Lamotrigine *(Lamictal®)* (Amber)

Prevention of depressive episodes in patients with bipolar disorder who experience predominantly depressive episodes. Lamotrigine is **not** indicated for the acute treatment of manic or depressive episodes.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines how responsibility for prescribing lamotrigine for the prevention of depressive episodes in patients with bipolar disorder (when lithium is contraindicated or not tolerated), might be shared between specialist and general practitioner (GP).GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

This shared care agreement is intended to apply to patients who have been initiated on treatment (and who have been assessed as benefiting) by a specialist in the care of patients with bipolar, in accordance with the guidance on Bipolar disorder (the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care) from NICE Clinical Guideline 185

Lamotrigine should not be routinely prescribed to women of child-bearing potential or nursing mothers due to risk of neural tube defects to the foetus or dermatological problems to the infant.

The doctor who prescribes this medication legally assumes clinical responsibility for lamotrigine and the consequences of its use.

RESPONSIBILITIES and ROLES (insert as much additional text as appropriate)

	Specialist responsibilities
1	Initiate treatment and prescribe the first 3 months of treatment of lamotrigine.
2	Discuss the benefits and side effects of treatment with the patient.
3	Ask the GP whether he or she is willing to participate in shared care (using the approved shared care agreement and signed shared care agreement signature sheet for lamotrigine). Discuss the shared care arrangement with the patient & obtain their consent (verbal is fine). Document in patients electronic records. If patient declines shared care, document this too.
4	Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay.
5	Review the patient's condition and monitor response to treatment regularly where indicated.
6	Give advice to the GP on when to adjust the dose / stop treatment.
7	Report adverse events to the MHRA & GP.
8	Ensure that clear backup arrangements exist for GPs to obtain advice and support.
9	Assess patient, establish the diagnosis and develop a care plan. Ensure care plan contains correct contact details of care co-ordinator/key worker and specialist. Forward copy of care plan to the GP.
10	To undertake baseline physical health check and assessment for the first 3 months.
11	To provide the patient with verbal and written information on lamotrigine including a patient information leaflet (PIL). Information on mental health conditions, treatments and medication can be found at: http://www.choiceandmedication.org/awp/
12	Provide counselling to patient and carer about implications of diagnosis; include written information about signs and symptoms, course, prognosis and treatments, local care and support groups, financial and legal advice.
13	The choice and formulation of drug for bipolar I should be a joint decision between the patient, (discuss with carer where patients lack capacity) and the specialist taking into consideration the risks and benefits of the treatment (including the relative potential of lamotrigine to cause side-effects) including any action to be taken should side effects occur.
14	To ensure the patient is fully informed about their treatment - for women of child bearing potential this should also include a discussion about plans for pregnancy as per NICE CG 192 (Antenatal and postnatal mental health) for guidance on the management of bipolar disorder during pregnancy and the postnatal period and in women and girls of childbearing potential. Effective contraception should also be discussed.
15	The medication regimen is regularly reviewed so that drugs that are not needed after the acute episode are stopped.
16	Do not offer lamotrigine to treat mania (unlicensed).
17	Be aware of its interaction with valproate where valproate is also prescribed.
18	Ensure that arrangements of appropriate blood tests has been made. Blood tests may be taken at the GP surgery providing appropriate communication with the GP and the GP is in agreement with this. The Specialist

	is responsible for the interpretation and monitoring of these blood test results for the first 3 months of treatment.
19	Review results of any baseline tests and relay any abnormal findings to the GP with appropriate advice.
20	Review concurrent medication for potential interaction prior to initiation of lamotrigine, including medication patient receives from the GP and purchases OTC or on-line.
21	To review the patient and treatment at least once a year until the patient is discharged from the mental health service where this is possible.
22	To review patient / provide advice as requested via the GP or Primary Care Liaison Service as necessary
23	Discuss appropriate lifestyle issues e.g. healthy eating, with the patient.
24	Communicate promptly with the GP when treatment is changed.
25	Inform GP if any appointments are not attended.
26	Any verbal communication between primary care and the specialist team should be confirmed in writing

General Practitioner responsibilities	
1	Reply to the request for shared care as soon as practicable (preferably within 3 weeks of receipt of request) using the shared care agreement signature sheet for lamotrigine.
2	Prescribe medicine at the dose recommended after the first 3 months.
3	Ensure compatibility with other concomitant medication.
4	Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
5	Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
6	Adjust dose / stop drug on the advice of the specialist.
7	Report adverse events to the specialist and MHRA.
8	If the GP decides not to prescribe lamotrigine, it should still be added to the patients repeat medication as a “non issued’ item for information and safety purposes. The quantity should be set to *0 or 1. On the dose line it should read: ‘Hospital prescribing only. Do not prescribe’. This should also be done during the stabilisation period before GP takes over the prescribing.
9	Monitor response to treatment including changes in symptoms and behaviour.
10	Monitor patient’s physical health through annual physical health check (under monitoring). A copy of the results should be sent to the care coordinator and psychiatrist (to file in the secondary care records).
11	Once the patient has been discharged, advice may be sought from the Patient Care Liaison Service on any aspect of patient’s mental health that is of concern to the GP.
12	Monitor patient’s overall health and compliance with medication.
13	Continue monitoring symptoms, mood and mental state for 2 years after medication has stopped entirely.
14	Ask patient / carer about particular problems e.g. side effects, concerns about treatment.
15	To notify specialist of any relevant changes in other medications or clinical status.

Primary Care Liaison Service (PCLS) responsibilities	
1.	Accept referrals by registered GPs in line with DoH guidance.
2.	To advise the GP on appropriate action regarding any issues they may have on patients management regarding shared care.
3.	To try and resolve the issue(s) raised by the GP or to refer to the specialist team as appropriate.
4.	Rapid & prioritised specialist mental health assessment with recommendation/s for care & treatment within multiple care pathways.
5.	Determination of the nature & severity of mental health needs with consequent sign posting and pathway facilitation
6.	Provide rapid and accessible ongoing support & advice to the non-specialist workforce

Patient's role	
1	Attend all appointments with GP and specialist.
2	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3	Share any concerns in relation to treatment with medicine.
4	Inform specialist or GP of any other medication being taken, including over-the-counter or those purchased on-line.
5	Report any adverse effects to the specialist or GP whilst taking the medicine.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:				
Care co-ordinator				
Primary Care Liaison Service Sandalwood Court, Swindon 8am – 8pm then Intensive service	01793 835787		01793 836817	

SUPPORTING INFORMATION

Summary of condition (NICE CG 185)

Bipolar disorder is a potentially lifelong and disabling condition characterised by episodes of mania (abnormally elevated mood or irritability and related symptoms with severe functional impairment or psychotic symptoms for 7 days or more) or hypomania (abnormally elevated mood or irritability and related symptoms with decreased or increased function for 4 days or more) and episodes of depressed mood. It is often comorbid with other disorders such as anxiety disorders, substance misuse, personality disorders and attention deficit hyperactivity disorder (ADHD). The peak age of onset is 15–19 years, and there is often a substantial delay between onset and first contact with mental health services. The lifetime prevalence of bipolar I disorder (mania and depression) is estimated at 1% of the adult population, and bipolar II disorder (hypomania and depression) affects approximately 0.4% of adults.

Licensed indications (SPC)
Bipolar disorder: Adults aged 18 years and above
Prevention of depressive episodes in patients with bipolar I disorder who experience predominantly depressive episodes. Lamotrigine is **not** indicated for the acute treatment of manic or depressive episodes.

Expected / established place in local treatment pathway
Lamotrigine is licensed for the prevention of depressive episodes in patients with bipolar I who experience predominantly depressive episodes. Continuation of treatment should be adapted individually using the lowest effective dose which produces the desired clinical effect. If stopping lamotrigine, the dose should be reduced gradually over at least 4 weeks to minimise the risk of relapse.

Dosage and administration
The starting dose and dose titration as outlined in the SPC and BNF should be followed, taking into account the need for slow titration in people who have not taken lamotrigine before.

Contra-indications and precautions for use
Hypersensitivity to the active substance or to any of the excipients.

Skin rash
Reports of adverse skin reactions generally occur within the first eight weeks after initiation of lamotrigine treatment. The majority of rashes are mild and self-limiting, however serious rashes requiring hospitalisation and discontinuation of lamotrigine have also been reported e.g. potentially life-threatening rashes such as Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS); also known as hypersensitivity syndrome (HSS).

Clinical worsening and suicide risk
In patients with bipolar disorder, worsening of depressive symptoms and/or the emergence of suicidality may occur whether or not they are taking medications for bipolar disorder, including lamotrigine. Therefore patients receiving lamotrigine for bipolar disorder should be closely monitored for clinical worsening (including development of new symptoms) and suicidality, especially at the beginning of a course of treatment, or at the time of dose changes. Certain patients, such as those with a history of suicidal behaviour or thoughts, young adults, and those patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment, may be at a greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

Hormonal contraceptives
The use of an ethinyloestradiol/levonorgestrel (30 µg/150 µg) combination increases the clearance of lamotrigine by approximately two-fold resulting in decreased lamotrigine levels (and risk of seizure). Following titration, higher maintenance doses of lamotrigine (by as much as two-fold) will be needed in most cases to attain a maximal therapeutic response. When stopping hormonal contraceptives, the clearance of

lamotrigine may be halved. Increases in lamotrigine concentrations may be associated with dose-related adverse events. Patients should be monitored with respect to this.

Renal failure
Plasma concentrations of lamotrigine were not significantly altered in those with end stage renal failure. However, accumulation of the glucuronide metabolite is to be expected; caution should therefore be exercised in treating patients with renal failure.

Patients taking other preparations containing lamotrigine
Lamictal should not be administered to patients currently being treated with any other preparation containing lamotrigine without consulting a doctor.

Use of lamotrigine in pregnancy & breastfeeding.

1. Lamotrigine carries the risk of oral cleft (estimated at nearly 9 in 1000 exposed fetuses).

2. If a woman who is taking lamotrigine is planning a pregnancy or has an unplanned pregnancy, healthcare professionals should advise her to stop taking these drugs because of the risk of neural tube defects and other malformations in the fetus. If appropriate an alternative drug (such as an antipsychotic) should be considered.

3. Lamotrigine should not be routinely prescribed for women who are pregnant because of the lack of evidence of efficacy and the risk of neural tube defects in the fetus.

4. Lamotrigine should not be routinely prescribed for women who are breastfeeding because of the risk of dermatological problems in the infant, such as Stevens–Johnson syndrome.

Side-effects

Please note that the following convention has been used for the classification of side-effects: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥ 1/10,000 to <1/1000) and very rare (<1/10,000).

Refer to the SPC for a full list of adverse effects & further information http://www.medicines.org.uk and the current BNF.

This medicine does not have black triangle (▼) status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Refer patient back to the specialist if any of these side-effects cause concern.

Very Common (> 1%)
Headache, skin rash,

Common (>1 % and <10%)
Aggression, irritability, Somnolence, dizziness, tremor insomnia, agitation, Nausea, vomiting, diarrhoea, dry mouth, Arthralgia, Tiredness, pain, back pain

Stopping lamotrigine

If stopping lamotrigine, reduce the dose gradually over at least 4 weeks to minimise the risk of relapse.

Referral back to specialist (NICE).

- there is a poor or partial response to treatment
- the person's functioning declines significantly
- treatment adherence is poor
- the person develops intolerable or medically important side effects from medication
- comorbid alcohol or drug misuse is suspected
- the person is considering stopping any medication after a period of relatively stable mood
- a woman with bipolar disorder is pregnant or planning a pregnancy.
- breast feeding - refer back for specialist advice

- any change in mood or development of suicidal thoughts likely to indicate a significant deterioration in the patient's condition.
- development of spontaneous bruising or bleeding.
- renal and hepatic impairment – refer back for specialist advice – dosage adjustment maybe necessary.

Advice to patient

- To contact their doctor immediately if they develop a rash while the dose of lamotrigine is being increased.
- To tell GP/Specialist/ care co-ordinator/ Allied Health Professional if they are pregnant or planning a pregnancy. See under 'Pregnancy and breastfeeding' above.

Monitoring

Parameter	Frequency of monitoring & responsibility	
	Specialist	**Primary care**
	Baseline physical health check	**Annual physical health check**
Blood pressure	✓	✓
Pulse	✓	✓
ECG	If indicated by history or clinical picture.	
Full blood count	✓	✓
Fasting blood glucose	✓	✓
Glycosylated haemoglobin		✓
Lipid Profile	✓	✓
Liver function	✓	✓
Renal function (U&Es)	✓	✓
Thyroid function	✓	✓
Weight or BMI		✓
Smoking status and alcohol use	✓	✓
Advice on diet, nutritional status and level of physical activity	✓	✓

- Secondary care/Specialist to do baseline physical health check.
- Primary care to do physical health monitoring at least annually (NICE).
- **Primary care to seek specialist advice from secondary care if results are abnormal**.
- People with bipolar have higher levels of physical morbidity and mortality than the general population [3].
- Do not routinely measure plasma lamotrigine levels unless there is evidence of ineffectiveness, poor adherence or toxicity.

Drug Interactions

- Weight gain can be exacerbated by other drugs that have this effect (e.g. antipsychotics, particularly clozapine and olanzapine).
- **Valproate** – Metabolism of lamotrigine reduced by valproate.
- **Phenytoin, carbamazepine, phenobarbitone and primidone** - Metabolism of lamotrigine increased by phenytoin, carbamazepine, phenobarbitone and primidone
- **Carbamazepine –** Reports of central nervous system events including dizziness, ataxia, diplopia, blurred vision and nausea in patients taking carbamazepine following the introduction of lamotrigine. These events usually resolve when the dose of carbamazepine is reduced.
- **Hormonal contraceptives** - ***Effect of hormonal contraceptives on lamotrigine pharmacokinetics***
  No adjustments to the recommended dose escalation guidelines for lamotrigine should be necessary solely based on the use of hormonal contraceptives, but the maintenance dose of lamotrigine will need to be increased or decreased in most cases when starting or stopping hormonal contraceptives
- **Hormonal contraceptives - *Effect of lamotrigine on hormonal contraceptive pharmacokinetics***
  A steady state dose of 300 mg lamotrigine had no effect on the pharmacokinetics of the ethinyloestradiol component of a combined oral contraceptive pill. The effects of doses of lamotrigine

other than 300 mg/day have not been studied and studies with other female hormonal preparations have not been conducted.

Reminder to ask patient about specific problems

- Report any adverse reactions to GP and/or specialist.
- Alert GP/specialist about any change in circumstances which could affect treatment (e.g. pregnancy or drug use).
- Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge and if they have any queries regarding their condition and/or medication.

Cost (Drug Tariff April 2016)

Name, formulation & strength	Quantity	Cost (£)
Lamotrigine tablets, 100mg	56	1.82
Lamotrigine tablets, 200mg	56	3.32
Lamotrigine tablets, 50mg	56	1.53
Lamotrigine tablets 25mg	56	1.56

References

1. Summary of Product Characteristics for Lamictal
2. British National Formulary
3. NICE CG 185 Bipolar Disorder Sept 2014 (Updated Feb 2016)
4. NICE CG 192 Antenatal and postnatal mental health Dec 2014
5. Maudsley Prescribing Guidelines 11th Edition
6. Drug Tariff April 2016

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