Directorate of Chief Medical Officer

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The Scottish Government
Riaghaltas na h-Alba

Dear Colleagues,

NATIONAL GUIDANCE FOR MONITORING LITHIUM

Following updated clinical evidence in relation to ECG monitoring I wish to recirculate this amended guidance. This is in keeping with the principles of Realistic Medicine - reducing harm and waste and reducing unwarranted variation in practice and outcomes. In addition, I wish to highlight that the percentage of people prescribed lithium who experienced lithium toxicity in the last 12 months is a mental health quality indicator which information services division will be reporting. https://www.gov.scot/publications/mental-health-quality-indicators-background-secondary-definitions/.

Lithium is an effective medicine, particularly in the maintenance treatment for bipolar disorder, recurrent depression, and with a growing evidence of suicide-protective effects. Research informs us that in Scotland the use of lithium has declined in recent years, despite lithium being recognised as the gold standard treatment for bipolar disorder.

Lithium has a narrow therapeutic index and requires careful monitoring to support patient safety. Lithium is teratogenic and special consideration is needed with women of child bearing potential. In addition, lithium can be associated with long term physical health issues. This guidance aims to support NHS Scotland maintain the safe use of this important drug, and defines a minimum standard for health monitoring for all patients taking lithium in Scotland.

Actions for NHS Boards and HSCPs

- Ensure current practice is reviewed against the guidance, and encourage its adoption as a basis for local audit and further research.
- Ensure that all clinicians and others with an interest are made aware of the guidance, including primary care, maternity and mental health services.

Kind regards,

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For action
Medical Directors, NHS Boards

For information
Chief Executives, NHS Boards
Chairs, NHS Boards
Directors of Public Health, NHS Boards
Directors of Pharmacy, NHS Boards
Royal College of Psychiatrists in Scotland
Royal College of General Practice
Royal Pharmaceutical Society
Voices of Experience
Mental Welfare Commission for Scotland
Chief Officers HSCPs

Background Note

The care and treatment of people with mental illnesses such as bipolar disorder is a priority for health services within Scotland.

It is important that we provide evidence based treatment for people. Recent research from Glasgow University has shown that Lithium is not being used enough in treating bipolar disorder (Lyall et al., 2019).

We are concerned not only with mental health and wellbeing, but physical health too. The physical health burden seen among some people with bipolar disorder is a concerning health inequality.

Lithium, a mood stabilising drug, is prescribed to some of our most ill, most vulnerable people with bipolar disorder in line with good practice guidelines such as those of NICE (NICE; Bipolar disorder: assessment and management (CG185), last update April 2018). While the outcomes of this treatment are good, side effects are common, as is the risk of developing toxicity.

Lithium is a known teratogen, although the absolute risks appear to be less than previously thought. In severe mental illness up to 80% of pregnancies are unplanned. Risks and benefits in relation to childbearing must be discussed fully with all women of childbearing potential prior to prescription and consent appropriately recorded. This should be revisited at least annually. Discussion should include review of contraception status and advice/signposting on effective contraception for the duration of prescribing, with preference for long-acting reversible methods.

For women who become pregnant on lithium it is important to review the risks and benefits of continuing treatment or discontinuation. Lithium should not be discontinued abruptly and specialist advice regarding ongoing prescribing should be sought.

This guidance intends to support the good clinical care that primary and secondary care services provide.

By setting national guidelines within Scotland to outline the monitoring requirements of people treated with lithium, we set a clear benchmark. Using this, we can improve the quality of care and treatment we provide, improve patient safety, and reduce the established health inequality.

Lithium currently should be prescribed by brand name.

I am pleased to have the opportunity to promote this guidance and encourage its adoption as the basis for local audit and further research.

NHS Scotland Lithium Monitoring (March 2019)

Lithium is an effective medicine, particularly in the maintenance treatment of bipolar affective disorder, recurrent depression and in reducing the risk of suicide in people with affective disorders. It is widely used, and most patients prescribed lithium are in primary care. The narrow therapeutic index of lithium, and the potential for acute and chronic side effects, place an absolute requirement to establish clear systems of work that protect patient safety. This should include robust systems to ensure monitoring is carried out irrespective of setting. Special consideration is needed with women of child bearing potential as lithium is potentially teratogenic, although recent data suggest that the risk of cardiac malformations with lithium is substantially lower than previously thought (Patorno et al., 2017). This document describes the monitoring required to support safe lithium use.

Individual Health Boards will determine how best to undertake this monitoring. This is likely to involve a combination of specialist services and primary care services, and good communication systems will be required to avoid duplication of effort and appropriate management of physical health problems.

Parameter/test	Frequency	Action / suggested Action if outside reference range
Lithium levels	**3 monthly** Trough samples for routine monitoring should be taken approximately 12 hours after the last dose. Additional levels should be taken 5 – 7 days after the initial dose, after any dose or formulation change or introduction/discontinuation of interacting medication, and if there is a suspicion of toxicity.	Confirm the timing of the blood test and compliance with lithium Review treatment and adjust dose if clinically indicated. Lithium toxicity is defined as any lithium level greater than 1.2mmol/L. However it should be noted that some patients may exhibit toxicity at lower levels e.g. over 65 year olds.
Urea & Electrolytes	**Baseline** (Include Sodium, Potassium, Urea, Creatinine & eGFR. Patients must have adequate renal function (eGFR>60ml/min) before commencing lithium. Note in some populations the eGFR may over estimate renal function and therefore calculation of creatinine clearance would be more appropriate), **6 monthly.** Monitor more frequently if evidence of deterioration, or if the patient is prescribed or takes medicines known to affect renal function e.g. ACE inhibitors, NSAIDs or diuretics.	If eGFR falls rapidly to <45ml/min review lithium treatment and refer to renal medicine. Investigate and correct for hyponatraemia /hypernatraemia.
Thyroid function	**Baseline & 6 monthly** Monitor more often if evidence of impaired thyroid function or an increase in mood symptoms that might be related to impaired thyroid function	Treat as necessary

ECG[1]	**Baseline only if appropriate** If no cardiac disease or no risk factors than baseline ECG is not necessary. Arrange an ECG for people with cardiovascular disease or risk factors for it.	Consider medical/ cardiology advice.
Calcium	**Baseline & 6 monthly**	Treat as necessary
Body Mass Index	**Baseline & 6 monthly**	Offer lifestyle advice
Side effects	**At every clinical contact** Check if recent diarrhoea and vomiting or dehydration / over-hydration due to other causes	Review lithium treatment if problematic
Signs & symptoms of toxicity	**At every clinical contact** Reinforce education on signs and symptoms of toxicity and avoiding dehydration. Lithium toxicity is defined as any lithium level greater than 1.2mmol/L. However it should be noted that some patients may exhibit toxicity at lower levels e.g. over 65 year olds.	Check an urgent lithium level and suspend lithium treatment. Lithium treatment can only be re-introduced once toxicity has resolved and if restoration of treatment is then deemed clinically appropriate. All episodes of toxicity must be clearly noted in the patient's clinical records and discussed with patients.
Interacting drugs	**At every clinical contact** Be aware that 'Over the counter' medications such as ibuprofen can interact with lithium	Review all drugs known to affect renal function.
Women of reproductive age	**Baseline and yearly discussion with patient** Lithium is potentially teratogenic. In severe mental illness up to 80% of pregnancies are unplanned. Risks and benefits in relation to childbearing must be discussed fully with all women of childbearing potential prior to prescription and consent appropriately recorded. This should be revisited at least annually. Discussion should include review of contraception status and advice/signposting on effective contraception for the duration of prescribing, with preference for long-acting reversible methods.	For all women of childbearing potential: Discussion of childbearing intentions and contraception status. Advice on risks and benefits in relation to childbearing. Advice/signposting on contraception (incl. LARC). Informed consent provided in writing. The 'BUMPS' website should be used to reinforce verbal information. www.medicinesinpregnancy.org. For women who become pregnant on lithium: Do not stop abruptly. Review risks and benefits of continuing treatment or discontinuation. Seek specialist advice regarding ongoing prescribing.

Patient & care education	**Baseline and ongoing as necessary**	Provide patients with the education necessary to support informed choice and suited to their individual needs. The Choice and Medication and ‘ BUMPS’ websites are recommended as below http://www.choiceandmedication.org/nhs24/ www.medicinesinpregnancy.org

Notes:

1. A literature search was undertaken to seek a rationale for the previous advice recommending twice yearly ECG. No RCTs could be found to support this recommendation. NICE guidelines and the Maudsley guidelines recommend baseline ECG prior to starting lithium for patients with cardiovascular disease or known risk factors although these are not defined. No recommendations could be found in either BAP or APA guidelines.

2. The audit criteria have been removed as it is considered more appropriate that NHS Boards and HSCPs determine their own audit processes.

References used in the production of these standards

NICE; Bipolar in Adults (QS95), July 2015
NICE; Bipolar disorder: assessment and management (CG185), last update April 2018
BNF 74; page339
Maudsley Prescribing Guidelines, 12th Edition 2015
Psychotropic Drug Directory 2016

Lyall, L., Penades, N., Smith D.J. (2019) Changes in prescribing for bipolar disorder between 2009 and 2016: national-level data linkage study in Scotland. *British Journal of Psychiatry.* https://doi.org/10.1192/bjp.2019.16

Patorno et al., (2017) Lithium Use in Pregnancy and the Risk of Cardiac Malformations. *New England Journal of Medicine,* 376:2245-2254. https://www.nejm.org/doi/full/10.1056/NEJMoa1612222

Tondo, L., & Baldessarini, Ross J. (2018). Antisuicidal Effects in Mood Disorders: Are They Unique to Lithium? *Pharmacopsychiatry*, 51.177-188. DOI: 10.1055/a-0596-7853

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