Bipolar disorder: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care

NICE guideline

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If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.
Contents

Patient-centred care ......................................................................................................... 4

Key priorities for implementation .................................................................................... 5

1 Guidance ....................................................................................................................... 8
   1.1 Common aspects of care for all people with bipolar disorder 9
   1.2 The assessment, recognition and diagnosis of bipolar disorder 12
   1.3 Assessment and diagnosis of children and adolescents 18
   1.4 The treatment and management of bipolar disorder 22
   1.5 The management of acute episodes 24
   1.6 Long-term management 39
   1.7 Overall treatment setting/pathways to care 51
   1.8 Treatment of children and adolescents with bipolar disorder 55
   1.9 Treatment and management of women of child-bearing potential 58

2 Notes on the scope of the guidance .............................................................................. 65

3 Implementation in the NHS ......................................................................................... 66
   3.1 Resource implications 66
   3.2 General 67
   3.3 Audit 67

4 Research recommendations ......................................................................................... 68

5 Other versions of this guideline .................................................................................... 68
   5.1 Full guideline 68
   5.2 Quick reference guide 69
   5.3 Information for the public 69

6 Related NICE guidance ............................................................................................... 69

7 Review date ................................................................................................................... 69

Appendix A: The Guideline Development Group ............................................................ 70

Appendix B: The Guideline Review Panel ................................................................... 73
Patient-centred care

This guideline offers best practice advice on the care of people with bipolar disorder.

Treatment and care should take into account people’s individual needs and preferences. People with bipolar disorder should have the opportunity to make informed decisions about their care and treatment. Where patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – *Reference guide to consent for examination or treatment* (2001) (available from www.dh.gov.uk).

Good communication between healthcare professionals and patients is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.

Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in decisions about the patient’s care and treatment.

Carers and relatives should also be provided with the information and support they need.
Key priorities for implementation

The following recommendations have been identified as recommendations for implementation:

- When diagnosing bipolar I disorder in adolescents, healthcare professionals should use the same criteria as for the adult disorder but modified so that:
  - mania must be present
  - euphoria must be present most of the time (for the past 7 days)
  - irritability can be helpful in making a diagnosis if it is episodic, severe, results in impaired function and is not in character or is out of keeping with the context. However, it should not be a core diagnostic criterion.

- For patients taking an antidepressant at the time of onset of an acute manic episode, healthcare professionals should stop the antidepressant drug. The decision about whether to discontinue the antidepressant abruptly or gradually should be based on current clinical need, previous experience of discontinuation/withdrawal symptoms, and the risk of discontinuation/withdrawal symptoms of the antidepressant in question.

- Healthcare professionals should not routinely prescribe valproate for women of child-bearing potential. If valproate is prescribed to women of child-bearing potential, ensure adequate contraception is used and explain the risks to the health of the unborn child.

- Healthcare professionals should normally consider initiating long-term treatment for bipolar disorder in the following circumstances:
  - following a manic episode which was associated with significant risk and adverse consequences
  - when there have been two or more acute episodes in patients with bipolar I disorder
- when there is evidence of significant functional impairment, significant risk of suicide or frequently recurring episodes in bipolar II disorder.

- Following successful treatment for an acute depressive episode, healthcare professionals should not routinely continue patients on long-term antidepressant treatment because there is no evidence that continuing antidepressants reduces relapse rates, and it may be associated with increased risk of switching to mania.

- For people with bipolar disorder who are relatively stable (but who may experience mild to moderate affective symptoms), healthcare professionals should consider individual structured psychological therapy (for at least 16 sessions over 6 to 9 months) in addition to medication which should:
  - include psychoeducation about the illness and the promotion of regular daily and routine sleep and of medication adherence
  - include monitoring of mood, detection of early warnings and strategies to prevent early stages from developing into full-blown episodes
  - enhance general coping strategies.

- When deciding on an agent for the long-term management of a patient with a diagnosis of bipolar disorder healthcare professionals should consider the following.
  - As first-line treatments an antipsychotic (olanzapine, quetiapine), lithium (particularly where there is a high risk of manic relapse), or valproate (but not for women of child-bearing potential).
  - For an incomplete response to optimum first-line treatment of at least 6 months consider the combination of two mood stabilizers (lithium, olanzapine, quetiapine, valproate) together with close monitoring of clinical state, side effects and, where relevant, blood levels. Appropriate combinations are lithium and valproate, lithium with quetiapine or olanzapine, or valproate and quetiapine or
olanzapine. The reasons for the use of such combinations and the discussion with the patient of the potential benefits and risks should be documented in the case notes.

- If a trial of one of the combination of mood stabilisers in the long-term management of bipolar disorder proves ineffective healthcare professionals should consider consulting with, or referring the patient to, a clinician with expertise in the pharmacological treatment of bipolar disorder.

- As third line treatments, lamotrigine (especially in bipolar II disorder) and carbamazepine.

- Base the treatment of an acute episode in the context of rapid cycling (which should normally be managed in secondary mental health services) on that for the treatment of manic and depressive episodes, but in addition do the following.
  - Undertake a thorough review of previous treatments for bipolar disorder, and consider a further trial of appropriate previous treatments that have been inadequately delivered or adhered to.
  - Focus on the optimisation of appropriate long-term treatment (with each trial of medication being usually of at least 6 months’ duration) rather than on treating individual episodes and symptoms.
  - Encourage patients to keep a regular mood diary (paper or electronic) to monitor changes in severity and frequency of symptoms, and the impact of interventions.
Guidance

This guideline makes recommendations for the identification, treatment and management of bipolar disorder for children (younger than 12), adolescents and adults in primary and secondary care, including those covered by prison medical services. Bipolar disorder is a serious mental illness that often has a long course and is characterised by episodes of both major depressed mood and elated mood (mania or hypomania). Both depression and elated mood must be present during the course of the illness for a diagnosis of bipolar disorder to be made. However, for many people the predominant experience is of low mood. In its more severe forms bipolar disorder is associated with significant impairment of both personal and social functioning. The peak age of onset for bipolar disorder is in late adolescence or early adult life, with a further small increase in incidence in mid to late life. In this guideline a distinction is drawn between bipolar I disorder (in which the presence of episodes of both depression and mania is required for the initial diagnosis) and bipolar II disorder (in which the presence of episodes of both depression and hypomania, but no evidence of mania, is required for the initial diagnosis).

The guideline draws on the best current available evidence for the treatment and management of bipolar disorder. However, there are some significant limitations to the current evidence base, which have considerable implications for this guideline. These include the limited data on the differential response of individuals to specific treatments, the long-term benefits of both pharmacological and psychosocial interventions and limited data on quality of life and social functioning for all interventions. The guideline makes evidence-based recommendations for the diagnosis and treatment of bipolar I disorder including psychological, pharmacological, service-level and self-help interventions. There is very little evidence for the treatment of people with bipolar II disorder. Therefore, except where specific recommendations for the treatment of bipolar II disorder have been stated, healthcare professionals should consider cautiously applying the recommendations for the treatment of bipolar I disorder to the treatment of people with bipolar II disorder. There are
also significant limitations with the evidence base for both under 18s and older adults (over 65 years).

1.1 Common aspects of care for all people with bipolar disorder

1.1.1 Providing good information, informed consent and mutual support

1.1.1.1 The provision of information about the nature, course, and treatment of bipolar disorder is important in promoting access to services and understanding and collaboration between patients, close family members, paid and unpaid carers and healthcare professionals.

1.1.1.2 Healthcare professionals should establish and maintain collaborative relationships with patients and families/carers (within the normal bounds of confidentiality) so as to provide the relevant information they need at every stage of assessment, diagnosis, course and treatment (including the proper use and likely side-effect profile of medication) and thereby help all make sense of the experience of the disorder and its treatment.

1.1.1.3 Patients, family and carers should be informed of self-help groups and support groups and be encouraged to regularly participate in such programmes, particularly on initial diagnosis, and regularly thereafter. Such groups may helpfully provide information on early warning signs, appropriate support in time of crisis and information on treatment and the management of side effects.

1.1.2 Language

1.1.2.1 When talking to people with bipolar disorder and their carers, healthcare professionals should use everyday, jargon-free language, and take into account the cultural needs, and the developmental,
intellectual and sensory capabilities of the individual person and their carer(s). Where access to services for people may be limited by language comprehension, services should ensure that:

- written material is provided in the preferred first language of the patient
- independent interpreters are used where appropriate
- consideration is given to providing psychosocial interventions and information about medications in the patient’s preferred first language.

1.1.3 Advance statements (directives)

1.1.3.1 Advance statements (directives) (for both mental health and physical health care) should be developed collaboratively by people with bipolar disorder and healthcare professionals, especially for people who are subject to severe manic or depressed episodes, and for those who have been treated under the Mental Health Act. These should be documented in care plans, and copies given to the person with bipolar disorder, and his or her care coordinator and general practitioner.

1.1.4 Supporting families and carers

1.1.4.1 When considering the needs of the family members/carers of a person with bipolar disorder, the following should be considered:

- the welfare of dependent children and vulnerable adults
- the requirement for a regular assessment of the physical and mental health needs of carers
- the impact of the disorder on relationships.

1.1.5 Additional considerations for children and adolescents

1.1.5.1 Healthcare professionals working in specialist services with children and adolescents with bipolar disorder should:
• be familiar with local and national guidelines on confidentiality and the rights of the child
• ensure appropriate consent is obtained, considering the adolescent’s position (including Gillick competence), parental consent and responsibilities, child protection matters, and the use of the Mental Health Act and of the Children Act (1989).

1.1.5.2 In planning the care of children and adolescents with bipolar disorder healthcare professionals should carefully consider:

• stressors and vulnerabilities within the child or adolescent’s social, educational and family environments including the quality of interpersonal relationships with family members, friends and peers
• the presence and impact of comorbid disorders, for example ADHD
• the impact of the disorder on the social inclusion and educational progression of the child or adolescent
• the vulnerability of the child or adolescent to exploitation, for example as a result of disinhibited behaviour
• the active involvement of parents/carers in the development of care plans so that parents/carers can give meaningful and properly informed consent before treatment is initiated.

1.1.5.3 Children and adolescents with bipolar disorder should be offered separate individual appointments with a healthcare professional in addition to those with their family members or carers. Consideration should be given to the involvement of siblings and other family members.

1.1.6 Treatment of people with disabilities with bipolar disorder

1.1.6.1 For people with bipolar disorder who have learning difficulties including those under 18 years of age, healthcare professionals
should ensure that they receive the same care as others, in particular taking into account interactions with concomitant medication.

1.1.7 Treatment of people with comorbid personality disorders with bipolar disorder

1.1.7.1 For people with bipolar disorder who have comorbid personality disorder healthcare professionals should ensure that they receive the same care as others with bipolar disorder because the presence of a personality disorder does not preclude the delivery of effective treatments for bipolar disorder.

1.2 The assessment, recognition and diagnosis of bipolar disorder

1.2.1 Introduction

The diagnosis and recognition of bipolar disorder in adults, particularly in those first presenting to services, can be difficult. For many individuals there are often periods of considerable psychological and social disturbance before diagnosis. In children and adolescents bipolar disorder is a relatively rare event, therefore considerable caution should be exercised before arriving at a diagnosis of bipolar disorder in this age group. First presentation of bipolar disorder in later life may be associated with greater incidence of comorbid physical disorders.

To achieve a diagnosis of bipolar disorder in adults ICD-10 requires at least two episodes (one of which must be mania or hypomania) in which the person’s mood and activity levels are significantly disturbed are required. (This contrasts with DSM-IV, where only a single manic or mixed episode of mania is required). The disturbance consists of either an elevation of mood and increased energy and activity (mania or hypomania). Episodes can be further specified as hypomanic, manic without psychotic symptoms, manic with psychotic symptoms, mild or moderate depression, severe depression without psychotic symptoms, severe depression with psychotic symptoms,
mixed, or in remission. Manic episodes usually begin abruptly and last for between 2 weeks and 4–5 months (median duration about 4 months). Depressions tend to last longer (median duration about 6 months). Recovery may be complete between episodes. The frequency of episodes and the pattern of remissions and relapses are both very variable, though remissions tend to get shorter as time goes on and depressions to become commoner and longer lasting.

1.2.2 New or suspected presentations of bipolar disorder

1.2.2.1 In cases of suspected bipolar disorder (which are not explained by drug misuse) primary care clinicians:

- should normally refer patients (for a specialist mental health assessment and development of a care plan) if any of the following are present:
  - a history of recurrent depressive episode on three or more occasions in the context of a history of overactive, disinhibited behaviour, or
  - periods of overactive disinhibited behaviour with or without periods of depression lasting at least 4 days and not entirely explained by drug misuse, or
  - overactive, disinhibited behaviour and a first period of depression before the age of 25 years
- must refer patients (for a specialist mental health assessment and development of a care plan) if there is a family history of affective disorder, particularly bipolar disorder, or two or more of the above are present.

1.2.3 Existing bipolar disorder in primary care

1.2.3.1 For all patients with existing bipolar disorder in primary care who are newly registered with a practice consideration should be given to a referral for assessment by specialist mental health services, including the development, where appropriate, of a care plan.
1.2.3.2 When a patient with bipolar disorder is managed solely in primary care an urgent referral to secondary care services should be made:

- where there is an acute exacerbation of symptoms, in particular the development of mania or severe depression
- where there is an increase or change in the degree of risk to self or others.

1.2.3.3 When a patient with bipolar disorder is managed solely in primary care consideration for a review by secondary care services or increased contact in primary care may be indicated:

- where there is a poor response to treatment
- where treatment adherence is a problem
- where comorbid substance misuse is suspected
- if the patient is considering stopping prophylactic medication following a period of relatively stable mood.

1.2.4 Assessment of bipolar disorder in secondary care

1.2.4.1 In the assessment of suspected bipolar disorder healthcare professionals should take a full history from the patient alongside an assessment of their symptom profile, triggers to previous episodes, and social and personal functioning. The assessment should also include a review of all previous episodes and any symptoms between episodes. Family history, comorbidities including substance use and abuse, anxiety, risk, physical health and current psychosocial stressors should be routinely and directly inquired about. A corroborative history should be obtained within the bounds of confidentiality. Additional help in reaching a diagnosis may be obtained by use of formal criteria aided by completion of self-rating scales such as the Mood Disorder Questionnaire.

1.2.4.2 When considering a diagnosis of bipolar disorder in individuals with more pronounced psychotic symptoms, increased suicidal ideation,
drug misuse, or more disturbed behaviour, healthcare professionals should remember that these symptoms may be a function of later presentation of bipolar disorder and not of a schizophrenia spectrum disorder. This may be particularly important when assessing patients such as those from black and minority ethnic groups who may have difficulty accessing services.

1.2.4.3 When a patient first presents with manic symptoms healthcare professionals should consider the possibility of drug and/or alcohol misuse inducing the manic-like symptoms. In inpatient settings, if there is evidence of drug/alcohol misuse, wait 7 days before confirming a diagnosis of bipolar disorder.

1.2.4.4 In the initial assessment of suspected bipolar disorder healthcare professionals should give consideration to underlying organic conditions, particularly for those presenting with late onset bipolar disorder (aged over 40 years), such as hypothyroidism and cerebrovascular insults, and other neurological disorders (such as dementia in older adults). Cardiovascular risk factors should be assessed. A full history of prescribed and non-prescribed drug exposure should be taken and appropriate investigations undertaken. For children and adolescents these investigations should include screening for previously undiagnosed learning difficulties.

1.2.4.5 Before diagnosing rapid cycling bipolar disorder, healthcare professionals should thoroughly review previous treatment history including the possibility of antidepressant-induced switching, physical health problems (such as thyroid disease) suboptimal doses of prophylactic medication and the effects of lithium withdrawal, together with the effects of erratic compliance and consider initiating a period of longitudinal self and/or carers’ assessment of mood for at least a year.

1.2.4.6 When considering the diagnosis of personality disorder in a person with mood swings, healthcare professionals should be cautious about
confirming such a diagnosis without first considering a diagnosis of bipolar disorder. Caution should also be exercised when considering a diagnosis of personality disorder in unstable bipolar patients without adequate treatment of bipolar disorder first.

1.2.5 Assessment of risk in primary and secondary care

1.2.5.1 Healthcare professionals should undertake a risk assessment in all people when:

- bipolar disorder is first diagnosed
- in established diagnosis of bipolar disorder where there is significant change in mental state or personal circumstances
- a patient with bipolar disorder is discharged from or is on leave from inpatient care.

1.2.6 Crisis and risk management plans

1.2.6.1 For patients at risk of suicide, exploitation, significant risk to others including neglect of dependents, severe self-neglect or where there is a history of compulsory admission, healthcare professionals must develop a crisis plan which should include the following.

- Identified or potential personal, social or environmental triggers, including early warning symptoms of relapse, which increase the risk of a deterioration in the patient’s mental state or circumstances.
- For patients at risk of rapid onset of mania and for whom clear early warning signs can be identified, a protocol for increasing the dose of existing medication or for taking additional medication (which may be given to the patient in advance). Such protocols should be reviewed regularly, and are not a substitute for an urgent review.
• The agreed response of primary and secondary healthcare services to any identified increase in risk including increased contact.
• How the individual (and where appropriate their carer[s]) can access help and identify the healthcare professionals in primary and secondary care who are designated as having responsibilities in the crisis plan.

1.2.6.2 Healthcare professionals should prescribe a limited quantity of psychotropic medication for patients at high risk of suicide.

1.2.7 Physical care of people with bipolar disorder

1.2.7.1 An annual review of the physical health of a person with bipolar disorder should ensure that over the course of a year the following are assessed:

• lipid levels including cholesterol (in patients over 40 even where there is no other indication of risk)
• glucose levels
• weight and waist measurement
• smoking status
• blood pressure.

1.2.7.2 Results of the annual review of a person with bipolar disorder should be made known to the person, documented in the person’s notes (including whether the person refused any tests) and communicated to relevant healthcare professionals in both primary and secondary care. Where a problem is detected clear agreement on responsibility for appropriate treatment should be made.

1.3 Assessment and diagnosis of children and adolescents

The diagnosis of bipolar disorder in children and adolescents, particularly prepubescent children, presents a considerable challenge because current diagnostic criteria developed for adults have limitations when applied to
children and adolescents. Therefore considerable caution, accompanied by careful long-term monitoring is required in the assessment of young people with possible bipolar disorder.

1.3.1 Diagnosing bipolar I disorder in prepubescent children

1.3.1.1 When diagnosing bipolar I disorder in prepubescent children healthcare professionals should use the same criteria as for the adult disorder but modified so that:

- mania must be present
- euphoria must be present most days, most of the time (for the past 7 days)
- irritability is not a core diagnostic criterion.

1.3.1.2 Bipolar I disorder should not be diagnosed in prepubescent children based solely on the diagnosis of a major depressive episode occurring in the context of a family history of bipolar disorder. However, children with a personal history of depression and family history of bipolar disorder should be carefully followed up.

1.3.2 Diagnosing bipolar I disorder in adolescents

1.3.2.1 When diagnosing bipolar I disorder in adolescents healthcare professionals should use the same criteria as for the adult disorder but modified so that:

- mania must be present
- euphoria must be present most days, most of the time (for the past 7 days)
- irritability can be helpful in making a diagnosis if it is episodic, severe, results in impaired function and is not in character or out of keeping with the context. However, it should not be a core diagnostic criterion.
1.3.2.2 Bipolar I disorder should not be diagnosed in adolescents based solely on the diagnosis of a major depressive episode occurring in the context of a family history of bipolar disorder. However, young people with a personal of depression and family history of bipolar disorder should be carefully followed up.

1.3.3 Diagnosing bipolar I disorder in older or developmentally advanced adolescents

1.3.3.1 When considering a diagnosis of bipolar I disorder in older or developmentally advanced adolescents, the same criteria as for establishing a diagnosis of bipolar I disorder in adults should be used.

1.3.4 Bipolar II disorder in both children and adolescents

1.3.4.1 Bipolar II disorder should not normally be diagnosed in children or adolescents because the criteria for establishing such a diagnosis are not well-enough established to support their use in routine clinical practice.

1.3.4.2 When considering a diagnosis of bipolar II disorder in older or developmentally advanced adolescents, the same criteria as for establishing a diagnosis of bipolar II disorder in adults should be used.

1.3.5 Differential diagnoses for both children and adolescents

1.3.5.1 When distinguishing bipolar I disorder from ADHD or conduct disorder the presence of clear-cut episodes of unduly elated mood, inappropriate and impairing grandiosity, and cycles of mood are normally indicative of bipolar disorder and so clinicians should focus of the presence of such symptoms before confirming a diagnosis of bipolar I disorder.

1.3.5.2 When distinguishing bipolar I disorder from schizophrenia the presence of mood cycles is normally indicative of bipolar disorder and
so clinicians should establish the presence of such cycles before confirming a diagnosis of bipolar I disorder.

1.3.5.3 When considering a diagnosis of bipolar I disorder in a child or adolescent clinicians should consider other possible explanations for presenting behaviour and symptoms including:

- sexual, emotional and physical abuse in a child or adolescent presenting with behaviours such as disinhibition, hypervigilance or hypersexuality before diagnosing mania
- the possibility of drug and/or alcohol misuse in children and adolescents presenting with mania-like symptoms, in which case consider a diagnosis of bipolar disorder only after a 7-day period of abstinence
- organic causes such as excited confusional states in children with epilepsy and akathisia resulting from neuroleptic medication.

1.3.6 Children and adolescents with learning difficulties

1.3.6.1 When diagnosing bipolar I disorder in a child or adolescent with learning difficulties, the same criteria as are applied to children and adolescents without learning difficulties should be used.

1.3.7 Assessment methods for children and adolescents

1.3.7.1 The diagnosis of bipolar disorder in children and adolescents should be made by a clinician with specialist training in child and adolescent mental health.

1.3.7.2 Assessment should include:

- a detailed mental state examination based on an individual interview with the child
- a medical evaluation to exclude organic causes
1.3.7.3 When assessing a child or adolescent for possible bipolar disorder a specialist diagnostic instrument such as the Wash-U-KSADS may be used; scales completed by parents/carers such as the Child Behaviour Checklist, Conners' Abbreviated Rating Scale, Parent Young Mania Rating Scale and Parent General Behaviour Inventory may also be used. These should not replace a full clinical interview.

1.3.7.4 In severely mentally ill children and adolescents with psychotic symptoms a diagnosis should be attempted as early as practical, and should be subject to regular specialist review.

1.4 The treatment and management of bipolar disorder

The treatment of bipolar disorder is based primarily on the provision of effective psychotropic medication, which aims to reduce the severity of symptoms, stabilise mood and prevent relapse. However, a range of psychological and psychosocial interventions can also have a significant impact on a person's well-being. It is also very important, given the long-term nature of bipolar disorder that care is effectively coordinated and monitored across both primary and secondary care settings.
1.4.1 General recommendations

1.4.1.1 In the treatment of bipolar disorder, the experience and outcome of previous treatment(s) together with patient preference should be considered when determining current treatment plans.

1.4.1.2 People with bipolar disorder, whether managed in primary or secondary care, should have continuity of care, including face-to-face contact as appropriate.

1.4.1.3 People started on any treatment who are not considered to be at increased risk of suicide should normally be seen within 2 weeks by a healthcare professional. Thereafter they should be seen on an appropriate and regular basis, for example, at intervals of 2–4 weeks in the first 3 months and at longer intervals thereafter, if response is good.

1.4.2 Special considerations for older adults with bipolar disorder

1.4.2.1 When determining the most appropriate care for an older adult with bipolar disorder (usually aged over 65 years) consideration should be given to the involvement of specialist old-age psychiatry services when:

- an existing patient of adult mental health services develops significant comorbid physical health and/or cognitive problems
- a new referral who has not previously been in contact with general adult psychiatry services or has had no contact with services for a significant period of time (usually 2 or more years) presents to services.

1.4.2.2 When treating older adults with bipolar disorder, healthcare professionals should:

- ensure that medication is given at an age-appropriate dose
• be aware of the increased frequency of drug interactions when prescribing psychotropic medication to older adults who are taking other medications
• ensure that medical comorbidities have been adequately recognised and addressed.

1.4.3 Weight gain management

1.4.3.1 For people who have gained weight during treatment for bipolar disorder, healthcare professionals should review the medication strategy, and consider:

• giving dietary advice and support from GP and mental health services
• advising regular increased aerobic exercise
• referring to a specialist mental health diet clinic or health delivery group, where available
• referring to a dietician for people with complex comorbidities (for example, additional physical problems/dietary difficulties, such as coeliac disease).

1.4.3.2 In people who have gained weight during long-term treatment, pharmacological treatment such as high-dose antidepressants, sibutramine or topiramate are not recommended for the promotion of weight loss.
1.5 The management of acute episodes

1.5.1 Recommendations relevant to all acute episodes

Assessment of patients with bipolar disorder prior to initiating pharmacological treatment

1.5.1.1 Prior to the initiation of any pharmacological treatment of bipolar disorder healthcare professionals should normally ensure that the following physical tests are performed:

- thyroid, liver and renal function tests, blood pressure, and full blood count
- chest X-ray and ECG if indicated
- EEG, CT scan or MRI scan in patients with evidence of an organic aetiology and/or a relevant comorbidity
- drug screening if suggested by the patient history.

1.5.2 The management of acute mania and hypomania

The pharmacological management of an acute manic or severe hypomanic episode depends on the severity of symptoms and whether patients are currently taking anti-manic drugs (lithium, valproate, antipsychotics). Clinicians should be guided by current medication doses and previous response. Only lithium, valproate semi-sodium, olanzapine, quetiapine and risperidone are licensed for the treatment of acute mania in the UK. Valproate is available in various forms including sodium valproate, valproic acid and valproate semisodium although only valproate semisodium is licensed for the treatment of manic episodes in the context of bipolar disorder. The active element in all formulations is the valproate ion.

General advice

1.5.2.1 To help reduce the negative consequences of manic symptoms, healthcare professionals should consider advising patients to avoid excessive stimulation, to engage in calming activities, to delay
important decisions, and to establish a structured routine (including a regular sleep pattern) in which the general level of activity is reduced.

1.5.2.2 In patients with severe acute hypomania healthcare professionals should consider treating such episodes as manic episodes and extrapolate from the recommendations for the treatment of acute mania as appropriate.

1.5.2.3 For patients taking an antidepressant at the time of onset of an acute manic episode, healthcare professionals should stop the antidepressant drug. The decision about whether to discontinue the antidepressant abruptly or gradually should be based on current clinical need, previous experience of discontinuation/withdrawal symptoms, and the risk of discontinuation/withdrawal symptoms of the antidepressant in question.

Pharmacological management of acute mania for those not currently taking anti-manic medication

1.5.2.4 In the treatment of acute mania in patients not currently taking anti-manic medication, treatment options include starting the patient on an antipsychotic, valproate or lithium. When choosing between these, bear in mind continuing long-term use, the likely side-effect profile, and:

- consider an antipsychotic for those who have severe manic symptoms or show marked behavioural disturbance as part of the syndrome of mania
- consider valproate or lithium for those who have showed previous response and good compliance to one of these drugs
- avoid valproate in women of child-bearing potential
- use lithium only for those with less severe symptoms due to the slower onset of action compared with antipsychotics and valproate.
1.5.2.5 In the initial management of acute behavioural disturbance and/or when there is severe insomnia, the short-term use of a benzodiazepine should be considered in addition to the anti-manic agent.

1.5.2.6 When treating acute mania with antipsychotics, healthcare professionals should generally use atypical antipsychotics (olanzapine, risperidone, quetiapine) because of the lower incidence of extrapyramidal side-effects but should take into account:

- individual risk factors regarding side effects (such as the risk of diabetes)
- the need to initiate treatment at the lower end of the dose range recommended in the Summary of Product Characteristics and titrate upwards based on response
- that if an antipsychotic proves ineffective in controlling symptoms of acute mania consideration should be given to augmenting the antipsychotic with valproate or lithium
- the greater risk of the sudden onset of depressive symptoms in older adults following recovery from a manic episode.

1.5.2.7 In the treatment of acute mania, carbamazepine should not be routinely used, and the following are not recommended: gabapentin, lamotrigine, topiramate.

**Pharmacological management of acute mania for those currently taking anti-manic medication**

1.5.2.8 When patients already taking lithium experience a manic episode healthcare professionals should check the plasma lithium levels and, for those with sub-optimal levels (that is, below 0.8 mmol/l), increase the dose until there is response (to a maximum level of 1.0 mmol/l). The patient should be monitored and, if there are no signs of improvement, consideration should be given to augmenting with an antipsychotic.
1.5.2.9 When patients already taking valproate experience a manic episode healthcare professionals should increase the dose until:

- symptoms start to improve
- side effects limit further dose increase
- or until the maximum licensed dose is reached

The patient should be monitored and, if there are no signs of improvement, consideration should be given to augmenting with an antipsychotic with anti-manic properties.

1.5.2.10 For patients already taking lithium or valproate, who present with severe mania, healthcare professionals should consider adding an antipsychotic at the same time as gradually increasing the dose of lithium or valproate. The decision depends on the severity of mania and the current dose of the mood stabiliser.

1.5.2.11 For patients already taking carbamazepine, healthcare professionals should not routinely increase the dose but should consider adding an antipsychotic depending on the severity of mania and the current dose of carbamazepine. Be aware of interactions with other medication, which are common with carbamazepine, and adjust doses as necessary.

1.5.3 Management of acute depression

The management of an acute depressive episode in bipolar disorder has some similarities but some important differences from the management of a unipolar depressive episode. The differences include the risk that antidepressants increase the rate of ‘switching’ to manic states and antidepressants have a possible role in causing cycle acceleration (mood destabilisation). In addition there is a more limited role in subsequent maintenance treatment with antidepressants in bipolar depression and a greater role for mood stabilisers. The choice of treatment will be influenced by the severity of present and past symptoms. When determining the choice of mood stabiliser, a mood stabiliser with anti-manic properties (that is, drugs
which in addition to having mood stabilising properties have also been shown to be of value in the management of acute mania: quetiapine, olanzapine, lithium or valproate) should be used. Lamotrigine may have a role to play in the management of depressive symptoms but its slow dose titration and onset of action limits its role in the treatment of acute depression.

The guidance below draws on the categorisation of severity for unipolar depression using ICD-10 criteria. This uses an agreed list of ten depressive symptoms to develop four categories, not depressed (fewer than four symptoms), mild depression (four symptoms), moderate depression (five to six symptoms), and severe depression (seven or more symptoms, with or without psychotic symptoms). In unipolar depression symptoms should be present for a month or more and every symptom should be present for most of every day. This categorisation is a helpful guide in bipolar disorder but it should be remembered that bipolar patients typically may experience more fluctuations in both the severity and duration of symptoms compared with unipolar patients, and so a strict application of these categories is not appropriate.

**General advice**

1.5.3.1 Healthcare professionals should consider advising patients with bipolar disorder and depressive symptoms to engage in a range of depression-management techniques, such as a structured exercise programme, activity scheduling, engaging in both pleasurable and achievement activities, ensuring adequate diet and sleep, and seeking appropriate social support, along with providing patients with an increased level of monitoring and formal support.

**Mild depressive episodes**

1.5.3.2 A further assessment should be arranged, normally within 2 weeks (‘watchful waiting’) for patients with bipolar disorder experiencing an acute mild depressive episode where:
mild depression has not in the past led to the development of a chronic or more severe depressive episode, or
• a healthcare professional judges the patient not to be at significant risk of developing a more severe depression.

Initiating treatment in patients not taking a mood stabiliser

1.5.3.3 In patients not taking a mood stabiliser experiencing mild depressive symptoms, if there is no improvement following a period of watchful waiting, or in patients who are assessed as requiring immediate treatment, healthcare professionals should consider an antidepressant (SSRI or moclobemide) plus a mood stabiliser with anti-manic properties. The choice of mood stabiliser should be based on the best choice for long-term treatment, the likely side effects and whether the patient is a woman of child-bearing potential.

1.5.3.4 Healthcare professionals should not normally prescribe an antidepressant alone (that is, in the absence of an anti-manic agent) for the management of acute depression. However, where a patient has refused a mood stabiliser with anti-manic properties and is assessed as at risk of developing moderate or severe depression, but is willing to take an antidepressant, healthcare professionals should explain the risks of switching to mania and the benefits of taking an adjunctive mood stabiliser and monitor carefully.

Initiating treatment in patients already taking an anti-manic agent

1.5.3.5 For people with bipolar disorder experiencing a mild acute depressive episode who are taking a mood stabiliser with anti-manic properties, healthcare professionals should check that the patient is taking the mood stabiliser at the appropriate dose, and adjust if necessary.
1.5.3.6 Healthcare professionals should consider initiating an antidepressant (SSRI or moclobemide) when a person with bipolar disorder:

- has experienced an acute depressive episode despite taking a mood stabiliser with anti-manic properties at an appropriate dose, or
- subsequent to developing an acute depressive episode, has been stabilised on an appropriate dose of a mood stabiliser, but has experienced no improvement in their depressive symptoms.

**Moderate and severe depressive episodes**

*Initiating treatment in patients not taking a mood stabiliser*

1.5.3.7 In patients experiencing a moderate or severe depressive episode, healthcare professionals should consider introducing an antidepressant (SSRI or moclobemide) plus a mood stabiliser with anti-manic properties or quetiapine. The choice of mood stabiliser should be based on the best choice for long-term treatment, the likely side effects and whether the patient is a woman of child-bearing potential.

1.5.3.8 For patients with moderate depressive symptoms with no history of recent rapid cycling, including those who have declined an antidepressant, healthcare professionals should consider offering a structured psychological therapy focused on depressive symptoms, problem solving, promoting social functioning, and further consideration of medication adherence.

1.5.3.9 When initiating an antidepressant in people not willing to take a mood stabiliser with anti-manic properties, healthcare professionals should explain the risks of switching to mania and the benefits of taking an adjunctive mood stabiliser and monitor carefully. Treatment should begin at a low dose and be increased gradually if necessary.
**Initiating treatment in patients taking a mood stabiliser with anti-manic properties**

1.5.3.10 For people with bipolar disorder experiencing a moderate or severe acute depressive episode and who are taking a mood stabiliser with anti-manic properties, healthcare professionals should first check that the patient is taking the mood stabiliser at the appropriate dose and adjust if necessary.

1.5.3.11 For those patients with bipolar disorder experiencing moderate depressive symptoms healthcare professionals should consider:

- the introduction of an adjunctive medication (antidepressant [SSRI or moclobemide] or quetiapine where the current mood stabiliser is not an antipsychotic), and
- a structured psychological treatment (focused on depressive symptoms, problem solving, promoting social functioning, and education about medication) if there has been no significant improvement after 2 to 4 weeks.

1.5.3.12 For those patients with bipolar disorder experiencing severe depressive symptoms healthcare professionals should consider the introduction of an adjunctive medication (antidepressant (SSRI or moclobemide), or quetiapine where the current mood stabiliser is not an antipsychotic.

**Depressed patients with recent unstable mood**

1.5.3.13 In patients who are depressed and have recent unstable mood, healthcare professionals should avoid the use of antidepressants, and consider increasing the dose of the mood stabiliser with anti-manic properties or the addition of a second mood stabiliser including lamotrigine.
Starting antidepressant treatment and monitoring risk

1.5.3.14 SSRIs or moclobemide (which are the only antidepressants with trial data in bipolar disorder) are recommended for the treatment of bipolar depression, since other MAOIs and the TCAs have increased side effects including higher rates of switching.

1.5.3.15 Healthcare professionals should address bipolar patients’ common concerns about taking antidepressants. For example, patients should be advised that craving and tolerance do not occur, and that taking medication should not be seen as a sign of weakness.

1.5.3.16 Healthcare professionals should ensure that all patients with bipolar disorder who are prescribed antidepressants are informed, at the time that treatment is initiated, of potential side effects including:

- the possibility of manic or hypomanic switching
- the delay in onset of effect, the gradual and fluctuating nature of improvement thereafter
- the need to take medication as prescribed and the risk of discontinuation/withdrawal symptoms
- the need to monitor for signs of akathisia, suicidal ideation, and increased anxiety and agitation (particularly in the initial stages of SSRI treatment)
- the need to seek help promptly if these side effects are at all distressing.

1.5.3.17 Patients with bipolar disorder started on antidepressants who are considered to present an increased suicide risk or are younger than 30 years (because of the potential increased risk of suicidal thoughts associated with the early stages of antidepressant treatment for this group) should normally be seen by a health professional after 1 week and frequently thereafter as appropriate until the risk is no longer considered significant.
1.5.3.18 When a patient with bipolar disorder develops marked and/or prolonged akathisia or agitation while taking an antidepressant, healthcare professionals should review the use of the drug.

1.5.3.19 Healthcare professionals should be cautious when prescribing SSRIs to people, in particular older adults, taking other medication known to cause intestinal bleeding such as non-steroidal anti-inflammatory drugs. The use of a gastro-protective drug may be considered.

**Stopping antidepressants after the treatment of acute depression**

1.5.3.20 When a patient has achieved remission (or maintained a significant reduction in symptoms for 8 weeks), healthcare professionals should consider tapering and discontinuing antidepressant medication over a period of several weeks, whilst maintaining the mood stabiliser, to avoid the risk of switching to mania and increased rapid cycling. Particular care is needed when discontinuing SSRIs (except fluoxetine) and venlafaxine.

**Additional guidance on specific treatments**

1.5.3.21 Healthcare professionals should not routinely provide the following treatments: lamotrigine as a single or first line agent for bipolar I disorder, or transcranial magnetic stimulation as an alternative to an antidepressant in the treatment of acute depressive episodes in people with bipolar disorder.

**Incomplete response to the treatment for acute depression**

1.5.3.22 When a patient with bipolar disorder has had an incomplete response to an antidepressant, healthcare professionals should reassess the patient, and consider evidence of substance abuse, psychosocial stressors, physical health problems, and inadequate adherence to medication.
1.5.3.23 In patients with depression who have had an incomplete response to an antidepressant healthcare professionals should consider:

- increasing the dose of the antidepressant within BNF limits, or
- switching to an alternative antidepressant (for example, mirtazapine or venlafaxine), or
- adding an atypical antipsychotic (quetiapine or olanzapine) or lithium, if these are not already being prescribed.

Management of treatment-resistant depression in bipolar disorder

1.5.3.24 When a patient’s depression has failed to respond to at least three courses of treatment for depression of adequate dose and duration, healthcare professionals should consider seeking the advice of, or referring to, a clinician with a specialist interest in treating bipolar disorder.

Recurrent depression in bipolar disorder

1.5.3.25 For patients with bipolar disorder who have experienced recurrent episodes of depression or chronic depressive symptoms with functional impairment whilst maintained on mood stabilising medication, healthcare professionals should consider (in the order set out below):

- individual psychological therapy focused on depressive symptoms, functioning particularly interpersonal functioning, detection of and coping with early signs, managing chronic social stress, promoting social functioning, and further consideration of medication adherence
- long-term treatment with antidepressants (SSRI or moclobemide) (at the minimum therapeutic dose and, in particular, for patients who have benefited from antidepressants for acute depression) in conjunction with a mood stabiliser with anti-manic properties
1.5.3.26 Healthcare professionals may consider lamotrigine alone as an option for long-term treatment for patients with bipolar II disorder with recurrent depression.

Management of severe depression with psychotic symptoms

1.5.3.27 For patients with a diagnosis of bipolar disorder experiencing a severe depressive episode with psychotic symptoms, healthcare professionals should consider augmenting the current treatment plan with antipsychotic medication, such as quetiapine, olanzapine or risperidone.

Sub-syndromal depression

In sub-syndromal depression in bipolar disorder symptoms are neither of sufficient number or duration (for example, persistent but intermittent symptoms) to meet criteria for major depression but, despite this, significantly impact on the personal and social functioning of an individual.

1.5.3.28 For patients with long-term sub-syndromal depression resulting in functional impairment healthcare professionals should initiate treatments recommended for mild depression unresponsive to watchful waiting.

1.5.4 The management of acute mixed episodes

An acute mixed episode is the presence of a mixture, or rapid alternation (usually within a few hours) of, manic/hypomanic and depressive symptoms. Both sets of symptoms should be prominent for the greater part of the current episode of illness, usually for at least 2 weeks. It should be distinguished from rapid cycling bipolar disorder (see below).
1.5.4.1 Healthcare professionals should consider treating patients with bipolar disorder experiencing an acute mixed episode as if they had an acute manic episode, and avoid prescribing an antidepressant.

1.5.4.2 Healthcare professionals should monitor patients with bipolar disorder experiencing an acute mixed episode closely (at least weekly) with emphasis on monitoring suicide risk.

1.5.5 The management of an acute episode in a patient with rapid cycling bipolar disorder

Rapid cycling bipolar disorder is defined as experiencing four or more acute episodes in a 1-year period. A key aspect of treatment should be to avoid medication-induced switching from one pole to another.

1.5.5.1 Base the treatment of an acute episode in the context of rapid cycling (which should normally be managed in secondary mental health services) on that for the treatment of manic and depressive episodes, but in addition do the following.

- Undertake a thorough review of previous treatments for bipolar disorder, and consider a further trial of appropriate previous treatments that have been inadequately delivered or adhered to.
- Focus on the optimisation of appropriate long-term treatment (with each trial of medication being usually of at least 6 months’ duration) rather than on treating individual episodes and symptoms.
- Encourage patients to keep a regular mood diary (paper or electronic) to monitor changes in severity and frequency of symptoms, and the impact of interventions.

1.5.6 The use of ECT in severe manic and depressive episodes

1.5.6.1 It is recommended that electroconvulsive therapy (ECT) is used only to achieve rapid and short-term improvement of severe symptoms after an adequate trial of other treatment options has

Bipolar disorder: NICE guideline DRAFT (November 2005) Page 36 of 75
proven ineffective and/or when the condition is considered to be potentially life-threatening, in individuals with:

- severe depressive illness
- catatonia
- a prolonged or severe manic episode.

1.5.6.2 The decision as to whether ECT is clinically indicated should be based on a documented assessment of the risks and potential benefits to the individual, including: the risks associated with the anaesthetic; current comorbidities; anticipated adverse events, particularly cognitive impairment; and the risks of not having treatment.

1.5.6.3 When using ECT in the treatment of bipolar disorder healthcare professionals should consider:

- stopping or reducing lithium or benzodiazepines, before giving ECT
- monitoring the length of fits carefully when anticonvulsants are used for the treatment of bipolar disorder
- monitor mental state carefully for evidence of switching to the opposite pole.

1.5.7 The prevention and management of behavioural disturbance

1.5.7.1 The management of disturbed behaviour in bipolar disorder should start with psychosocial and environmental interventions which are aimed at developing an approach to care which seeks to de-escalate any potential violent situations and moves to the use of restraint and pharmacological interventions only when these approaches are judged to be insufficient.

1.5.7.2 When a patient with bipolar disorder exhibits seriously disturbed behaviour or is judged to be at risk of doing so healthcare professionals should:
ensure the patient is placed in the least stimulating, most supportive and most non-confrontational environment available

review the safety and physical status of the patient, including hydration levels, and take appropriate action

consider the use of the use of distraction techniques and the diversion of energy into less risky or more productive activities to help prevent or reduce behavioural disturbance.

Pharmacological management of severe behavioural disturbance in people with bipolar disorder

This section on the pharmacological management on severe behavioural disturbance should be read in conjunction with the NICE guideline on the short-term management of disturbed/violent behaviour in in-patient psychiatric settings and emergency departments.

1.5.7.3 In the pharmacological management of severe behavioural disturbance in bipolar disorder healthcare professionals should normally try to use oral medication such as olanzapine before the use of intramuscular preparations.

1.5.7.4 When a severely disturbed patient with bipolar disorder cannot be effectively managed with oral medication and rapid tranquillisation is required healthcare professionals should consider:

- the use of intramuscular olanzapine (10 mg), lorazepam (2 mg) or haloperidol (2–10 mg); wherever possible as a single agent
- that olanzapine or lorazepam should be preferred to haloperidol on grounds of the propensity of haloperidol to cause movement disorders, in particular dystonia and akathisia
- that olanzapine and parenteral benzodiazepines should not be given intramuscularly within 1 hour of each other
- that repeat intramuscular doses can be given up to 20 mg per day (olanzapine), or 4 mg per day (lorazepam) or 18 mg per day
(haloperidol) – total daily dose including concurrent oral 
medication should not normally exceed BNF limits
• previous response and tolerability, the availability of flumazenil, 
and the current regular medication when choosing between olanzapine and lorazepam.

1.5.7.5 Intravenous preparations of any psychotropic drug, intramuscular 
diazepam, intramuscular chlorpromazine, paraldehyde and 
zuclopenthixol acetate are not recommended for routine use in the 
pharmacological management of behavioural disturbances in people 
with bipolar disorder.

1.6 Long-term management
Bipolar disorder is a chronic relapsing and remitting disorder. Long-term 
treatment and support are required to minimise the risk of recurrence and 
optimise quality of life, and social and personal functioning. The primary long-
term treatment methods are pharmacological, but psychological and 
psychosocial interventions have an important part to play. Whether an 
individual is managed long term in either primary or secondary care a 
coordinated care programme, with rapid access to support at times of crisis, is 
essential.

1.6.1 Pharmacological treatment following recovery from an acute episode

Initiating long-term treatment

1.6.1.1 Healthcare professionals should normally consider initiating long-
term treatment for bipolar disorder in the following circumstances:

• following a manic episode which was associated with significant 
  risk and adverse consequences
• when there have been two or more acute episodes in patients 
  with a diagnosis of bipolar I disorder
• when there is evidence of significant functional impairment, significant risk of suicide or frequently recurring episodes in patients with bipolar II disorder.

1.6.1.2 When choosing long-term pharmacological treatment for patients with bipolar disorder, healthcare professionals should:

• carefully review response to previous treatments, the relationship between, and pattern of, mood changes and life events (using a life chart where appropriate)
• review medical history and any risk assessment
• consider patient preference and history of adherence
• consider a brief assessment of cognitive state (for example, the mini mental state examination) in particular for older adults.

1.6.1.3 When deciding on an agent for the long-term management of a patient with a diagnosis of bipolar disorder healthcare professionals should consider the following.

• As first-line treatments an antipsychotic (olanzapine, quetiapine), lithium (particularly where there is a high risk of manic relapse), or valproate (but not for women of child-bearing potential).
• For an incomplete response to optimum first-line treatment of at least 6 months consider the combination of two mood stabilizers (lithium, olanzapine, quetiapine, valproate) together with close monitoring of clinical state, side effects and, where relevant, blood levels. Appropriate combinations are lithium and valproate, lithium with quetiapine or olanzapine, or valproate and quetiapine or olanzapine. The reasons for the use of such combinations and the discussion with the patient of the potential benefits and risks should be documented in the case notes.
• If a trial of one of the combination of mood stabilisers in the long-term management of bipolar disorder proves ineffective healthcare professionals should consider consulting with, or
referring the patient to, a clinician with expertise in the pharmacological treatment of bipolar disorder.

- As third line treatments, lamotrigine (especially in bipolar II disorder) and carbamazepine.

1.6.1.4 Healthcare professionals should normally expect long-term pharmacological treatment to continue for at least 5 years following an episode of bipolar disorder. They should discuss this with the patient and ensure that regular reviews take place.

1.6.1.5 If, after careful discussion with a healthcare professional, a patient with bipolar disorder declines long-term medication, they should still be offered regular contact and regular reassessment with primary or secondary care services as appropriate.

1.6.1.6 Long-acting intramuscular formulations of antipsychotics (‘depots’) are not recommended for routine use in the treatment of bipolar disorder, although they may be considered in the long-term treatment of people in whom oral antipsychotics have proved effective in the treatment of mania, but in whom poor concordance has led to relapse.

The use of antipsychotics in long-term pharmacological treatment

Initiating antipsychotics

1.6.1.7 When initiating long-term treatment of bipolar disorder with antipsychotics healthcare professionals should measure baseline weight and waist measurement, and:

- for olanzapine – plasma glucose and lipids
- for quetiapine – thyroid function.

1.6.1.8 When initiating quetiapine healthcare professionals should be aware of the need to titrate the dose gradually in order to help maintain normal blood pressure.
Monitoring antipsychotics

1.6.1.9 For patients with bipolar disorder taking antipsychotics healthcare professionals should monitor weight and waist measurement, and initiate weight management techniques if necessary, as well as for olanzapine monitoring plasma glucose and lipids 3 months after the start of treatment, and then annually, or more frequently if there is evidence of elevated levels.

Stopping antipsychotics

1.6.1.10 Patients with bipolar disorder stopping an antipsychotic, but continuing with other mood stabilising medication, should discontinue the antipsychotic gradually over at least 4 weeks.

1.6.1.11 Patients with bipolar disorder stopping an antipsychotic but not continuing with other mood stabilising medication, and those with a history of manic relapse, should discontinue the antipsychotic over a period of up to 3 months.

Risks associated with the use of antipsychotics

1.6.1.12 Healthcare professionals should be aware of the possibility of the development of malignant neuroleptic syndrome and diabetic ketoacidosis with the use of antipsychotic medication, particular caution may need to be exercised when treating manic patients. They should discuss with patients the potential for weight gain.

The use of lithium in long-term pharmacological treatment

Initiating lithium

1.6.1.13 When initiating lithium as long-term treatment in patients with bipolar disorder, healthcare professionals should:
• advise patients that erratic compliance or rapid discontinuation may be harmful and that regular fluid intake should be maintained
• arrange for the following tests to be undertaken – full blood counts, urea and electrolyte, and thyroid function
• arrange for an ECG to be carried out in patients with risk factors for cardiac disease
• establish a shared-care protocol for the prescribing and monitoring of lithium and potential adverse effects.
• not routinely initiate lithium in primary care
• be aware that the effectiveness of lithium as a long-term treatment can only be established over at least a 6 month period.

1.6.1.14 Healthcare professionals should normally aim to maintain serum lithium levels at between 0.6 mmol/l and 0.8 mmol/l for people with bipolar disorder who have not previously been prescribed lithium.

1.6.1.15 Healthcare professionals should consider a trial of lithium for at least 6 months with serum lithium levels between 0.8 mmol/l and 1.0 mmol/l for people with bipolar disorder who have relapsed previously while taking lithium or continue to have sub-syndromal symptoms with functional impairment while receiving lithium.

Monitoring lithium

1.6.1.16 For patients with bipolar disorder on long-term lithium treatment healthcare professionals should do the following.

• Monitor serum lithium levels weekly until stable and every 3 months thereafter.
• Monitor carefully with older adults because of the propensity for older adults to develop high serum levels of lithium at doses within the normal range, and the possibility of lithium toxicity at moderate serum lithium levels.
• Undertake blood tests more frequently if there is evidence of clinical deterioration, abnormal results, or symptoms suggestive of abnormal renal or thyroid function, such as unexplained fatigue, or the presence of other risk factors, for example initiation of concurrent medication such as ACE inhibitors, non-steroidal anti-inflammatory drugs, or diuretics.

• Monitor for the symptoms of neurotoxicity including paraesthesia, ataxia, tremor and cognitive impairment which can occur at therapeutic levels.

• Initiate closer monitoring of dose and blood serum levels if urea and creatinine levels become elevated, and assess the rate of deterioration of renal function. The decision to continue lithium depends on clinical efficacy, and degree of renal impairment, and healthcare professionals should consider seeking the advice of a renal specialist and a clinician with expertise in the management of bipolar disorder to arrive at this decision.

**Stopping lithium**

1.6.1.17 Lithium should be discontinued gradually over at least 4 weeks, and preferably over a longer period of up to 3 months, particularly in patients with a history of manic relapse and even where the patient has been started on another mood stabiliser.

1.6.1.18 Where lithium has been, or is about to be, stopped abruptly, switch patients to either an atypical antipsychotic or valproate to reduce the likelihood of relapse. Patients should be closely monitored for early signs of mania and depression during this period.

**Risks associated with the use of lithium**

1.6.1.19 Healthcare professionals should avoid prescribing non-steroidal anti-inflammatory drugs to patients taking lithium if possible, and should warn patients taking lithium not to take over-the-counter non-
steroidal anti-inflammatory drugs. Patients prescribed non-steroidal anti-inflammatory drugs should be closely monitored.

1.6.1.20 Healthcare professionals should be cautious when prescribing diuretics to older adults taking lithium.

1.6.1.21 Healthcare professionals should warn patients to seek medical attention if they develop diarrhoea and/or vomiting, and to maintain fluid levels if they experience these symptoms after taking exercise or when in hot climates. This is particularly important for older adults and people with learning difficulties, suffering from chest infections or pneumonia, or who are immobile for long periods.

The use of valproate in long-term pharmacological treatment

Initiating valproate

1.6.1.22 When initiating valproate as long-term treatment for patients with bipolar disorder healthcare professionals should arrange a full blood count and liver function tests.

1.6.1.23 Healthcare professionals should not routinely prescribe valproate for women of child-bearing potential with bipolar disorder. If valproate is prescribed to women of child-bearing potential ensure adequate contraception is used, and explain the risks to the health of the unborn child.

1.6.1.24 Healthcare professionals should not routinely prescribe valproate for females with bipolar disorder under the age of 18 because of the increased risk of polycystic ovary syndrome and unplanned pregnancy in this age group.
Monitoring valproate

1.6.1.25 Routine measurement of valproate blood levels is not recommended unless there is evidence of ineffectiveness, poor adherence or toxicity.

Stopping valproate

1.6.1.26 When stopping valproate in patients with bipolar disorder reduce the dose gradually over a period of at least 4 weeks to minimise the potential for destabilisation.

Risks associated with the use of valproate

1.6.1.27 Healthcare professionals should advise patients and their carers how to recognise signs of blood or liver disorders and to seek immediate medical attention if symptoms develop. If abnormal liver function or blood dyscrasia is detected stop the drug immediately.

1.6.1.28 When prescribing valproate healthcare professionals should be aware of:

- drug interactions between valproate and other anticonvulsants
- the need for more careful monitoring of sedation, tremor and gait disturbance in older adults.

Lamotrigine

Initiating lamotrigine

1.6.1.29 Healthcare professionals should titrate lamotrigine upwards gradually to minimise the risk of skin rashes, including Stevens-Johnson syndrome. Titration should be slower in patients taking concurrent valproate.

1.6.1.30 When considering prescribing lamotrigine to women taking oral contraceptives, healthcare professionals should discuss with the
patient the need to use another method of contraception, and/or increase the dose of lamotrigine.

**Monitoring lamotrigine**

1.6.1.31 Healthcare professionals do not need to undertake routine monitoring of blood levels for patients taking lamotrigine.

**Stopping lamotrigine**

1.6.1.32 When stopping lamotrigine in patients with bipolar disorder reduce the dose gradually over a period of at least 4 weeks to minimise the potential for destabilisation.

**Risks associated with the use of lamotrigine**

1.6.1.33 Healthcare professionals should advise patients taking lamotrigine, particularly when starting the drug, that if a rash develops they should seek medical attention urgently. The drug should be stopped unless it is clear that the rash is not lamotrigine-related. If an appointment cannot be arranged within a few days or if the rash is worsening the patient should be advised to stop the drug.

**Carbamazepine**

**Initiating carbamazepine**

1.6.1.34 Healthcare professionals should not routinely initiate carbamazepine in the long-term treatment of bipolar disorder without consulting a specialist in the treatment of bipolar disorder.

1.6.1.35 When initiating carbamazepine for the long-term treatment of bipolar disorder healthcare professionals should gradually increase the dose to reduce the risk of ataxia.
Monitoring carbamazepine

1.6.1.36 Healthcare professionals should arrange for 6-monthly tests of plasma levels of carbamazepine to exclude toxicity because therapeutic levels and toxic levels are close.

1.6.1.37 Healthcare professionals should monitor closely possible interactions of carbamazepine with a wide range of other drugs, including oral contraceptives, particularly if the person starts a new medication.

Stopping carbamazepine

1.6.1.38 When stopping carbamazepine in patients with bipolar disorder reduce the dose gradually over a period of at least 4 weeks to minimise the potential for destabilisation.

Risks associated with the use of carbamazepine

1.6.1.39 Be careful when prescribing carbamazepine for patients taking concomitant medications, for example, older adults (older than 65 years) and people with multiple physical problems, because of the problems of interactions with other drugs.

Additional considerations for long-term treatment following an acute depressive episode

1.6.1.40 Following successful treatment for an acute depressive episode, healthcare professionals should not routinely continue patients on long-term antidepressant treatment because there is no evidence that continuing antidepressants reduces relapse rates, and it may be associated with increased risk of switching to mania.

Treatment for chronic depressive symptoms

1.6.1.41 For people with an established diagnosis of bipolar disorder who are not taking a mood stabiliser and who have not had a
manic/hypomanic episode for 5 years but who are experiencing chronic depressive symptoms consider:

- long-term antidepressant medication (SSRIs or moclobemide) in combination with a mood stabiliser, or
- cognitive behavioural psychotherapy (16–20 sessions) in combination a mood stabiliser.

In the absence of clear evidence, patient preference should influence the choice of the above treatments.

1.6.2 Long-term management of rapid cycling

1.6.2.1 For the long-term pharmacological management of people with rapid cycling bipolar disorder healthcare professionals should:

- consider as first line treatment a combination of lithium and valproate
- avoid monotherapy with lithium or the use of an antidepressant, except on advice from a specialist in bipolar disorder
- consider combinations of lithium or valproate with lamotrigine, especially in bipolar II disorder
- check thyroid function every 6 months together with levels of thyroid antibodies in people with a personal or family history of thyroid problems.

1.6.3 Harmful drug/alcohol use in bipolar disorder

1.6.3.1 For patients with bipolar disorder and comorbid harmful drug and/or alcohol use healthcare professionals should consider providing a psychosocial intervention specifically targeted at the drug and/or alcohol use (for example, psychoeducation and motivational enhancement). In most cases this should normally be delivered by general mental health services where appropriate in conjunction with specialist substance use services.
1.6.4 Promoting a healthy lifestyle and relapse prevention

1.6.4.1 Healthcare professionals should give patients with bipolar disorder advice on:

- the importance of maintaining good sleep hygiene, and a regular lifestyle
- the avoidance of shift work, night flying or flying across time zones, and of routinely working excessively long hours for those with a history of relapse related to not maintaining good sleep hygiene or a regular lifestyle
- the need for and provision of additional support when a person with bipolar disorder experiences a significant life event (loss of job, close bereavement) including increased monitoring of mood and general well-being, and encouraging the patient to discuss difficulties with family and friends
- appropriate methods for self-monitoring of physical and mental state.

1.6.4.2 For people with bipolar disorder healthcare professionals should develop a programme to identify the symptoms and indicators of a potential exacerbation of the disorder and a plan of how to respond (including both psychosocial and pharmacological interventions) should be put in place.

1.6.5 Psychological therapy following recovery from an acute episode

1.6.5.1 For people with bipolar disorder who are relatively stable (but who may experience mild to moderate affective symptoms), healthcare professionals should consider individual structured psychological therapy (for at least 16 sessions over 6 to 9 months) in addition to medication which should:

- include psychoeducation about the illness and the promotion of regular daily and routine sleep and of medication adherence
• include monitoring mood, detection of early warnings and strategies to prevent early stages from developing into full-blown episodes
• enhance general coping strategies.

1.6.5.2 Healthcare professionals should ensure that psychological interventions are delivered by people with competence in the intervention and experience of bipolar disorder.

1.6.5.3 For people with bipolar disorder in regular contact with their families and where an agreed focus for a family intervention can be identified, healthcare professionals should consider offering a focused family intervention over a period of 6 to 9 months, comprising elements of psychoeducation about the illness, communication enhancement and problem solving.

1.6.6 Psychosocial support

1.6.6.1 For people with bipolar disorder, particularly those with chronic depressive symptoms, who would benefit from additional social support, healthcare professionals should consider offering befriending in addition to pharmacological and psychological treatments. Befriending should be by trained volunteers providing, typically, at least weekly contact for between 2 and 6 months.

1.7 Overall treatment setting/pathways to care

Bipolar disorder is a long-term illness that needs long-term care. The service needs of a person with bipolar disorder will depend on their phase of illness, age, function and recent history. No specific service will be able to meet all these needs throughout the person’s life so inevitably there will be a need for the transfer of care and sharing of care by services, requiring good communication between people with bipolar disorder, carers and health professionals in different services.
1.7.1 Models of service provision

Service provision in primary and secondary care

1.7.1.1 Primary and secondary care organisations should jointly consider establishing integrated care programmes for the care of people with bipolar disorder. These should include:

- Clearly specified regular reviews in primary and secondary care, so as to ensure that symptoms (including sub-threshold symptoms) are managed if they significantly impair social functioning
- Clearly specified protocols for the delivery and monitoring of appropriate pharmacological, psychosocial, psychological and psycho-educational interventions
- Clear agreements between healthcare professionals on their specific responsibilities for assessment, monitoring and treatment
- Written treatment plans that are shared with the patient and, where appropriate, with families and carers.

1.7.1.2 The organisation and development of primary care based practice case registers for people with severe mental illness including bipolar disorder is recommended for the monitoring of the physical and mental health of people with bipolar disorder in primary care.

1.7.1.3 The provision of telephone support by appropriately trained members of the primary care team, informed by clear treatment protocols, should be considered for all patients with bipolar disorder, in particular for the monitoring of medication regimes.

Community mental health teams (CMHTs)

1.7.1.4 Consideration should be given to referral to coordinated care provided by a CMHT for people with bipolar disorder who:
• have problems in engaging with, and maintaining regular contact with, services such as outpatient care
• experience frequent relapses, poor symptom control, continuing functional impairment, or comorbid anxiety disorders
• are at risk of suicide, or harm to self or others, including self-neglect or exploitation
• have problems with medication adherence or chronic substance misuse.

Crisis resolution and home treatment teams

1.7.1.5 Crisis resolution and home treatment teams should be developed as a means to manage crises for people with bipolar disorder, and as a means of delivering high-quality acute care. In this context, teams must pay particular attention to existing care plans, which should be immediately available to the crisis team.

1.7.1.6 When delivering crisis care at home for bipolar patients, particular attention should be given to managing risk, and monitoring behavioural disturbance particularly in the case of mania, and the burden on family and carers.

1.7.1.7 Crisis resolution and home treatment teams should be considered for people with bipolar disorder who may benefit from early discharge from hospital following a period of inpatient care.

Early intervention services

1.7.1.8 Early intervention services focused on the needs of people under the age of 35 presenting with bipolar disorder for the first time should be developed. These should include access to specialist expertise in diagnosis, and tailored pharmacological, psychological, social, occupational and educational interventions.

1.7.1.9 Where the needs of the patient and/or carer exceed the capacity of early intervention services, referral to crisis resolution and home
treatment teams, acute day hospitals or inpatient services should be considered.

**Assertive outreach teams**

1.7.1.10 Assertive community treatment should be considered for people with bipolar disorder, particularly those who make high use of inpatient services and who have a history of poor engagement with services leading to frequent relapse and/or social breakdown (as manifest by homelessness or seriously inadequate accommodation).

**Inpatient care**

1.7.1.11 Admission to an inpatient unit should be available to patients with bipolar disorder who present with significant risk of harm.

1.7.1.12 The hospital environment should provide facilities for containment within a supportive, low stimulation environment including where necessary access to a psychiatric intensive care unit.

**Day hospitals**

1.7.1.13 Acute day hospitals should be considered for the provision of acute care, both as an alternative to acute admission to inpatient care and particularly to facilitate early discharge from inpatient care. The degree of risk to the patient or others, level of behavioural disturbance, and the burden to family and/or carer(s) should be considered.

**Vocational rehabilitation**

1.7.1.14 Vocational rehabilitation, specifically individual supported placements, should be considered for those people with bipolar disorder who want help to return to work or gain employment.

1.7.1.15 Mental health services, in partnership with social care providers and other local stakeholders, should help people to use local employment,
education and a range of other structured purposeful activities opportunities, to suit the different needs and level of skill, for people with severe mental health problems, including people with bipolar disorder.

**Enhanced outpatient care**

1.7.1.16 For patients with bipolar disorder who would benefit from close monitoring, and have a particular physical health risk such as renal damage, and have a record of regular attendance without the need for outreach services, healthcare professionals should consider referral to enhanced multi-professional outpatient clinics, such as lithium clinics.

**Specialist services**

1.7.1.17 Trusts providing specialist mental health services should ensure that all clinicians (in primary and secondary care) have access to specialist advice on the management of bipolar disorder for adults, and separately for children and adolescents.

**1.8 Treatment of children and adolescents with bipolar disorder**

The evidence base for the pharmacological and psychological treatment of bipolar disorder in children and adolescents is extremely limited. In a number of cases recommendations for treatment can be based on a careful extrapolation for the evidence for the treatment of bipolar disorder in adults, in other cases this cannot be justified. With regard to pharmacological treatment at the date of publication (XXXXX 2006), there are no psychotropic drugs with a current UK Marketing Authorisation for bipolar disorder in children and adolescents (younger than 18 years). However, in 2000, the Royal College of Paediatrics and Child Health issued a policy statement on the use of unlicensed medicines, or the use of licensed medicines for unlicensed applications, in children and adolescents. This states that such use is
necessary in paediatric practice and that doctors are legally allowed to prescribe unlicensed medicines where there are no suitable alternatives and where the use is justified by a responsible body of professional opinion. General management principles for the pharmacological treatment of bipolar disorder in children and adolescents include reduced starting doses compared with those used in adults, and closer monitoring during treatment because children and adolescents may be more prone to adverse effects of medication including sedation, obesity, extrapyramidal symptoms, metabolic changes and raised prolactin.

1.8.1 The pharmacological treatment of acute mania in children and adolescents

1.8.1.1 In the pharmacological management of children or adolescents experiencing an acute manic episode healthcare professionals should follow the recommendations set out for adults with bipolar disorder and in addition they should:

- measure baseline, then chart height and weight
- measure prolactin levels for all children and adolescents
- consider an atypical antipsychotic, such as quetiapine, as first line treatment
- where there is an inadequate response to an antipsychotic, consider adding lithium or valproate. Valproate should normally be avoided in females because of risks during pregnancy and potential increased risk of polycystic ovary syndrome.

1.8.2 The pharmacological and psychological treatment of depression in children and adolescents

Mild depression in children and adolescents

1.8.2.1 For children and adolescents with bipolar disorder experiencing a mild depressive episode, monitor weekly and offer additional support, for example at home and in school.
Moderate and severe depression in children and adolescents

1.8.2.2 In the pharmacological and psychological management of children or adolescents with bipolar disorder experiencing a moderate or severe depressive episode healthcare professionals, who should normally be specialist clinicians (based in at least Tier 3 level services), should follow the recommendations set out for adults with bipolar disorder except that they should be normally first offer children and adolescents a structured psychological therapy in addition to a mood stabiliser which should be monitored weekly.

1.8.2.3 For a child or adolescent with bipolar disorder, if there has been no response after 4 weeks to psychological therapy for the treatment of depression in combination with a mood stabiliser healthcare professionals should consider:

- the addition of fluoxetine starting at 10 mg per day, continuing at this dose if there is an adequate response but if not increase to 20 mg per day
- changing to sertraline or citalopram if there is no response to fluoxetine after an adequate trial, and if there is still no response seek advice from a specialist in affective disorders.

1.8.2.4 For adolescents who are experiencing a moderate or severe depressive episode but are developmentally advanced, use the guidance for the management of depression provided for adults in this guideline.

1.8.3 Long-term treatment of children and adolescents

1.8.3.1 In the long-term pharmacological and psychological management of children or adolescents with bipolar disorder healthcare professionals, who should normally be specialist clinicians (based in at least Tier 3 level services) should follow the recommendations set out for adults with bipolar disorder except that they should:
use quetiapine as the first line mood stabiliser
consider lithium as the second line mood stabiliser in females and valproate as the second line mood stabiliser in males
consider providing support to parents/carers in helping the child or adolescent maintain a regular lifestyle
consider offering specific advice to the school/college (with permission of the patient and those with parental responsibility) on the management of the child or adolescent.

1.8.4 Inpatient service for children and adolescents

1.8.4.1 For children and adolescents who are at risk of suicide or other serious harm as a consequence of bipolar disorder, admission as an inpatient or day patient, or the provision of more intensive community treatment, should be considered.

1.8.4.2 For children and adolescents with bipolar disorder who require inpatient care this should be provided in specialist units designed specifically for young people which are able to provide an age appropriate setting and support the educational social and personal needs of the child or adolescent.

1.8.4.3 In the management of children and adolescents with bipolar disorder and severe behavioural disturbance healthcare professionals should follow the guidance for adults. However, rapid tranquillisation with haloperidol in children and adolescents is not recommended because of increased propensity to extrapyrimidal side effects in this age group.

1.9 Treatment and management of women of child-bearing potential

The treatment and management of pregnant women with bipolar disorder, in particular its pharmacological management, is a challenging and complex problem. In significant part this is because the evidence base is weak and the
precise nature of the risks of use of medication is not always well understood. However, all pregnancies and deliveries carry some risk, and these risks are increased if serious mental illness goes untreated throughout pregnancy.

1.9.1 General principles of management for women of childbearing potential and for women with bipolar disorder who are pregnant

1.9.1.1 At the initial appointment for (and subsequently as appropriate) women of child-bearing potential with bipolar disorder, healthcare professionals should provide information (documented in the notes) about:

- the relative risks associated with the continuation and discontinuation of medication both to themselves and to the fetus if they were to become pregnant
- appropriate contraception.

1.9.1.2 When presenting information about risk healthcare professionals should take care to use the most effective methods to communicate the nature and extent of the absolute and relative risks of both treating and not treating the bipolar disorder.

1.9.1.3 Consideration should be given to an increased frequency of contact by specialist mental health services with pregnant women with bipolar disorder, who should also maintain close liaison with obstetric services, because of the increased risk of relapse during pregnancy and the postnatal period.

1.9.1.4 A pregnant woman with bipolar disorder who is stable on an antipsychotic and whose history shows that she is likely to relapse without medication, should be maintained by healthcare professionals on the antipsychotic. Such a patient should be monitored for weight gain and diabetes.
1.9.1.5 Healthcare professionals should note that the following drugs should not be routinely prescribed as treatment for pregnant women with bipolar disorder:

- valproate – because of risk to the fetus and subsequent child development. If valproate is used it should be limited to a maximum of 1 gram per day, administered in divided doses and in the slow release form, with 5 mg/day folic acid
- carbamazepine – because of its limited efficacy and risk of harm to the fetus
- long-term treatment with benzodiazepines – because of risks during pregnancy and the immediate postnatal period.

1.9.1.6 Healthcare professionals should ensure that appropriate advice and psychological support is offered by obstetric services to a woman if congenital defects are identified, regardless of whether she has decided to continue with the pregnancy or have a termination.

1.9.2 Women planning a pregnancy

1.9.2.1 Women taking antipsychotics who are planning a pregnancy should be advised that some antipsychotics may be associated with raised prolactin levels, with the likelihood that this will decrease the possibility of successful conception. Measure prolactin levels and if raised levels are confirmed consider an alternative drug less associated with raised prolactin levels.

1.9.2.2 For a woman who plans to become pregnant and whose history shows that she is at particular risk of developing mania and cannot be managed without mood stabilising medication, the drug of least risk would be an antipsychotic (quetiapine or olanzapine) and so consideration should be given to changing to an antipsychotic.

1.9.2.3 In women with existing bipolar disorder who are planning a pregnancy and are currently taking lithium healthcare professionals should consider the following.
• Stopping lithium if the patient is well and not at high risk of relapse.
• If the patient is not well or at high risk of relapse:
  − consider switching gradually to an antipsychotic throughout pregnancy, or
  − if there is a previous good response to lithium above other drugs consider restarting lithium in second trimester if not planning to breastfeed
  − consider continuing with lithium, after full discussion with the patient of the attendant risks, while trying to conceive and throughout the pregnancy if the patient had manic episodes which significantly complicated previous pregnancies, and where there is a documented good response to lithium.

1.9.2.4 Women with bipolar disorder who are considering pregnancy should normally be advised to discontinue taking sodium valproate and consideration should be given to the use of an alternative mood stabiliser such as an antipsychotic.

1.9.2.5 For women with bipolar disorder who are considering pregnancy, who have discontinued a mood stabiliser and who have become depressed, consider offering psychological therapy (CBT) in preference to an antidepressant because of the risk of switching associated with the use of antidepressants. If antidepressants are used SSRIs (but not paroxetine because of the risk of cardiovascular malformations in the fetus) should be preferred and close monitoring of the woman instigated.

1.9.3 Women with an unplanned pregnancy

1.9.3.1 For a woman with bipolar disorder who has an unplanned pregnancy healthcare professionals should:

• confirm the pregnancy as quickly as possible
• normally advise the woman to discontinue taking sodium valproate or carbamazepine
• if the pregnancy is confirmed in the first trimester, reduce the dose of lithium but be aware that rapid discontinuation of lithium has a high risk of precipitating relapse, and that discontinuation on confirmation of pregnancy does not avoid cardiac defects in the fetus
• offer the choice of an alternative mood stabiliser (an antipsychotic)
• offer appropriate screening and counselling concerning the continuation of the pregnancy, additional monitoring and information from appropriate healthcare professionals of the risks to the fetus if it is agreed she stay on the existing medication.

1.9.3.2 If women with bipolar disorder and an unplanned pregnancy continue with the pregnancy, a full paediatric assessment of the newborn baby is required with appropriate social and medical help being provided for mother and child.

1.9.4 Pregnant women experiencing acute mania or depression

Acute mania

1.9.4.1 For women who are pregnant, on no current appropriate psychotropic medication and experiencing acute mania healthcare professionals should consider antipsychotics (for example, quetiapine, risperidone or a low-dose typical antipsychotic) as the first choice and monitor carefully.

1.9.4.2 For women who are pregnant, currently taking an anti-manic mood stabiliser and experiencing acute mania healthcare professionals should:

• check dose/adherence to the mood stabilisers
increase dose of the antipsychotic or consider changing to an antipsychotic if not on such medication
if there is no response and the patient is severely manic consider the use of ECT, lithium and rarely valproate.

1.9.4.3 Where no effective alternative to sodium valproate can be identified women should be informed of the increased risk to the fetus and subsequently to the child's intellectual development. The lowest possible effective dose should be used and consideration should be given to augmenting the low-dose with other mood stabilising drug, other than carbamazepine.

**Acute depression**

1.9.4.4 In the treatment of mild depression in pregnant women with bipolar disorder avoid antidepressant medication and use the recommendations set out for adults with bipolar disorder.

1.9.4.5 In the treatment of moderate to severe depression in pregnant women with bipolar disorder consider:

- psychological treatment (CBT) for moderate depression
- combined medication and structured psychological intervention for severe depression.

1.9.4.6 In the treatment of moderate to severe depression in bipolar disorder in pregnant women quetiapine alone or SSRIs (but excluding paroxetine) in combination with a mood stabiliser should be preferred as they are less likely to be associated with switching that the tricyclic antidepressants. Monitor closely for signs of switching and stop the drug if patients start to develop manic or hypomanic symptoms.

1.9.4.7 Women with bipolar disorder who are prescribed an antidepressant during pregnancy and the immediate postnatal period should be informed by healthcare professionals of the potential adverse but predominantly short-lived effects of antidepressants on the neonate.
1.9.5 Care in the perinatal period

1.9.5.1 For pregnant women, especially towards the end of pregnancy, and for women in the immediate post-partum phase the serum levels of lithium should be carefully monitored (within 24 hours of childbirth and every 4 weeks during pregnancy) and the dose adjusted to maintain appropriate serum levels within the therapeutic range.

1.9.5.2 For women with bipolar disorder in the immediate postnatal period who are not medicated but at high risk of developing an acute episode, healthcare professionals should consider establishing or reinstating medication as soon as the patient is medically stable (once the fluid balance is established).

1.9.5.3 For women with bipolar disorder who develop severe manic or psychotic symptoms and associated behavioural disturbance in the intrapartum period healthcare professionals should consider the use of rapid tranquillisation with an antipsychotic not a benzodiazepine because of the risk of floppy baby syndrome. Such women should be managed in close collaboration with an anaesthetist.

1.9.6 Breast feeding

1.9.6.1 For women with bipolar disorder continuing/starting on psychotropic medication after childbirth healthcare professionals should:

- give appropriate advice on the risks and benefits of breast feeding
- advise not to breastfeed if taking lithium, benzodiazepines or lamotrigine
- offer an alternative mood stabiliser if the woman wishes to continue breastfeeding – an antipsychotic should be the preferred option
- when prescribing an antidepressant for a woman wishing to breastfeed use an SSRI or moclobemide.
1.9.7 Care of the infant

Symptoms including irritability, constant crying, shivering, tremor, restlessness, increased tone, feeding and sleeping difficulties and rarely seizures have been reported in children born to mothers taking SSRIs at delivery. Many of these symptoms are mild and self-limiting. In many cases these symptoms appear causally related to antidepressant exposure although there is debate as to what extent they represent serotonergic toxicity or a withdrawal reaction.

1.9.7.1 Any child born to a mother prescribed a psychotropic drug during pregnancy should be monitored by healthcare professionals for the development of adverse drug effects, drug toxicity or withdrawal (for example, floppy baby syndrome, irritability, constant crying, shivering, tremor, restlessness, increased tone, feeding and sleeping difficulties and rarely seizures) in the first 7 to 10 days after delivery.

1.9.7.2 When a neonate presents with irritability, constant crying, shivering, tremor, restlessness, increased tone, feeding, sleeping difficulties or seizures healthcare professionals should be aware that in a neonate whose mother was prescribed antidepressants the symptoms may be the result of a serotonergic toxicity syndrome rather than withdrawal and the normal course of action should be to monitor the neonate carefully.

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from www.nice.org.uk/page.aspx?o=20

This guideline is relevant to adults, young people and children who meet the standard diagnostic criteria of bipolar disorder, their families or carers, and all healthcare professionals involved in the help, treatment and carer of people with bipolar disorder and their families or carers. These include the following.
• Professional groups (including general practitioners, psychiatrists, clinical psychologists, psychotherapists, mental health, community psychiatric and practice nurses, secondary care professionals, occupational therapists and physicians) who share in the treatment and care of people with a diagnosis of bipolar disorder.

• Professionals in other health and non-health sectors who may have direct contact with, or are involved in the provision of health and other public services for, people diagnosed with bipolar disorder. These may include staff from schools and other educational settings, paediatric and community child health services, social services, the voluntary sector and prison doctors, the police, and professionals who work in the criminal justice sectors.

• Those with responsibility for planning services for people with a diagnosis of bipolar disorder and their families or carers, including directors of public health, NHS trust managers and managers in primary care trusts.

This guideline does not specifically address treatments that are not normally available on the NHS.

3 Implementation in the NHS

3.1 Resource implications

Local health communities should review their existing practice in the management of bipolar disorder against this guideline. The review should consider the resources required to implement the recommendations set out in section 1, the people and processes involved, and the timeline over which full implementation is envisaged. It is in the interests of people with bipolar disorder that the implementation timeline is as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly.
Information on the cost impact of this guideline in England is available on the NICE website and includes a template that local communities can use (www.nice.org.uk/CG0XXcosttemplate). Detailed implementation advice and a slide set are also available on the NICE website. [Note: the costing information will be available when the guideline is published.]

3.2 General

The Healthcare Commission considers implementation of clinical guidelines to be a developmental standard. The implementation of this guideline will build on the National Service Frameworks for Mental Health in England and Wales and should form part of the service development plans for each local health community in England and Wales.

The National Service Framework for Mental Health is available for England from the Department of Health website (www.dh.gov.uk) and for Wales from the NHS Wales website (www.wales.nhs.uk).

This guideline should be used in conjunction with the NICE technology appraisal on electroconvulsive therapy, the NICE clinical guideline on violent behaviour, and the NICE clinical guideline on antenatal and postnatal mental health when it is available (publication expected in early 2007), see section 6.

3.3 Audit

Suggested audit criteria based on the key priorities for implementation are listed in Appendix D, and can be used to audit practice locally.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, on the basis of its review of the evidence. The Group regards these recommendations as the most important research areas to improve NICE guidance and patient care in the future. The Guideline Development Group’s full set of research recommendations is detailed in the full guideline (see Section 5).
5 Other versions of this guideline

The National Institute for Health and Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Mental Health. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in Appendix B. Information about the independent Guideline Review Panel is given in Appendix C.

The booklet ‘The guideline development process: an overview for stakeholders, the public and the NHS’ has more information about the Institute’s guideline development process. It is available from www.nice.org.uk/guidelinesprocess and copies can also be ordered by telephoning 0870 1555 455 (quote reference N0472).

5.1 Full guideline

The full guideline, ‘Bipolar disorder: the management of bipolar disorder in adults, children and young people, in primary and secondary care’, is published by the National Collaborating Centre for Mental Health. It is available from [website details to be added], the NICE website (www.nice.org.uk/CGXXX/fullguideline) and the website of the National Library for Health (www.nlh.nhs.uk). [Note: these details will apply to the published full guideline.]

5.2 Quick reference guide

A quick reference guide for health professionals is also available from the NICE website (www.nice.org.uk/CGXXX/quickrefguide) or from the NHS Response Line (telephone 0870 1555 455; quote reference number N0XXX). [Note: these details will apply when the guideline is published.]
5.3 Information for the public

A version of this guideline for people with bipolar disorder and their carers, and for the public, is available from the NICE website (www.nice.org.uk/CGXXXpublicinfo) or from the NHS Response Line (0870 1555 455); quote reference number N0xxx). [Note: these details will apply when the guideline is published.]

6 Related NICE guidance


NICE is in the process of developing the following guidance (details available from www.nice.org.uk):

- Antenatal and postnatal mental health: clinical management and service guidance. NICE clinical guideline. (Publication expected February 2007.)

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin before this if significant evidence that affects the guideline recommendations is identified. The updated guideline will be available within 2 years of the start of the review process.
Appendix A: The Guideline Development Group

**Professor Nicol Ferrier** (Chair, Guideline Development Group)
Professor of Psychiatry and Head of School of Neurology, Neurobiology and Psychiatry, University of Newcastle upon Tyne

**Mr Stephen Pilling** (Facilitator, Guideline Development Group)
Co-Director, National Collaborating Centre for Mental Health; Director, Centre for Outcomes Research and Effectiveness; Consultant Clinical Psychologist, Camden and Islington Mental Health and Social Care Trust

**Mr Stephen Bazire**
Director Pharmacy Services, Norfolk and Wavenely Mental Health Partnership NHS Trust

**Dr Roger Beer**
Psychiatrist, Gwent Healthcare NHS Trust

**Dr Tamsin Black**
Clinical Psychologist, The Coborn Adolescent Service, East London and the City Mental Health Trust

**Ms Ellen Boddington**
Research Assistant, National Collaborating Centre for Mental Health

**Ms Rachel Burbeck**
Systematic Reviewer, National Collaborating Centre for Mental Health

**Ms Julie Charles**
Service user representative

**Ms Josephine Foggo**
Project Manager, National Collaborating Centre for Mental Health, (October 2004–August 2005)
DRAFT FOR FIRST CONSULTATION

Mr Robert Westhead
Service user representative

Ms Marilyn Wilson
Occupational Therapist, Community Mental Health Team, Essex

Mr Stephen Yorke
Carer representative
Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows

[To be added at 2nd consultation]
Appendix C: Technical detail on the criteria for audit

[To be added at 2nd consultation]

Possible objectives for an audit

People that could be included in an audit and time period for selection

Measures that could be used as a basis for an audit
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Exception</th>
<th>Definition of terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. [Label criteria numerically (1, 2, 3 etc, one number per row; use a, b, c for subdivisions within rows)]</td>
<td>[Insert exception(s)]</td>
<td>[Insert definitions]</td>
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<tr>
<td>2. [Label criteria numerically (1, 2, 3 etc, one number per row; use a, b, c for subdivisions within rows)]</td>
<td>[Insert exception(s)]</td>
<td>[Insert definitions]</td>
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