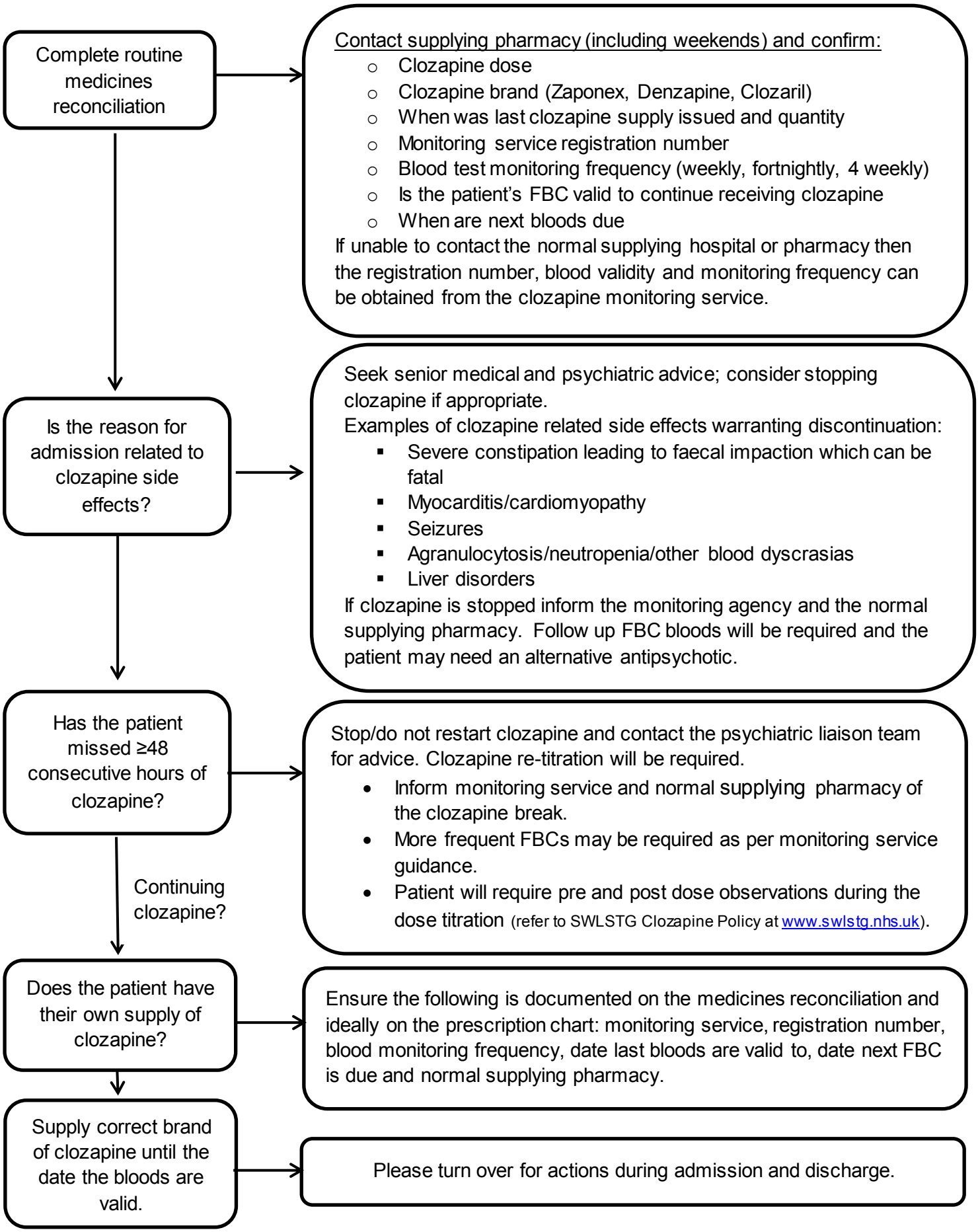
Guidance for pharmacy staff managing clozapine for patients admitted to Acute Hospitals

Introduction:

- Clozapine is an antipsychotic used most commonly in the management of treatment resistant schizophrenia. Patients prescribed clozapine tend to have a more severe and enduring illness.
- Patients on clozapine have a relatively high (~1%) risk of developing neutropenia/ agranulocytosis. Therefore patients prescribed clozapine are required to have regular mandatory FBC monitoring.
- There are 3 brands of clozapine - Zaponex® which is monitored by the Zaponex Treatment Access System (ZTAS), Clozaril® monitored by the Clozaril Patient Monitoring Service (CPMS) and Denzapine® monitored by the Denzapine Monitoring System (DMS) (details at end of document).
- It is a requirement that all patients prescribed clozapine, their consultant psychiatrist and the dispensing pharmacy are registered with the relevant clozapine monitoring agency, listed above.
- Clozapine is available in tablet, orodispersible tablet and liquid form. There are two liquid forms of clozapine, Denzapine® suspension, and a specials clozapine solution, monitored by ZTAS.
- Co-prescription of clozapine with other medicines that may cause blood dyscrasia increases the risk of neutropenia/agranulocytosis and is generally contra-indicated.
- Clozapine has a short half life. If clozapine has been omitted for more than 48 hours it must be re-titrated. Restarting at the previous dose would result in a high risk of seizures, tachycardia, hypotension and circulatory collapse. The speed of re-titration is multifactorial and advice should be sought from the patient's community psychiatrist or the liaison psychiatry team.
- Clozapine should be considered a critical medicine and supplies should be provided in a timely manner to avoid omission of clozapine for more than 48 hours. Sudden discontinuation of clozapine commonly results in an abrupt and severe psychotic relapse.
- In some medical scenarios e.g. acute infection, certain cardiac symptoms, or following a sudden cessation or reduction in smoking, patients may need a lower dose of clozapine than usual. The management of individual cases is best discussed with the liaison psychiatry team.
- Cigarette smoking induces clozapine metabolism, hence smoking cessation or reduction upon admission can lead to an increase in clozapine plasma levels (normal levels 0.35 – 0.6mg/L). Raised clozapine levels may cause drowsiness, ataxia, confusion and seizures.
- Acute hospital pharmacies must be registered with the monitoring services in order to place emergency orders, and ideally keep a small stockholding of clozapine to avoid delays in supply. It is recommended that local Acute Trusts register as emergency supply pharmacy with ZTAS if they are not already registered. To do this the Trust must liaise with the service providing a procedure outlining:
    - How clozapine (Zaponex) will be dispensed to patients
    - Checks in place to ensure a patient fulfils the criteria for being dispensed Zaponex (e.g. registered with ZTAS?
    - Checks in place to confirm whether the prescription is made by a ZTAS registered consultant or physician?
- For other manufacturers the pharmacy will need to contact the monitoring agencies directly to confirm their exact requirements.
- Clozapine is a hospital only medicine and will not normally be prescribed in primary care.

On Admission

NB – if the last dose was taken >48 hours ago, clozapine must not automatically be prescribed. Clozapine re-titration will be required



During Admission:

- Review the management of common clozapine side effects such as hypersalivation, constipation and sedation.
- Consider interactions with other medications that may affect clozapine plasma levels such as CYP1A2 inhibitors (e.g. ciprofloxacin, erythromycin) and inducers (e.g. phenytoin, rifampicin).
- Avoid concurrent prescribing of medicines that have a substantial potential for causing agranulocytosis.
- For patients who are smokers monitor any change in smoking habit during their admission, monitoring plasma levels and adjusting the dose accordingly to avoid both toxicity and sub-therapeutic plasma levels.
- Clozapine levels can be done using a "Magna pack" (obtained from Magna labs – contact below) which needs to be sent to Magna labs via Royal Mail post.
- Ensure FBC monitoring is done as required by the monitoring service and is reported to the monitoring service.
- Ensure the patient has enough supply and there is a new supply if the patient's own supply runs out.

On Discharge:

- Supply clozapine for the same duration as other medication unless it needs to be reduced as per FBC monitoring allowance.
- Inform the normal supplying pharmacy of the patient's discharge, and of the details, including amount of clozapine supplied. For SWLStG patients the TTA can be emailed to Medicines Information (see below) who will ensure a continued supply of clozapine is arranged and the prescription is altered accordingly by the community psychiatrist.

Contacts:

Monitoring Agencies		
ZTAS (Zaponex brand)	DMS (Denzapine brand)	CPMS (Clozaril brand)
Tel: 0207 365 5842 Fax: 0207 365 5843 Email: info@ztas.co.uk Supplier: Alloga UK LTD Tel: 01773441700	Tel: 0333 200 4141 Fax: 0333 200 4142 Email: Denzapine@britannia-pharm.com	Tel: 0845 769 8269 Fax: 0845 769 8379 or 8541 Email: cpms@mylan.co.uk
Dispensing Pharmacy		
South West London & St George's Mental Health Trust, Springfield hospital, SW17 7DJ	Tel: 0203 513 6829 / On-call pharmacist via security 0203 513 5000 Email Medicines Information: medinfo@swlstg.nhs.uk	
South London and Maudsley, SE5 8AZ	Tel: 0203 228 2317	
Magna Labs		
Tel: 01989 763 533		

Further Information:

Clozapine SmPCs – available from www.medicines.org.uk

SWLStG Clozapine Prescribing Policy – available from www.swlstg.nhs.uk