required until haematological recovery has occurred. **If Clozaril has been withdrawn and either a further drop in the WBC count below 2.0x10^9 /l occurs or the ANC falls below 1.0x10^9 /l the management of this condition must be guided by an experienced haematologist.** The patient should be educated to contact the treating physician immediately if any kind of infection, fever, sore throat or other flu-like symptoms develop. WBC and differential blood counts must be performed immediately if any symptoms or signs of an infection occur.
Low WBC count/ANC: If, during Clozaril therapy, either the WBC count falls to between 3.5x10^9/l and 3.0x10^9/l or the ANC falls to between 2.0x10^9/l and 1.5x10^9/l, haematological evaluations must be performed at least twice weekly until the patient's WBC count and ANC stabilise within the range 3.0-3.5x10^9/l and 1.5-2.0x10^9/l respectively, or higher.

Eosinophilia: Discontinuation of Clozaril is recommended if the eosinophil count rises above $3.0x10^9$ /l; therapy should be restarted only after the eosinophil count has fallen below $1.0x10^9$ /l. Discontinuation of Thrombocytopenia: Clozaril therapy is recommended if the platelet count falls below $50x10^9$ /l. Cardiovascular disorders: Orthostatic hypotension, with or without syncope, can occur during Clozaril treatment. Rarely, collapse can be profound and may be accompanied by cardiac and/or respiratory arrest which is more likely to occur with concurrent use of certain medications (See SPC for more details) and during initial titration with rapid dose escalation. Patients starting Clozaril treatment require close medical supervision. Clozaril is associated with an increased risk of myocarditis, pericarditis/pericardial effusion and cardiomyopathy; and if suspected, Clozaril treatment should be promptly stopped and the patient immediately referred to a cardiologist. Patients with clozapine-induced myocarditis or cardiomyopathy should not be re-exposed to Clozaril. In patients who are diagnosed with cardiomyopathy while on Clozaril treatment, there is potential to develop mitral valve incompetence, including mild or moderate mitral regurgitation. Myocarditis or cardiomyopathy should be suspected in patients who experience persistent tachycardia at rest, especially in the first two months of treatment, and/or palpitations, arrhythmias, chest pain and other signs and symptoms of heart failure or symptoms mimicking myocardial infarction. Flu-like symptoms may also be present. Myocardial infarction (MI): There have been post marketing reports of MI which include fatal cases. Epilepsy: Patients with a history of epilepsy should be closely observed during Clozaril therapy since dose related convulsions have been reported. Hepatic impairment: Patients with stable pre-existing liver disorders or liver dysfunction need regular liver function tests. If the LFTs are elevated, discontinue Clozaril and resume only if LFTs return to normal. Dyslipidemia: Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics, including Clozaril. Clinical monitoring, including baseline and periodic follow-up lipid evaluations in patients using clozapine, is recommended.
Anticholinergic effects: Use with care in patients with a history of colonic disease, a history of lower abdominal surgery, glaucoma, narrow angle glaucoma, prostatic enlargement and in patients receiving concomitant medications known to cause constipation, megacolon and intestinal infarction/ischaemia, paralytic ilius. Pyrexia: High temperatures should be evaluated carefully to rule out underlying infection, agranulocytosis or Neuroleptic Malignant Syndrome (NMS). If NMS is confirmed, discontinue Clozaril immediately and administer appropriate medical measures. Patients with rare hereditary problems of galactose intolerance should not take Clozaril. Impaired glucose tolerance and/or development or exacerbation of diabetes mellitus has been reported rarely during treatment with clozapine. Falls: Clozaril may cause seizures, somnolence and other conditions that could lead to falls. Fall risk assessments should be performed on patients with exacerbating conditions. Risk of thromboembolism: Immobilisation of patients should be avoided due to reports of thromboembolism. Increased mortality in elderly patients with dementia. Caution when prescribing to pregnant women. Mothers receiving Clozaril should not breast-feed. Adequate contraceptive measures must be ensured in women of childbearing potential. Neonates exposed to antipsychotic drugs (including Clozaril), during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress or feeding disorder. Consequently, newborns should be monitored carefully. Activities such as driving or operating machinery should be avoided, especially during the initial weeks of treatment.
Interaction with other medicinal products and other forms of interaction
Clozaril must not be used concomitantly with substances having a well-known potential to suppress bone marrow function. (See Section 4.3 of the SmPC, Contraindications).
Long-acting depot antipsychotics (with myelosuppressive potential) must not be used with Clozaril because these cannot be removed from the body in situations where they may be required e.g. neutropenia. Alcohol should not be used with Clozaril due to possible potentiation of sedation.

Caution is advised if Clozaril is used concomitantly with other CNS active agents such as, MAOIs, perazine, SSRIs especially fluvoxamine, caffeine, CNS depressants including narcotics, antihistamines and benzodiazepines, Caution is advised if Clozaril is used concomitantly with antihypertensive agents, highly protein bound drugs (e.g. warfarin and digoxin), phenytoin, lithium, rifampicin, valproic acid, noradrenaline [norepinephrine], adrenaline [epinephrine] or omeprazole. Cases have been reported of an interaction between citalopram and clozapine, which may increase the risk of adverse events associated with clozapine. The nature of this interaction has not been fully elucidated. Hormonal contraceptives (including combinations of estrogen and progesterone or progesterone only) are CYP 1A2, CYP 3A4 and CYP 2C19 inhibitors. Therefore initiation or discontinuation of hormonal contraceptives, may require dose adjustment of clozapine according to the individual medical need. In cases of sudden cessation of smoking, the plasma clozapine concentration may be increased, thus leading to an increase in adverse effects. See SPC for more details.

Fertility, Pregnancy and Lactation
Pregnancy: Caution should be exercised when prescribing to pregnant women. Neonates exposed to antipsychotics (including Clozaril) during the third trimester are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.
Lactation: Animal studies suggest that clozapine is excreted in breast milk and has an effect in the nursing infant; therefore, mothers receiving Clozaril should not breast-feed.
Fertility: Limited data available on the effects of clozapine on human fertility are inconclusive.
Women of child-bearing potential: A return to normal menstruation may occur as a result of switching from other antipsychotics to Clozaril. Adequate contraceptive measures must therefore be ensured in women of childbearing potential.

Ability to Drive and Operate Machinery
Owing to the ability of Clozaril to cause sedation and lower the seizure threshold, activities such as driving or operating machinery should be avoided, especially during the initial weeks of treatment.

Undesirable effects
Adverse reactions are ranked under headings of frequency. Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), including isolated reports.
The most serious adverse reactions experienced with clozapine are agranulocytosis, seizure, cardiovascular effects and fever.

Very common: Drowsiness/sedation, dizziness, tachycardia, constipation, hypersalivation.
Common: Leukopenia/decreased WBC/neutropenia, eosinophilia, leukocytosis, weight gain, blurred vision, headache, tremor, rigidity, akathisia, extrapyramidal symptoms, seizures, convulsions, myoclonic jerks, ECG changes, hypertension, postural hypotension, syncope, nausea, vomiting, anorexia, dry mouth, elevated liver enzymes, urinary incontinence, urinary retention, fatigue, fever, benign hyperthermia, disturbances in sweating/temperature regulation, dysarthria.
Uncommon: Agranulocytosis, neuroleptic malignant syndrome, dysphemia, falls.
For details of rare, very rare and not known undesirable effects please refer to SmPC."
Package Quantities and basic NHS price
28 x 25 mg tablets : £2.95 ; 84 x 25 mg tablets : £6.30; 100 x 25 mg tablets : £7.50
28 x 100 mg tablets : £11.76 ; 84 x 100 mg tablets : £25.21 ; 100 x 100 mg tablets : £30.01
Supply of Clozaril is restricted to hospital pharmacies registered with the CLOZARIL Patient Monitoring Service.
Marketing Authorisation Holder
Mylan Products Limited, 20 Station Close, Potters Bar, Herts, EN6 1TL, UK.
Product Authorisation Numbers
25 mg tablets: PL 46302/0054
100 mg tablets: PL 46302/0057
Legal Category: POM
Further information is available in the UK from: BGP Products Ltd., Building Q1, Quantum House, 60 Norden Road, Maidenhead, Berkshire, SL6 4AY, UK.
Date of last revision: May 2020
Clozaril is a registered Trademark

Reporting of adverse reactions:
Please continue to report suspected adverse drug reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme.
It is easiest and quickest to report adverse drug reactions online via the Yellow Card website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, you can report via some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) or by calling the Commission on Human Medicines (CHM) free phone line: 0800-731-6789. Adverse reactions/events should also be reported to Viatris via cpms@viatris.com

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Clozaril® (clozapine)

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