Clopine CENTRAL™

YOUR Connection to Clopine® (Clozapine) patient care

1800 656 403

www.clopine.com.au

Contents

About ClopineCentral™

Introduction

Clopine® (clozapine) is an atypical antipsychotic agent for treatment resistant schizophrenia. A tricyclic dibenzodiazepine derivative, Clopine® has antipsychotic effects in patients with schizophrenia, particularly those resistant to other drug therapies. Clopine® improves both positive and negative symptoms in the patient with schizophrenia whilst being relatively free of extrapyramidal side-effects compared with traditional antipsychotic agents[1].

Agranulocytosis and neutropenia are serious adverse reactions that may occur with clozapine therapy. Because of this risk, the use of clozapine should be limited to patients with schizophrenia:

- Who do not respond satisfactorily to, or cannot tolerate, other antipsychotic drug therapies
- Whose initial white blood cell (WBC) parameters are normal
- And in whom regular blood counts can be carried out

It is important to review both this document and the full Product Information for Clopine®, particularly the Boxed Warning, Contraindications, Precautions and Adverse Reactions sections, before prescribing Clopine®.

Cases of myocarditis and cardiomyopathy have been reported in patients on clozapine. For this reason, baseline screening of patients is recommended prior to commencing Clopine® therapy. Periodic monitoring is advisable.

ClopineCentral™ has been designed to provide a mechanism for monitoring patients receiving Clopine® and identifying adverse haematological effects.

1. Clopine® (clozapine) TGA Approved Prescribing Information v18.0 Feb 2015.

ClopineCentral™

ClopineCentral™ is administered by Pfizer Australia Pty Ltd (Pfizer).

A full description of the ClopineCentral™ Protocol is provided in the 'Patients and ClopineCentral™' section of this document.

Purpose

The purpose of the ClopineCentral™ Protocol is:

- To serve as a safeguard against the risk of patients developing agranulocytosis or neutropenia during treatment with Clopine® via a system of regular monitoring and recording of white blood cell (WBC) and neutrophil counts for all patients on Clopine®
- To ensure that patients who have previously discontinued therapy because of haematological effects are not rechallenged with clozapine
- To provide prescribers and prescribing Centres with an opportunity to record baseline and ongoing data on their use of clozapine in clinical practice
- To provide a support network of Centres and patients

Registration

ClopineCentral™ requires all patients, prescribing doctors, dispensing pharmacists, Centre Coordinators and Centres using Clopine® to be registered with ClopineCentral™ (see 'Registration and Roles' section).

Pre-treatment screening

Prior to commencing therapy with Clopine®:

- Patients' details are cross-checked against a combined database – the Clozapine Exclusion Database (CED) – to identify any patient who has discontinued clozapine therapy because of haematological adverse events, and is therefore ineligible for treatment with Clopine® or any other brand of clozapine. The CED is a database established, in conjunction with Novartis Australia Pty Ltd and Pfizer. This database details any patient who has had a 'red' blood level reading, and should not be rechallenged with clozapine treatment.
- Total WBC and neutrophil count must be assessed before a patient's eligibility to receive Clopine® is confirmed.
- Cases of myocarditis and cardiomyopathy have been reported in patients receiving clozapine, some of which have been fatal. Therefore baseline screening for myocardial damage (including patient clinical exam and family history of heart failure), echocardiogram (ECHO), electrocardiogram (ECG), and measurement of troponin I or T and C-reactive protein (CRP) has been recommended in the literature (Ronaldson 2011, See 'References' section, page 20).

Ongoing monitoring

Full details of the monitoring protocol are provided in the 'Patients and ClopineCentral™' section.

WBC and neutrophil counts must be performed weekly for the first 18 weeks of treatment with Clopine®, and at least every 28 days thereafter. In some situations, WBC and neutrophil counts must be monitored more frequently. Monitoring is also required after cessation of treatment with Clopine®. See section regarding 'Post-therapy blood testing', page 18.

Monitoring of patients for cardiac changes while on Clopine® therapy is also recommended.

ClopineCentral™ Contacts

ClopineCentral™ is administered by Pfizer. For information and enquiries, contact the Clopine® Services Manager on 1800 656 403.

Access to the web based ClopineCentral™ database is found at http://www.clopine.com.au

Amendments to the ClopineCentral™ Protocol

All Centres will be notified of changes to the ClopineCentral™ Protocol.

Changes to the protocol are also reviewed by the TGA before distribution.

Registration and roles of Centres and Personnel

The 'stakeholders' involved in ClopineCentral™ are:

- Centres – hospital, clinic or other health facility that is involved with the use of Clopine®
- Clinics – defined General Practitioner Clinics or Retail Pharmacies registered under the governing Clopine® Centre
- The Centre Coordinator – the staff member who is responsible for administration of the Clopine® program for that Centre
- Pharmacists
- Specialists/prescribers ('Medical Practitioners')
- Patients

Each individual and institution must be registered with ClopineCentral™.

Privacy

The ClopineCentral™ monitoring system has been established taking patient privacy issues into account. To ensure appropriate privacy notification is given to the patient and/or carer about the collection, use, disclosure and security of patient information, a Clopine® Monitoring System Privacy Statement must be signed by any new Clopine® Patient. In addition, every patient's acceptance of the Privacy Statement should be recorded within ClopineCentral™. The Clopine® Monitoring System Privacy Statement can be found on page 28.

Registration of a Centre

A Centre is defined as a hospital, clinic or other health facility that is involved with the use of Clopine®, in conjunction with ClopineCentral™. Patients are listed as 'belonging' to a specific Centre through their registration at the Centre.

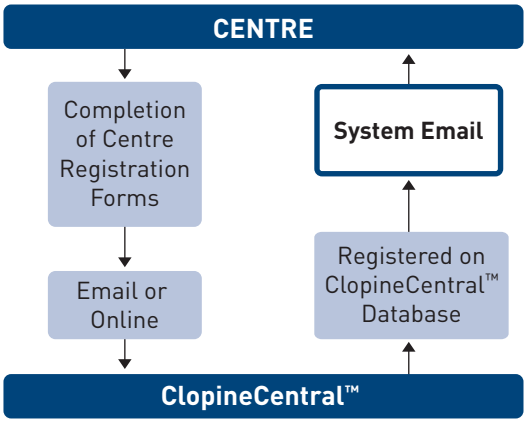
Pfizer will provide Clopine® only to Centres that are registered in accordance with the ClopineCentral™ Protocol.

Centres wishing to register with ClopineCentral™ can do so via the Centre Registration Form (see page 22). The completed form must be signed by:

- The Centre's Director of Psychiatry or Clinical director of Mental Health or Practice Principle Psychiatrist
- The Director/Manager of pharmacy or delegate, and
- The Centre Coordinator

By signing the Centre Registration Form, the directors and the Centre signify their agreement to comply with the ClopineCentral™ Protocol. It is also the responsibility of the directors/managers listed above to see that other departmental staff members who are registered with ClopineCentral™ abide by the protocol, and those who are not registered do not prescribe or dispense Clopine®.

Centre Registration



Once a Centre has been registered with ClopineCentral™, an email link is established between the Centre and ClopineCentral™. ClopineCentral™ will confirm the Centre's registration by email.

Registration of a Clinic

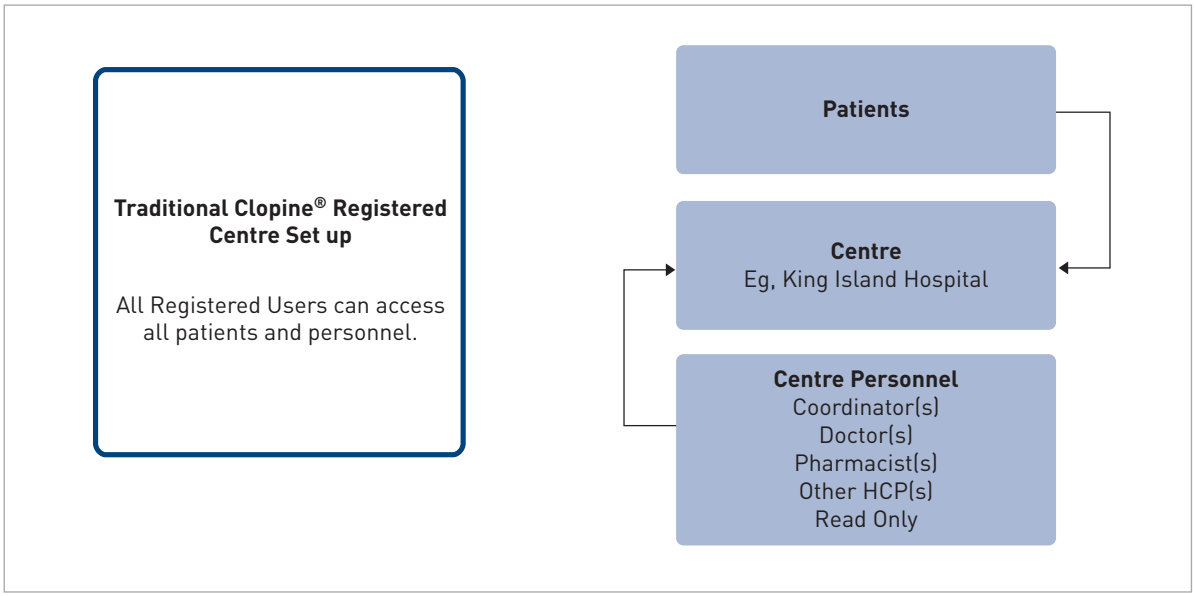
ClopineCentral™ gives your Hospital or Mental Health Centre the ability to group patients into Clinics.

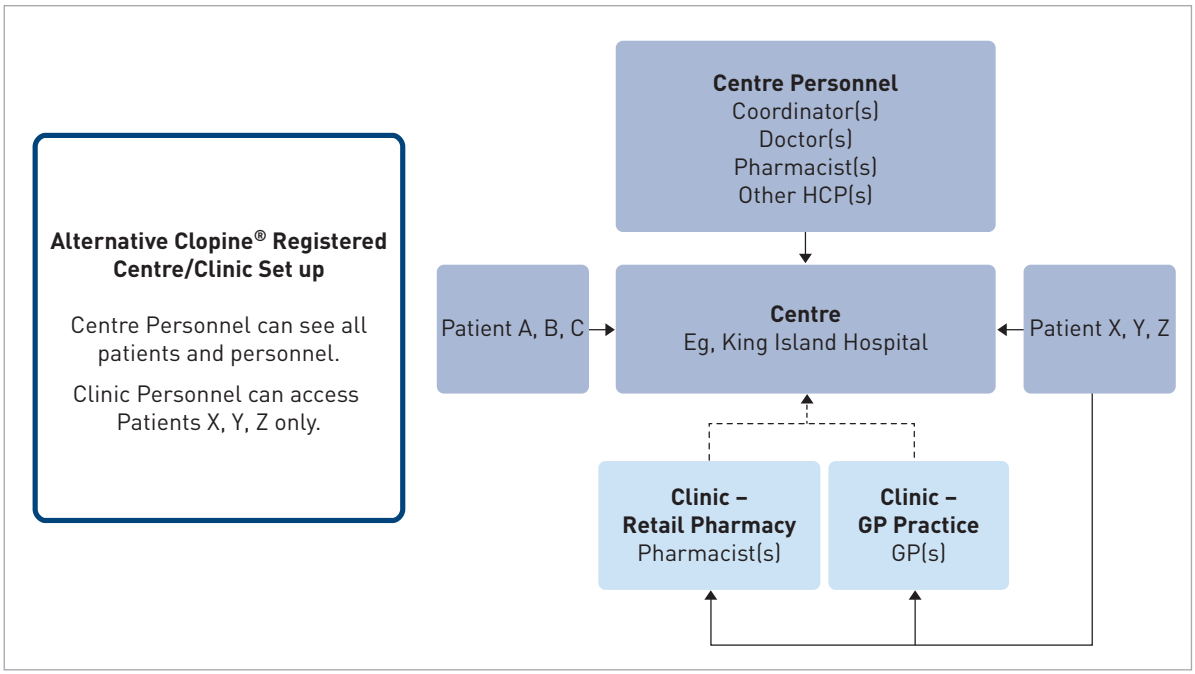
These clinics can be used to group patients under a specific Mental Health Community Centre or attach a General Practitioner Clinic or Pharmacy.

The Centre can then register specific users to have access to their specific Clinic, rather than having access to the entire Centre the patient is registered under.

Clinic setup also allows sites to search for those patients linked to a specific pharmacy, or those that have a General Practitioner Clinic attached to their record.

To register a new Clinic, complete the Clinic Registration form (page 23) or go online to www.clopine.com.au.





HCP = Healthcare Professional
GP = General Practitioner

Centre Personnel requirements

Every healthcare professional who is involved in the supply of Clopine® to patients must be registered in the ClopineCentral™ database.

All personnel must complete the relevant registration form and return the form to ClopineCentral™. Alternatively the Centre Coordinator also has the ability to register Centre Personnel online at www.clopine.com.au.

If the Centre Coordinator, Medical Practitioner or Pharmacist is away from the Centre, another ClopineCentral™ registered person must be available to take responsibility for patients attending the Centre.

Upon receipt of each faxed or electronic form, ClopineCentral™ will confirm each registration by email. The Centre Coordinator will be advised each time a new registration is confirmed at their Centre.

Registration and role of the Centre Coordinator

Every Centre that is part of ClopineCentral™ must nominate a Centre Coordinator who will oversee and facilitate successful adherence to the ClopineCentral™ Protocol at the Centre. The Centre Coordinator must register with ClopineCentral™ as described previously.

The responsibilities of the Centre Coordinator are:

- To ensure that the required blood tests are carried out for each patient, the results checked promptly and appropriate action is taken whenever necessary
- To transmit or process all registrations, patient data and blood test results from the Centre to ClopineCentral™
- To act as the point of contact for, and to be aware of, all communication between the Centre and ClopineCentral™
- To ensure that the Centre operates within the ClopineCentral™ Protocol
- Ensure that ClopineCentral™ has the most up to date details as soon as available.

If the Centre Coordinator relocates, the Centre must nominate another registered person to take on the role of Coordinator until a new Centre Coordinator is appointed and registered with ClopineCentral™.

Registration and role of Medical Practitioners

Medical Practitioners must be registered with ClopineCentral™ before prescribing Clopine®.

When a Medical Practitioner relocates, he or she must re-register with ClopineCentral™ at the new Centre/Clinic either by completion of a new 'Medical Practitioner Registration Form' or contacting ClopineCentral™. Medical Practitioners must notify the Centre Coordinator if they are no longer an active prescriber at that Centre/Clinic.

If a Medical Practitioner is working at more than one Centre, he or she must register with ClopineCentral™, under each Centre using the 'Medical Practitioner Registration Form'.

It is the Medical Practitioner's duty to ensure that, if they are unavailable, another ClopineCentral™ registered Medical Practitioner is available to assume their responsibilities.

Registered Medical Practitioners may only prescribe Clopine® to patients who are registered with ClopineCentral™ (see 'Patient' section of this document). It is the Medical Practitioner's responsibility to register the patient with ClopineCentral™ before Clopine® treatment is commenced.

Before prescribing Clopine®, Medical Practitioners must review the Full Approved Product Information for Clopine®.

It is the Medical Practitioner's responsibility to ensure that each patient for whom he/she prescribes Clopine® is monitored in accordance with the requirements of the ClopineCentral™ Protocol as described in this document.

A WBC and neutrophil count must be performed and the results checked by the Medical Practitioner to ensure

that they comply with the ranges before Clopine® is prescribed.

In the first 18 weeks of treatment, each prescription for Clopine® must be for no more than seven day supply. After the first 18 weeks treatment, up to four weeks (28 days) supply may be prescribed.

The Medical Practitioner must ensure that each prescription for Clopine® is either accompanied by a WBC and neutrophil count result or this information has been entered online (www.clopine.com.au). The prescription and (if not entered online) Clopine® Blood Count Results must be forwarded by the Medical Practitioner to a ClopineCentral™ registered Pharmacist for review before Clopine® can be dispensed.

Registration and role of Pharmacist

Pharmacists must register with ClopineCentral™ before dispensing Clopine®, by the completing the 'Pharmacist Registration Form' which can be found on page 27.

If a Pharmacist is working at more than one Centre/Clinic, he or she must register with ClopineCentral™ under each Centre/Clinic. If a Pharmacist relocates to another Centre/Clinic, his or her registration at the original Centre/Clinic terminates he or she must register again with ClopineCentral™ at the new Centre/Clinic. Pharmacists must notify the Center Coordinator or ClopineCentral™ when they cease dispensing from a Centre/Clinic.

Registered Pharmacists may only dispense Clopine® to patients who are registered with ClopineCentral™ (see 'Patient' section of this document) upon receipt of a prescription for Clopine® written by a Medical Practitioner who is also registered with ClopineCentral™.

Before dispensing each Clopine® prescription, the registered Pharmacist should be satisfied that the prescription has been signed by a Medical Practitioner who is registered with ClopineCentral™ and that the prescription is accompanied by the results of a WBC and neutrophil count or this information has been entered online (www.clopine.com.au), which is no older than 48 hours and has been reviewed and approved by the patient's Medical Practitioner.*

For the first 18 weeks of treatment, each prescription for Clopine® must be for no more than seven day supply. After 18 weeks of treatment, up to four weeks (28 days) supply of Clopine® may be dispensed.

A prescription for Clopine® must not be dispensed unless it is accompanied by or entered online the results of a WBC and neutrophil count and is reviewed by the Pharmacist and deemed acceptable. An acceptable result is a WBC and neutrophil count within defined ranges (see page 13) and the test was performed no more than 48 hours prior to presentation of the prescription. (Refer to Appendix 1 on page 39 for further details regarding the 48 hour rule).

After each Clopine® prescription is dispensed, if not already done so, the results of the WBC and neutrophil counts are entered onto the ClopineCentral™ database or returned to the Centre Coordinator to be transmitted to the ClopineCentral™ database, or faxed directly to ClopineCentral™ by pharmacy. The Pharmacist must then enter the relevant dispensing information that accompanies that result either online, faxed directly to ClopineCentral™ or the Coordinator. If an increase in the dose of Clopine® is required before the next blood test is due, the Medical Practitioner may prescribe sufficient medication to maintain the increased dose until the next blood test, and the Pharmacist may dispense this extra medication. However, a patient must not be given extra medication to last beyond the date of their next scheduled blood test.

Registration for other types of personnel

A Centre can register their personnel at their Centre under other roles for the purpose of giving these users access to their Clopine® Patients via the online ClopineCentral™ platform.

Healthcare professionals – this allows users to access patient profiles, add blood test results, patient assessments, notes, recommended tests. This role may be appropriate for a Case Manager or psychologist.

Read Only – this allows users to access patient profiles and run certain reports but are not able to add information. This role may be appropriate for a Network Director or Director of Pharmacy.

Patients and ClopineCentral™

Initiation of treatment

Please review the approved Product Information for Clopine® before prescribing.

Clopine® Monitoring System Privacy Statement

The Clopine® Monitoring System Privacy Statement provides important information and privacy notification to patients and/or carers and to ensure that patients and/or carers are aware that de-identified data from the ClopineCentral™ database may be used as part of a cross-check with an existing database or other databases of patients to ensure non-rechallenge if they are or have been terminated for haematological reasons and may also be used for research, which may subsequently be published.

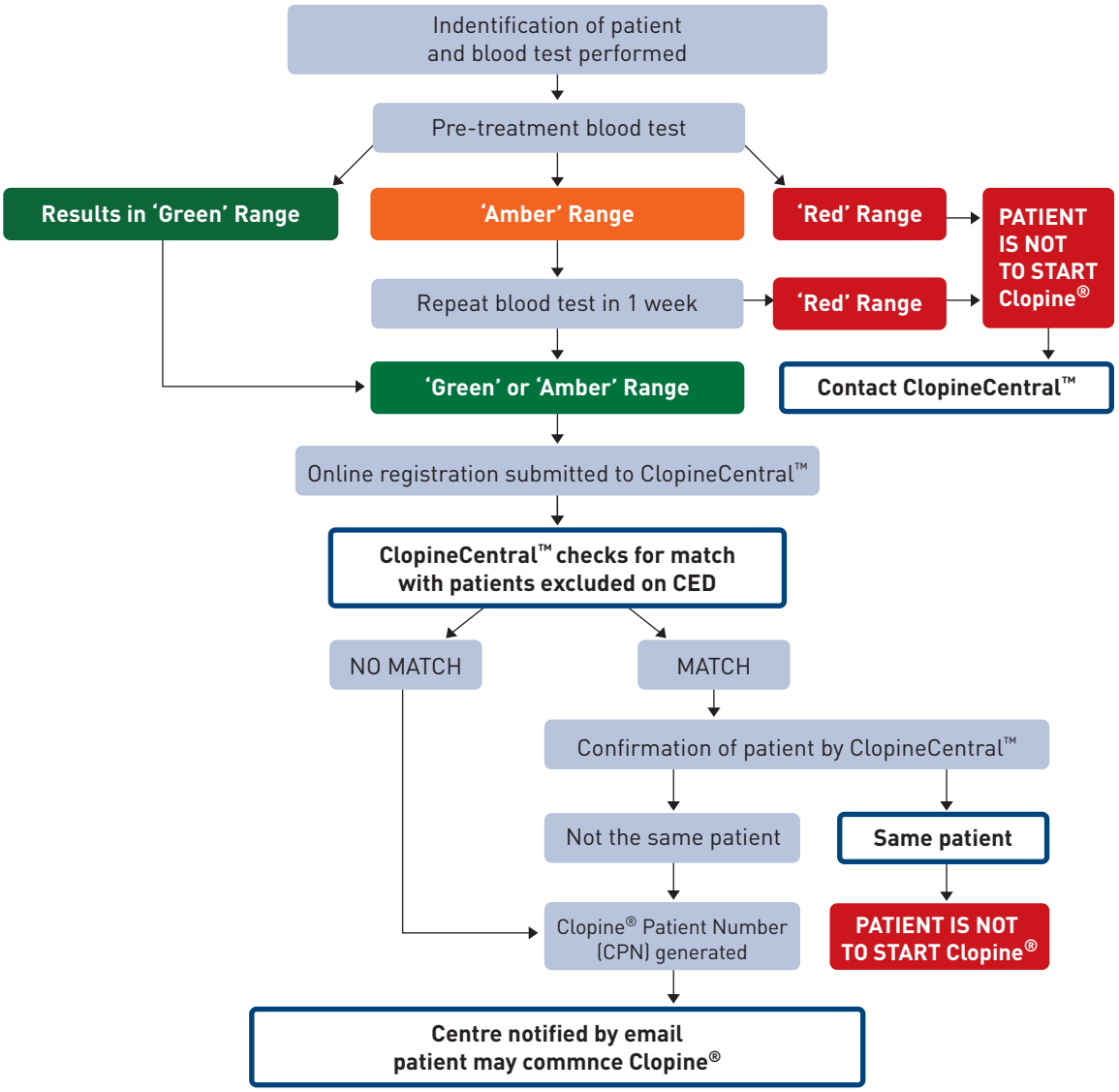
If the patient is involuntary or under age, Medical Practitioners should follow the treating institution's policy or the Mental Health Act for that state to treat the patient with Clopine®.

The Patient Registration Forms (pages 30, 31 and 32) must record that the Clopine® Monitoring System Privacy Statement has been signed by the patient (page 28).

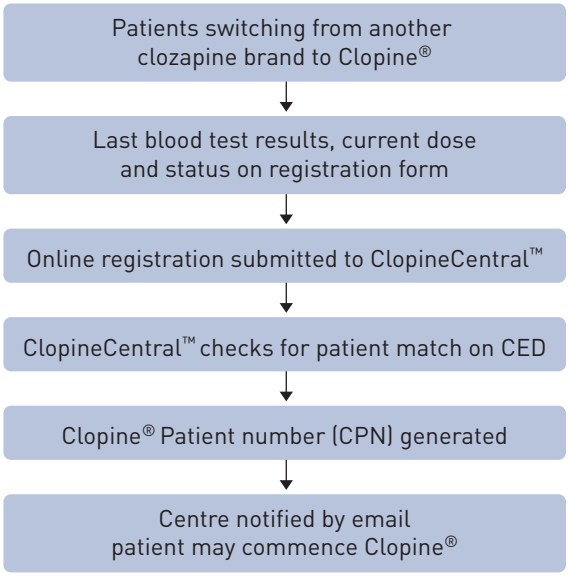
Please note: the signed Clopine® Monitoring System Privacy Statement must not be sent to Pfizer, and should be retained in the patient's own medical records.

Patient Registration Procedure

New Patient Registration



Registration for patients switching from other brands of clozapine



Prior to initiation of therapy, a Patient Registration Form must be submitted online to ClopineCentral™ and a pre-treatment WBC and neutrophil count obtained for that patient. This blood sample must be collected no more than 10 days prior to starting treatment with Clopine®. Patient registrations can be submitted online (www.clopine.com.au) or by using the forms on pages 31 and 32.

The details required with the patient registration are:

- Patient's initials*
- Date of birth*
- Sex*
- Blood group*
- Weight (optional)
- Name of Centre
- Name of Centre Coordinator
- Name of Clinic (if applicable)
- Has the patient agreed and signed the privacy statement? Y/N
- Has the patient given Recommended Tests Consent? Y/N
- History of previous drug-induced neutropenia? Y/N
- History of bone marrow disorders? Y/N
- Is there a family history of schizophrenia? Y/N
- Is the patient diabetic? Y/N
- Name of prescribing Medical Practitioner (who must be registered with ClopineCentral™)
- Results of baseline WBC and neutrophil count (which must be performed no more than 10 days before commencing treatment) - refer to table below

Status	WBC and neutrophil count result	Action
'Green' range	WBC >3.5 x 10^9/L AND Neutrophils >2.0 x 10^9/L	Following successful registration, commencement of Clopine® therapy is at the discretion of the treating Medical Practitioner.
'Amber' range	WBC 3.0 – 3.5 x 10^9/L AND/OR Neutrophils 1.5 – 2.0 x 10^9/L	Wait one week and repeat blood count. If haematological results are still in this range, Clopine® therapy **may** be commenced under the supervision of the treating Medical Practitioner once registration has been completed.
'Red' range	WBC <3.0 x 10^9/L AND/OR Neutrophils <1.5 x 10^9/L	***Patient is permanently ineligible for treatment with Clopine®. Consult haematologist.***

- Date of blood test

* These details are used to identify the individual patient and are compulsory for registration.

The person who completes the Patient Registration Form must also ascertain whether the patient has a history of previous drug-induced neutropenia or bone marrow disorders, which may place him or her at increased risk of developing agranulocytosis or neutropenia while on Clopine® therapy. This is still applicable should the patient have trialed Clopine® previously.

The Medical Practitioner must also determine any reasons that may make the patient unsuitable for treatment with Clopine® e.g. cardiac concerns.

Upon receipt of the completed Patient Registration Form, ClopineCentral™ will cross-check the patient's details against the CED to ascertain whether the patient has ever previously discontinued clozapine therapy due to agranulocytosis or neutropenia. If this has occurred, that patient is ineligible for treatment with Clopine® because of the high risk of recurrence if he or she is rechallenged with clozapine.

Generation of a Clopine® Patient Number

As part of the registration process, once a patient has been deemed eligible for treatment with Clopine®, he or she is allocated a Clopine® Patient Number (CPN). This number will be used in all subsequent correspondence with ClopineCentral™.

The Clopine® Patient Number comprises the following:

Followed by an **F** to differentiate a Clopine® Patient Number from all other Clozapine Patient Numbers.
Clopine® therapy cannot be commenced until a Clopine® Patient Number is generated.

Concurrent therapy with other agents

Drugs known to have a substantial potential to depress bone marrow function (e.g. phenothiazines or carbamazepine) should not be used concurrently with clozapine. In addition, the concomitant use of long acting depot antipsychotics should be avoided because of the inability of these medications (which may have the potential to be myelosuppressive) to be rapidly removed from the body in situation where this may be required, e.g. granulocytopenia. Please see the Full Clopine® Product Information for other potential interactions with medicines. For a copy of the Full Clopine® Product Information please direct any medical queries to Pfizer's Medical Information team on 1800 675 229.

Switching from other antipsychotic agents

It is generally recommended that clozapine should not be used in combination with other antipsychotics. When clozapine therapy is to be initiated in a patient undergoing oral antipsychotic therapy, other antipsychotic drugs should first be discontinued by tapering the dosage downward over a period of approximately one week. Once the other antipsychotic is completely discontinued for at least 24 hours, begin clozapine as described previously.

If, in a particular patient, discontinuation of the antipsychotic is not a realistic option prior to institution of clozapine, combination therapy can be cautiously undertaken in hospital during a transition period. Taper the dose of antipsychotic downward over a period of a week, while gradually adding clozapine in increasing doses.

Initial dosage

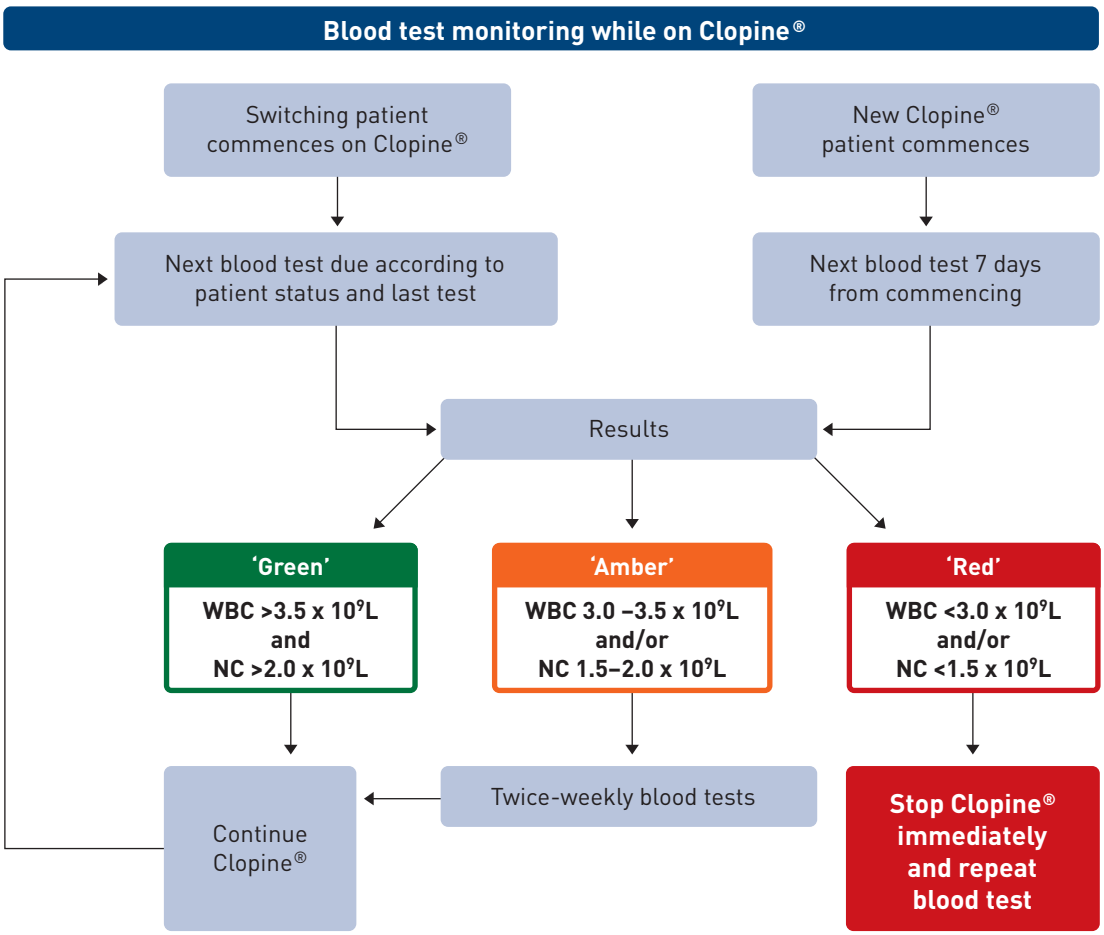
The dosage must be adjusted individually. For each patient the lowest effective dose should be used. Appropriate resuscitative facilities should be available and the patient adequately supervised during initiation of therapy. The recommended dosages that follow are for oral administration.

12.5mg once or twice daily on the first day, followed by 25mg, once or twice, on the second day. If well tolerated, the daily dose may then be increased slowly in increments of 25-50mg in order to achieve a dose level of up to 300mg/day within two to three weeks. Thereafter, if required, the daily dose may be further increased in increments of 50 to 100mg at half-weekly or, preferably, weekly intervals.

Monitoring vital signs

Patients should be kept under close supervision and their vital signs monitored, in an environment with appropriate resuscitative facilities, for approximately six hours following the first dose of Clopine® so that any adverse events associated with the initial dose can be detected and treated.

Haematological monitoring during therapy with Clopine®



All patients receiving Clopine® must have WBC and neutrophil counts performed before commencing therapy, regularly during therapy and after ceasing therapy.

All prescriptions for Clopine® must be accompanied by a WBC and neutrophil count that have been performed and evaluated no more than 48 hours prior to the prescription being dispensed. The Medical Practitioner must have reviewed the results and confirmed that they are satisfactory.

If a patient's WBC and/or neutrophil count fall into the specified 'Amber' range during therapy, twice weekly monitoring is required. If WBC or neutrophil counts fall into specified 'Red' range, Clopine® therapy must be discontinued and that patient becomes permanently ineligible for Clopine® therapy.

Status	WBC and neutrophil count result	Action
'Green' range	WBC >3.5 x 10^9/L AND Neutrophils >2.0 x 10^9/L	Continue Clopine® therapy
'Amber' range	WBC 3.0 – 3.5 x 10^9/L AND/OR Neutrophils 1.5 – 2.0 x 10^9/L	**Continue Clopine® therapy with twice-weekly blood tests until return to 'green' range**
'Red' range	WBC <3.0 x 10^9/L AND/OR Neutrophils <1.5 x 10^9/L	**Stop Clopine® therapy immediately. This patient is permanently ineligible for treatment with Clopine®. Refer to 'red' range section for more information on treatment of 'red' patients.**

The ClopineCentral™ database will automatically show which of these categorises apply to a patient when the patient's blood test results are entered.

The following must take place within a 48-hour period:

- Collection of a blood sample
- Haematological examination by the Centre's laboratory
- Clinical examination of the patient
- Review of the blood test results by the ClopineCentral™ registered Medical Practitioner
- Generation of a prescription
- Dispensing medication
- Enter blood test results (including responsible Medical Practitioner, pharmacist and dispensing details) onto the ClopineCentral™ database

Once the Medical Practitioner has reviewed the blood test results, a prescription can be written. Upon receipt of both these, the Pharmacist can dispense the patient's Clopine® medication.

Blood test results must be entered into the ClopineCentral™ database by the Centre during the 48-hour period.

Blood test results which are faxed to ClopineCentral™ for entry into the database must be on the Clopine® Blood Count Record Form with corresponding registered Medical Practitioner sign off. Pathology reports should not be sent directly to Pfizer. Please use the blood count record form on page 34.

Overdue blood test results

ClopineCentral™ automatically alerts the Centre Coordinator to any overdue blood tests so that follow-up can be arranged.

The Centre should notify ClopineCentral™ if a patient absconds or refuses to allow any further blood testing to be performed.

Frequency of monitoring

WBC and neutrophil counts must be performed for all patients on Clopine® therapy:

- At least weekly for the first 18 weeks of therapy
- At least every four weeks (28 days) after the first 18 weeks of therapy.

In some cases, more frequent monitoring is required (see next section).

Situations requiring increased frequency of blood testing

Clinical signs of infection

If a patient on Clopine® therapy develops symptoms of infection and/or of neutropenia (e.g. flu-like symptoms, mouth ulcers, sore throat or fever) the Medical Practitioner should obtain an immediate differential blood count in addition to performing a clinical assessment of the patient. If both are normal, Clopine® therapy should continue in conjunction with twice-weekly (i.e. within four days of each other) WBC and neutrophil counts and clinical review until the symptoms resolve.

'AMBER' RANGE: WBC count 3.0 – 3.5 x 10^9/L and/or neutrophil 1.5 – 2.0 x 10^9/L

If a patient's WBC count is 3.0 – 3.5 x 10^9/L and/or neutrophil 1.5 – 2.0 x 10^9/L ('amber' range), Clopine® therapy may be continued, but blood testing and clinical review of this patient must be increased to twice a week until both counts return to the target ('green') range (WBC > 3.5 x 10^9/L and neutrophils > 2.0 x 10^9/L). During this time, Clopine® therapy may only be dispensed until the time of the next blood test.

'RED' RANGE: WBC < 3.0 x 10^9/L and/or neutrophils < 1.5 x 10^9/L

If a patient's WBC count falls below 3.0 x 10^9/L and/or the neutrophil count falls below 1.5 x 10^9/L, CLOPINE® THERAPY MUST BE DISCONTINUED IMMEDIATELY.

The 'red' blood test results must be transmitted immediately to ClopineCentral™ and another differential blood count performed within 24 hours and each day thereafter, until the patient has a 'green' blood test result, in conjunction with close clinical monitoring. Once the patient has attained a 'green' blood test result, post-therapy monitoring must still be adhered to. From the day a patient attains a 'green' result, a weekly patient must have four weeks of weekly monitoring and a monthly patient must have a blood test 28 days after that 'green' result. All blood test results following the first 'red' results must also be transmitted to ClopineCentral™.

Management of a patient whose WBC and/or neutrophil counts decrease further following withdrawal of Clopine® should be under the supervision of a clinical haematologist. It may be advisable to refer the patient to a specialised haematologist unit where facilities for protective isolation are available. Upon receipt of a 'red' blood result, ClopineCentral™ will contact the Centre to discuss the case and confirm that Clopine® therapy has been discontinued in this patient. The treating Medical Practitioner and clinical haematologist must inform ClopineCentral™ of any adverse events or changes to the patient's condition throughout their management.

Patients in whom Clopine® therapy has been discontinued as a result of white blood cell deficiencies (WBC < 3.0 x 10^9/L and/or absolute neutrophil count < 1.5 x 10^9/L) must not be re-exposed to clozapine.

Additional haematological support

Whilst the management of any patient remains the responsibility of the treating Medical Practitioner, ClopineCentral™ may be contacted for additional information and protocol advice. Enquiries should be directed to ClopineCentral™ at Pfizer on 1800 656 403.

Eosinophilia

Unexplained eosinophilia may occur, especially in the initial weeks of treatment with Clopine®. Discontinuation of therapy is recommended if the eosinophil count rises above 3.0 x 10^9/L, Therapy should restart only after the eosinophil count has fallen below 1.0 x 10^9/L.

Reporting of serious or unexpected adverse event(s)

All adverse events, whether expected or unexpected, must be reported to ClopineCentral™ within 24 hours of the event. Even if initial information is scant, these details should be forwarded to ClopineCentral™ pending provision of further data.

Supply of additional medication to patients – Dispensation

In special circumstances, Pfizer and ClopineCentral™ may authorise Centres to dispense one-off additional medication to patients, with a corresponding extension of the time between blood tests. This request is called a Dispensation. Requests for such extensions must be submitted to ClopineCentral™ online (www.clopine.com.au) or by using the form on page 37. Patients must also have an up-to-date, complete blood history on their ClopineCentral™ profile for dispensations to be approved.

There are two types of dispensations that can be applied for as approved by the Clopine® Haematologist - 'Medication only' (no extension between blood tests) and 'Medication and Blood tests'.

Medication only

Request for medication supply under 180 days is approved without the need to contact the haematologist, even for patients with history of 'amber' and 'reds'. However patients must have their usual blood test monitoring.

Personnel applying for this type of dispensation should be aware that it is up to the Centre Coordinator and the Medical Practitioner to decide whether the dispensation is appropriate for their patient. And in particular, whether they believe that patient will be compliant with their mandatory blood tests.

Medication and blood tests

If the patient has 'green' blood history the following can be approved without the need to contact the haematologist:

- Monthly patients can have their blood test date extended by 14 days
- Weekly patients can have their blood test date extended by 2 days

Please note patient treatment decisions are the physicians responsibility therefore they can request to extend blood test dates and/or medication supply based on their clinical decision.

Dosage of Clopine®

Please review the approved Full Product Information for Clopine® before prescribing.

Therapeutic dose range

In most patients, antipsychotic efficacy can be expected with 200 to 450mg/day in divided doses. The total daily dose may be divided unevenly, with the larger portion at bedtime.

Because of the significant risk of agranulocytosis and seizure, events which both present a continuing risk over time, the extended treatment of patients failing to show an acceptable level of clinical response should ordinarily be avoided.

Maximum dose

For most patients, the recommended maximum dose is 600mg/day. However, a few patients may require larger doses to obtain maximum therapeutic benefit in which case judicious increments (i.e. not exceeding 100mg) are permissible up to a maximum of 900mg/day.

Maintenance dose

After achieving optimum therapeutic benefit, many patients can be maintained effectively on lower doses. Careful downward titration is recommended. With daily doses not exceeding 200mg, a single administration in the evening may be appropriate.

Discontinuing therapy with Clopine®

In the event of planned termination of Clopine® therapy, a gradual reduction in dose is recommended over a one to two week period. If abrupt discontinuation is necessary, the patient's mental state should be followed carefully. The patient should also be carefully observed for symptoms related to cholinergic rebound such as profuse sweating, headache, nausea, vomiting and diarrhoea.

The Medical Practitioner must notify ClopineCentral™ of the date and reason of discontinuation. These details can be submitted online (www.clopine.com.au) or by using the form on page 38.

Post-therapy blood testing

Weekly

In patients who are on weekly monitoring at the time of discontinuation for non-haematological reason, testing must occur at the time of therapy interruption and must be continued weekly for at least four weeks.

Monthly

Patients who are on monthly blood testing at the time of discontinuation for non-haematological reason should have one further blood count performed one month after therapy ceases. Note that the patient should have a blood test performed close to the time of discontinuation and then four weeks later. It is not desirable for a patient to cease therapy just before the next blood test is due and then to wait a further four weeks before the post-therapy blood count is performed as this would represent an unacceptable eight-week period between blood tests.

Twice-weekly (increased frequency) testing

Patients who are being monitored twice weekly because of WBC and/or neutrophil counts in the 'amber' range (WBC 3.0 – 3.5 x 10^9/L and/or neutrophils 1.5 – 2.0 x 10^9/L) or signs of infection, should continue to have twice weekly blood tests until the WBC count returns to > 3.5 x 10^9/L and the neutrophil count to > 2.0 x 10^9/L, the 'green' range. Once the patient is back in the 'green range' their post-monitoring blood test frequency should reflect their pre-'amber' protocol. i.e. if they were weekly, they should receive 4 weeks of weekly blood tests.

Restarting therapy after discontinuation

Re-registration of a patient

A new Patient Registration Form must be submitted to ClopineCentral™ for patients who are recommencing when the:

- patient has ceased for ≥ three months or;
- patient is recommencing at a new Centre

Patient registrations can be submitted online (www.clopine.com) or by using the form on page 31.

All patients recommencing Clopine® following an interruption in treatment must have a pre-treatment blood test. This includes patients with therapy interruptions of less than a week.

Clopine® must not be recommenced in patients who have previously developed blood dyscrasias related to clozapine therapy.

Recommencing therapy after interruption

In patients for whom the interval since the last dose of clozapine exceeds two days, treatment should be reinstated with 12.5mg (half a 25mg tablet) given once or twice daily on the first day. If this dose is tolerated, it may be feasible to titrate the dose to the therapeutic level more quickly than is recommended for initial treatment. However, in any patient who has previously experienced respiratory or cardiac arrest with initial dosing (please review 'Other Precautions' section of the approved Product Information for Clopine®) but was then able to be successfully titrated to a therapeutic dose, retitration should be done with extreme caution.

Haematological monitoring after interruption of therapy

Three days or less interruption

Continue monitoring as normal.

More than three days and less than four weeks of interruption

If the interruption in therapy occurs during the first 18 weeks of treatment i.e. while patients are on a schedule of weekly monitoring, weekly monitoring should continue for at least six weeks after treatment is recommenced, or for as long as is necessary to achieve a total of 18 weeks of weekly monitoring. For example, a patient whose therapy is interrupted after 15 weeks should have weekly blood tests for six weeks after therapy is reinstituted; a patient whose therapy was interrupt at week nine should be monitored for a further nine weeks after therapy is resumed.

Patients who were on a schedule of monthly monitoring when treatment was interrupted should be monitored weekly for six weeks on resumption of therapy, then monthly thereafter if no abnormalities have been detected.

Four weeks or more interruption of therapy

If treatment with Clopine® is interrupted for more than four weeks, monitoring should recommence as for a new patient.

Transferring a patient to another Centre

Within Australia

The Centre Coordinator at the original Centre should contact the Centre Coordinator at the new Centre to discuss the transfer and confirm that the new Coordinator accepts responsibility for the monitoring of the patient.

ClopineCentral™ should be advised in advance when a patient on Clopine® therapy is to be transferred to a new Centre. The Centre Coordinator at the originating Centre should notify ClopineCentral™ of the transfer by submitting the request online (www.clopine.com.au) or by using the form on page 35. This form includes the following information:

- Clopine® Patient Number
- Name of new Centre
- Date to present at new Centre
- Last blood test results and dose prescribed/dispensed
- Has the new Centre been notified of the transfer?

ClopineCentral™ will provide the new Centre with the relevant haematological history for the patient, as well as any additional information input by the originating Centre.

Outside Australia

If a patient on Clopine® therapy is to transfer outside Australia, the Centre Coordinator and/or treating Medical Practitioner should contact ClopineCentral™ on 1800 656 403 to discuss arrangements for the ongoing care and monitoring of the patient on an individual basis.

The Patient Overseas Travel Form (see page 36) may assist with this process. This form is also available online (www.clopine.com.au).

References

- Approved Full Product Information for Clopine® (clozapine), Pfizer Australia Pty Ltd, available on request from Medical Information, phone 1800 675 229 or email medicalaffairs.anz@Pfizer.com.
- Ronaldson KJ, Fitzgerald PB, Taylor AJ, *et al.*, A New Monitoring Protocol for Clozapine-Induced Myocarditis Based on an Analysis of 75 Cases and 94 Controls. *Aust N Z J Psychiatry*, 2011; 45(6):458-465.

Contacts for ClopineCentral™

Phone: 1800 656 403

Fax: 1800 657 454

Email: ClopineCentral@pfizer.com

Clopine® Services Manager
Pfizer Australia Pty Limited
38-42 Wharf Rd
West Ryde NSW 2114
AUSTRALIA

Web Address: http://www.clopine.com.au

Please review the approved Full Product Information for Clopine® before prescribing.

The approved Full Production Information for Clopine® can be obtained from Pfizer by contacting our Medical Information Department on 1800 675 229.

REGISTRATION FORM FOR ClopineCentral™ CENTRES

All sections of this form must be completed

This document signifies the intent of the following parties to be involved in prescribing Clopine® (clozapine) at the Centre named below, within the patient monitoring protocol set by ClopineCentral™: Director of Psychiatry/ Clinical Director of Mental Health, Director of Pharmacy, Centre Coordinator.

By signing this form, the undersigned signify their commitment and that of the Centre to abide by the ClopineCentral™ Protocol and to ensure that staff members within their respective departments register with ClopineCentral™ and comply appropriately with the ClopineCentral™ Protocol.

CENTRE NAME:

NAME OF PSYCHIATRIC UNIT:

ADDRESS:

STATE: POSTCODE:

PHONE: FAX:

EMAIL ADDRESS:

DIRECTOR OF PSYCHIATRY/CLINICAL DIRECTOR OF MENTAL HEALTH

FIRST NAME:

SURNAME: SALUTATION:

SIGNATURE: DATE: / /

PHONE: FAX:

DIRECTOR OF PHARMACY

FIRST NAME:

SURNAME: SALUTATION:

ADDRESS (IF NOT LOCATED IN CENTRE):

STATE: POSTCODE:

SIGNATURE: DATE: / /

PHONE: FAX:

NOMINATED CENTRE COORDINATOR

FIRST NAME:

SURNAME: SALUTATION:

SIGNATURE: DATE: / /

ADDRESS (IF NOT LOCATED IN CENTRE):

STATE: POSTCODE:

PHONE: FAX:

EMAIL ADDRESS:

Note: To be registered with ClopineCentral™, this completed form must be emailed to ClopineCentral@pfizer.com, submitted online (www.clopine.com.au) or faxed to 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone 1800 656 403. Requests for access to your own personal information held for registration purposes may also be directed to ClopineCentral™. Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR ClopineCentral™ CLINICS

All sections of this form must be completed

This document signifies the intent of the following parties to be involved in Clopine® (clozapine) monitoring at the clinic named below, within the patient monitoring protocol set by ClopineCentral™: Practice Manager/ Pharmacist In Charge/Clopine® Centre Coordinator.

By signing this form, the undersigned signify their commitment and that of the clinic to abide by the ClopineCentral™ Protocol and to ensure that staff members within their respective departments register with ClopineCentral™ and comply appropriately with the ClopineCentral™ Protocol.

*** Indicates areas that must be completed before form may be submitted**

* CLINIC NAME:

* NAME OF ASSOCIATED CLOPINE® CENTRE(S):

CLINIC ADDRESS:

STATE: POSTCODE:

* PHONE: FAX:

EMAIL ADDRESS:

PRACTICE MANAGER/PHARMACIST IN CHARGE

* FIRST NAME:

* SURNAME: SALUTATION:

* SIGNATURE: DATE: / /

* PHONE: FAX:

CENTRE COORDINATOR CONFIRMATION:

☐ I have contacted my Clopine® Centre Coordinator for pre-approval of this new Clinic Registration.

* CENTRE COORDINATOR NAME:

* PHONE/EMAIL:

Pre-approval from your Clopine® Centre Coordinator is required prior to the submission of a new Clinic Registration. If you have not done so, please contact ClopineCentral™ to obtain their contact details.

Note: To be registered with ClopineCentral™, this completed form must be emailed to ClopineCentral@pfizer .com, submitted online (www.clopine.com.au) or faxed to 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone 1800 656 403. Requests for access to your own personal information held for registration purposes may also be directed to ClopineCentral™.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR CENTRE COORDINATOR/ COORDINATOR ASSISTANTS

By signing this document, I signify that:

- I intend to participate in the distribution of Clopine® (clozapine) in association with the ClopineCentral™ program
- I agree to abide by the ClopineCentral™ Protocol.

PRESCRIBING REMINDERS

1. Only patients who are registered with ClopineCentral™ may be prescribed Clopine®.
2. For the first 18 weeks of treatment, no more than 1 weeks supply of Clopine® may be prescribed at once. After 18 weeks, no more than 28 days supply may be prescribed. The patient's haematological profile must be assessed before each prescription for Clopine® is written.
3. A WBC and Neutrophil count no more than 48 hours old must accompany each prescription or be entered online (www.clopine.com.au) for Clopine® to be supplied.

*** Indicates areas that must be completed before form may be submitted**

* FIRST NAME: SALUTATION:

* SURNAME:

POSITION HELD:

CLOPINE® CENTRE:

☐ Coordinator Assistant Registration

* ADDRESS:

* SUBURB: * STATE: * POSTCODE:

* PHONE: FAX:

* MOBILE PHONE NUMBER:

* EMAIL ADDRESS:

* COORDINATOR SIGNATURE: DATE: / /

Note: To be registered with ClopineCentral™, this completed form must be emailed to ClopineCentral@pfizer.com, submitted online (www.clopine.com.au) or faxed to 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone 1800 656 403. Requests for access to your own personal information held for registration purposes may also be directed to ClopineCentral™.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR CLINIC COORDINATOR/ COORDINATOR ASSISTANTS

By signing this document' I signify that:

- I intend to participate in the distribution of Clopine® (clozapine) in association with the ClopineCentral™ program
- I agree to abide by the ClopineCentral™ Protocol.

PRESCRIBING REMINDERS

1. Only patients who are registered with ClopineCentral™ may be prescribed Clopine®.
2. For the first 18 weeks of treatment' no more than 1 weeks supply of Clopine® may be prescribed at once. After 18 weeks' no more than 28 days supply may be prescribed. The patient's haematological profile must be assessed before each prescription for Clopine® is written.
3. A WBC and Neutrophil count no more than 48 hours old must accompany each prescription or be entered online (www.clopine.com.au) for Clopine® to be supplied.

*** Indicates areas that must be completed before form may be submitted**

* FIRST NAME: SALUTATION:

* SURNAME:

POSITION HELD:

* CLOPINE® CLINIC:

☐ Coordinator Assistant Registration

* ADDRESS:

* SUBURB: * STATE: * POSTCODE:

* PHONE: FAX:

* MOBILE PHONE NUMBER:

* EMAIL ADDRESS:

* COORDINATOR SIGNATURE: DATE: / /

Note: To be registered with ClopineCentral™, this completed form must be emailed to ClopineCentral@pfizer.com, submitted online (www.clopine.com.au) or faxed to 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone 1800 656 403. Requests for access to your own personal information held for registration purposes may also be directed to ClopineCentral™.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR MEDICAL PRACTITIONERS

Registration can also be submitted online (www.clopine.com.au) by the Centre Coordinator.

By prescribing Clopine® (clozapine) I intend to participate in ClopineCentral™ and the ClopineCentral™ Protocol.

I agree to abide by the obligations of a Medical Practitioner as described in the ClopineCentral™ Protocol and I agree that, notwithstanding these obligations, I remain solely responsible for the management of patients for whom I prescribe Clopine®.

PRESCRIBING REMINDERS

1. Only patients who are registered with ClopineCentral™ may be prescribed Clopine®.
2. For the first 18 weeks of treatment, no more than 1 week supply of Clopine® may be prescribed at once. After 18 weeks, no more than 28 days supply may be prescribed. The patient's haematological profile must be assessed before each prescription for Clopine® is written.
3. A WBC and Neutrophil count no more than 48 hours old must accompany each prescription or be entered online (www.clopine.com.au) for Clopine® to be supplied.

*** Indicates areas that must be completed before form may be submitted**

MEDICAL PRACTITIONER

* FIRST NAME:

* SURNAME:

CLOPINE® CENTRE:

* **OR**

CLOPINE® CLINIC: (if applicable)

* PRACTICE NAME:

* PRACTICE ADDRESS:

* STATE: * POSTCODE:

* PHONE: * FAX:

* MOBILE PHONE NUMBER: PAGER:

* EMAIL ADDRESS:

☐ General Practitioner ☐ Consultant ☐ Registrar ☐ Other

Note: To be registered with ClopineCentral™, this completed form must be emailed to ClopineCentral@pfizer.com, submitted online (www.clopine.com.au) or faxed to 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone 1800 656 403. Requests for access to your own personal information held for registration purposes may also be directed to ClopineCentral™.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR PHARMACISTS

Registration can also be submitted online (www.clopine.com.au) by the Centre Coordinator.

By dispensing Clopine® (clozapine) I intend to participate in the distribution of Clopine® within ClopineCentral™ and I hereby agree to comply with the ClopineCentral™ Protocol.

I agree to abide by the obligations of a Pharmacist as described in the ClopineCentral™ Protocol and I agree that, notwithstanding these obligations, I remain solely responsible for the professional dispensing of Clopine® as prescribed by a responsible Medical Practitioner.

DISPENSING REMINDERS

1. Only patients who are registered with ClopineCentral™ may be prescribed Clopine®.
2. For the first 18 weeks of treatment, no more than 1 weeks supply of Clopine® may be dispensed at once. After 18 weeks, prescriptions may be for up to 28 days supply. The patient's haematological profile must be assessed by the responsible Medical Practitioner before each prescription for Clopine® is written.
3. A WBC and Neutrophil count must accompany each prescription or be entered online (www.clopine.com.au) for Clopine® to be supplied, and the blood test must have been performed no more than 48 hours prior to the presentation of the prescription; and without the blood test results, the prescription must not be dispensed.

*** Indicates areas that must be completed before form may be submitted**

PHARMACIST:

* FIRST NAME: * SALUTATION:

* SURNAME:

CLOPINE® CENTRE:

* **OR**

CLOPINE® CLINIC: (if applicable)

* NAME OF PHARMACY:

* ADDRESS OF PHARMACY:

* SUBURB: * STATE: * POSTCODE:

* PHONE: * FAX:

* MOBILE PHONE NUMBER:

* EMAIL ADDRESS:

Note: To be registered with ClopineCentral™, this completed form must be emailed to ClopineCentral@pfizer.com, submitted online (www.clopine.com.au) or faxed to 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone 1800 656 403. Requests for access to your own personal information held for registration purposes may also be directed to ClopineCentral™.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

CLOPINE® (clozapine) MONITORING SYSTEM PRIVACY STATEMENT

In order for you to be treated with Clopine®, it is a Therapeutic Goods Administration (TGA) requirement that you undergo regular blood tests and your healthcare professional register you on the Clopine® monitoring system facilitated by Pfizer Australia Pty Ltd (Pfizer), the supplier of Clopine®.

This document provides important information about how your personal information is handled under the Clopine® monitoring system.

PART A: Essential information required for treatment with Clopine®

Collection of information: Pfizer may be provided with the following personal information about you for inclusion in the Clopine® monitoring system:

Registration Information	As part of the registration process, your healthcare professional will enter into the monitoring system: • your initials, date of birth, blood group and gender • the name of your healthcare professionals and their place of business • your dose of Clopine® • blood test results (white blood cell and neutrophil counts)
Pathology Results	Your ongoing blood test results will be sent by your healthcare professional for entry into the monitoring system.
Other information provided by your healthcare professionals	Pfizer may be provided with the following mandatory personal information about you by your healthcare professionals through the monitoring system: • any changes to your dose of Clopine® • if you stop Clopine® therapy for any reason • the name of the pharmacy which dispenses Clopine® to you • any adverse events potentially associated with your treatment

Use of information: Pfizer will provide healthcare professionals involved in your care with access to your personal information to assist them to manage your treatment on Clopine®. Pfizer also uses de-identified information: to administer, develop and improve the Clopine® monitoring system; to satisfy its regulatory and reporting requirements; for research and publication purposes.

Disclosure of information: Pfizer engages a consultant haematologist and cardiologists to assist your healthcare professional if they have queries about your treatment and these specialists may be provided with your de-identified information. Pfizer may also engage third party IT vendors to administer and host the Clopine® monitoring system and your personal information may be disclosed to such organisations in order for them to perform their IT services.

Your personal information in the Clopine® monitoring system will be cross-checked with the Clozapine Exclusion Database, a database of patients who have received clozapine under other brand names or from other suppliers, and/or other Australian suppliers of clozapine in order to ensure that patients who discontinue clozapine on the basis of their blood test results do not recommence therapy. Whilst on clozapine if your blood tests results indicate you should discontinue treatment with Clopine® certain information (including your

initials, date of birth, gender, blood group, name of treating healthcare professional and white cell/neutrophil count) will be added to the Database and be accessible by other suppliers of clozapine in order to ensure that you do not recommence treatment with clozapine if your treatment was discontinued for clinical reasons.

If you experience an adverse event associated with your Clopine® treatment, Pfizer is required to provide de-identified information about the adverse event to the TGA. Pfizer may also disclose de-identified information about your adverse event or product safety complaint to Pfizer's affiliated companies for data entry and record management purposes. In addition, Pfizer is required to provide de-identified statutory reports to the TGA regarding the national use of clozapine.

PART B: Additional personal information provided by your healthcare professionals

In addition to the tests and other mandatory information referred to above, healthcare professionals involved in your Clopine® treatment may provide additional personal information about you to Pfizer which will also be collected and held in the Clopine® monitoring system to assist your healthcare professionals to monitor and facilitate clinical management of potential cardiac changes, cholesterol levels, blood glucose levels, and other general health related parameters. For administrative purposes your healthcare may also include identifying information such as your name, address and telephone number and certain health information in the Clopine® monitoring system. You should discuss with your healthcare professionals whether they intend to collect and store additional personal information in the Clopine® monitoring system, and if required request information on their privacy practices.

You may choose to withdraw your consent to the collection, storage, use and disclosure of your personal information in accordance with this Part B of the consent form at any time. You may do this by informing your healthcare professional.

PART C: Other information

Your personal information will be stored in the Clopine® monitoring system in an electronic format with high levels of security to protect it from loss or misuse.

Pfizer is unlikely to transfer your identifiable personal information overseas. In the event that Pfizer transfers your identifiable personal information outside Australia, Pfizer will comply with the requirements of the Privacy Act that relate to transborder data flows.

The Privacy Policy of Pfizer is available at www.pfizer.com.au and contains further information about how you may access and/or correct the personal information held about you as required by law, as well as information about making a complaint about a breach of the Privacy Act and how Pfizer will deal with such a complaint.

Patient Consent

I have been informed by my medical practitioner about the drug Clopine®. This medical practitioner has explained to me the procedures that must be followed with Clopine® treatment and the associated Clopine® monitoring system which the TGA requires Pfizer to maintain.

I confirm that I have read and understood this consent form. I have also had the opportunity to ask the medical practitioner questions and I understand and am satisfied with the answers I have received.

I consent to the collection, storage, use and disclosure of my personal information as set out in this statement.

Patient name (and authorised representative, if applicable)

Patient (or authorised representative) **signature**

Date:

Medical Practitioner Acknowledgment

I, the patient's medical practitioner, confirm that I have explained to the patient why the collection, storage, use and disclosure of their personal information is required for their treatment with Clopine® and the nature of the Clopine® monitoring system.

Medical practitioner name

Medical practitioner signature

Date:

REGISTRATION FORM FOR NEW PATIENTS

Patient registrations can also be submitted online (www.clopine.com.au) by the Centre Coordinator or Medical Practitioner.

Clopine® (clozapine) therapy must not be commenced until ClopineCentral™ has approved this registration and a Clopine® Patient Number is generated.

*** Indicates areas that must be completed before this form may be submitted**

* PATIENT INITIALS: * DATE OF BIRTH: / /

* BLOOD GROUP: * SEX: WEIGHT: KG

* 1. HAS THE PATIENT EVER HAD AN EPISODE OF DRUG-INDUCED NEUTROPENIA? YES ☐ / NO ☐

* 2. HAS THE PATIENT EVER HAD A BONE MARROW DISORDER? YES ☐ / NO ☐

* 3. HAS THE PATIENT AGREED AND SIGNED THE PRIVACY STATEMENT? ? YES ☐ / NO ☐

4. DOES THE PATIENT HAVE A FAMILY HISTORY OF SCHIZOPHRENIA? YES ☐ / NO ☐

5. DOES THE PATIENT HAVE DIABETES? YES ☐ / NO ☐

6. HAS THE PATIENT AGREED TO RECOMMENDED TEST CONSENT? YES ☐ / NO ☐

If the answer is 'yes' to either question 1 and/or 2, do not initiate Clopine® (clozapine) therapy in this patient.

* DATE OF PRE-TREATMENT BLOOD TEST: / /

* WHITE BLOOD CELL COUNT#: x 10^9/L

* NEUTROPHIL COUNT#: x 10^9/L

The results for the pre-treatment WBC/neutrophil count must be from a blood sample collected within 10 days of the date of treatment initiation.

* CLOPINE® CENTRE:

* CLOPINE® CLINIC: (if applicable)

* MEDICAL PRACTITIONER NAME:

* PHONE: * EMAIL:

CENTRE COORDINATOR NAME:

* NAME OF PERSON COMPLETING FORM:

(Please Print Name)

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone: 1800 656 403.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR PATIENTS SWITCHING FROM ANOTHER CLOZAPINE BRAND TO CLOPINE® (clozapine)

Patient registrations can also be submitted online (www.clopine.com.au) by the Centre Coordinator or Medical Practitioner.

Clopine® therapy must not be commenced until ClopineCentral™ has approved this registration and a Clopine® Patient Number is generated.

*** Indicates areas that must be completed before this form may be submitted**

* PATIENT INITIALS: * DATE OF BIRTH: / /

* BLOOD GROUP: * SEX: WEIGHT: KG

* 1. HAS THE PATIENT PREVIOUSLY RECEIVED CLOZAPINE? YES ☐ / NO ☐
(If answer to question 1 is NO, then please complete the New Patient Registration Form)

* 2. HAS THE PATIENT EVER HAD AN EPISODE OF DRUG-INDUCED NEUTROPENIA? YES ☐ / NO ☐

* 3. HAS THE PATIENT EVER HAD A BONE MARROW DISORDER? YES ☐ / NO ☐

* 4. HAS THE PATIENT AGREED AND SIGNED THE PRIVACY STATEMENT? YES ☐ / NO ☐

5. DOES THE PATIENT HAVE A FAMILY HISTORY OF SCHIZOPHRENIA? YES ☐ / NO ☐

6. DOES THE PATIENT HAVE DIABETES? YES ☐ / NO ☐

7. HAS THE PATIENT AGREED TO THE RECOMMENDED TEST CONSENT? YES ☐ / NO ☐

If the answer is 'yes' to either question 1 and/or 2, do not initiate Clopine® (clozapine) therapy in this patient.

* DATE OF LAST BLOOD TEST: / /

* WHITE BLOOD CELL COUNT#: x 10^9/L

* NEUTROPHIL COUNT: x 10^9/L * DOSAGE: mg/Day

* PATIENT STATUS (Please tick): ☐ WEEKLY ☐ MONTHLY ☐ TWICE WEEKLY

* Please indicate date of clozapine commencement: / /

Has there been any recent therapy interruptions? YES ☐ / NO ☐

If yes, please indicate date treatment was ceased: / /

And date treatment was recommenced: / /

* CLOPINE® CENTRE:

* CLOPINE® CLINIC: (if applicable)

* MEDICAL PRACTITIONER NAME:

CENTRE COORDINATOR NAME:

* NAME OF PERSON COMPLETING FORM:

(Please Print Name)

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone: 1800 656 403.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

REGISTRATION FORM FOR MULTIPLE PATIENTS SWITCHING TO CLOPINE® (clozapine)

Patient registrations can also be submitted online (www.clopine.com.au) by the Centre Coordinator or Medical Practitioner.

Clopine® therapy must not be commenced until ClopineCentral™ has approved this registration and a Clopine® Patient Number is generated.

*** Indicates areas that must be completed before this form may be submitted**

	1	2	3	4	5
* PATIENT INITIALS:					
* DATE OF BIRTH:					
* SEX:					
* BLOOD GROUP:					
* 1. HAS THE PATIENT EVER HAD AN EPISODE OF DRUG-INDUCED NEUTROPENIA OR A BONE MARROW DISORDER? *(please circle)*	Y/N	Y/N	Y/N	Y/N	Y/N
* 2. HAS THE PATIENT AGREED AND SIGNED THE PRIVACY STATEMENT?	Y/N	Y/N	Y/N	Y/N	Y/N
3. DOES THE PATIENT HAVE A FAMILY HISTORY OF SCHIZOPHRENIA?	Y/N	Y/N	Y/N	Y/N	Y/N
4. DOES THE PATIENT HAVE DIABETES?	Y/N	Y/N	Y/N	Y/N	Y/N
5. HAS THE PATIENT AGREED TO THE RECOMMENDED TEST CONSENT?	Y/N	Y/N	Y/N	Y/N	Y/N
* CURRENT STATUS OF PATIENT: #W/M/A	W/M/A	W/M/A	W/M/A	W/M/A	W/M/A
* CLOZAPINE COMMENCEMENT DATE:					
* DATE OF LAST BLOOD TEST:					
* WHITE CELL COUNT x 10^9/L					
* NEUTROPHIL COUNT x 10^9/L					
* DOSAGE: mg/Day					

#W=WEEKLY, M=MONTHLY, A='AMBER'

If the answer to question 1 is 'yes' do not initiate Clopine® (clozapine) therapy in this patient.

* CLOPINE® CENTRE:

* CLOPINE® CLINIC: (if applicable)

* MEDICAL PRACTITIONER NAME:

CENTRE COORDINATOR NAME:

* NAME OF PERSON COMPLETING FORM:

(Please Print Name)

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. Registration will be confirmed by email. ClopineCentral™ Phone: 1800 656 403.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

CLOPINE® (clozapine)
BLOOD COUNT RECORD FORM

* Indicates areas that must be completed before this form may be submitted

Blood count results can also be submitted online (www.clopine.com.au) by either the Medical Practitioner, pharmacist or Centre Coordinator.

This form is for recording the patient's WBC and neutrophil count at commencement of Clopine® therapy, during treatment and after discontinuation of therapy.

Each prescription for Clopine® must be accompanied by a WBC and neutrophil count no more than 48 hours old. Unless a current WBC and neutrophil count has been performed and assessed as satisfactory, the next prescription for Clopine® cannot be dispensed.

PATIENT STATUS (Tick appropriate box)

☐ ON TREATMENT

☐ DISCONTINUED DATE DISCONTINUED: / /

• TERMINATION OF TREATMENT FORM COMPLETED? YES/NO (please circle)

COMMENCEMENT DATE: / /

(PLEASE PRINT ALL DETAILS)

* Clopine® PATIENT NUMBER:

* DATE BLOOD TAKEN: / / WEIGHT: kg

LABORATORY:

* WBC COUNT: x 10^9/L

* NEUTROPHIL COUNT: x 10^9/L

* PRESCRIBED CLOPINE® DOSAGE: mg/DAY

PRESENTATION: ☐ TABLET ☐ CLOPINE® SUSPENSION

* CENTRE:

* MEDICAL PRACTITIONER NAME:

* MEDICAL PRACTITIONER SIGNATURE:

* PHARMACIST NAME:

* PHARMACIST SIGNATURE:

PRESCRIPTION FILLED? YES ☐ / NO ☐ DATE DISPENSED: / /

DAYS DISPENSED:

PHARMACY NAME:

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. ClopineCentral™ Phone: 1800 656 403.

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PATIENT TRANSFER FORM

All sections of this form must be completed.

The Centre Coordinator at the receiving Centre must be contacted before submitting this form. Patient transfers can also be submitted online (www.clopine.com.au).

CLOPINE® PATIENT NUMBER:

NAME OF ORIGINATING CENTRE (TRANSFER FROM):

NAME OF CENTRE COORDINATOR:

REQUESTOR NAME: (if different from above)

PHONE: FAX:

EMAIL ADDRESS:

NAME OF NEW CENTRE (TRANSFER TO):

NAME OF CENTRE COORDINATOR:

PHONE: FAX:

EMAIL ADDRESS:

REASON:

DATE OF LAST BLOOD TEST: / /

WBC COUNT: x 10^9/L

NEUTROPHIL COUNT: x 10^9/L

DATE NEXT TEST IS DUE: / /

DAILY CLOPINE® DOSAGE: mg

DATE TO PRESENT TO NEW CENTRE: / /

HAS THIS FORM BEEN FAXED/EMAILED TO THE NEW CENTRE? YES ☐ / NO ☐

HAS THIS FORM BEEN FAXED/EMAILED TO ClopineCentral™? YES ☐ / NO ☐

HAS THE BLOOD HISTORY BEEN FAXED/EMAILED TO THE NEW CENTRE? YES ☐ / NO ☐

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. ClopineCentral™ Phone: 1800 656 403.

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PATIENT OVERSEAS TRAVEL FORM

All sections of this form must be completed.

Please fax the completed form to ClopineCentral™ on 1800 657 454.

Patient overseas travel requests can also be submitted online (www.clopine.com.au).

CLOPINE® PATIENT NUMBER:

CURRENT CENTRE:

COORDINATOR NAME:

PHONE: FAX:

ADDRESS(ES) WHILE OVERSEAS (if known):

PROPOSED DATE OF DEPARTURE:

PROPOSED DATE OF RETURN:

DATE OF LAST BLOOD TEST DUE BEFORE DEPARTURE: / /

DATES BLOOD TESTS ARE DUE WHILE AWAY:

TOTAL WEEKS REQUESTED EXTRA DISPENSATION:

DATE OF BLOOD TEST UPON RETURN:

TRAVELLING WITH CARER / FAMILY MEMBER:

PATIENT / CARER AWARE / INFORMED OF HOW TO TRANSMIT RESULTS BACK TO CENTRE:

CONTACT DETAILS OF TREATING PSCYHIATRIST:

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. ClopineCentral™ Phone: 1800 656 403.

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ADDITIONAL CLOPINE® (clozapine) TREATMENT DISPENSATION FORM

All sections of this form must be completed.

Dispensations can also be applied for online (www.clopine.com.au).

Additional medication cannot be prescribed or dispensed until approval is obtained from ClopineCentral™.

Please fax the completed form to ClopineCentral™ on 1800 657 454.

CLOPINE® PATIENT NUMBER:

CENTRE:

COORDINATOR NAME:

PHONE: FAX:

REASON FOR DISPENSATION:

TYPE OF DISPENSATION REQUIRED: Medication only ☐ **OR** Blood test and Medication ☐

TOTAL NUMBER OF EXTRA DAYS ADDITIONAL MEDICATION REQUIRED:

PROPOSED DISPENSATION DATE: / /

PROPOSED DATE OF NEXT BLOOD TEST: / /

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. Outcome of the request will be communicated by email. ClopineCentral™ Phone: 1800 656 403.

Your personal information will be handled at all times in accordance with Pfizer Australia's Privacy Policy (available at Pfizer Privacy www.pfizer.com.au/privacy).

THERAPY EVENT/TERMINATION OF TREATMENT FORM

*** Indicates areas that must be completed before this form may be submitted.**

This form is to record the discontinuation of Clopine® (clozapine) treatment and the reason for the discontinuation. Once completed, the form must be faxed to ClopineCentral™ on 1800 657 454.

Therapy events and adverse events can also be recorded online (www.clopine.com.au).

Please print all details

* CLOPINE® PATIENT NUMBER:

* DATE OF EVENT (DD/MM/YY)): / /

* DATE CLOPINE® THERAPY DISCONTINUED (DD/MM/YY): / /

PRESENTATION AT TIME OF EVENT: TABLET ☐ /CLOPINE® SUSPENSION ☐

* HAS THERAPY BEEN RECOMMENCED: YES ☐ / NO ☐

* DATE OF RECOMMENCEMENT (DD/MM/YY)): / /

*** TICK REASON(S) FOR INTERRUPTION / DISCONTINUATION:**

- ☐ CEASED DUE TO INADEQUATE RESPONSE
- ☐ CEASED DUE TO NO EFFICACY
- ☐ CEASED DUE TO NON-COMPLIANCE
- ☐ DEATH OF PATIENT
- ☐ CEASED DUE TO WEIGHT GAIN
- ☐ CEASED DUE TO PERSONAL REASONS
- ☐ CEASED DUE TO FAMILY/CARER OBJECTIONS
- ☐ CEASED DUE TO AGRANULOCYTOSIS
- ☐ CEASED DUE TO NEUTROPENIA
- ☐ CEASED DUE TO LEUCOPENIA/NEUTROPENIA
- ☐ CEASED DUE TO LEUCOPENIA
- ☐ CEASED DUE TO SEIZURES
- ☐ CEASED DUE TO POSTURAL HYPOTENSION
- ☐ CEASED DUE TO CARDIAC COMPLICATIONS
- ☐ CEASED DUE TO OTHER SIDE-EFFECTS (NOT LISTED ABOVE)
  Please specify:
- ☐ CEASED DUE TO MEDICAL REASONS (NOT LISTED ABOVE)
  Please specify:
- ☐ CEASED DUE TO EOSINOPHILIA
- ☐ OTHER (PLEASE SPECIFY):

* NAME OF MEDICAL PRACTITIONER:

* SIGNATURE OF MEDICAL PRACTITIONER: DATE: / /

* NAME OF CENTRE COORDINATOR:

* NAME OF CONTACT: (if different to above)

Note: This form must be emailed to ClopineCentral@pfizer.com or submitted online (www.clopine.com.au) or faxed to ClopineCentral™ on 1800 657 454. ClopineCentral™ Phone: 1800 656 403.

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Appendix 1 – 48 hour blood test rule

A valid blood test (no older than 48 hours) must accompany the Clopine® (clozapine) prescription or be entred online to enable a patient to have Clopine® dispensed (no more than 7 days for a weekly patient or 28 days for a monthly patient, if patients blood tests are within the 'green' range).[1]

The following is a suggested example of how to address the issue of a blood test that is older than 48 hours. It should be noted that consideration regarding a patient's adherence and current tablet supply should be addressed, including communication back to the Medical Practitioner or Centre Coordinator.

If the patient presents after the 48 hour window of the blood test, and the patient has not had an interruption in treatment, the amount supplied would be the original quantity minus the number of days late presenting. i.e. if a monthly patient presented on Thursday for a blood test taken on Monday then up to 27 days could be supplied.

Ultimately, the decision to supply clozapine is a clinical one and at the discretion of the registered Pharmacist and in accordance with their local clozapine protocols.

CLOPINE® (clozapine) MINIMUM PRODUCT INFORMATION

WARNING: Cases of myocarditis, some of which have been fatal, and cardiomyopathy have been reported in patients on clozapine.

Before prescribing, physicians must be registered with a monitoring program and comply with the relevant safety measures. Mandatory haematological monitoring is required.

Please review Full Product Information before prescribing.

I**NDICATIONS:** For people with treatment-resistant schizophrenia, non-responsive to, or intolerant of other antipsychotics. **DOSAGE:** Adults and children → 16 years: Starting at 12.5mg once or twice daily on the first day, slowly titrate to the lowest effective dose usually 200-450mg/day (given in divided doses). Maximum daily dose is usually 600mg. Occasionally doses up to 900mg/day have been used. Complex dosing schedule and specific instructions for suspension, see full PI. **CONTRAINDICATIONS:** History of drug induced granulocytopenia/agranulocytosis; bone marrow disorders; circulatory collapse; drug intoxication; comatose conditions; CNS depression; hypersensitivity to clozapine or any components; alcoholic and toxic psychoses; severe renal, cardiac, hepatic disease; uncontrolled epilepsy; paralytic ileus. **PRECAUTIONS:** History of bone marrow disorders. Not to be used with bone marrow suppressants or long acting depot antipsychotics. Discontinue therapy in cases of myocarditis, eosinophilia (→3000/mm^3) or a decrease in platelet count (←50,000/mm^3). Consider discontinuation if cardiomyopathy occurs. Others include history of seizures; cardiac, renal or hepatic disorders (monitor LFTs); infection; fever; abrupt withdrawal; rapid dose escalation; anticholinergic effects; hyperglycaemia and diabetes (Check BSLs); immobilisation; elderly especially those with dementia related psychosis; extrapyramidal effects; pregnancy (category C); lactation; children ←16. Caution is advised in patients with known cardiovascular disease or family history of QT prolongation. Interactions: Bone marrow-, CNS-, respiratory-depressants; anticholinergic-, hypotensive-, protein bound-, antipsychotic-drugs; alcohol; MAOIs; valproic acid; lithium; cytochrome P450 isoenzyme inhibitors and inducers; adrenaline and its derivatives; CNS active agents; medicines known to increase the QTc interval, or causing electrolyte imbalance. **ADVERSE REACTIONS:** Agranulocytosis; other haematological disturbances; fatigue; drowsiness; sedation; dizziness; headache; weight gain; postural hypotension; hypertension; syncope; tachycardia; disturbance in temperature regulation; myocarditis; cardiomyopathy; extrapyramidal symptoms; seizures; neuroleptic malignant syndrome; tremor; rigidity; akathisia; dysarthria; urinary incontinence/retention; impaired glucose tolerance; diabetes mellitus; hypersalivation; GI upset; confusion; agitation; delirium and restlessness; elevated liver enzymes; constipation; ECG changes; sudden death. See full PI.

Full Product Information is available on request from Pfizer Australia Pty Ltd 38-42 Wharf Rd, West Ryde NSW 2114, Australia. CLO V17.0 09/16

PBS Information: Section 100

Treatment of schizophrenia in patients who are non-responsive to, or intolerant of, other neuroleptic agents.

ANZ-CL001-LSOP-SD1 Version 1.0 Effective 01 April 2017
Author Andrew Chao

Please review Product Information before prescribing Clopine® (clozapine). See Boxed Warning.

Full Product Information is available on request from Pfizer Australia Pty Ltd
38-42 Wharf Rd, West Ryde NSW 2114, Australia Medical Information Phone: 1800 675 229
PP-CPE-AUS-0016

Last Reviewed March 2017