Development of user-friendly consumer and health professional resources for the antipsychotic clozapine: a New Zealand example

Nicola J Holmes,1 S Wayne Miles,2,3 Amanda J Wheeler4,5

ABSTRACT
The antipsychotic clozapine has been shown to have superior efficacy to most other treatments for psychosis, especially where treatment-resistant schizophrenia has been diagnosed. Like all medications, clozapine has a number of well-recognised adverse effects, some of which can be fatal. Evidence also suggests that those for whom clozapine is the most suitable treatment option do not receive it because the doctor or health system views the risks as too great to prescribe. The provision of guidelines including innovative consumer and general practitioner resources regarding the ways to most safely monitor and manage people who are exposed to clozapine has the potential to increase the safe use of the product and also to provide potential prescribers with more confidence in using it. This paper outlines both the process for development and the final package produced by a large metropolitan District Health Board service in Auckland, New Zealand. This material was aimed at non-specialist prescribers as well as consumers and their family/carers and other supports.

INTRODUCTION
Clozapine, the only antipsychotic recommended for treatment-resistant schizophrenia, has been available as a registered medicine in most English-speaking countries since the early 1990s. It was reintroduced after concerns related to fatal agranulocytosis had led to its withdrawal in 1975. A number of other life-threatening adverse effects have been associated with clozapine, including myocarditis and cardiomyopathy, insulin resistance and diabetes, and constipation and bowel obstruction. Typically, owing to the risk of serious adverse effects, clozapine prescribing and dispensing is generally restricted to secondary care services. However, shared-care arrangements with primary healthcare services, that is, general practitioners (GPs) and community pharmacies, are increasing for those people who are stable and well established on this medication. Despite its superior efficacy and beneficial health outcomes,1 many studies show underutilisation,2–5 delayed access4,6 7 and a reluctance by psychiatrists to prescribe clozapine.8 9 In response to both safety and access concerns, clinical guidelines that recommend appropriate monitoring and management of mental and physical health for people initiated on clozapine are available in many countries.10–12

At a large public secondary care mental health service in Auckland, New Zealand, an organisation-wide evidence-based consensus-agreed clozapine best-practice guideline had been in place since 1999. This guideline had been developed primarily for those clinicians involved in the prescribing, dispensing, administration and monitoring of clozapine within the secondary care mental health service. Regular reviews of the guideline addressed new evidence, as well as responding to outcomes of local case reviews and relevant Coronial enquiries throughout the country. Clozapine use had been reviewed regularly in the service as part of an audit and feedback cycle over 7 years between March 2000 and March 2007.6 13–16
Call for the tool
In late 2007, a New Zealand Coroner’s report regarding a clozapine-induced fatal blood dyscrasia that occurred 9 months after clozapine initiation highlighted that community-based people taking clozapine were being managed by both secondary care mental health services and GP services. It was felt that this conferred a potential for people to fall between the two services with respect to monitoring and management of adverse effects. The Coroner recommended that a “medication booklet to be carried by the patient” be developed that could act as an aide memoire for the consumer, their family and carers regarding the signs and symptoms of important adverse effects and how to respond to these, and provide advice to a practitioner (particularly non-regular practitioners and those in after-hours situations) about these adverse effects. Another Coroner’s recommendation was that GPs be provided with “appropriate information about clozapine by specialist prescribers”.

In response to this, the planned guideline review in 2008 included incorporating the Coroner’s recommendations for developing appropriate, portable, user-friendly clozapine information resources for consumers and health practitioners who were not specialist clozapine prescribers. Other areas of concern identified by clinicians from within the organisation that were to be included in the review were
1. More detailed guidance on utility, rationale and interpretation of clozapine serum levels;
2. Initiation of clozapine in outpatient settings;
3. Monitoring and management of gastrointestinal adverse effects, particularly constipation;
4. Identification and management of significant and potentially fatal cardiovascular adverse effects, such as myocardi-tis and cardiomyopathy.

The work conducted around these areas is not presented here in detail, but is noted as it informed some content of the consumer and non-specialist health practitioner resources that were developed.

METHOD
Development of the tool
A multidisciplinary clozapine working group was established with different members leading the process for each of the four areas outlined above. The working group consulted with national and international specialists and the organisation’s consumer advisor group as needed. The main tasks of the resource development workstream were to design and produce the portable resource for people taking clozapine and any healthcare professionals they came in contact with and also an information resource for GPs, as recommended by the Coroner’s report.

An extensive search of the literature, Google and mental health pharmacy network groups in the UK, Australia and New Zealand was carried out to identify existing portable consumer resources and quick reference information for GPs about clozapine, the risk of adverse effects, and how to respond to these. Only one example of a portable consumer resource was identified from a mental health service in the UK, but this was more as a medical alert card than as a portable resource (personal correspondence Dr Dave Branford 30 December 2008). The card recorded the consumer’s name, the prescriber’s details, a warning that clozapine can cause neutropenia and to be on the alert for signs of infection, and emergency medical contact numbers at the Clozaril Patient Monitoring Service (CPMS). This UK mental health service added a sticker to the reverse side of this standard card provided by the CPMS, which included advice about restarting treatment, and the impact of smoking and contact details for the pharmacy supplying the clozapine.

A letter for GPs who would be working with people taking clozapine had already been developed for use by the Auckland mental health service prior to this most recent guideline update; however it required updating. Several other formal letter templates were identified, but these did not outline the benefits and risks of clozapine or give specific advice to the GP about the need for close haematological monitoring, the additional monitoring that should be carried out (by the GP) and in which circumstances, and when to contact the mental health team. Many of these letters had been developed by the pharmaceutical manufacturers of clozapine.

RESULTS
Three draft resources were developed over an 18-month period
1. A double-sided wallet leaflet that folded up to bankcard size to be carried by consumers (one side detailing information for consumers and the other side for health professionals) (see online supplementary appendix A);
2. A two-page letter for GPs alerting them that someone under their care had been started on clozapine and summarising important related information (see online supplementary appendix B);
3. A one-page quick reference sheet available on the organisation’s external website (see online supplementary appendix C).

The three resources were designed to supplement the very detailed information about clozapine that is included in the manufacturers’ registration documentation available on the Medsafe® website (http://www.medsafe.govt.nz).

Coroner’s findings in New Zealand are available free online for all completed cases opened after 1 July 2007. Cases opened prior to 30 June 2007 are available on request http://www.justice.govt.nz/courts/coroners-court/publications/findings-recommendations-and-records.

Medsafe is the New Zealand Medicines and Medical Devices Safety Authority. It is a business unit of the Ministry of Health and is the authority responsible for the regulation of therapeutic products in New Zealand.
The consumer resource was developed with significant input from the organisation’s consumer advisor group. Space was included to document personal details and the mental health professionals working with the person carrying the card. This document could be folded to the same size as a bankcard to fit in a wallet or purse (figure 1). Two consumer advisors then piloted the prototype with eight people taking clozapine, and minor changes were made to the wording based on their feedback. The information letter for GPs was piloted with three GPs who had consumers taking clozapine in their practice, and again minor amendments were made due to their feedback.

While working towards final versions of the consumer and GP resources, it became apparent that there needed to be a more detailed summary resource that could easily be accessed by people taking clozapine, their families/carers, and healthcare professionals working with people taking clozapine. This quick reference sheet was developed to be accessible on the internal intranet and external organisation website, and it is referred to in both the GP resource and the wallet card as an additional resource.

Finally, the resources were presented widely across the organisation at staff and professional meetings as part of the consultation process for the updated guideline. Overall feedback from staff, consumers and GPs was positive. Suggested amendments were incorporated where relevant, and roadblocks solved where possible.

All three resources were incorporated into the final version of the guideline, with signposting on the wallet card directing staff to order bulk supplies of the printed and folded cards from the pharmacy department (see online supplementary Appendices A–C). The GP letter and quick reference sheet were made available on the internal intranet, and additionally the reference sheet was available on the external website to facilitate ease of access (http://www.waitematadhb.govt.nz/HealthProfessionals/Medicinesresources.aspx).

Prior to the final sign-off and publication, the guideline was reviewed and approved by the organisation’s Drug and Therapeutics Committee.

**DISCUSSION**

**Strategies for innovation**

The strategies used to update the guideline to support evidence-based practice in a consensus-agreed manner were undertaken to maximise awareness of and adherence with the best-practice recommendations and have been discussed previously. With respect to dissemination, the updated guideline was emailed electronically to all mental health clinical staff, discussed with medical staff employed at the time, and then embedded into induction training for new staff starting with the organisation. This occurred across inpatient, community and forensic services. Copies of the consumer wallet card, GP letter and summary resources were placed in the organisation’s consumer advice folders available in all clinical areas. In addition, a specific initiative took place whereby care coordinators were tasked with ensuring that all community-based consumers taking clozapine received a wallet card.

An informal clozapine initiation checklist (aimed specifically at junior medical staff but available for any staff to use) had previously been in place within the organisation; however, it had not explicitly been part of the best practice guideline. In order to facilitate clarity regarding the monitoring and steps required prior to starting clozapine (especially for junior medical staff not necessarily as familiar with this medication as more senior medical staff), this checklist was reviewed and updated and integrated within the guideline (see online supplementary appendix D). Junior medical staff were consulted on the checklist and it was piloted on an inpatient forensic unit prior to being finalised and implemented; feedback regarding the clarity and ease of use of the document was positive. The checklist was also made accessible separately on the internal intranet to facilitate ease of access.

**Figure 1** (A and B) Portable information resource for consumers and health professionals (wallet card).
In the final stages of guideline dissemination, a subsequent Coroner’s report (following a cardiac adverse event) recommended that the updated guideline be available to other health services throughout the country, to Medsafe and to the Health Quality and Safety Commission.iii More specifically, the Coroner recommended that the Commission:

Assists in providing national leadership to ensure that the clozapine guidelines of all District Health Boards are aligned with international best practice standards and consistent across the country;

Identifies a process for developing national best practice guidelines for the prescription and monitoring of medications such as clozapine for which practitioners throughout New Zealand require particular guidance.

The guideline developers were aware that, as the guideline had been developed for local application, it would not meet international criteria set by the Appraisal of Guidelines for Research and Evaluation (AGREE) Trust (http://www.agreetrust.org). It was also acknowledged that a guideline that was consensus-agreed in one setting would need to be assessed by another organisation independently to elucidate utility, and agreement from clinicians; otherwise, adherence could be compromised. To help clarify these considerations for organisations, the guideline was shared with a cover note that highlighted these issues and also provided a summary of the process followed and staff involved with respect to the expert consensus groups and associated consultees.

Lessons and messages
The guideline took an extended amount of time to update and disseminate (approximately 2.5 years). This was partially due to (1) the logistical difficulties associated with gathering all the relevant expertise together for the working group, and especially for consultation outside the organisation, plus, (2) the work was undertaken by busy health practitioners who had to incorporate this work into their current workload with no backfill. Ideally, ring-fenced time would have been available to expedite the process. The extended nature of the review meant that some enlisted staff moved on to other settings or organisations during the review process; replacements had to be enlisted and brought up to speed prior to being able to contribute meaningfully.

Another complication was a succession of relevant evidence and reports being published during guideline development. It was a challenge to incorporate newly available information as and when it became available, and also to make a decision on when to stop developing the guideline so that it could be signed off and implemented.

The use of a widely consultative, consensus-agreed and collaborative approach with clinicians and other health professionals throughout the guideline and resource review and development process, alongside inclusion within the guideline of content requested by staff, facilitated implementation of the finished guideline, as many staff were already aware of and familiar with the content.

Informal feedback from clinical pharmacists and cardiology services suggested that the guideline was being followed throughout inpatient and community mental health services within the organisation. Informal feedback from consumers, mental health clinicians and other staff indicated that they felt the guideline contents, especially the associated resources, were useful.

For guidelines and best practice summaries to have the most impact on clinical decision-making, it is crucial that they remain current and that essential details are readily available at both the time and site of that decision. This has historically not been easy to achieve, partly due to the workload involved with updating guidelines in the absence of specific resourcing for this, and also due to limitations in the logistics of information technology. The organisation has developed CeDSS (Clinical electronic Decision Support System), which provides practitioners with key information at the bedside. It has yet to be extended to outside hospital use. When that is achieved, then this clozapine-related material will be easily and rapidly accessed. The material on this site is regularly reviewed by expert content holders and this will ensure that information is regularly updated.

The guideline was due for review in mid-2013. Many of the original working group members have left the organisation. Efforts have been made to maintain relevant expertise and knowledge base within the organisation’s mental health pharmacy services to facilitate seamless progress of further guideline updates.

Ideally, the implementation of the guideline would improve the safe and quality use of clozapine within the organisation. This is difficult to state with certainty, given the lack of available formal evidence regarding this, as a post-implementation audit has not occurred. Post-implementation audits are important to identify adherence with guideline recommendations and identify strategies to address any areas of poor adherence. The significant adverse effects discussed, while being potentially fatal, are rare, and as concluded in the Coroner’s reports and evidence from the literature examining the utility of the mandatory full blood count monitoring, even good monitoring does not guarantee good outcomes. If people with difficult-to-treat schizophrenia are to have the best opportunity to minimise the effects of that illness and thereby maximise their recovery of roles and function, then it is important that they have

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iii The Health Quality & Safety Commission (http://www.hqsc.govt.nz) was established in November 2010 to ensure that all New Zealanders receive the best health care and disability care within available resources and with an expectation from the Government that it would lead quality and safety improvements in the health sector.


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access to well-informed clinicians who have well-developed systems for safe and reliable monitoring of mental and physical health. The described set of tools to inform consumers and their families, as well as clinicians at the secondary and primary levels, meet these requirements. Future audit of clozapine use at the organisation will allow evaluation of the impact of the set of tools on enhancing quality use of clozapine.

Acknowledgements The authors would like to thank all the members of the organisation’s clozapine working group, the organisation’s consumer advisor team, the many other clinicians and consumers who contributed their expertise in the consultation and piloting process, and the administrative staff who assisted in the development of resources and document formatting.

Contributors Each author contributed to the guideline review, consultation and dissemination. NJH led the overall review process and the dissemination process. SWM was a member of the working group specifically reviewing cardiac monitoring. AJW led the overall review process and development of the resources. Each author contributed to and approved the final version of the manuscript.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

Clozapine can be very helpful for the relief of distressing mental health symptoms. However, the potential side effects can be serious.

Health professionals such as your family doctor, dentist, pharmacist or any other doctors, need to know that you are taking Clozapine so they can assess any health problems you may have and choose the right medicine for you.

Please read this information carefully and keep it in mind while taking Clozapine.

Things you need to know about Clozapine

Potential side effects and interactions with other substances:

- **Clozapine can affect the production of white blood cells which fight infection.** At the first sign of infection (such as fever, cold or flu symptoms), you will need to contact your doctor or mental health worker for an urgent blood test to check your white blood cell levels.

- **Constipation from Clozapine can result in serious bowel damage.** Drink lots of water, exercise regularly, and eat fibre-filled foods such as porridge, bran, fruit and vegetables, brown rice and whole grain breads. If constipation becomes a problem, talk to your doctor, mental health worker, or pharmacist immediately.

- **Sudden changes in smoking or caffeine intake can affect how Clozapine works.** If you are making changes to your smoking or caffeine intake, talk to a doctor or mental health worker so your Clozapine levels can be checked.

Your details

If you are receiving health care, please give the health professionals the following information to ensure you receive the best care:

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Clozapine can be very helpful for the relief of distressing mental health symptoms. However, the potential side effects can be serious. Special care is needed when arranging any kind of medical treatment for people taking Clozapine, or when prescribing any other medications.

**Side effects and interactions with other medications**

The possible side effects of Clozapine can include:

- Agranulocytosis
- Constipation
- Hypersalivation
- Metabolic disturbances
- Myocarditis and cardiomyopathy
- Epileptic seizures
- Nocturnal urinary incontinence

Avoid prescribing medications with the potential to cause interaction. Eating fibre-filled foods, drinking plenty of water and exercising will help reduce the risk. Close management with laxatives may also be needed on a regular basis.

Take care when co-prescribing. Some drugs raise or lower Clozapine’s potency by their interaction with the liver. Sudden changes in smoking or caffeine intake may affect clozapine metabolism. Clozapine levels need to be monitored in these situations.

Avoid prescribing drugs with the potential for bone marrow suppression as Clozapine can affect the production of white blood cells resulting in agranulocytosis. An urgent blood test is needed to check WBC levels at the first sign of infection (such as fever or cold/flu symptoms).

If you need to stop Clozapine suddenly because of a medical emergency (such as myocarditis or agranulocytosis) please contact the Mental Health Team as mental distress may occur. Close monitoring is needed.
Dear Colleague,

Your patient,

is taking clozapine (Clopine®), an antipsychotic that can be effective in patients who have failed to respond to, or are intolerant of, other antipsychotics.

This medication can only be initiated by a psychiatrist or psychiatric registrar under supervision. GP prescribing is only permitted for stable patients in collaboration with the treating psychiatrist. However we recognise that we share this patient’s care with you, and that clozapine can have serious side effects, so would appreciate your help. Even if you are not prescribing clozapine you may wish to enter clozapine on the patient’s medication list, e.g. in MedTech, so that an alert is added to their record and drug interaction warnings will come up even though you are not the prescribing doctor. If you wish to discuss prescribing clozapine please contact the treating psychiatrist.

About 30% of patients with schizophrenia have a limited response to other antipsychotics. Clozapine is indicated after trials of two other antipsychotics have been unsuccessful in controlling symptoms or poorly tolerated. The response rate to clozapine is up to 60% by 12 months. However there are various issues to be aware of when a patient is taking clozapine and we have detailed these below.

Problems with clozapine

Haematological

The risk of agranulocytosis (about 0.7% in the first six months), means regular blood monitoring must be carried out for the duration of treatment. Tests are weekly for the first 18 weeks (because the risk is highest in this period), and every four weeks thereafter.

Blood collection, collation and dissemination of results is coordinated by a system involving pharmacies (both hospital and some community pharmacies), all the pathology laboratories, and mental health teams, and is backed up by a monitored database run by Douglas Pharmaceuticals called ClopineConnect. You can freephone the 24-hour ClopineConnect number (0800 435 811) should you have queries about the database or results for one of your patients. The dispensing pharmacy will not provide clozapine for a patient unless they have a recent normal white blood cell (WBC) and neutrophil result.

If signs of infection occur, or blood tests indicate a significant drop in WBCs, a repeat test - marked urgent - should be carried out.

A significant drop would be:

- A WBC count falling below 3.5 $10^9/L$ in the first 18 weeks of treatment; or
- A neutrophil count falling below 1.5 $10^9/L$; or
- A WBC count falling below 3.0 $10^9/L$, or a neutrophil count below 1.0 $10^9/L$, after week 18; or
- A single WBC drop of ≥ 3 $10^9/L$; or
- A cumulative drop of ≥ 3 $10^9/L$ within three weeks.

Any of these events require contact with Mental Health Services as the clozapine may need to be stopped.

Patients on clozapine should be reminded to contact their doctor immediately if any kind of infection begins to develop. Particular attention should be paid to flu-like complaints, such as fever or sore throat, and to other evidence of infection which may be indicative of neutropenia. Patients on clozapine who present to any medical centre with signs or symptoms of infection must have an immediate WBC check, with results sought urgently to rule out agranulocytosis.

Each time the patient has a blood test done it is important to request that a copy be sent to both the dispensing pharmacy, and to ClopineConnect. This ensures that the pharmacist can check the results before any medication is dispensed. The Mental Health Team is responsible for coordinating the blood monitoring and supply of treatment but if you would like to routinely receive a copy of the regular blood results then please let the Mental Health Team know.
**Interruption of treatment**

Clozapine is a continuing therapy. If a patient stops taking their medication, there is a high risk that their previous mental health symptoms will return. The patient should take the correct dose as soon as the error is recognised, unless more than two days worth of doses have been missed. If you are required to restart it, please consult the clozapine data sheet, Re-starting Therapy and let the Mental Health Team and Pharmacy know.

**Other important adverse effects**

Constipation is common (up to 15%), can be severe and requires active management (such as regular osmotic laxatives, e.g. lactulose, and short-term stimulant laxative use, e.g. docusate and senokot). In severe cases (especially when other constipating medication such as anticholinergic drugs and opiates have been co-prescribed), toxic megacolon has developed, which in some cases has been fatal. Avoid co-prescribing any other medication that causes constipation.

Hypersalivation is common (up to 20%), unpleasant for the patient and occurs more often at night, but treatment is often successful. In particular, prescribing terazosin (1-2mg at night) may be effective. Benztrapine (1-2mg) at night may also be effective but must be used cautiously because it can cause constipation.

Metabolic disturbances including weight gain, lipid abnormalities and diabetes are potential complications and we would appreciate you monitoring these three-monthly after starting and then annually (more frequently if indicated).

Myocarditis and cardiomyopathy can occur rarely (reports range from 1 in 500 to 1 in 10,000). The first month of treatment is the highest risk period for myocarditis, however it may occur very rarely later in treatment and some cases have been fatal. Any signs or symptoms of cardiac adverse effects including unexplained fatigue, fever, chest pain, palpitations, shortness of breath, or other symptoms of heart failure need urgent investigation (e.g. ECG, FBC, troponin, CRP, chest x-ray and possible cardiology referral). If myocarditis is suspected then immediate withdrawal of clozapine is recommended and you should contact the Mental Health Team.

Epileptic seizures are uncommon (around 3%) and usually occur at higher doses. Clozapine does not necessarily need to be stopped as addition of sodium valproate will usually be effective. If seizures occur, you should contact the Mental Health Team.

Nocturnal urinary incontinence may occur (5-10%) but treatment is often successful (desmopressin, oxybutynin and ephedrine may be effective). If this occurs, you should contact the Mental Health Team.

**Drug Interactions**

Any drug with the potential for bone-marrow suppression should not be used with clozapine. The commonest examples are cotrimoxazole and carbamazepine. Some drugs and substances can increase or reduce serum levels of clozapine by inducing or inhibiting liver enzymes responsible for clozapine breakdown - and care needs to be taken if co-prescribing (please consult the clozapine datasheet or speak to the dispensing pharmacy).

Chemicals in cigarette smoke (not the nicotine) can lower serum levels of clozapine so sudden cessation of smoking can cause a large rise in clozapine serum levels with associated toxicity. Conversely the serum level of clozapine can be increased by caffeine intake so sudden cessation of regular caffeine can cause a decrease in clozapine levels and possible return of mental health symptoms.

**Please find enclosed:**

- A Clozapine® datasheet
- A Clozapine ‘Quick Reference Sheet’ summarising the information in this letter

Thank you. Should you have any questions please contact the treating psychiatrist or a hospital/community pharmacist dispensing clozapine.

Regards
Blood collection, collation and dissemination of results is coordinated by a system involving pharmacies, all the pathology laboratories and mental health teams, and is backed up by a monitored database called ClopineConnect run by Douglas Pharmaceuticals. You can freephone the 24-hour ClopineConnect number should you have queries about the database or results for one of your patients.

**CLOPINECONNECT: 0800 435 812**

### Agranulocytosis

**KEY ACTION:** Regular full blood counts. Test white blood cell (WBC) count weekly for the first 18 weeks and every four weeks thereafter. Request that copy of results be sent to the dispensing pharmacy and ClopineConnect (0800 435 812).

**Immediately withdraw clozapine and contact Mental Health Services if:**
- A WBC count falls below 3.5 (10^9/L) in the first 18 weeks of treatment; or
- A neutrophil count falls below 1.5 (10^9/L); or
- A WBC count falls below 3.0 (10^9/L), or there is a neutrophil count below 1.0, after week 18; or
- There is a single WBC drop of ≥ 3 (10^9/L); or
- There is a cumulative drop of ≥ 3 (10^9/L) within three weeks.

Because clozapine may need to be stopped.

### Interruption of treatment

**KEY ACTION:** Resume at correct dose unless more than two days of doses have been missed. If two or more days of doses missed, consult the clozapine data sheet, *Re-starting Therapy* and let the Mental Health Team know.

### Constipation

**KEY ACTION:** Immediate and active management such as regular osmotic laxatives and short-term stimulant laxative use. Avoid prescribing medication that causes constipation.

### Hypersalivation

**KEY ACTION:** Treatment often successful. Prescribing terazosin (1-2mg at night) may be effective. Benztrapine (1-2mg) at night may also be effective but must be used cautiously because of constipation side effects.

### Metabolic disturbances

**KEY ACTION:** Monitor for weight gain, lipid abnormalities and diabetes at baseline, three-monthly after starting, then annually (or more frequently if indicated). Primary care to take the lead with any indicated treatment.

### Myocarditis and cardiomyopathy

**KEY ACTION:** Urgently investigate signs/symptoms of any adverse cardiac effects including unexplained fatigue, fever, chest pain, palpitations, and shortness of breath (e.g. ECG, FBC, troponin, CRP, chest x-ray and possible cardiology referral). If myocarditis is suspected immediately withdraw clozapine and contact the Mental Health Team.

### Epileptic seizures

These are uncommon and clozapine does not necessarily need to be stopped as addition of sodium valproate will usually be effective. If seizures occur, contact the Mental Health Team.

### Nocturnal urinary incontinence

**KEY ACTION:** Treatment often successful (desmopressin, oxybutynin and ephedrine may be effective). Please let the Mental Health Team know if this is a problem.

### Drug interactions

**KEY ACTION:** Avoid drugs with the potential for bone-marrow suppression. The commonest examples are cotrimoxazole and carbamazepine. Some drugs and substances increase or reduce serum levels of clozapine - especially liver enzyme inducers and inhibitors. Care needs to be taken if co-prescribing.

**Chemicals in cigarette smoke** (not nicotine) can lower clozapine serum levels so sudden smoking cessation can cause a large rise in serum levels with associated toxicity. **Caffeine** can raise clozapine serum levels so sudden cessation of regular caffeine can cause a decrease in clozapine levels and possible return of mental health symptoms.

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**Quick reference: Clozapine**

- Can be effective when other antipsychotics have failed
- Can have serious side effects
- High risk that mental health symptoms will return if treatment interrupted
- Risk of agranulocytosis
- Patients with signs/symptoms of infection need an immediate full blood count
- Other important side effects can include:
  - Constipation
  - Hypersalivation
  - Metabolic disturbances
  - Myocarditis and cardiomyopathy
  - Epileptic seizures
  - Nocturnal urinary incontinence
- Avoid drugs with potential for bone marrow suppression or constipation
- Some drugs and substances can increase or reduce clozapine serum levels, especially liver enzyme inhibitors or inducers
- Can interact adversely with cigarettes and caffeine

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**Our core values**

- Customer Focus ‘eye’
- Integrity ‘sunrise’
- Compassion ‘bird’
- Respect ‘kōru’
- Openness ‘flower’

Publication number 0182-01-059 (Review date: September 2012)
**Clozapine Initiation Checklist**

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<td>Clozapine information fully discussed with consumer (and whanau/caregivers where available), including use of WDHB clozapine information resources.</td>
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<td>Verbal consent given or second opinion obtained and process documented in clinical notes.</td>
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<td>Baseline clinical assessment performed of function and symptoms.</td>
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<td>Medical history reviewed (past and current comorbidity and family history of cardiovascular disease).</td>
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<td>Physical examination performed (abdominal examination, weight, waist circumference, body mass index, pulse and blood pressure (lying and standing) and temperature).</td>
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<td>Baseline ECG within the four weeks prior to starting clozapine.</td>
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<td>Referral made for baseline echocardiogram. N.B. test does not need to occur prior to starting clozapine. On referral form please state “pre-clozapine baseline” and give an indication of approximately when it is intended to start clozapine.</td>
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<td>Referral made for baseline chest X-ray if none available within past five years. N.B. X-ray does not need to occur prior to starting clozapine.</td>
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<td>Baseline blood tests within ten days prior to starting clozapine (FBC, electrolytes, renal and liver function tests, creatinine kinase, troponin-I, C-reactive protein, fasting blood sugar and lipid profile).</td>
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<td>Consumer registered with and approved by the relevant FBC monitoring system.</td>
<td></td>
</tr>
<tr>
<td>Clozapine wallet card given to consumer (available in all clinical areas).</td>
<td></td>
</tr>
</tbody>
</table>

Signed: _______________ Date: _______________

Name (print): _______________ Designation: _______________

Once completed this form should be filed in the consumer’s clinical notes.
For further information see Clozapine Best Practice Guidelines.