

Bipolar disorder: assessment and management

Clinical guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

Contents

Overview	4
Who is it for?	4
Recommendations.....	5
1.1 Care for adults, children and young people across all phases of bipolar disorder	5
1.2 Recognising and managing bipolar disorder in adults in primary care	8
1.3 Assessing suspected bipolar disorder in adults in secondary care	11
1.4 Managing crisis, risk and behaviour that challenges in adults with bipolar disorder in secondary care.....	12
1.5 Managing mania or hypomania in adults in secondary care	14
1.6 Managing bipolar depression in adults in secondary care	17
1.7 Managing bipolar disorder in adults in the longer term in secondary care	21
1.8 Monitoring physical health in secondary care	25
1.9 Promoting recovery and return to primary care	26
1.10 How to use medication.....	27
1.11 Recognising, diagnosing and managing bipolar disorder in children and young people	36
Terms used in this guideline.....	40
Recommendations for research	42
1 Maintenance treatment.....	42
Context.....	43
Safeguarding children.....	43
Finding more information and committee details.....	45
Update information	46

This guideline replaces CG38.

This guideline is the basis of QS102, QS95 and QS167.

Overview

This guideline covers recognising, assessing and treating bipolar disorder (formerly known as manic depression) in children, young people and adults. The recommendations apply to bipolar I, bipolar II, mixed affective and rapid cycling disorders. It aims to improve access to treatment and quality of life in people with bipolar disorder.

Valproate: In September 2024, the [Medicines and Healthcare products Regulatory Agency \(MHRA\)](#) published a [Drug Safety Update on valproate use in men and their partners](#). Effective contraception (condoms, plus contraception used by the female sexual partner) is recommended throughout the valproate treatment period and for 3 months after stopping valproate. See the [MHRA's advice for healthcare professionals](#). NICE is assessing the impact of this alert on recommendations in this guideline.

Recommendations on valproate in this guideline are in line with the [MHRA guidance on valproate use by women and girls](#) and [Drug Safety Update on the risks associated with valproate in men and women under 55](#). For more details see [update information](#).

Who is it for?

- Healthcare professionals
- People working in occupational health, social services and the independent sector
- Children, young people and adults with bipolar disorder
- Families of and people who care for children, young people and adults with bipolar disorder

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [making decisions about your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

Health and care professionals should follow our general guidelines for people delivering care:

- [babies, children and young people's experience of healthcare](#)
- [decision making and mental capacity](#)
- [medicines adherence](#)
- [medicines optimisation](#)
- [multimorbidity](#)
- [service user experience in adult mental health](#)
- [shared decision making](#)
- [supporting adult carers](#)
- [transition from children's to adults' services](#).

The recommendations cover children, young people and adults with suspected or diagnosed bipolar disorder and apply to bipolar I, bipolar II, mixed affective and rapid cycling disorders.

1.1 Care for adults, children and young people

across all phases of bipolar disorder

Treatment and support for specific populations

See [NICE's guideline on antenatal and postnatal mental health](#) for guidance on the management of bipolar disorder during pregnancy and the postnatal period and in women and girls of childbearing potential.

- 1.1.1 Ensure that [older people](#) with bipolar disorder are offered the same range of treatments and services as younger people with bipolar disorder. **[2014]**
- 1.1.2 Offer people with bipolar disorder and coexisting disorders, such as personality disorder, attention deficit hyperactivity disorder, anxiety disorders or substance misuse, treatment in line with the relevant NICE guideline, in addition to their treatment for bipolar disorder. See [NICE's guidelines on antisocial personality disorder](#), [borderline personality disorder](#), [attention deficit hyperactivity disorder](#), [generalised anxiety disorder](#) and [psychosis with coexisting substance misuse](#), be alert to the potential for drug interactions and use clinical judgement. **[2014]**
- 1.1.3 Offer people with rapid cycling bipolar disorder the same interventions as people with other types of bipolar disorder because there is currently no strong evidence to suggest that people with rapid cycling bipolar disorder should be treated differently. **[2014]**

Information and support

- 1.1.4 Consider identifying and offering assistance with education, financial and employment problems that may result from the behaviour associated with bipolar disorder, such as mania and hypomania. If the person with bipolar disorder agrees, this could include talking directly with education staff, creditors and employers about bipolar disorder and its possible effects, and how the person can be supported. **[2014]**
- 1.1.5 Explain and discuss making a lasting power of attorney with adults with bipolar disorder and their [carers](#) if there are financial problems resulting from mania or

hypomania. **[2014]**

Support for carers of people with bipolar disorder

- 1.1.6 Give carers written and verbal information in an accessible format about:
- diagnosis and management of bipolar disorder
 - positive outcomes and recovery
 - types of support for carers
 - role of teams and services
 - getting help in a crisis. **[2014]**
- 1.1.7 As early as possible negotiate with the person with bipolar disorder and their carers about how information about the person will be shared. When discussing rights to confidentiality, emphasise the importance of sharing information about risks and the need for carers to understand the person's perspective. Foster a collaborative approach that supports both people with bipolar disorder and their carers, and respects their individual needs and interdependence. **[2014]**
- 1.1.8 Offer a carer-focused education and support programme, which may be part of a family intervention for bipolar disorder, as early as possible to all carers. The intervention should:
- be available as needed
 - have a positive message about recovery. **[2014]**
- 1.1.9 Identify children, young people and adults at risk of abuse or neglect who are dependent on, living with or caring for a person with bipolar disorder and:
- review the need for an assessment according to local safeguarding procedures for children or adults as appropriate
 - offer psychological and social support as needed. **[2014]**

1.2 Recognising and managing bipolar disorder in adults in primary care

Recognising bipolar disorder in primary care and referral

- 1.2.1 When adults present in primary care with depression, ask about previous periods of overactivity or disinhibited behaviour. If the overactivity or disinhibited behaviour lasted for 4 days or more, consider referral for a specialist mental health assessment. **[2014]**
- 1.2.2 Refer people urgently for a specialist mental health assessment if mania or severe depression is suspected or they are a danger to themselves or others. **[2014]**
- 1.2.3 Do not use questionnaires in primary care to identify bipolar disorder in adults. **[2014]**

Managing bipolar disorder in primary care

- 1.2.4 When working with people with bipolar disorder in primary care:
- support them to carry out care plans developed in secondary care and achieve their recovery goals
 - follow crisis plans developed in secondary care and liaise with secondary care specialists if necessary
 - review their treatment and care, including medication, at least annually and more often if the person, carer or healthcare professional has any concerns. **[2014]**
- 1.2.5 Offer people with bipolar depression:
- a psychological intervention that has been developed specifically for bipolar disorder and has a published evidence-based manual describing how it should be delivered **or**
 - a choice of psychological intervention (cognitive behavioural therapy,

interpersonal therapy or behavioural couples therapy) in line with the [advice on treatment options for more severe depression in the NICE guideline on depression](#).

Discuss with the person the possible benefits and risks of psychological interventions and their preference. Monitor mood and if there are signs of hypomania or deterioration of the depressive symptoms, liaise with or refer the person to secondary care. If the person develops mania or severe depression, refer them urgently to secondary care. **[2014]**

- 1.2.6 Psychological therapists working with people with bipolar depression in primary care should have training in and experience of working with people with bipolar disorder. **[2014]**
- 1.2.7 Do not start lithium to treat bipolar disorder in primary care for people who have not taken lithium before, except under shared-care arrangements. **[2014]**
- 1.2.8 Do not start [valproate](#) in primary care to treat bipolar disorder. **[2014]**
- 1.2.9 If bipolar disorder is managed solely in primary care, re-refer to secondary care if any one of the following applies:
- there is a poor or partial response to treatment
 - the person's functioning declines significantly
 - treatment adherence is poor
 - the person develops intolerable or medically important side effects from medication
 - comorbid alcohol or drug misuse is suspected
 - the person is considering stopping any medication after a period of relatively stable mood
 - a woman with bipolar disorder is pregnant or planning a pregnancy. **[2014]**

Physical health

- 1.2.10 Develop and use practice case registers to monitor the physical and mental health of people with bipolar disorder in primary care. **[2014]**
- 1.2.11 Monitor the physical health of people with bipolar disorder when responsibility for monitoring is transferred from secondary care, and then at least annually. The health check should be comprehensive, including all the checks recommended in recommendation 1.2.12 and focusing on physical health problems such as cardiovascular disease, diabetes, obesity and respiratory disease. A copy of the results should be sent to the care coordinator and psychiatrist, and put in the secondary care records. **[2014]**
- 1.2.12 Ensure that the physical health check for people with bipolar disorder, performed at least annually, includes:
- weight or BMI, diet, nutritional status and level of physical activity
 - cardiovascular status, including pulse and blood pressure
 - metabolic status, including fasting blood glucose or glycosylated haemoglobin (HbA1c), and blood lipid profile
 - liver function
 - renal and thyroid function, and calcium levels, for people taking long-term lithium. **[2014, amended 2021]**
- 1.2.13 Identify people with bipolar disorder who have hypertension, have abnormal lipid levels, are obese or at risk of obesity, have diabetes or are at risk of diabetes (as indicated by abnormal blood glucose levels), or are physically inactive, at the earliest opportunity. Follow [NICE's guidelines on hypertension](#), [lipid modification](#), [prevention of cardiovascular disease](#), [overweight and obesity management](#), [physical activity](#) and [preventing type 2 diabetes](#). **[2014]**
- 1.2.14 Offer treatment to people with bipolar disorder who have diabetes and/or cardiovascular disease in primary care in line with [NICE's guidelines on type 1 diabetes in adults: diagnosis and management](#), [type 2 diabetes in adults: management](#) and [lipid modification](#). **[2014]**

1.3 Assessing suspected bipolar disorder in adults in secondary care

1.3.1 Assessment of suspected bipolar disorder, and subsequent management, should be conducted in a service that can:

- offer the full range of pharmacological, psychological, social, occupational and educational interventions for people with bipolar disorder consistent with this guideline
- be competent to provide all interventions offered
- place emphasis on engagement as well as risk management.

This might be an early intervention in psychosis service, a specialist bipolar disorder team, or a specialist integrated community-based team. **[2014]**

1.3.2 When assessing suspected bipolar disorder:

- undertake a full psychiatric assessment, documenting a detailed history of mood, episodes of overactivity and disinhibition or other episodic and sustained changes in behaviour, symptoms between episodes, triggers to previous episodes and patterns of relapse, and family history
- assess the development and changing nature of the mood disorder and associated clinical problems throughout the person's life (for example, early childhood trauma, developmental disorder or cognitive dysfunction in later life)
- assess social and personal functioning and current psychosocial stressors
- assess for potential mental and physical comorbidities
- assess the person's physical health and review medication and side effects, including weight gain
- discuss treatment history and identify interventions that have been effective or ineffective in the past
- encourage people to invite a family member or carer to give a corroborative

history

- discuss possible factors associated with changes in mood, including relationships, psychosocial factors and lifestyle changes
- identify personal recovery goals. **[2014]**

- 1.3.3 Take into account the possibility of differential diagnoses including schizophrenia spectrum disorders, personality disorders, drug misuse, alcohol-use disorders, attention deficit hyperactivity disorder and underlying physical disorders such as hypo- or hyperthyroidism. **[2014]**
- 1.3.4 If bipolar disorder is diagnosed, develop a care plan in collaboration with the person with bipolar disorder based on the assessment carried out in recommendation 1.3.2 as soon as possible after assessment and, depending on their needs, using the care programme approach. Give the person and their GP a copy of the plan, and encourage the person to share it with their carers. **[2014]**
- 1.3.5 Carry out a risk assessment in conjunction with the person with bipolar disorder, and their carer if possible, focusing on areas that are likely to present possible danger or harm, such as self-neglect, self-harm, suicidal thoughts and intent, risks to others, including family members, driving, spending money excessively, financial or sexual exploitation, disruption in family and love relationships, disinhibited and sexualised behaviour, and risks of sexually transmitted diseases. For the management of risk, follow the recommendations in the section on managing crisis, risk and behaviour that challenges. **[2014]**

1.4 Managing crisis, risk and behaviour that challenges in adults with bipolar disorder in secondary care

- 1.4.1 Develop a risk management plan jointly with the person, and their carer if possible, covering:
- identifiable personal, social, occupational, or environmental triggers and early

warning signs and symptoms of relapse

- a protocol for applying the person's own coping strategies and increasing doses of medication or taking additional medication (which may be given to the person in advance) for people at risk of onset of mania or for whom early warning signs and symptoms can be identified
- agreements between primary and secondary care about how to respond to an increase in risk or concern about possible risk
- information about who to contact if the person with bipolar disorder and, if appropriate, their carer, is concerned or in a crisis, including the names of healthcare professionals in primary and secondary care who can be contacted.

Give the person and their GP a copy of the plan, and encourage the person to share it with their carers. **[2014]**

- 1.4.2 Offer crisis services to support people with bipolar disorder who are in crisis, in line with recommendations 1.4.1.1 to 1.4.1.4 in NICE's guideline on psychosis and schizophrenia in adults. **[2014]**

If people with bipolar disorder pose an immediate risk to themselves or others during an acute episode, see:

- NICE's guideline on violence and aggression: short-term management in mental health, health and community settings for advice on managing agitation, challenging behaviour and imminent violence, and on rapid tranquillisation **or**
- NICE's guideline on self-harm for advice on managing acts of self-harm and suicide risk.

1.5 Managing mania or hypomania in adults in secondary care

Support and advice

- 1.5.1 Ensure that people with mania or hypomania have access to calming environments and reduced stimulation. Advise them not to make important decisions until they have recovered from mania or hypomania and encourage them to maintain their relationships with their [carers](#) if possible. **[2014]**

Pharmacological interventions

Valproate: NICE is assessing the impact of the following Medicines and Healthcare products Regulatory Agency (MHRA) drug safety update on recommendations in this guideline:

- [valproate use in men and their partners](#) (September 2024).

- 1.5.2 If a person develops mania or hypomania and is taking an antidepressant (as defined by the [British National Formulary \[BNF\]](#)) as monotherapy:
- consider stopping the antidepressant and
 - offer an antipsychotic as set out in recommendation 1.5.3, regardless of whether the antidepressant is stopped. **[2014]**
- 1.5.3 If a person develops mania or hypomania and is not taking an antipsychotic or mood stabiliser, offer haloperidol, olanzapine, quetiapine or risperidone, taking into account any advance statements, the person's preference and clinical context (including physical comorbidity, previous response to treatment and side effects). Follow the [recommendations on using antipsychotics](#). **[2014]**
- 1.5.4 If the first antipsychotic is poorly tolerated at any dose (including rapid weight gain) or ineffective at the maximum licensed dose, offer an alternative

antipsychotic from the drugs listed in recommendation 1.5.3, taking into account any advance statements, the person's preference and clinical context (including physical comorbidity, previous response to treatment and side effects). **[2014]**

- 1.5.5 If an alternative antipsychotic is not sufficiently effective at the maximum licensed dose, consider adding lithium.

Although its use is common in UK clinical practice, in September 2014 this was an off-label use of lithium. See [NICE's information on prescribing medicines](#). **[2014, amended 2023]**

- 1.5.6 If adding lithium is ineffective, or if lithium is not suitable (for example, because the person does not agree to routine blood monitoring), consider adding [valproate](#) instead. **[2014]**

- 1.5.7 Do not start valproate for the first time in people (male or female) younger than 55 years, unless 2 specialists independently agree and document that there is no other effective and tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. Ensure the pregnancy prevention programme is in place if valproate is used in women and girls of childbearing potential. Follow the [MHRA safety advice on the use of valproate](#).

In September 2014 semi-sodium valproate had a UK marketing authorisation for the treatment of mania if lithium is not tolerated or is contraindicated; this was an off-label use of sodium valproate, although its use was common in UK clinical practice. See [NICE's information on prescribing medicines](#). **[2014, amended 2023]**

- 1.5.8 If a person develops mania or hypomania and is taking an antidepressant (as defined by the [BNF](#)) in combination with a mood stabiliser, consider stopping the antidepressant. **[2014]**

- 1.5.9 If the person is already taking lithium, check plasma lithium levels to optimise treatment (see the [section on how to use medication](#)). Consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment. **[2014]**

1.5.10 If the person is already taking a mood stabiliser as prophylactic treatment, consider increasing the dose, up to the maximum level in the [BNF](#) if necessary, depending on clinical response. If there is no improvement, consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment. Follow the [recommendations on using antipsychotics in the section on how to use medication](#). **[2014]**

1.5.11 If the person is already taking valproate and develops mania or hypomania, review their treatment including adherence and:

- consider increasing the dose if tolerated, but be aware of the increased risk of side effects at higher doses, **or**
- consider changing to an alternative treatment.

Follow the [recommendations on using valproate in the section on how to use medication](#). **[2014, amended 2023]**

1.5.12 If a woman or girl of childbearing potential is already taking valproate, advise her to gradually stop the drug under medical supervision because of the risk of fetal malformations and adverse neurodevelopmental outcomes after any exposure in pregnancy. Follow the [MHRA safety advice on the use of valproate](#). **[2014, amended 2023]**

1.5.13 If the clinical presentation is of a mixed affective state, characterised by both manic and depressive symptoms, follow recommendations 1.5.1 to 1.5.12 for the treatment of mania, and monitor closely for the emergence of depression. **[2014]**

1.5.14 Do not offer lamotrigine to treat mania. **[2014]**

For a short explanation of why the recommendations were amended in 2023 and full details of the evidence see the [evidence review for changes to valproate recommendations after revised MHRA safety advice](#).

Electroconvulsive therapy

For the treatment of severe mania that has not responded to other interventions, see

Reviewing treatment for mania

- 1.5.15 Within 4 weeks of resolution of symptoms, discuss with the person, and their carers if appropriate, whether to continue treatment for mania or start long-term treatment (see the [section on managing bipolar disorder in adults in the longer term in secondary care](#)). Explain the potential benefits of long-term treatment and the risks, including side effects of medication used for long-term treatment. **[2014]**
- 1.5.16 If the person decides to continue treatment for mania, offer it for a further 3 to 6 months, and then review. **[2014]**

1.6 Managing bipolar depression in adults in secondary care

Psychological interventions

- 1.6.1 Offer adults with bipolar depression:
- a psychological intervention that has been developed specifically for bipolar disorder and has a published [evidence-based manual](#) describing how it should be delivered **or**
 - a choice of psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with the [advice on treatment options for more severe depression in the NICE guideline on depression](#).
- Discuss with the person the possible benefits and risks of psychological interventions and their preference. Monitor mood for signs of mania or hypomania or deterioration of the depressive symptoms. **[2014]**
- 1.6.2 Psychological therapists working with people with bipolar depression should have

training in, and experience of, working with people with bipolar disorder. [2014]

Pharmacological interventions

Valproate: NICE is assessing the impact of the following MHRA drug safety update on recommendations in this guideline:

- [valproate use in men and their partners](#) (September 2024).

1.6.3 If a person develops moderate or severe bipolar [depression](#) and is not taking a drug to treat their bipolar disorder, offer fluoxetine combined with olanzapine, or quetiapine on its own, depending on the person's preference and previous response to treatment.

- If the person prefers, consider either olanzapine (without fluoxetine) or lamotrigine on its own.
- If there is no response to fluoxetine combined with olanzapine, or quetiapine, consider lamotrigine on its own.

Follow the [recommendations on using antipsychotics and lamotrigine in the section on how to use medication](#).

In September 2014, this was an off-label use of olanzapine. Although their use was common in UK clinical practice, in September 2014 this was an off-label use of fluoxetine and of lamotrigine. See [NICE's information on prescribing medicines](#). [2014]

1.6.4 If a person develops moderate or severe bipolar depression and is already taking lithium, check their plasma lithium level. If it is inadequate, increase the dose of lithium; if it is at maximum level, add either fluoxetine combined with olanzapine or add quetiapine.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine to lithium.

- If there is no response to adding fluoxetine combined with olanzapine, or adding quetiapine, stop the additional treatment and consider adding lamotrigine to lithium.

Follow the [recommendations in the section on how to use medication on using lithium, antipsychotics and lamotrigine](#).

In September 2014, these were off-label uses of olanzapine, risperidone, haloperidol, quetiapine, lamotrigine and lithium for children and young people. See [NICE's information on prescribing medicines](#). **[2014]**

- 1.6.5 If a person develops moderate or severe bipolar depression and is already taking [valproate](#), review their treatment including adherence and consider increasing the dose if tolerated but be aware of the increased risk of side effects at higher doses. Follow the [recommendations in the section on how to use medication on using valproate](#). **[2014, amended 2023]**

- 1.6.6 If the maximum tolerated dose, or the top of the therapeutic range for valproate, has been reached and there is a limited response, add either of the following options, depending on the person's preference and previous response to treatment:

- fluoxetine combined with olanzapine **or**
- quetiapine.

Follow the [recommendations in the section on how to use medication on using valproate and antipsychotics](#).

In September 2014, these were off-label uses of olanzapine, quetiapine and valproate for children and young people. See [NICE's information on prescribing medicines](#). **[2014, amended 2023]**

- 1.6.7 If the person does not wish to try adding fluoxetine combined with olanzapine or adding quetiapine, consider:

- adding olanzapine (without fluoxetine) **or**

- adding lamotrigine **or**
- changing from valproate to an alternative treatment.

Follow the [recommendations in the section on how to use medication on using valproate, antipsychotics and lamotrigine](#).

In September 2014, these were off-label uses of olanzapine, quetiapine, lamotrigine and valproate for children and young people. See [NICE's information on prescribing medicines](#). **[2014, amended 2023]**

1.6.8 If there is no response to adding fluoxetine combined with olanzapine or adding quetiapine, consider stopping the additional medications and:

- adding lamotrigine to valproate **or**
- changing from valproate to an alternative treatment.

Follow the [recommendations in the section on how to use medication on using valproate, antipsychotics and lamotrigine](#).

In September 2014, these were off-label uses of olanzapine, quetiapine, lamotrigine and valproate for children and young people. See [NICE's information on prescribing medicines](#). **[2014, amended 2023]**

1.6.9 If a woman or girl of childbearing potential is already taking valproate, advise her to gradually stop the drug under medical supervision because of the risk of fetal malformations and adverse neurodevelopmental outcomes after any exposure in pregnancy. Follow the [MHRA safety advice on the use of valproate](#). **[2014]**

1.6.10 Follow the [recommendations on using antipsychotics in the section on how to use medication](#) and be aware of the potential interactions between valproate and fluoxetine, lamotrigine and olanzapine. Follow the [MHRA safety advice on the use of valproate](#). **[2014, amended 2020]**

1.6.11 Take into account toxicity in overdose when prescribing psychotropic medication during periods of high suicide risk. Assess the need to limit the quantity of medication supplied to reduce the risk to life if the person overdoses. **[2014]**

For a short explanation of why the recommendations were amended in 2023 and full details of the evidence see the [evidence review for changes to valproate recommendations after revised MHRA safety advice](#).

Reviewing treatment for bipolar depression

- 1.6.12 Within 4 weeks of resolution of symptoms, discuss with the person, and their [carers](#) if appropriate, whether to continue psychological or pharmacological treatment for bipolar depression or start long-term treatment (see the [section on managing bipolar disorder in adults in the longer term in secondary care](#)). Explain the potential benefits of long-term treatment and the risks, including side effects of medication used for long-term treatment. **[2014]**
- 1.6.13 If the person decides to continue psychological or pharmacological treatment for bipolar depression, offer it for a further 3 to 6 months, and then review. **[2014]**

1.7 Managing bipolar disorder in adults in the longer term in secondary care

Discussing long-term treatment

- 1.7.1 After each episode of mania or bipolar [depression](#), discuss with the person, and their [carers](#) if appropriate, managing their bipolar disorder in the longer term. Discussion should aim to help people understand that bipolar disorder is commonly a long-term relapsing and remitting condition that needs self-management and engagement with primary and secondary care professionals and involvement of carers. The discussion should cover:
- the nature and variable course of bipolar disorder
 - the role of psychological and pharmacological interventions to prevent relapse and reduce symptoms
 - the risk of relapse after reducing or stopping medication for an acute episode

- the potential benefits and risks of long-term medication and psychological interventions, and the need to monitor mood and medication
- the potential benefits and risks of stopping medication, including for women who may wish to become pregnant
- the person's history of bipolar disorder, including:
 - the severity and frequency of episodes of mania or bipolar depression, with a focus on associated risks and adverse consequences
 - previous response to treatment
 - symptoms between episodes
 - potential triggers for relapse, early warning signs, and self-management strategies
- possible duration of treatment, and when and how often this should be reviewed.

Provide clear written information about bipolar disorder, including [NICE's information for the public](#), and ensure there is enough time to discuss options and concerns. **[2014]**

Psychological interventions

- 1.7.2 Offer a family intervention to people with bipolar disorder who are living, or in close contact, with their family in line with [recommendation 1.3.7.2 in NICE's guideline on psychosis and schizophrenia in adults](#). **[2014]**
- 1.7.3 Offer a structured psychological intervention (individual, group or family), which has been designed for bipolar disorder and has a published [evidence-based manual](#) describing how it should be delivered, to prevent relapse or for people who have some persisting symptoms between episodes of mania or bipolar depression. **[2014]**
- 1.7.4 Individual and group psychological interventions for bipolar disorder to prevent

relapse should:

- provide information about bipolar disorder
- consider the impact of thoughts and behaviour on moods and relapse
- include self-monitoring of mood, thoughts and behaviour
- address relapse risk, distress and how to improve functioning
- develop plans for relapse management and staying well
- consider problem-solving to address communication patterns and managing functional difficulties.

In addition:

- individual programmes should be tailored to the person's needs based on an individualised assessment and psychological formulation
- group programmes should include discussion of the information provided with a focus on its relevance for the participants. **[2014]**

Pharmacological interventions

Valproate: NICE is assessing the impact of the following MHRA drug safety update on recommendations in this guideline:

- valproate use in men and their partners (September 2024).

- 1.7.5 When planning long-term pharmacological treatment to prevent relapse, take into account drugs that have been effective during episodes of mania or bipolar depression. Discuss with the person whether they prefer to continue this treatment or switch to lithium, and explain that lithium is the most effective long-term treatment for bipolar disorder. **[2014]**
- 1.7.6 When considering long-term treatment, discuss with the person the possible

benefits and risks of each drug for them, following the [recommendations in the section on how to use medication](#). **[2014, amended 2023]**

- 1.7.7 Offer lithium as a first-line, long-term pharmacological treatment for bipolar disorder. **[2014]**
- 1.7.8 If lithium is ineffective, poorly tolerated, or is not suitable (for example, because the person does not agree to routine blood monitoring), consider an antipsychotic (for example, asenapine, aripiprazole, olanzapine, quetiapine or risperidone). **[2014, amended 2023]**
- 1.7.9 If the first antipsychotic is poorly tolerated at any dose (including rapid weight gain) or ineffective at the maximum licensed dose, consider an alternative antipsychotic from the drugs listed in recommendation 1.7.8). **[2014, amended 2023]**
- 1.7.10 If an alternative antipsychotic is ineffective, consider a combination of [valproate](#) with either:
- an antipsychotic or
 - lithium. **[2014]**
- 1.7.11 Do not start valproate for the first time in people (male or female) younger than 55 years, unless 2 specialists independently agree and document that there is no other effective and tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. Ensure the pregnancy prevention programme is in place if valproate is used in women and girls of childbearing potential. Follow the [MHRA safety advice on the use of valproate](#).
- In September 2014 semi-sodium valproate had a UK marketing authorisation for this indication in people who have had mania that has responded to treatment with semi-sodium valproate; it was an off-label use of sodium valproate, although its use was common in UK clinical practice. See [NICE's information on prescribing medicines](#). **[2014, amended 2023]**
- 1.7.12 If a woman or girl of childbearing potential is already taking valproate, advise her to gradually stop the drug under medical supervision because of the risk of fetal

malformations and adverse neurodevelopmental outcomes after any exposure in pregnancy. Follow the [MHRA safety advice on the use of valproate](#).

In September 2014 semi-sodium valproate had a UK marketing authorisation for this indication in people who have had mania that has responded to treatment with semi-sodium valproate; it was an off-label use of sodium valproate, although its use was common in UK clinical practice. See [NICE's information on prescribing medicines](#). **[2014, amended 2020]**

1.7.13 If stopping long-term pharmacological treatment:

- discuss with the person how to recognise early signs of relapse and what to do if symptoms recur
- stop treatment gradually (see the [section on how to use medication](#)) and monitor the person for signs of relapse. **[2014]**

1.7.14 Continue monitoring symptoms, mood and mental state for 2 years after medication has stopped entirely. This may be undertaken in primary care (see [recommendation 1.9.3](#)). **[2014]**

For a short explanation of why the recommendations were amended in 2023 and full details of the evidence see the [evidence review for changes to valproate recommendations after revised MHRA safety advice](#).

1.8 Monitoring physical health in secondary care

1.8.1 Healthcare professionals in secondary care should ensure, as part of the care programme approach, that people with bipolar disorder receive physical healthcare from primary care as described in [recommendations 1.2.10 to 1.2.14](#) after responsibility for monitoring has been transferred from secondary care. **[2014]**

1.8.2 People with bipolar disorder, especially those taking antipsychotics and long-term medication, should be offered a combined healthy eating and physical activity programme by their mental healthcare provider. **[2014]**

- 1.8.3 If a person has rapid or excessive weight gain, abnormal lipid levels or problems with blood glucose management, take into account the effects of medication, mental state, other physical health and lifestyle factors in the development of these problems. **[2014]**

For physical health and lifestyle interventions, see [NICE's guidelines on overweight and obesity management](#), [lipid modification](#) or [preventing type 2 diabetes](#).

- 1.8.4 Routinely monitor weight and cardiovascular and metabolic indicators of morbidity in people with bipolar disorder. These should be audited in the annual team report. **[2014]**
- 1.8.5 Trusts should ensure that they take account of relevant guidelines on the monitoring and treatment of cardiovascular and metabolic disease in people with bipolar disorder through board-level performance indicators. **[2014]**

1.9 Promoting recovery and return to primary care

Continuing treatment in secondary care

- 1.9.1 Continue treatment and care in an early intervention in psychosis service, a specialist bipolar disorder service or a specialist integrated community-based team. Share physical health monitoring with primary care as outlined in the [sections on physical health](#) and [monitoring physical health in primary care](#). **[2014]**
- 1.9.2 Consider intensive case management for people with bipolar disorder who are likely to disengage from treatment or services. **[2014]**

Return to primary care

- 1.9.3 Offer people with bipolar disorder whose symptoms have responded effectively to treatment and remain stable the option to return to primary care for further management. If they wish to do this, record it in their notes and coordinate transfer of responsibilities through the care programme approach. **[2014]**

- 1.9.4 When making transfer arrangements for a return to primary care, agree a care plan with the person, which includes:
- clear, individualised social and emotional recovery goals
 - a crisis plan indicating early warning symptoms and triggers of both mania and depression relapse and preferred response during relapse, including liaison and referral pathways
 - an assessment of the person's mental state
 - a medication plan with a date for review by primary care, frequency and nature of monitoring for effectiveness and adverse effects, and what should happen in the event of a relapse.
- Give the person and their GP a copy of the plan, and encourage the person to share it with their carers. **[2014]**
- 1.9.5 Encourage and support the person to visit their GP and discuss the care plan before discharge and transfer. **[2014]**

Employment, education and occupational activities

- 1.9.6 Offer supported employment programmes to people with bipolar disorder in primary or secondary care who wish to find or return to work. Consider other occupational or educational activities, including pre-vocational training, for people who are unable to work or unsuccessful in finding employment. **[2014]**

1.10 How to use medication

- 1.10.1 When using any psychotropic medication for bipolar disorder ensure that:
- the person is given information that is suitable for their developmental level about the purpose and likely side effects of treatment including any monitoring that is required, and give them an opportunity to ask questions
 - the choice of medication is made in collaboration with the person with bipolar

disorder, taking into account the carer's views if the person agrees

- the overall medication regimen is regularly reviewed so that drugs that are not needed after the acute episode are stopped. **[2014]**

1.10.2 Discuss the use of alcohol, tobacco, prescription and non-prescription medication and illicit drugs with the person, and their carer if appropriate. Explain the possible interference of these substances with the therapeutic effects of prescribed medication and psychological interventions. **[2014]**

1.10.3 When offering psychotropic medication to older people, take into account its impact on cognitive functioning in older people and:

- use medication at lower doses
- take into account the increased risk of drug interactions
- take into account the negative impact that anticholinergic medication, or drugs with anticholinergic activity, can have on cognitive function and mobility
- ensure that medical comorbidities have been recognised and treated. **[2014]**

1.10.4 Do not offer gabapentin or topiramate to treat bipolar disorder. **[2014]**

Using antipsychotic medication

Starting antipsychotic medication

1.10.5 Before starting antipsychotic medication, measure and record the person's:

- weight or BMI
- pulse
- blood pressure
- fasting blood glucose or HbA1c

- blood lipid profile. **[2014]**

1.10.6 Before starting antipsychotic medication, offer the person an electrocardiogram (ECG) if:

- it is specified in the drug's summary of product characteristics (SPC) **or**
- a physical examination has identified a specific cardiovascular risk (such as hypertension) **or**
- there is a family history of cardiovascular disease, a history of sudden collapse, or other cardiovascular risk factors such as cardiac arrhythmia **or**
- the person is being admitted as an inpatient. **[2014]**

1.10.7 Treatment with antipsychotic medication should be considered an explicit individual therapeutic trial. Carry out the following:

- Discuss and record the side effects that the person is most willing to tolerate.
- Record the indications and expected benefits and risks of antipsychotic medication, and the expected time for a change in symptoms and appearance of side effects.
- At the start of treatment prescribe a dose that is appropriate for the phase and severity of the illness.
- Do not routinely prescribe a dose above the maximum recommended in the BNF or SPC.
- Justify and record reasons for doses outside the range given in the BNF or SPC, and inform the person that such treatment is unlicensed.
- Record the rationale for continuing, changing or stopping medication, and the effects of such changes. **[2014]**

Monitoring antipsychotic medication

1.10.8 Monitor and record the following during dose titration and then regularly and

systematically throughout treatment:

- pulse and blood pressure after each dose change
- weight or BMI weekly for the first 6 weeks, then at 12 weeks
- fasting blood glucose or HbA1c, and blood lipid profile at 12 weeks
- response to treatment, including changes in symptoms and behaviour
- side effects and their impact on physical health and functioning
- the emergence of movement disorders
- adherence. **[2014, amended 2021]**

- 1.10.9 The secondary care team should maintain responsibility for monitoring the efficacy and tolerability of antipsychotic medication for at least the first 12 months or until the person's condition has stabilised, whichever is longer. Thereafter, the responsibility for this monitoring may be transferred to primary care under shared-care arrangements. **[2014]**
- 1.10.10 If out-of-range test results are reported at any stage of treatment, the healthcare professional who ordered the tests should ensure that the person is offered further investigations and treatment as needed. **[2014]**
- 1.10.11 'As required' (p.r.n.) prescriptions of antipsychotic medication should be made as described in recommendation 1.10.7. Review clinical indications, frequency of administration, therapeutic benefits and side effects each week or more often if needed. Ensure that p.r.n. prescriptions have not unintentionally led to a total antipsychotic dosage above the maximum specified in the BNF or SPC. **[2014]**
- 1.10.12 Do not start regular combined antipsychotic medication, except for short periods (for example, when changing medication). **[2014]**

Stopping antipsychotic drugs

- 1.10.13 If stopping an antipsychotic drug, reduce the dose gradually over at least 4 weeks to minimise the risk of relapse. **[2014]**

Using lithium

Starting lithium

1.10.14 When starting lithium:

- advise the person that poor adherence or rapid discontinuation may increase the risk of relapse
- measure the person's weight or BMI and arrange tests for urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR), thyroid function and a full blood count
- arrange an ECG for people with cardiovascular disease or risk factors for it
- ensure the person is given appropriate national information (or a locally available equivalent) on taking lithium safely
- establish a shared-care arrangement with the person's GP for prescribing lithium and monitoring adverse effects. **[2014]**

1.10.15 Measure plasma lithium levels 1 week after starting lithium and 1 week after every dose change, and weekly until the levels are stable. Aim to maintain plasma lithium level between 0.6 and 0.8 mmol per litre in people being prescribed lithium for the first time. **[2014]**

1.10.16 Consider maintaining plasma lithium levels at 0.8 to 1.0 mmol per litre for a trial period of at least 6 months for people who:

- have had a relapse while taking lithium in the past **or**
- are taking lithium and have subthreshold symptoms with functional impairment. **[2014]**

1.10.17 Advise people taking lithium to:

- seek medical attention if they develop diarrhoea or vomiting or become acutely ill for any reason
- ensure they maintain their fluid intake, particularly after sweating (for

example, after exercise, in hot climates or if they have a fever), if they are immobile for long periods or if they develop a chest infection or pneumonia

- talk to their doctor as soon as possible if they become pregnant or are planning a pregnancy. **[2014]**

1.10.18 Warn people taking lithium not to take over-the-counter non-steroidal anti-inflammatory drugs and avoid prescribing these drugs for people with bipolar disorder if possible; if they are prescribed, this should be on a regular (not p.r.n.) basis and the person should be monitored monthly until a stable lithium level is reached and then every 3 months. **[2014]**

Monitoring lithium

1.10.19 Measure the person's plasma lithium level every 3 months for the first year. **[2014]**

1.10.20 After the first year, measure plasma lithium levels every 6 months, or every 3 months for people in any of the following groups:

- older people
- people taking drugs that interact with lithium
- people who are at risk of impaired renal or thyroid function, raised calcium levels or other complications
- people who have poor symptom control
- people with poor adherence
- people whose last plasma lithium level was 0.8 mmol per litre or higher. **[2014]**

1.10.21 Measure the person's weight or BMI and arrange tests for urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR) and thyroid function every 6 months, and more often if there is evidence of impaired renal or thyroid function, raised calcium levels or an increase in mood symptoms that might be

related to impaired thyroid function. **[2014]**

- 1.10.22 Monitor lithium dose and plasma lithium levels more frequently if urea levels and creatinine levels become elevated, or eGFR falls over 2 or more tests, and assess the rate of deterioration of renal function. For further information see [NICE's guidelines on chronic kidney disease](#) and [acute kidney injury](#). **[2014]**
- 1.10.23 When discussing whether to continue lithium, take into account clinical efficacy, other risk factors for renal impairment and cardiovascular disease, and degree of renal impairment; if needed seek advice from a renal specialist and a clinician with expertise in managing bipolar disorder. **[2014]**
- 1.10.24 Monitor the person at every appointment for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels of lithium. **[2014]**

Stopping lithium

- 1.10.25 If stopping lithium, reduce the dose gradually over at least 4 weeks, and preferably up to 3 months, even if the person has started taking another antimanic drug. **[2014]**
- 1.10.26 During dose reduction and for 3 months after lithium treatment is stopped, monitor the person closely for early signs of mania and depression. **[2014]**

Using valproate

Valproate: NICE is assessing the impact of the following MHRA drug safety update on recommendations in this guideline:

- [valproate use in men and their partners](#) (September 2024).

- 1.10.27 Do not start valproate for the first time in people (male or female) younger than

55 years, unless 2 specialists independently agree and document that there is no other effective and tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. Ensure the pregnancy prevention programme is in place if valproate is used in women and girls of childbearing potential. Follow the [MHRA safety advice on the use of valproate](#). **[2014, amended 2023]**

- 1.10.28 If a woman or girl of childbearing potential is already taking valproate, advise her to gradually stop the drug under medical supervision because of the risk of fetal malformations and adverse neurodevelopmental outcomes after any exposure in pregnancy. Follow the [MHRA safety advice on the use of valproate](#). **[2014, amended 2020]**

Starting valproate

- 1.10.29 When starting [valproate](#), measure the person's weight or BMI and carry out a full blood count and liver function tests. **[2014]**
- 1.10.30 Advise people taking valproate, and their carers, how to recognise the signs and symptoms of blood and liver disorders and to seek immediate medical help if any of these develop. Stop valproate immediately if abnormal liver function or blood dyscrasia is detected.

Although the absolute values of hepatic enzymes are a poor indicator of the extent of hepatic damage, it is generally accepted that if these are persistently elevated to over 3 times the upper normal limit, continuing to rise or accompanied by clinical symptoms, the suspected drug should be withdrawn. Raised hepatic enzymes of any magnitude accompanied by reduced albumin or impaired clotting suggest severe liver disease. **[2014]**

- 1.10.31 When prescribing valproate, be aware of its interactions with other anticonvulsants (particularly carbamazepine and lamotrigine) and with olanzapine and smoking. **[2014]**

Monitoring valproate

- 1.10.32 Do not routinely measure plasma valproate levels unless there is evidence of ineffectiveness, poor adherence or toxicity. **[2014]**
- 1.10.33 Measure the person's weight or BMI and carry out liver function tests and a full blood count again after 6 months of treatment with valproate and repeat annually. **[2014]**
- 1.10.34 Monitor sedation, tremor and gait disturbance carefully in older people. **[2014]**

Stopping valproate

- 1.10.35 If stopping valproate, to change to an alternative medication, reduce the dose gradually over at least 4 weeks to minimise the risk of relapse. **[2014]**

Using lamotrigine

Starting lamotrigine

- 1.10.36 When starting lamotrigine:
- carry out a full blood count, urea and electrolytes and liver function tests
 - be aware of its interaction with valproate
 - follow the instructions for initial dosage and dosage titration outlined in the SPC and BNF, taking into account the need for slow titration in people who have not taken lamotrigine before. **[2014]**
- 1.10.37 Advise people taking lamotrigine to:
- contact their doctor immediately if they develop a rash while the dose of lamotrigine is being increased
 - tell you if they are pregnant or planning a pregnancy. **[2014]**

Monitoring lamotrigine

- 1.10.38 Do not routinely measure plasma lamotrigine levels unless there is evidence of ineffectiveness, poor adherence or toxicity. **[2014]**

Stopping lamotrigine

- 1.10.39 If stopping lamotrigine, reduce the dose gradually over at least 4 weeks to minimise the risk of relapse. **[2014]**

1.11 Recognising, diagnosing and managing bipolar disorder in children and young people

Recognition and referral

- 1.11.1 Do not use questionnaires in primary care to identify bipolar disorder in children or young people. **[2014]**
- 1.11.2 If bipolar disorder is suspected in primary care in children or young people aged under 14 years, refer them to child and adolescent mental health services (CAMHS). **[2014]**
- 1.11.3 If bipolar disorder is suspected in primary care in young people aged 14 years or over, refer them to a specialist early intervention in psychosis service or a CAMHS team with expertise in the assessment and management of bipolar disorder in line with the recommendations in this guideline. The service should be multidisciplinary and have:
- engagement or assertive outreach approaches
 - family involvement and family intervention
 - access to structured psychological interventions and psychologically informed care

- vocational and educational interventions
- access to pharmacological interventions
- professionals who are trained and competent in working with young people with bipolar disorder. **[2014]**

Diagnosis and assessment

- 1.11.4 Diagnosis of bipolar disorder in children or young people should be made only after a period of intensive, prospective longitudinal monitoring by a healthcare professional or multidisciplinary team trained and experienced in the assessment, diagnosis and management of bipolar disorder in children and young people, and in collaboration with the child or young person's parents or carers. **[2014]**
- 1.11.5 When diagnosing bipolar disorder in children or young people take account of the following:
- mania must be present
 - euphoria must be present on most days and for most of the time, for at least 7 days
 - irritability is not a core diagnostic criterion. **[2014]**
- 1.11.6 Do not make a diagnosis of bipolar disorder in children or young people on the basis of depression with a family history of bipolar disorder but follow them up. **[2014]**
- 1.11.7 When assessing suspected bipolar disorder in children or young people, follow recommendations 1.3.2 to 1.3.4 for adults, but involve parents or carers routinely and take into account the child or young person's educational and social functioning. **[2014]**

Management in young people

- 1.11.8 When offering treatment to young people with bipolar disorder, take into account their cognitive ability, emotional maturity, developmental level, their capacity to consent to treatment, the severity of their bipolar disorder and risk of suicide or self-harm or any other risk outlined in [recommendation 1.3.5](#). **[2014]**

Mania

- 1.11.9 To treat mania or hypomania in young people see [NICE's technology appraisal guidance on aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder](#) and also consider the [recommendations for adults in the section on managing mania or hypomania in adults in secondary care](#). Refer to the [BNF for children](#) to modify drug treatments, be aware of the increased potential for a range of side effects, and do not routinely continue antipsychotic treatment for longer than 12 weeks.

In September 2014 aripiprazole had a UK marketing authorisation for up to 12 weeks of treatment for moderate to severe manic episodes in bipolar I disorder in young people aged 13 and older.

In September 2014, this was an off-label use of olanzapine, risperidone, haloperidol, quetiapine, lamotrigine, lithium and valproate for children and young people. See [NICE's information on prescribing medicines](#). **[2014]**

- 1.11.10 Do not offer [valproate](#) to children unless there is no other effective and tolerated treatment. Follow the [MHRA safety advice on the use of valproate](#). **[2014, amended 2023]**

Bipolar depression

- 1.11.11 Offer a structured psychological intervention (individual cognitive behavioural therapy or interpersonal therapy) to young people with bipolar depression. The intervention should be of at least 3 months' duration and have a published [evidence-based manual](#) describing how it should be delivered. **[2014]**

- 1.11.12 If after 4 to 6 weeks there is no or a limited response to cognitive behavioural therapy or interpersonal therapy, carry out a multidisciplinary review and consider an alternative individual or family psychological intervention. **[2014]**
- 1.11.13 If there is a risk of suicide or self-harm or any other risk outlined in [recommendation 1.3.5](#), carry out an urgent review and develop a risk management plan as outlined in [recommendation 1.4.1](#). **[2014]**
- 1.11.14 After the multidisciplinary review, if there are coexisting factors such as comorbid conditions, persisting psychosocial risk factors such as family discord, or parental mental ill-health, consider:
- an alternative psychological intervention for bipolar depression for the young person, their parents or other family member **or**
 - an additional psychological intervention for any coexisting mental health problems in line with relevant NICE guidance for the young person, their parents or other family member. **[2014]**
- 1.11.15 If the young person's bipolar depression is moderate to severe, consider a pharmacological intervention in addition to a psychological intervention. Follow the [recommendations for pharmacological interventions for adults in the section on managing bipolar depression in adults in secondary care](#), but do not routinely continue antipsychotic treatment for longer than 12 weeks. At 12 weeks, carry out a full multidisciplinary review of mental and physical health, and consider further management of depression or long-term management.

In September 2014, this was an off-label use of olanzapine, quetiapine and lamotrigine for children and young people. See [NICE's information on prescribing medicines](#). **[2014]**

Long-term management

- 1.11.16 After the multidisciplinary review, consider a structured individual or family psychological intervention for managing bipolar disorder in young people in the longer term. **[2014]**

Terms used in this guideline

Carer

A person who provides unpaid support to a partner, family member, friend or neighbour who is ill, struggling or disabled.

Children

People aged 12 years and under.

Depression

The severity of bipolar depression is defined as follows:

- **Mild depression** Few, if any, symptoms in excess of the 5 required to make the diagnosis, with symptoms resulting in minor functional impairment.
- **Moderate depression** Symptoms or functional impairment that are between mild and severe.
- **Severe depression** Most symptoms, with symptoms markedly interfering with functioning. Can occur with or without psychotic symptoms.

Evidence-based manual

A manual based on at least 1 randomised controlled trial published in a peer-reviewed journal showing effectiveness of the intervention in reducing depression symptoms in bipolar depression or, when used as long-term treatment, reducing relapse in people with bipolar disorder.

Older people

People aged 65 years and over.

Young people

People aged 13 to 17 years.

Valproate

Refers to 3 formulations of valproate available in the UK: sodium valproate, valproic acid and semi-sodium valproate. At the time of publication (September 2014), sodium valproate and valproic acid had UK marketing authorisation for the treatment of epilepsy.

Semi-sodium valproate had a UK marketing authorisation for the treatment of acute mania and for continuation treatment in people who have had mania that has responded to treatment with semi-sodium valproate. Both semi-sodium and sodium valproate are metabolised to valproic acid (also known as valproate), which is the pharmacologically active component. Follow the [MHRA safety advice on the use of valproate](#).

Recommendations for research

The Guideline Development Group has made the following recommendation for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The [Guideline Development Group's full set of recommendations for research are detailed in the full guideline](#).

1 Maintenance treatment

In the maintenance treatment of bipolar disorder, what is the relative effect on quality of life of lithium, an antipsychotic (haloperidol, olanzapine, quetiapine or risperidone), or a combination of lithium and an antipsychotic?

Why this is important

Lithium and antipsychotic medication are known to reduce the risk of relapse when used long-term in people with bipolar disorder. Relapses do still occur and the response is usually to add another mood-stabilising drug. However, lithium and antipsychotics are associated with a number of side effects, some of which can adversely affect physical health. The relative effects of lithium, an antipsychotic or a combination of these drugs, regarding efficacy, tolerability, cost effectiveness and quality of life, are unknown. Such information is important to people with bipolar disorder to help them make an informed choice about the treatment options available to them, and to the NHS to inform the best use of resources.

The suggested programme of research should involve a pragmatic 3-arm RCT comparing lithium monotherapy with antipsychotic monotherapy (haloperidol, olanzapine, quetiapine or risperidone) and a combination of lithium and an antipsychotic. The study should last at least 1 year with the primary outcome being quality of life. Symptom control, relapse, function and economic outcomes should also be measured.

Context

Bipolar disorder is a potentially lifelong and disabling condition characterised by episodes of mania (abnormally elevated mood or irritability and related symptoms with severe functional impairment or psychotic symptoms for 7 days or more) or hypomania (abnormally elevated mood or irritability and related symptoms with decreased or increased function for 4 days or more) and episodes of depressed mood. It is often comorbid with other disorders such as anxiety disorders, substance misuse, personality disorders and attention deficit hyperactivity disorder (ADHD).

The peak age of onset is 15 to 19 years, and there is often a substantial delay between onset and first contact with mental health services. The lifetime prevalence of bipolar I disorder (mania and depression) is estimated at 1% of the adult population, and bipolar II disorder (hypomania and depression) affects approximately 0.4% of adults. Bipolar disorder in children under 12 years is very rare.

Since the publication of the previous NICE guideline (CG38) in 2006, there have been some important advances in our knowledge of the care pathway and treatment approaches that are most likely to benefit people with bipolar disorder. All areas of CG38 have been updated.

This guideline covers the recognition, assessment and management of bipolar disorder in children, young people and adults. It includes specific recommendations for diagnosis in children and young people because presentation in these age groups can be complicated by other conditions such as ADHD. The recommendations apply to people with bipolar I, bipolar II, mixed affective and rapid cycling disorders. Non bipolar affective disorders are not covered because these are addressed by other guidelines, and this guideline does not make specific recommendations about other mental disorders that commonly coexist with bipolar disorder.

Safeguarding children

Remember that child maltreatment:

- is common

- can present anywhere, such as emergency departments, primary and secondary care and community settings (such as the child's home).

Be aware of or suspect abuse as a contributory factor to or cause of bipolar disorder in children. Abuse may also coexist with bipolar disorder. See [NICE's guideline on child maltreatment](#) for clinical features that may be associated with maltreatment.

This section has been agreed with the Royal College of Paediatrics and Child Health.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE topic page on bipolar disorder](#).

For full details of the evidence and the guideline committee's discussions, see the [full guideline and evidence review](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources](#) to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see [resources to help you put guidance into practice](#).

Update information

December 2023: We amended recommendations on valproate in line with [Medicines and Healthcare products Regulatory Agency \(MHRA\) safety advice](#), that valproate must not be started for the first time in people (male or female) younger than 55 years, unless 2 specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.

June 2022: We updated the advice on choice of psychological intervention for bipolar depression, to link to the information in the new [NICE guideline on depression in adults: treatment and management](#).

December 2021: Following a [surveillance review](#) we have updated recommendation 1.2.12 to say that either glycosylated haemoglobin (HbA1c) or fasting blood glucose may be used to test for diabetes, and 1.10.8 to clarify that the test is of fasting blood glucose.

February 2020: We amended recommendations on valproate in line with the [MHRA guidance on valproate use by women and girls](#). The MHRA states that valproate must not be used in women and girls of childbearing potential (including young girls who are likely to need treatment into their childbearing years), unless other options are unsuitable, and the pregnancy prevention programme is in place. We did this by:

- moving cautions and links to the MHRA's latest advice on valproate into the recommendations
- adding information about valproate use to recommendations rather than relying on cross-references to other recommendations in the guideline.

Medicines containing valproate taken in pregnancy can cause malformations in 11% of babies and developmental disorders in 30 to 40% of children after birth. Valproate treatment must not be used in girls and women including in young girls below the age of puberty, unless alternative treatments are not suitable and unless the terms of the pregnancy prevention programme are met. This programme includes: assessment of patients for the potential of becoming pregnant; pregnancy tests; counselling patients about the risks of valproate treatment; explaining the need for effective contraception throughout treatment; regular (at least annual) reviews of treatment by a specialist, and

completion of a risk acknowledgement form. In pregnancy, valproate is contraindicated and an alternative treatment should be decided on, with appropriate specialist consultation. See the [MHRA toolkit to ensure female patients are better informed about the risks of taking valproate during pregnancy](#).

November 2017: Some recommendations were updated with current UK marketing authorisations and MHRA advice. Links to other guidelines have also been updated. Some recommendations for research have been stood down.

February 2016: The MHRA has produced a toolkit to ensure female patients are better informed about the risks of taking valproate during pregnancy. Healthcare professionals are advised to use the NICE guideline in conjunction with the latest MHRA advice and resources. Notes have been added to the guideline to link to the MHRA's latest advice and resources.

April 2015: Recommendations related to valproate in the section on how to use medication have been reordered, and a new recommendation on withdrawal of valproate in women of childbearing potential added. These changes are in line with the revised MHRA warning on valproate.

January 2015: The MHRA has strengthened its warnings on the use of valproate in women of childbearing potential.

Minor changes since publication

March 2025: Links were updated following publication of NICE's guideline on overweight and obesity management.

October 2024: We added links to the [MHRA Drug Safety Update on valproate use in men and their partners](#).

July 2024: We have simplified the guideline by removing recommendations that are covered in other sources (such as other NICE guidelines or the BNF), and recommendations that are general good practice advice with no supporting evidence.

This is a presentational change only, and no changes to practice are intended.

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