Northamptonshire Healthcare NHS
NHS Trust

GUIDELINES FOR THE MONITORING OF ANTIMANIC AND PROPHYLACTIC MEDICATION IN BIPOLAR DISORDER

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Freedom of information category	**Guidelines**

GUIDELINES FOR THE MONITORING OF ANTIMANIC AND PROPHYLACTIC MEDICATION IN BIPOLAR DISORDER

This document is based on NICE Clinical guidance 28, Bipolar Disorder with some locally agreed additions which are indicated in the text. It replaced NHT MM-G-010 Guidelines for the monitoring of lithium, carbamazepine and valproate when used as mood stabilisers.

For all patients on these medicines agreed arrangements for prescribing, monitoring and treating any problems either by the GP or the CMHT should be considered

This is in addition to the annual health check in primary care for all patients with bipolar disorder which should include thyroid function, blood (plasma) glucose, lipid levels, including cholesterol, for all patients over 40, and blood pressure. Weight, smoking status and alcohol use should also be included in the GP's annual health check. The results of the health check should be given to the patient and healthcare professionals in primary and secondary care (including whether the person refused any tests)

LITHIUM

When starting lithium as long-term treatment a shared-care protocol for prescribing and monitoring should be established with the GP.

Baseline Measurements

- Blood Urea
- Electrolytes
- Serum Creatinine
- T_3, T_4, TSH
- Full Blood Count (only if clinically indicated)
- ECG if risk factors for, or existing, cardiovascular disease
- 24 hour creatinine clearance if history of renal infection or renal problems
- Calcium *(not included in NICE)*
- Weight and height

Initial Monitoring

Lithium Level

- 0.6 – 0.8mmol/L normally, or 0.8 – 1.0mmol/L if patient has relapsed previously on lithium or has sub-syndromal symptoms. (Elderly patients are more sensitive to undesirable effects. Aim for a lower range). Monitor carefully for symptoms of lithium toxicity.
- Levels need to be taken 12 hours post dose and should always be taken at the same time to give consistent results.
- A single night-time dose of Priadel m/r tablets is recommended. If lithium needs to be given as a liquid this should be taken BD as it is not a modified release preparation.

When a liquid preparation is used the level should be taken prior to the morning dose with a target of 0.5-0.8mmol/L. Similarly if tablets are taken BD for any reason.

- Testing should be done 5-7 days after initiation and after every change of dose or formulation or interacting drug.
- Weekly monitoring is required until patient is stabilised at the target level (usually 4 to 5 weeks),.
- The Path Lab should be requested to also send results of any lithium level tests to the GP.

Routine Monitoring

Weight. When needed if patient gains weight rapidly.
FBC. Only if clinically indicated.

Three monthly:

- Lithium level . More frequently if any changes in medication with potential interactions.

Six Monthly:

- Serum creatinine (care if levels rising, monitor more frequently; over 100μmol/L (female) or 120μmol/L (male) – warning sign; over 140μmol/L – refer to renal physician)[1,2] . Measure more frequently if patient starts taking medicines such as ACE inhibitors, diuretics or NSAIDs.
- T_3, T_4 and TSH (every 4-6 weeks if TSH raised)
- Electrolytes

Annually (or more frequently if clinical concerns)**:**

- ECG if history of cardiac dysfunction or suspected cardiac dysfunction. (ECG changes which have been seen in patients on lithium include reversible flattening or inversion of T-waves and QT prolongation). (*Not included in NICE)*
- Calcium (monitor for increased levels) *(Not included in NICE)*

Drug Interactions

Lithium levels increased by:

- diuretics
- ACE inhibitors and angiotension ll antagonists
- NSAIDs except aspirin and sulindac. (NSAIDs should not be used PRN. If regular NSAID is essential lithium dose should be decreased and levels monitored carefully **N.B.** Ibuprofen is available OTC).

Lithium levels deceased by:

- Xanthines e.g. theophylline
- increase in dietary salt including sodium containing antacids

Neurotoxicity or other adverse effects (possibly without increased lithium level) may occur with: diltiazem, verapamil, fluoxetine, fluvoxamine, antipsychotics, metronidazole, methyldopa, metoclopramide, domperidone, carbamazepine, steroids.

Because of the narrow therapeutic index of lithium, the possibility of an interaction should be checked before adding or removing any concurrent medication.

Signs of Toxicity

Ataxia, nausea, confusion, blurred vision, coarse tremor, giddiness.,paraesthesia.

NOTES:

- Any patient started on lithium must be informed of the need for regular monitoring and the reasons for this. They must also be educated about signs of toxicity, interactions etc. Pharmacy can help with patient counselling when required.
- Lithium should always be prescribed by brand name, as different preparations are not bioequivalent.
- Lithium carbonate 200mg tablet is approximately equivalent to 509mg lithium citrate liquid but any changes require weekly monitoring initially.

CARBAMAZEPINE

Initial Monitoring

FBC

- Low incidence of agranulocytosis and aplastic anaemia
- Early leucopenias usually transient and benign. Discontinue if it is severe, progressive or accompanied by clinical manifestations e.g. fever or sore throat.

LFTs

- If any clinical symptoms occur monitor more frequently and consider discontinuation.
- Discontinue if aggravated liver dysfunction or acute liver disease.

Weight and height

Carbamazepine level

- Induces its own metabolism so steady state is not reached for 2-4 weeks. Steady state following any further changes after this time is reached in a few days.

Six months after starting

- FBC
- LFTs
- U&Es
- Carbamazepine level
- Weight and height if patient gains weight rapidly

Routine Monitoring

Six monthly

- U&Es
- Carbamazepine level. NB therapeutic and toxic levels are close.

Additional Monitoring

Carbamazepine level

- Consider if toxicity suspected (>12mg/L) or possible noncompliance.
- May be helpful if adequate response not obtained. Trough levels >7mg/L are associated with therapeutic response in bipolar disorder but evidence is limited.
- Levels are taken pre-dose unless toxicity is suspected. Details of time sample is taken, dose etc., must be given.

FBC

- if fever, sore throat, etc.

U+Es

- If symptoms of SIADH

Monitor for **rashes and skin reactions.** May indicate hypersensitivity. If toxic epidermal necrolysis or Stevens-Johnson syndrome is suspected, discontinue immediately.

Drug Interactions

There are many potential serious interactions including:-

- Levels of carbamazepine raised by: dextropropoxyphene
  erythromycin/clarithromycin
  diltiazem/verapamil
  cimetidine
  fluoxetine/fluvoxamine
- Complex interactions with other antiepileptic drugs
- Reduction in contraceptive effect of oral contraceptives
- Reduction of anticoagulant effect of warfarin
- As carbamazepine is an enzyme inducer it reduces levels of many other medicines
- Contraindicated with clozapine
- Neurotoxicity with lithium without increased plasma levels

Signs of Toxicity

Double vision, ataxia, headache, nausea, dizziness

NOTES:

- Warn patient to report immediately any fever, sore throat, rash, ulcers in the mouth, easy bruising or bleeding.
- See also Trust guidance for the use of carbamazepine in acute mania MM-G-016.

VALPROATE

Initial Monitoring

LFTs

- Risk of severe liver damage is highest in first 6 months and if multiple therapy is involved.
- Raised liver enzymes may be seen and are usually transient or respond to a reduction in dose.
- Prothrombin rate most relevant. An abnormally prolonged prothrombin time, especially if associated with other abnormalities, requires cessation of treatment.

FBC

Weight and height

Six months after starting

- FBC
- LFTs
- Weight and height if patient gains weight rapidly

Routine Monitoring

None required

Additional Monitoring

Valproate level

- Not required routinely unless inadequate response obtained or evidence of poor adherence or toxicity. Trough levels of 50-100mg/L are associated with therapeutic response in bipolar disorder.

Spontaneous bruising or bleeding

- indicates the need for a FBC with bleeding time and coagulation tests[5]

Drug interactions

- Complex interactions with other antiepileptics. Toxic effect of carbamazepine may be potentiated.
- Anticoagulant effect of warfarin possibly increased.
- The effects of antipsychotics, MAOIs, antidepressants and benzodiazepines may be potentiated.
- Cimetidine and erythromycin may increase levels.

NOTE: Patients should be told to seek immediate medical attention if they develop symptoms of panceatitis e.g. abdominal pain, nausea and vomiting. They should also be told to immediately report sudden onset of anorexia, lethargy, drowsiness or aesthenia. Monitor sedation, tremor and gait disturbance in older people.

LAMOTRIGINE

No special monitoring tests required in addition to annual health check.

ANTIPSYCHOTICS

Initial Monitoring

- Blood (plasma) glucose at start and after 3 months. Olanzapine only – additional test one month after starting.
- Lipid profile at start and after 3 months (more often if evidence of elevated levels)
- Weight and height. Weight every 3 months for first year (more often if patient gains weight rapidly)
- Prolactin (risperidone only). Repeat if symptoms of raised prolactin develop
- ECG if risk factors for, or existing, cardiovascular disease

For full prescribing information see the relevant Summary of Product Characteristics (SPC) available at http://emc.medicines.org.uk

REFERENCES:

1. Gitlin M. Lithium and the kidney: an updated review *Drug Saf* 1999;20(3):231-43
2. Lepkifker E, Sverdlik A, Iancu I *et al* Renal insufficiency in long-term lithium treatment *J Clin Psychiatry* 2004;65(6):850-6
3. *The Maudsley Prescribing Guidelines* 8th Ed. 2005/6
4. *Psychotropic Drug Directory.* Stephen Bazire 2005
5. Depakote SPC
6. Epilim SPC
7. Priadel SPC
8. Tegretol SPC
9. Jules Sutherland, Southdown Health. Lithium, carbamazepine and valproate monitoring May 2002
10. Letter from Sanofi-Synthelabo Monitoring patients on lithium July 2002
11. Drug & Therapeutics Bulletin 1999, 37(3), 22-24 (*Ca monitoring*)
12. NICE, clinical guidance 38 Bipolar disorder July 2006

Equality Impact Assessment			
Title of Policy or Function:	**Guidelines for the monitoring of antimanic and prophylactic medication in bipolar disorder**	**Directorate:**	
Name of person completing Impact Assessment:	Catherine Mortimer, Pharmacy Manager, Princess Marina Hospital		

- For each of the following checks please remember to check is this policy and/or function sensitive to peoples of different age, ethnicity, gender, disability, religion or belief and sexual orientation?
- The checklists below will help you to see any strength and/or highlight improvements required to ensure that the policy/procedure is compliant with equality legislation.

1. Who will be affected by the policy/procedure/strategy/service/project/function? Who is intended to benefit from it and how?

***(Ask yourself:** Who are the target customer groups? Who will if affect directly and indirectly? What do you know about these groups already in relation to the policy/procedure/strategy/service/project/function?)*

Inpatients and outpatients with bipolar disorder.
To ensure they receive appropriate physical monitoring while on antimanic and prophylactic medication.

2. What involvement has there been with the people that might be affected directly or indirectly by the policy/procedure/strategy/service/project/function?
(Ask yourself: *Who have we engaged and how? Who else needs to be involved at this stage? What information do we have to support the development of the policy/strategy/project/function in relation to our duty to promote all equalities?)*
Approved by the Medicines Management Committee

3. What data and information have you gathered or have available to support the impact assessment?
(Ask yourself: *What qualitative data and complaints, audits, needs analysis and anecdotal evidence will be relevant here? Has your data reflected equality and diversity issues? Do you have enough to proceed at this stage?*
It is consistent with NICE guidelines.

4. Check for DIRECT and INDIRECT discrimination against any of the following groups of SERVICE USERS:						
Question: Is there any evidence that the following groups and individuals from these groups have different needs in relation to this policy or function?		**Positive**	**Negative**	**Action Required**		**Reason/ comment**
				Yes	**No**	
1.0	Age?				**x**	**Prescribers should aim for lower lithium levels in the elderly. This is covered in the guidelines.**
1.1	Gender (male/female/transgender)?				**x**	
1.2	Learning Difficulties/Disability or Cognitive Impairment?				**x**	
1.3	Mental Health Need?				**x**	
1.4	Sensory Impairment?				**x**	
1.5	Physical Disability?				**x**	
1.6	Race, Ethnicity, Religion, Language or Culture?				**x**	
1.7	Religious, Spiritual belief (including other belief)?				**x**	
1.8	Sexuality?				**x**	
1.9	Any Long Term Medical Conditions?				**x**	**The guidelines support the safe use of medicines used in bipolar disorder**
If 'YES' is answered to any of the above items, the policy or function may be considered discriminatory and require review and further work to ensure compliance with legislation.						

5. Check for DIRECT and INDIRECT discrimination against any of the following groups of SERVICE USERS:						
Question: Does your policy or function contain any conditions or requirements which are applied equally to everyone, but disadvantage particular groups or person's because they cannot comply due to:		**Positive Impact**	**Negative Impact**	**Action Required**		**Reason/ comment**
				Yes	**No**	
2.0	Age?				**x**	
2.1	Gender (male/female/transgender)?				**x**	
2.2	Learning Difficulties/Disability or Cognitive Impairment?				**x**	
2.3	Mental Health Need?				**x**	
2.4	Sensory Impairment?				**x**	
2.5	Physical Disability?				**x**	
2.6	Race, Ethnicity, Religion, Language or Culture?				**x**	
2.7	Religious, Spiritual belief (including other belief)?				**x**	
2.8	Sexuality?				**x**	
2.9	Any Long Term Medical Conditions?				**x**	
If 'YES' is answered to any of the above items, the policy or function may be considered discriminatory and require review and further work to ensure compliance with legislation.						

6. Check for DIRECT and INDIRECT discrimination against any of the following groups of SERVICE USERS:						
Question: Does your policy or function contain any statements which may exclude employees from operating the policy or function on the grounds of their:		**Positive Impact**	**Negative Impact**	**Action Required**		**Reason/ comment**
				Yes	**No**	
3.0	Age?				**x**	
3.1	Gender (male/female/transgender)?				**x**	
3.2	Learning Difficulties/Disability or Cognitive Impairment?				**x**	
3.3	Mental Health Need?				**x**	
3.4	Sensory Impairment?				**x**	
3.5	Physical Disability?				**x**	
3.6	Race, Ethnicity, Religion, Language or Culture?				**x**	
3.7	Religious, Spiritual belief (including other belief)?				**x**	
3.8	Sexuality?				**x**	
3.9	Any Long Term Medical Conditions?				**x**	
If 'YES' is answered to any of the above items, the policy or function may be considered discriminatory and require review and further work to ensure compliance with legislation.						

7. What further information do you need to collect to provide a full picture to carry out the impact assessment?
***(Ask yourself:** What qualitative data and anecdotal evidence will be relevant here? Who are you going to consult with and when?*
None

8. What is the priority of the impact assessment for the action plan?
*(Ask yourself**: where does this fit with existing priorities for your service and the Trust? Where does it fit in terms of meeting the specific and general equality duties?*)
No action plan required

9. What is the summary of your impact assessment?
(Ask yourself: **What are you going to do? Who else needs to know? How will you test it out? What outcomes are you looking for? Who will benefit and how will you measure and report your outcomes?**
No action required

10. Any other comments?

Action Planning

1. What are you going to do differently as a result of this equality impact assessment?

Action	Outcome Measure	Who	When	Monitoring Arrangements

2. How and when are you going to consult on this action plan?

Action	Outcome Measure	Who	When	Monitoring Arrangements

3. Who else needs to know about this action plan?				
Action	**Outcome Measure**	**Who**	**When**	**Monitoring Arrangements**

4. What other formats do you need to have it produced in?				
Action	**Outcome Measure**	**Who**	**When**	**Monitoring Arrangements**

Review date for action plan:	

NAME:		**SIGNATURE:**		**DATE:**	

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