NHS Greater Glasgow & Clyde
Mental Health Services
Clozapine review group

Guidelines for the assessment and treatment of Clozapine Induced Constipation

Scope

This guideline is intended to support the appropriate assessment of patients prescribed clozapine to enable the early identification and treatment of clozapine induced constipation. It is relevant to healthcare professionals across NHS Greater Glasgow & Clyde involved in the care of people prescribed clozapine.

Background

Clozapine is a second generation antipsychotic licensed for treatment resistant schizophrenia, for use in patients intolerant of other antipsychotics and for the treatment of psychosis in Parkinson's disease. Clozapine has a range of potentially troublesome side effects, some of which can have significant impacts on patients' physical health. National guidelines to support improved physical health monitoring of patients prescribed clozapine were published by the Scottish Government in 2013 (*1*).

Constipation is a very common side effect of clozapine. It is estimated that up to 60% of patients who are prescribed clozapine experience constipation (*2*). Although rare, death from complications arising from constipation is estimated at more than three times the rate of death from agranulocytosis (2). Severe complications associated with clozapine induced constipation include intestinal obstruction, faecal impaction and paralytic ileus. Despite this however, unlike for blood dyscrasias, there are no mandatory requirements to monitor patients for and actively treat clozapine induced constipation.

Many services have begun to introduce more structured processes for physical health monitoring but there is a need for a systematic, frequent assessment to identify patients experiencing clozapine induced constipation and then implement effective treatment.

Risk factors for constipation are:

- Recent initiation of clozapine (greatest risk is during the first four months of treatment, but the risk persists)
- High dose or plasma clozapine level
- Intercurrent illness
- History of bowel surgery
- Concurrent use of other drugs known to cause constipation (opioids, drugs with anticholinergic properties. This includes most of the treatments for clozapine-induced hypersalivation e.g. hyoscine hydrobromide).
- Lifestyle issues e.g. poor diet and lack of exercise.
- Learning disability
- Old age
- Obesity

This guideline provides advice to services in NHS GG&C to support systematic assessment and treatment of clozapine induced constipation.

Assessment

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Patients prescribed clozapine are regularly in contact with NHS services in order to undergo mandatory full blood count testing. That frequent contact presents an opportunity to systematically assess patients for common serious side effects. There are two distinct phases to clozapine treatment, a titration/stabilisation phase and a maintenance phase. Assessment of clozapine induced constipation is appropriate in both phases. There must be a systematic, documented and reliable process of assessment throughout clozapine treatment.

It should be noted that clozapine has a greater potential for gastro-intestinal side effects compared with other antimuscarinic agents, possibly because of its anti-serotonergic properties. This may lead to slower colon transit, reduced gastro-colonic reflexes, increased colonic compliance and perhaps reduced intestinal sensitivity to distension. This means that patients may not complain about constipation and therefore should be asked regularly about bowel habit.

The risk of developing clozapine induced constipation should be clearly identified within care plans.

1. Titration/stabilisation phase

- During the work up for clozapine treatment, patients should be assessed for risk factors for constipation including previous history, concurrent treatments likely to induce constipation and lifestyle factors.
- Active bowel monitoring should occur throughout this phase at each clinically appropriate contact (Appendix 1 and 2). The use of daily bowel charts should be considered. Tools like the Bristol Stool Chart (see clozapine care plan in GG&C Clozapine Standards) should be used to help identify constipation.
- Any change in bowel habit should be immediately reported to the multi-disciplinary team and constipation actively treated (Appendix 3).
- Educate patients and carers about the risk of constipation. Consider providing the Choice and Medication Clozapine and Constipation Handy Fact Sheet (http://www.choiceandmedication.org/nhs24/)

2. Maintenance phase.

Patients with no history of constipation

- Patients should be assessed for constipation at every visit for their full blood count (Appendix 1). Tools like the Bristol Stool Chart should be used to help identify constipation.
- Any patient reporting changes in their bowel habit, abdominal pain or having less than 3 bowel movements per week must be immediately referred for a thorough medical assessment* including an abdominal examination if necessary (Appendix 3).
- Any patient with a high clozapine plasma level should be immediately examined for constipation.

Patients undergoing treatment for clozapine induced constipation

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- Any patient who is already receiving laxative treatment for clozapine induced constipation who continues to report problems should be referred for further medical assessment* including an abdominal examination if necessary.
- Any patient with a high clozapine plasma level should be immediately assessed for constipation.

***Note:** for the CMHTs referral would be to the patient's GP or if symptoms are severe to A&E. For patients in hospital contact the duty doctor. The patient's Responsible Medical Officer (RMO) must always be informed.

Re-introducing clozapine to patients who have experienced bowel obstruction, paralytic ileus or bowel surgery

For patients who have experienced severe bowel related clozapine adverse effects including obstruction, paralytic ileus or bowel surgery re-introducing clozapine carries considerable risks and is best avoided. Indeed, clozapine treatment is contra-indicated in existing ileus. If clozapine is the only effective treatment option for the patient an individualised care plan should be developed that considers and includes the following

- Use of the lowest possible clozapine dose with consideration of augmentation strategies to allow the minimum possible dosing
- Aggressive regular laxative therapy from the outset e.g. combination of osmotic and stimulants and consideration of novel agents
- Consider non-pharmacological approaches where appropriate e.g. abdominal massage
- Frequent assessment of bowel function (at least daily while in hospital and weekly as an out-patient). For patient's incapable of reporting bowel function reliably abdominal examination should be considered
- Regular plasma level monitoring
- Withdrawal of all drugs with the potential to worsen bowel motility including drugs with anti-cholinergic properties used to treat clozapine induced hypersalivation
- Seek advice from a clinical pharmacist
- Obtaining informed consent where possible or an appropriate second opinion (DMP if necessary) before recommencing clozapine.

Recording bowel function

A standardised approach to recording bowel function should be adopted and include numerical values for Bristol Stool Chart type and frequency. For example:

BSC (Bristol Stool Chart) - 4

BM (Bowel motion) - 2/7

Treatment

When clozapine induced constipation has been identified the following steps are recommended

- Recommend changes in lifestyle, diet and fluid intake
- Consider reducing the clozapine dose
- Stop or reduce medications that can cause constipation

- Consider non-pharmacological approaches where appropriate e.g. abdominal massage
- Flowcharts in appendices 2 and 3 give guidance on the recommended management of clozapine induced constipation.
- Review compliance regularly and if necessary prescribe more palatable options e.g. docusate. Patients frequently have issues complying with laxative treatment as they may be quite unpalatable.
- If severe symptoms emerge e.g. abdominal pain, distension, vomiting, overflow diarrhoea*, absent bowel sounds, acute abdomen, feculent vomitus or symptoms of sepsis, take the following steps
    - Stop clozapine and all other anti-muscarinic medicines
    - Refer for emergency medical treatment
    - Assess for bowel obstruction
- Patients presenting with diarrhoea may be constipated with main symptom presenting as overflow and that should be excluded before any treatment is considered.

For patients who cannot reliably identify bowel problems, the use of preventative laxative treatment throughout clozapine treatment may be appropriate. It should be noted that prolonged use of stimulant laxatives may lead to degenerative changes in colonic muscles and nerves.

References

1. National Standard for Monitoring the Physical Health of People Being Treated with Clozapine. Scottish Government. CMO (2013)12
2. Fact Sheet; Constipation. ZTAS December 2013
3. Lactulose versus polyethylene glycol for Chronic Constipation (Review). Cochrane Collaboration (2011)

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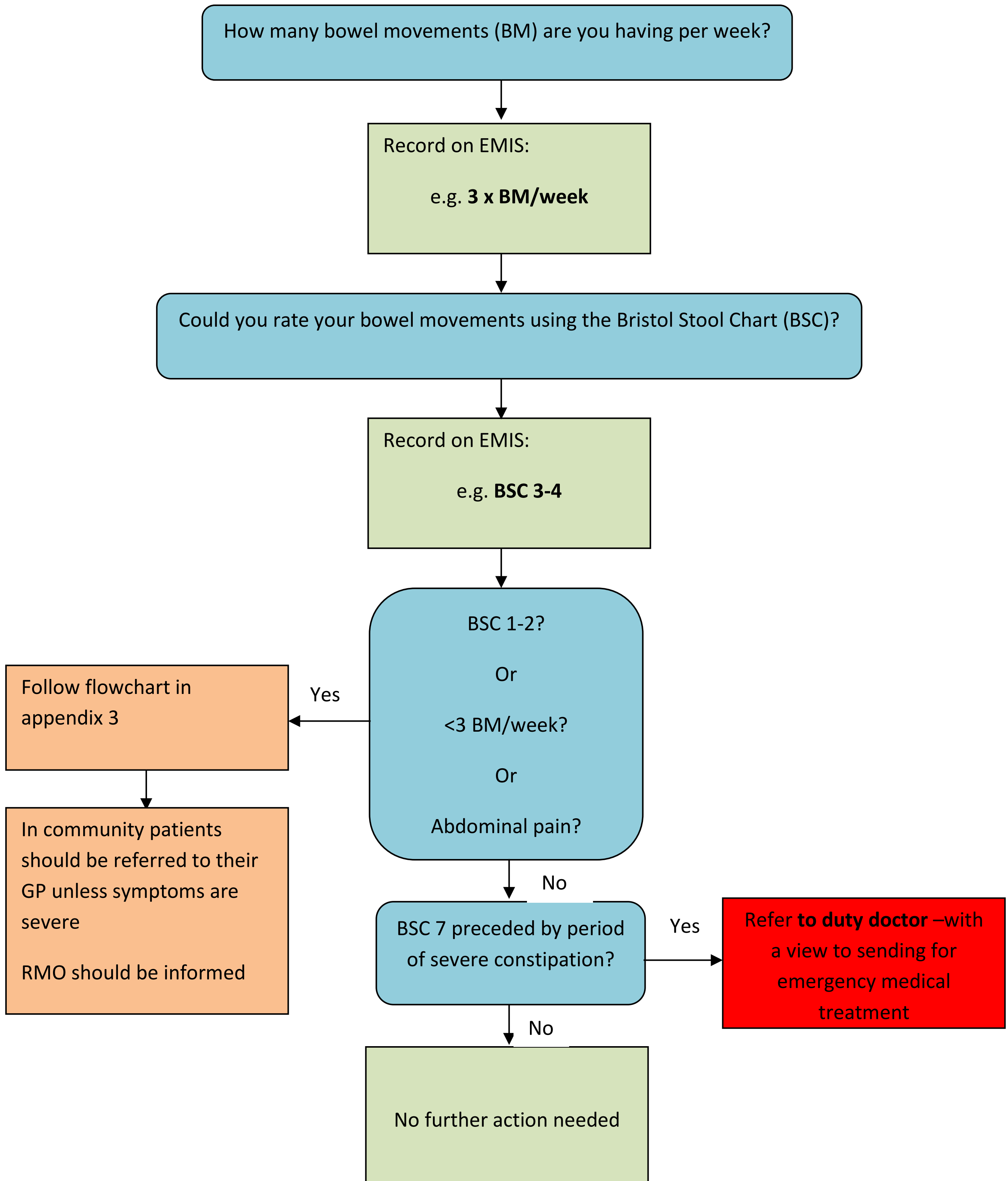
Appendix 1- Clozapine induced constipation monitoring



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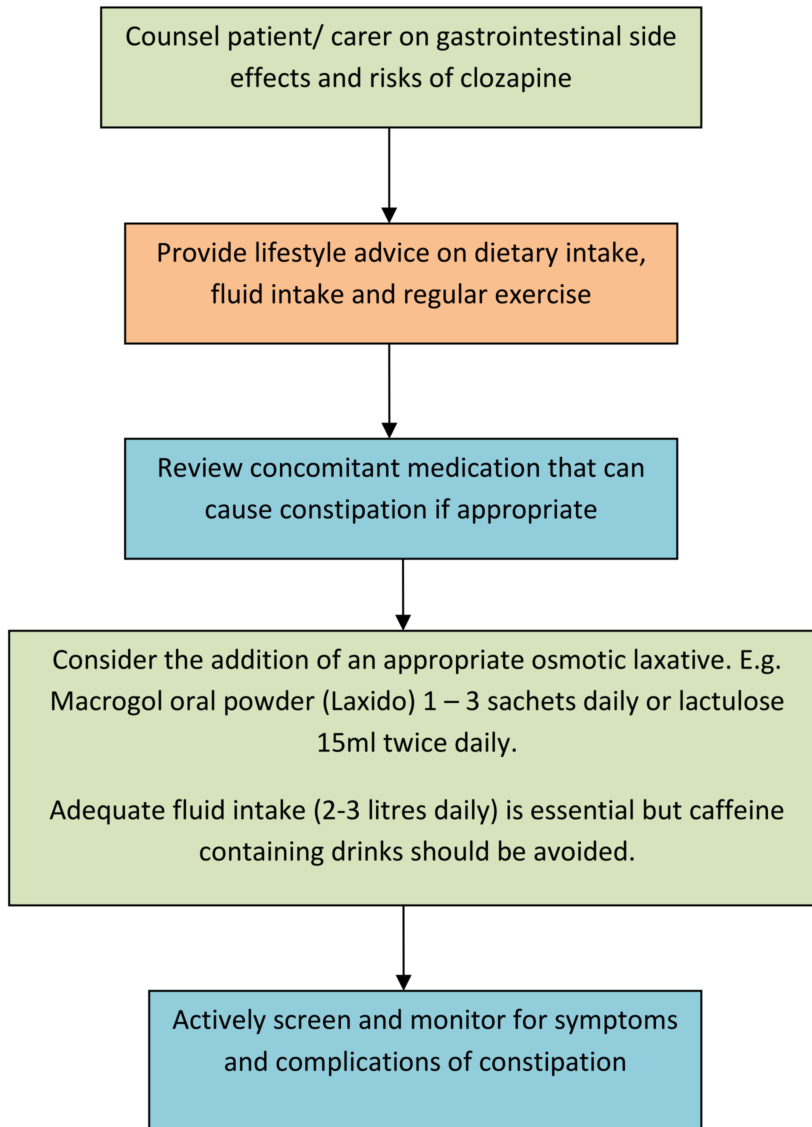
Appendix 2- When commencing clozapine



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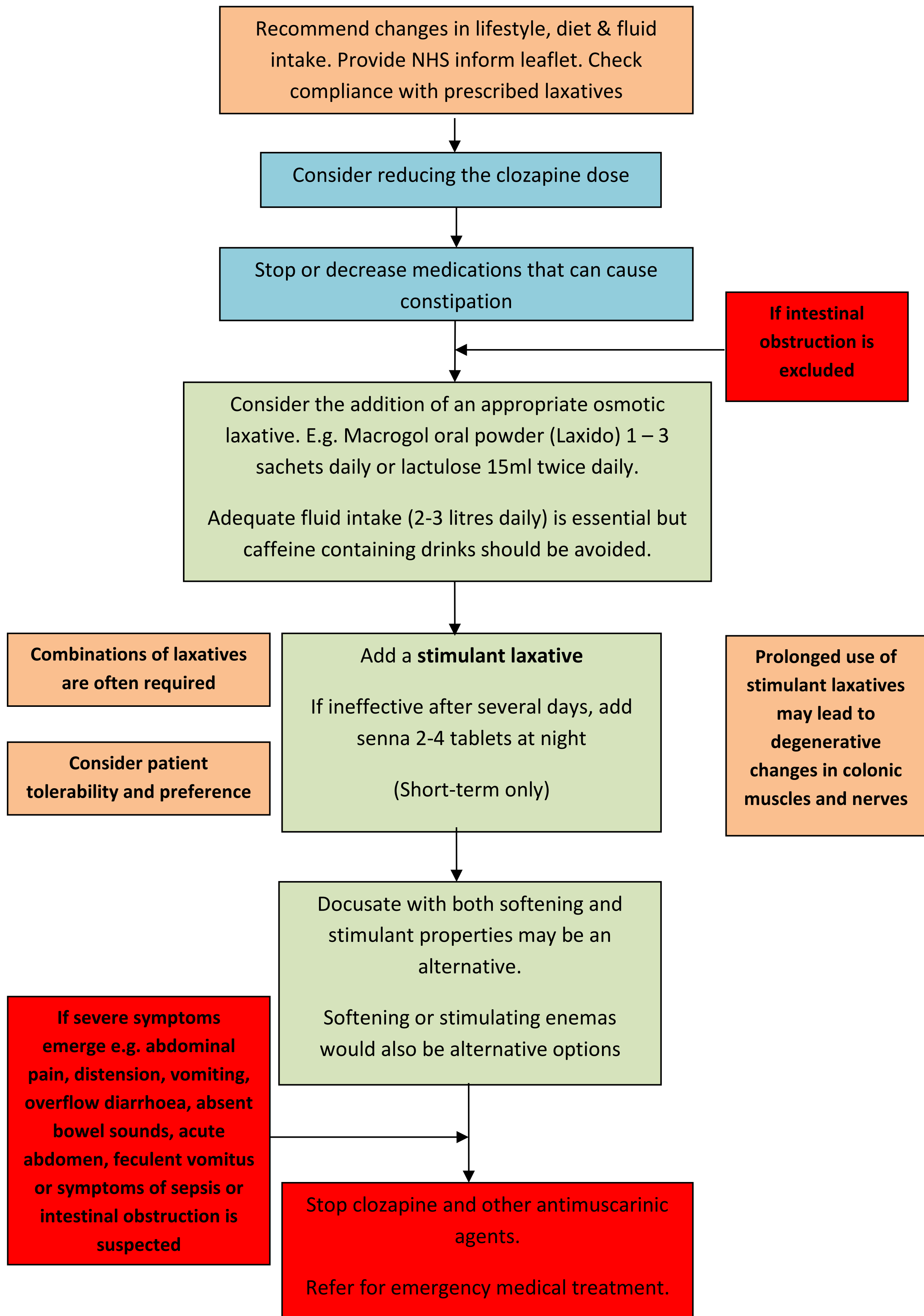
Appendix 3- Clozapine induced constipation treatment



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