Guideline Summary NGC-10556

Guideline Title

Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care.

Bibliographic Source(s)

National Collaborating Centre for Mental Health. Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Sep. 58 p. (Clinical guideline; no. 185).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Mental Health. Bipolar disorder: the management of bipolar disorder in adults, children, and adolescents, in primary and secondary care. Leicester (UK): British Psychological Society, Royal College of Psychiatrists; 2006. 592 p.

This guideline meets NGC's 2013 (revised) criteria.

Scope

Disease/Condition(s)

Bipolar disorder, including bipolar I, bipolar II, mixed affective and rapid cycling disorders

Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Internal Medicine

Pediatrics

Psychiatry

Psychology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Occupational Therapists

Pharmacists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Guideline Objective(s)

- To improve access and engagement with treatment and services for people with bipolar disorder
- To evaluate the role of specific psychological, psychosocial and pharmacological interventions in the treatment of bipolar disorder
- To evaluate the role of psychological and psychosocial interventions in combination with pharmacological interventions in the treatment of bipolar disorder
- To evaluate the role of specific service-level interventions for people with bipolar disorder

- To integrate the above to provide best-practice advice on the care of individuals throughout the course of their treatment
- To promote the implementation of best clinical practice through the development of recommendations tailored to the requirements of the National Health Service (NHS) in England and Wales

Target Population

Children, young people and adults with suspected or diagnosed bipolar disorder, including bipolar I, bipolar II, mixed affective and rapid cycling disorders

Interventions and Practices Considered

1. Care for adults, children and young people across all phases of bipolar disorder
   - Improving the experience of care
   - Treatment and support for specific populations (e.g., during pregnancy and postnatal period, women and girls of childbearing potential, older people, people with coexisting learning disabilities, and people with coexisting mental disorders)
   - Providing information and support on education, financial and employment problems and legal issues
   - Providing support for carers of people with bipolar disorder
2. Recognising and managing bipolar disorder in adults in primary care
   - Referral for specialist mental health assessment
   - Establishing an ongoing relationship with patients and carers
   - Psychological interventions: cognitive behavioural therapy, interpersonal therapy, behavioural couples therapy
   - Referral to secondary care, if appropriate
   - Monitoring physical health (e.g., weight, nutritional status, physical activity, cardiovascular and metabolic status, liver function, renal function, thyroid function, calcium levels)
   - Lithium use (not recommended in primary care for people who have not taken lithium before, except under shared-care arrangements)
3. Assessing suspected bipolar disorder in adults in secondary care
   - Full psychiatric assessment and mental/physical health history
   - Differential diagnosis
   - Development of care plan
   - Risk assessment for possible danger or harm (self-harm or risk to others)
4. Managing crisis, risk and behaviour that challenges in adults with bipolar disorder in secondary care
   - Developing a risk management plan jointly with the patient and their carers
   - Offering crisis services
   - Managing agitation, challenging behaviour, imminent violence, and self-harm according to established guidelines
5. Managing mania or hypomania in adults in secondary care
   - Offering support and advice
   - Pharmacological interventions: stopping antidepressants, starting or changing antipsychotics (haloperidol, olanzapine, quetiapine or risperidone, lithium, valproate)
   - Electroconvulsive therapy
   - Reviewing treatment for mania
6. Managing bipolar depression in adults in secondary care
   - Psychological interventions: cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy
   - Pharmacological interventions (single drugs or combination): fluoxetine, quetiapine, olanzapine, lamotrigine, lithium, valproate
   - Reviewing treatment for bipolar depression
7. Managing bipolar disorder in adults in the longer term in secondary care
   - Discussing long-term treatment with patient and carers
   - Psychological intervention: family intervention, structured psychological intervention
   - Long-term pharmacological interventions: lithium (first-line), valproate, olanzapine, stopping long-term treatment
   - Monitoring mood and mental state
8. Monitoring physical health in secondary care
   - Ensuring that physical healthcare is provided from primary care
   - Healthy eating and physical activity program
   - Interventions for obesity, lipid modification or type 2 diabetes prevention according to established guidelines
   - Monitoring weight and cardiovascular and metabolic indicators
9. Promoting recovery and return to primary care
   - Continuing treatment and care in an early intervention in psychosis service, a specialist bipolar disorder service or a specialist integrated community-based team
   - Intensive case management
   - Return to primary care, as appropriate
   - Offering supported employment programs and educational and occupational activities
10. How to use medication
    - Patient education on medication use
    - Regular medication review
    - Starting, monitoring, and stopping medications: antipsychotic drugs, lithium, valproate, lamotrigine
11. Recognising, diagnosing and managing bipolar disorder in children and young people

- Recognition (questionnaires not recommended in primary care)
- Referral to specialist intervention in early intervention in psychosis service or a child and adolescent mental health services team
- Diagnosis of bipolar disorder only after intensive, prospective, longitudinal monitoring by trained professional
- Management of mania or hypomania: aripiprazole, antipsychotics
- Management of bipolar depression: structured psychological interventions, risk management plans for self-harm, considering comorbid conditions or other coexisting psychosocial factors, pharmacological interventions
- Long-term management

Major Outcomes Considered

- Symptoms, frequency, and time to event for:
  - Mania
  - Hypomania
  - Depression
  - Mixed episodes
- Side effects of interventions
- Physical health
- Quality of life
- Functional disability (including work, educational, family, and social domains)
- Carer outcomes
- Service use
- Dropout (including all-cause and dropout because of side effects)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Review Protocols

Review questions drafted during the scoping phase were discussed by the Guideline Development Group (GDG) at the first few meetings and amended as necessary. The review questions were used as the starting point for developing review protocols for each systematic review. Where appropriate, the review questions were refined once the evidence had been searched and, where necessary, sub-questions were generated.

For questions about interventions, the PICO (Population, Intervention, Comparison and Outcome) framework was used to structure each question (see Table 2 in the full version of the original guideline document).

Questions relating to diagnosis or case identification do not involve an intervention designed to treat a particular condition, and therefore the PICO framework was not used. Rather, the questions were designed to pick up key issues specifically relevant to clinical utility, for example their accuracy, reliability, safety and acceptability to the service user.

To help facilitate the literature review, a note was made of the best study design type to answer each question. There are four main types of review question of relevance to NICE guidelines. These are listed in Table 3 in the full version of the original guideline document. For each type of question, the best primary study design varies, where 'best' is interpreted as 'least likely to give misleading answers to the question'. For questions about the effectiveness of interventions, where randomised controlled trials (RCTs) were not available, the review of other types of evidence was pursued only if there was reason to believe that it would help the GDG to formulate a recommendation.

However, in all cases, a well-conducted systematic review (of the appropriate type of study) is likely to always yield a better answer than a single study.

Clinical Review Methods

The aim of the clinical literature review was to systematically identify and synthesise relevant evidence from the literature in order to answer the specific review questions developed by the GDG. Thus, clinical practice recommendations are evidence-based, where possible, and, if evidence is not available, informal consensus methods are used to try and reach general agreement between GDG members and the need for future research is specified.

The Search Process

Scoping Searches

A broad preliminary search of the literature was undertaken in August 2011 to obtain an overview of the issues likely to be covered by the scope, and to help define key areas. Searches were restricted to clinical guidelines, Health Technology Assessment (HTA) reports, key systematic reviews and RCTs. A list of databases and websites searched can be found in Appendix 8 in the full version of the original guideline document.

Systematic Literature Searches

After the scope was finalised, a systematic search strategy was developed to locate as much relevant evidence as possible. The balance between sensitivity (the power to identify all studies on a particular topic) and specificity (the ability to exclude irrelevant studies from the results) was carefully considered, and a decision made to utilise a broad approach to most of the searches to maximise retrieval of evidence to all parts of the guideline. Searches were restricted to certain study designs if specified in the review protocol, and conducted in the following databases:

- Cochrane Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Database of Systematic Reviews (CDSR)
- CENTRAL

- EMBASE
- HTA database (technology assessments)
- MEDLINE/MEDLINE In-Process
- Psychological Information Database (PsycINFO)

The search strategies were initially developed for MEDLINE before being translated for use in other databases/interfaces. Strategies were built up through a number of trial searches and discussions of the results of the searches with the review team and the GDG to ensure that all possible relevant search terms were covered. The search terms for each search are set out in full in Appendix 8 in the full version of the original guideline document.

Reference Management

Citations from each search were downloaded into reference management software and duplicates removed. Records were then screened against the eligibility criteria of the reviews before being appraised for methodological quality. The unfiltered search results were saved and retained for future potential re-analysis to help keep the process both replicable and transparent.

Search Filters

To aid retrieval of relevant and sound studies, filters were used to limit a number of searches to randomised controlled trials and systematic reviews. Both of these search filters are adaptations of filters designed by the Health Information Research Unit of McMaster University. Each filter comprises index terms relating to the study type(s) and associated text words for the methodological description of the design(s).

Date and Language Restrictions

Systematic database searches were initially conducted in July 2012 up to the most recent searchable date. Search updates were generated on a 6-monthly basis, with the final re-runs carried out in January 2014 ahead of the guideline consultation.

After this point, studies were only included if they were judged by the GDG to be exceptional (for example, if the evidence was likely to change a recommendation).

Although no language restrictions were applied at the searching stage, foreign language papers were not requested or reviewed, unless they were of particular importance to a review question.

For review questions that update Bipolar disorder (NICE clinical guideline 38), searching was limited to updating pre-existing reviews, covering the time period since the searches for the published reviews were conducted. For new review questions, no date restriction was imposed.

Other Search Methods

Other search methods involved: (a) scanning the reference lists of all eligible publications (systematic reviews, stakeholder evidence and included studies) for more published reports and citations of unpublished research; (b) sending lists of studies meeting the inclusion criteria to subject experts (identified through searches and the GDG) and asking them to check the lists for completeness, and to provide information of any published or unpublished research for consideration (see Appendix 6 in the full version of the original guideline document and "Unpublished Evidence," below); (c) contacting included study authors for unpublished or incomplete datasets. Searches conducted for existing NICE guidelines were updated where necessary.

Full details of the search strategies and filters used for the systematic review of clinical evidence are provided in Appendix 8 in the full version of the original guideline document.

Study Selection and Assessment of Methodological Quality

All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility at the time they were being entered into the study information database. More specific eligibility criteria were developed for each review question and are described in the relevant clinical evidence chapters. The eligibility of each study was confirmed by at least one member of the GDG.

For some review questions, it was necessary to prioritise the evidence with respect to the UK context (that is, external validity). To make this process explicit, the GDG took into account the following factors when assessing the evidence:

- Participant factors (for example, gender, age and ethnicity)
- Provider factors (for example, model fidelity, the conditions under which the intervention was performed and the availability of experienced staff to undertake the procedure)
- Cultural factors (for example, differences in standard care and differences in the welfare system)

It was the responsibility of the GDG to decide which prioritisation factors were relevant to each review question in light of the UK context.

Unpublished Evidence

Stakeholders, authors and principle investigators were approached for unpublished evidence (see Appendices 4 and 6 in the full version of the original guideline document). The GDG used a number of criteria when deciding whether or not to accept unpublished data. First, the evidence must have been accompanied by a trial report containing sufficient detail to properly assess risk of bias. Second, the evidence must have been submitted with the understanding that data from the study and a summary of the study's characteristics would be published in the full version of the original guideline document.

Health Economics Methods

Search Strategy for Economic Evidence

Scoping Searches

A broad preliminary search of the literature was undertaken in August 2011 to obtain an overview of the issues likely to be covered by the scope, and help define key areas. Searches were restricted to economic studies and HTA reports, and conducted in the following databases:

- EMBASE
- MEDLINE/MEDLINE In-Process
- HTA database (technology assessments)
- National Health Service Economic Evaluation Database (NHS EED)

Any relevant economic evidence arising from the clinical scoping searches was also made available to the health economist during the same period.

Systematic Literature Searches

After the scope was finalised, a systematic search strategy was developed to locate as much relevant evidence as possible. The balance between sensitivity (the power to identify all studies on a particular topic) and specificity (the ability to exclude irrelevant studies from the results) was carefully considered, and a decision made to utilise a broad approach to most of the searches to maximise retrieval of evidence to all parts of the guideline. Searches were restricted to economic studies and health technology assessment reports, and conducted in the following databases:

- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- EMBASE
- HTA database (technology assessments)
- MEDLINE/MEDLINE In-Process

- NHS EED
- PsycINFO

Any relevant economic evidence arising from the clinical searches was also made available to the health economist during the same period.

The search strategies were initially developed for MEDLINE before being translated for use in other databases/interfaces. Strategies were built up through a number of trial searches, and discussions of the results of the searches with the review team and GDG to ensure that all possible relevant search terms were covered.

The search terms are set out in full in Appendix 9 in the full version of the original guideline document.

Reference Management

Citations from each search were downloaded into reference management software and duplicates removed. Records were then screened against the inclusion criteria of the reviews before being quality appraised. The unfiltered search results were saved and retained for future potential re-analysis to help keep the process both replicable and transparent.

Search Filters

The search filter for health economics is an adaptation of a pre-tested strategy designed by the Centre for Reviews and Dissemination. The search filter is designed to retrieve records of economic evidence (including full and partial economic evaluations) from the vast amount of literature indexed to major medical databases such as MEDLINE. The filter, which comprises a combination of controlled vocabulary and free-text retrieval methods, maximises sensitivity (or recall) to ensure that as many potentially relevant records as possible are retrieved from a search. A full description of the filter is provided in Appendix 9 in the full version of the original guideline document.

Date and Language Restrictions

Systematic database searches were initially conducted in July 2012 up to the most recent searchable date. Search updates were generated on a 6-monthly basis, with the final re-runs carried out in January 2014 ahead of the guideline consultation. After this point studies were included only if they were judged by the GDG to be exceptional (for example, the evidence was likely to change a recommendation).

For review questions that update Bipolar disorder (NICE clinical guideline 38), searching was limited to updating pre-existing reviews, covering the time period since the searches for the published reviews were conducted. For new review questions, searches were restricted to research published from 1998 onwards in order to obtain data relevant to current healthcare settings and costs.

Other Search Methods

Other search methods involved scanning the reference lists of all eligible publications (systematic reviews, stakeholder evidence and included studies from the economic and clinical reviews) to identify further studies for consideration.

Full details of the search strategies and filter used for the systematic review of health economic evidence are provided in Appendix 9 in the full version of the original guideline document.

Inclusion Criteria for Economic Studies

The following inclusion criteria were applied to select studies identified by the economic searches for further consideration:

1. Only studies from Organisation for Economic Co-operation and Development countries were included, as the aim of the review was to identify economic information transferable to the UK context.
2. Only studies published from 2003 onwards were included in the review. This date restriction was imposed so that retrieved economic evidence was relevant to current healthcare settings and costs.
3. Selection criteria based on types of clinical conditions and service users as well as interventions assessed were identical to the clinical literature review.
4. Studies were included provided that sufficient details regarding methods and results were available to enable the methodological quality of the study to be assessed, and provided that the study's data and results were extractable. Poster presentations and abstracts in conference proceedings were excluded.
5. Full economic evaluations that compared two or more relevant options and considered both costs and consequences were included in the review.
6. Economic studies were included if they used clinical effectiveness data from RCTs, prospective cohort studies, or systematic reviews and meta-analyses of clinical studies. Studies that had a mirror-image or other retrospective design were excluded from the review. Studies that utilised clinical effectiveness parameters based on expert opinion or assumptions were also excluded.
7. Studies were included only if the examined interventions were clearly described. This involved the dosage and route of administration and the duration of treatment in the case of pharmacological interventions; and the types of health professionals involved as well as the frequency and duration of treatment in the case of psychological interventions. Evaluations in which drugs were treated as a class were excluded from further consideration.
8. Studies that adopted a very narrow perspective, ignoring major categories of costs to the NHS, were excluded; for example studies that estimated exclusively drug acquisition costs or hospitalisation costs were considered non-informative to the guideline development process.

Number of Source Documents

Clinical Evidence Review

The number of publications retrieved in the literature search and that were included in the formulation of guideline recommendations is stated in the relevant chapter for each clinical question in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Results of the Systematic Search of Economic Literature

The titles of all studies identified by the systematic search of the literature were screened for their relevance to the topic (that is, economic issues and information on health-related quality of life). References that were clearly not relevant were excluded first. The abstracts of all potentially relevant studies (250 references) were then assessed against the inclusion criteria for economic evaluations by the health economist. Full texts of the studies potentially meeting the inclusion criteria (including those for which eligibility was not clear from the abstract) were obtained. Studies that did not meet the inclusion criteria, were duplicates, were secondary publications of one study, or had been updated in more recent publications were subsequently excluded. Economic evaluations eligible for inclusion (20 studies in 19 publications) were then appraised for their applicability and quality using the methodology checklist for economic evaluations. Finally, 17 publications reporting 18 economic analyses that fully or partially met the applicability and quality criteria were considered at formulation of the guideline recommendations.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Clinical Review Methods

Evidence Synthesis

Study characteristics, aspects of methodological quality, and outcome data were extracted from all eligible studies, using Microsoft Excel and Review Manager 5.2 (The Cochrane Collaboration).

The method used to synthesize evidence depended on the review question and availability and type of evidence (see below for full details). In the absence of high-quality research, an informal consensus process was used (see Section 3.5.6 in the full version of the original guideline document).

Synthesising the Evidence from Test Accuracy Studies

Meta-analysis

Review Manager was used to summarise test accuracy data from each study using forest plots and summary receiver operator characteristic (ROC) plots.

Refer to Section 3.5.2 in the full version of the original guideline document for discussions of sensitivity and specificity, ROC curves, negative and positive likelihood ratios, and heterogeneity.

Synthesising the Evidence for the Effectiveness of Interventions

Pairwise Meta-analysis

Where appropriate, meta-analysis was used to synthesise evidence for the effectiveness of interventions using Review Manager Version 5.2. If necessary, re-analyses of the data or sub-analyses were used to answer review questions not addressed in the original studies or reviews.

Dichotomous outcomes were analysed as relative risks (RR; also called a risk ratio) with the associated 95% confidence interval (CI) (see Figure 2 in the full version of the original guideline document for an example of a forest plot displaying dichotomous data).

Continuous outcomes were analysed using the mean difference (MD) or standardised mean difference (SMD) when different measures were used in different studies to estimate the same underlying effect (see Figure 3 in the full version of the original guideline document for an example of a forest plot displaying continuous data). If reported by study authors, intention-to-treat (ITT) data, using a valid method for imputation of missing data, were preferred over data only from people who completed the study.

Heterogeneity

To check for consistency of effects among studies, both the I^2 statistic and the chi-squared test of heterogeneity, as well as a visual inspection of the forest plots were used. The I^2 statistic describes the proportion of total variation in study estimates that is due to heterogeneity. For meta-analyses of comparative effectiveness studies, the I^2 statistic was interpreted in the following way based on guidelines from the Cochrane Collaboration:

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

The Cochrane Collaboration advice suggests that overlapping categories are less misleading than simple thresholds since the importance of inconsistency depends on (1) the magnitude and direction of effects, and (2) the strength of evidence for heterogeneity (for example, p value from the chi-squared test, or a CI for I^2).

Network Meta-analysis

Standard models for network meta-analysis (NMA) with binary outcomes were used for two outcomes: a) discontinuation, and b) response given no discontinuation. Information on the log-odds ratio of response in trials reporting on more than one scale was combined and information on the standardised mean difference on different symptoms scales was used to inform the log-odds ratio of response. Baseline probabilities of discontinuation and response given no discontinuation were calculated based on all trials with a Placebo arm reporting these outcomes. Further information about the method used and the winBUGS code can be found in Appendix 15 in the full version of the original guideline document.

Grading the Quality of Evidence

For questions about the effectiveness of interventions, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to grade the quality of evidence for each outcome. For questions about the experience of care and the organisation and delivery of care, methodology checklists were used to assess the risk of bias, and this information was taken into account when interpreting the evidence. The technical team produced GRADE evidence profiles using GRADEprofiler (GRADEpro) software (Version 3.6), following advice set out in the GRADE handbook.

Evidence Profiles

A GRADE evidence profile was used to summarise both the quality of the evidence and the results of the evidence synthesis for each "critical" outcome. The GRADE approach is based on a sequential assessment of the quality of evidence, followed by judgment about the balance between desirable and undesirable effects, and subsequent decision about the strength of a recommendation.

Within the GRADE approach to grading the quality of evidence, the following is used as a starting point:

- Randomised controlled trials (RCTs) without important limitations provide high quality evidence
- Observational studies without special strengths or important limitations provide low quality evidence

For each outcome, quality may be reduced depending on five factors: limitations, inconsistency, indirectness, imprecision and publication bias. For the purposes of the guideline, each factor was evaluated using criteria provided in Table 4 in the full version of the original guideline document.

For observational studies without any reasons for down-grading, the quality may be up-graded if there is a large effect, all plausible confounding would reduce the demonstrated effect (or increase the effect if no effect was observed), or there is evidence of a dose-response gradient (details would be provided under the "other" column).

Presenting Evidence to the Guideline Development Group

Study characteristics tables and, where appropriate, forest plots generated with Review Manager Version 5.2 and GRADE summary of findings tables were presented to the GDG.

Where meta-analysis was not appropriate and/or possible, the reported results from each primary-level study were reported in the study characteristics table and presented to the GDG. The range of effect estimates were included in the GRADE profile, and where appropriate, described narratively.

Summary of Findings Tables

Summary of findings tables generated from GRADEpro were used to summarise the evidence for each outcome and the quality of that evidence. The tables provide illustrative comparative risks, especially useful when the baseline risk varies for different groups within the population.

Extrapolation

When answering review questions, if there is no direct evidence from a primary dataset (defined as a data set which contains evidence on the population and intervention under review), based on the initial search for evidence, it may be appropriate to extrapolate from another data set. In this situation, the following principles were used to determine when to extrapolate:

- A primary dataset is absent, of low quality or is judged to be not relevant to the review question under consideration, and
- A review question is deemed by the GDG to be important, such that in the absence of direct evidence, other data sources should be considered, and
- Non-primary data source(s) is in the view of the GDG available, which may inform the review question.

When the decision to extrapolate was made, the following principles were used to inform the choice of the non-primary dataset:

- The populations (usually in relation to the specified diagnosis or problem which characterises the population) under consideration share some common characteristic but differ in other ways, such as age, gender or in the nature of the disorder (for example, a common behavioural problem; acute versus chronic presentations of the same disorder), and
- The interventions under consideration in the view of the GDG have one or more of the following characteristics:
  - Share a common mode of action (e.g., the pharmacodynamics of drug; a common psychological model of change - operant conditioning)
  - Be feasible to deliver in both populations (e.g., in terms of the required skills or the demands of the health care system)
  - Share common side effects/harms in both populations, and
- The context or comparator involved in the evaluation of the different datasets shares some common elements which support extrapolation, and
- The outcomes involved in the evaluation of the different datasets shares some common elements which support extrapolation (for example, improved mood or a reduction in challenging behaviour).

When the choice of the non-primary dataset was made, the following principles were used to guide the application of extrapolation:

- The GDG should first consider the need for extrapolation through a review of the relevant primary dataset and be guided in these decisions by the principles for the use of extrapolation
- In all areas of extrapolation datasets should be assessed against the principles for determining the choice of datasets. In general the criteria in the four principles set out above for determining the choice should be met
- In deciding on the use of extrapolation, the GDG will have to determine if the extrapolation can be held to be reasonable, including ensuring that:
  - The reasoning behind the decision can be justified by the clinical need for a recommendation to be made
  - The absence of other more direct evidence, and by the relevance of the potential dataset to the review question can be established
  - The reasoning and the method adopted is clearly set out in the relevant section of the guideline.

Method Used to Answer a Review Question in the Absence of Appropriately Designed, High-Quality Research

In the absence of appropriately designed, high-quality research (including indirect evidence where it would be appropriate to use extrapolation), an informal consensus process was adopted.

The process involved a group discussion of what is known about the issues. The views of GDG were synthesised narratively by a member of the review team, and circulated after the meeting. Feedback was used to revise the text, which was then included in the appropriate evidence review chapter.

Health Economic Methods

The aim of the health economics was to contribute to the guideline's development by providing evidence on the cost-effectiveness of interventions for adults, children and young people with bipolar disorder covered in the guideline. This was achieved by:

- Systematic literature review of existing economic evidence
- Decision-analytic economic modelling

Systematic reviews of economic literature were conducted in all areas covered in the guideline. Economic modelling was undertaken in areas with likely major resource implications, where the current extent of uncertainty over cost-effectiveness was significant and economic analysis was expected to reduce this uncertainty, in accordance with *The Guidelines Manual* (NICE, 2012). Prioritisation of areas for economic modelling was a joint decision between the Health Economist and the GDG. The rationale for prioritising review questions for economic modelling was set out in an economic plan agreed between NICE, the GDG, the Health Economist and the other members of the technical team. The following economic questions were selected as key issues that were addressed by economic modelling:

- Cost-effectiveness of pharmacological interventions for adults with bipolar disorder in a manic episode
- Cost-effectiveness of pharmacological interventions for adults with bipolar disorder in an acute depressive episode
- Cost-effectiveness of pharmacological interventions for the maintenance treatment of adults with bipolar disorder

In addition, literature on the health-related quality of life of people with bipolar disorder was systematically searched to identify studies reporting appropriate utility values that could be utilised in a cost-utility analysis.

Methods employed in economic modelling are described in the relevant economic sections of the evidence chapters in the full version of the original guideline document.

Applicability and Quality Criteria for Economic Studies

All economic papers eligible for inclusion were appraised for their applicability and quality using the methodology checklist for economic evaluations recommended by NICE (NICE, 2012). The methodology checklist for economic evaluations was also applied to the economic models developed specifically for this guideline. All studies hat fully or partially met the applicability and quality criteria described in the methodology checklist were considered during the guideline development process, along with the results of the economic modelling conducted specifically for this guideline. The completed methodology checklists for all economic evaluations 9 considered in the guideline are provided in Appendix 31 in the full version of the original guideline document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The Guideline Development Group

During the consultation phase, members of the Guideline Development Group (GDG) were appointed by an open recruitment process. GDG membership consisted of:

professionals in psychiatry, clinical psychology, nursing, social work, and general practice; academic experts in psychiatry and psychology; and service users. The guideline development process was supported by staff from the NCCMH, who undertook the clinical and health economic literature searches, reviewed and presented the evidence to the GDG, managed the process, and contributed to drafting the guideline.

Guideline Development Group Meetings

Thirteen GDG meetings were held between October 2012 and June 2014. During 30 each day-long GDG meeting, in a plenary session, review questions and clinical and economic evidence were reviewed and assessed and, at later meetings, recommendations formulated. At each meeting, all GDG members declared any potential conflicts of interest (see Appendix 2 in the full version of the original guideline document [see the "Availability of Companion Documents" field]), and service user and carer concerns were routinely discussed as a standing agenda item.

Service Users and Carers

Individuals with direct experience of services gave an integral service-user focus to the GDG and the guideline. The GDG included service users. They contributed as full GDG members to writing the review questions, providing advice on outcomes most relevant to service users and carers, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline, and bringing service user research to the attention of the GDG. In drafting the guideline, they contributed to the chapter on experience of carers and to writing the guideline's introduction and identified recommendations from the service user and carer perspective.

Special Advisors

Special advisors, who had specific expertise in one or more aspects of treatment and management relevant to the guideline, assisted the GDG, commenting on specific aspects of the developing guideline and making presentations to the GDG. Appendix 3 in the full version of the original guideline document lists those who agreed to act as special advisors.

National and International Experts

National and international experts in the area under review were identified through the literature search and through the experience of the GDG members. These experts were contacted to identify unpublished or soon-to-be published studies, to ensure that up-to-date evidence was included in the development of the guideline. They informed the GDG about completed trials at the pre-publication stage, systematic reviews in the process of being published, studies relating to the cost effectiveness of treatment and trial data if the GDG could be provided with full access to the complete trial report. Appendix 6 in the full version of the original guideline document lists researchers who were contacted.

Using NICE Evidence Reviews and Recommendations from Existing Guidelines

When review questions overlap and evidence from another guideline applies to a question in the current guideline, it might be desirable and practical to incorporate or adapt recommendations published in NICE guidelines. Adaptation refers to the process by which an existing recommendation is modified in order to facilitate its placement in a new guideline. Incorporation refers to the placement of a recommendation that was developed for another guideline into a new guideline, with no material changes to wording or structure. Incorporation would be used in relatively rare circumstances, as cross-referring to the other guideline will often be all that is necessary.

Incorporation or adaptation is likely to be substantially more complex where health economics were a major part of the decision making. In these circumstances, these methods are only used rarely after full and detailed consideration. Refer to the full version of the original guideline document for the criteria used for incorporation and adaptation in this guideline.

In deciding whether to choose between incorporation or adaptation of existing guideline recommendations, the GDG considered whether the direct evidence obtained from the current guideline dataset was of sufficient quality to allow development of recommendations. It was only where (a) such evidence was not available or insufficient to draw robust conclusions and (b) where methods used in other NICE guidelines were sufficiently robust that the 'incorporate and adapt' method could be used. Recommendations were only incorporated or adapted after the GDG had reviewed evidence supporting previous recommendations and confirmed that they agreed with the original recommendations.

When adaptation is used, the meaning and intent of the original recommendation is preserved but the wording and structure of the recommendation may change. Preservation of the original meaning (that is, that the recommendation faithfully represents the assessment and interpretation of the evidence contained in the original guideline document evidence reviews) and intent (that is, the intended action[s] specified in the original recommendation will be achieved) is an essential element of the process of adaptation.

From Evidence to Recommendations

Once the clinical and health economic evidence was summarised, the drafted the recommendations. In making recommendations, the GDG took into account the trade-off between the benefits and harms of the intervention/instrument, as well as other important factors, such as economic considerations, values of the GDG and society, the requirements to prevent discrimination and to promote equality, and the GDG's awareness of practical issues.

Finally, to show clearly how the GDG moved from the evidence to the recommendations, each chapter has a section called 'from evidence to recommendations'. Underpinning this section is the concept of the 'strength' of a recommendation. This takes into account the quality of the evidence but is conceptually different. Some recommendations are 'strong' in that the GDG believes that the vast majority of healthcare professionals and service users would choose a particular intervention if they considered the evidence in the same way that the GDG has. This is generally the case if the benefits clearly outweigh the harms for most people and the intervention is likely to be cost effective. However, there is often a closer balance between benefits and harms, and some service users would not choose an intervention whereas others would. This may happen, for example, if some service users are particularly averse to some side effect and others are not. In these circumstances the recommendation is generally weaker, although it may be possible to make stronger recommendations about specific groups of service users. The strength of each recommendation is reflected in the wording of the recommendation, rather than by using ratings, labels or symbols (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

The economic evidence identified by the health economics systematic review was summarised in the respective chapters of the full version of the original guideline document, following presentation of the clinical evidence. The characteristics and results of all economic studies included in the review were provided in the form of evidence tables in Appendix 32 in the full version of the original guideline document.

Methods and results of economic modelling undertaken alongside the guideline development process are presented in the relevant evidence chapters. Characteristics and results of all economic studies considered during the guideline development process (including modelling studies conducted for this guideline) are summarised in economic evidence profiles that are presented in Appendix 33 nm the full version of the original guideline document.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Validation of the Guideline

Registered stakeholders had an opportunity to comment on the draft guideline, which was posted on the National Institute for Health and Care Excellence (NICE) website during the consultation period. Following the consultation, all comments from stakeholders and experts (see Appendix 5 in the full version of the original guideline document) were responded to, and the guideline updated as appropriate. NICE also reviewed the guideline and checked that stakeholders' comments had been addressed.

Following the consultation period, the Guideline Development Group (GDG) finalised the recommendations and the National Collaborating Centre for Mental Health (NCCMH) produced the final documents. These were then submitted to NICE for a quality assurance check. Any errors were corrected by the NCCMH, then the guideline was formally approved by NICE and issued as guidance to the National Health Service (NHS) in England and Wales.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The wording used in the recommendations in this guideline (for example words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Care for Adults, Children and Young People Across All Phases of Bipolar Disorder

Improving the Experience of Care

Use this guideline in conjunction with the NICE guideline Service user experience in adult mental health: improving the experience of care for people using adult NHS mental health services (NICE clinical guideline 136) to improve the experience of care for adults with bipolar disorder using mental health services, and for adults, children and young people:

- Promote a positive recovery message from the point of diagnosis and throughout care.
- Build supportive and empathic relationships as an essential part of care.

Follow the recommendations in general principles of care in the NICE clinical guideline on psychosis and schizophrenia in children and young people to improve the experience of care for children and young people with bipolar disorder (see the NGC summary of the NICE guideline Psychosis and schizophrenia in children and young people: recognition and management [NICE clinical guideline 155]).

Treatment and Support for Specific Populations

Follow the recommendations in race, culture and ethnicity in the NICE clinical guideline on psychosis and schizophrenia in adults when working with people with bipolar disorder from black, Asian and minority ethnic groups (see the NGC summary of the NICE guideline Psychosis and schizophrenia in adults: treatment and management [NICE clinical guideline 178]).

See the NICE clinical guideline Antenatal and postnatal mental health: Clinical management and service guidance (NICE clinical guideline 45) for guidance on the management of bipolar disorder during pregnancy and the postnatal period and in women and girls of childbearing potential.

Ensure that people with bipolar disorder and a coexisting learning disability are offered the same range of treatments and services as other people with bipolar disorder.

Ensure that older people with bipolar disorder are offered the same range of treatments and services as younger people with bipolar disorder.

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 clinical guideline, in addition to their treatment for bipolar disorder. See the NICE guidelines Antisocial personality disorder. Treatment, management and prevention (NICE clinical guideline 77); Borderline personality disorder: treatment and management (NICE clinical guideline 78); Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults (NICE clinical guideline 72); Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. Management in primary, secondary and community care (NICE clinical guideline 113); and Psychosis with coexisting substance misuse. Assessment and management in adults and young people (NICE clinical guideline 120). Be alert to the potential for drug interactions and use clinical judgement.

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.

Information and Support

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.

Encourage people with bipolar disorder to develop advance statements while their condition is stable, in collaboration with their carers if possible.

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.

Support for Carers of People with Bipolar Disorder

Offer carers of people with bipolar disorder an assessment (provided by mental health services) of their own needs and discuss with them their strengths and views. Develop a care plan to address any identified needs, give a copy to the carer and their general practitioner (GP) and ensure it is reviewed annually.[1]

Advise carers about their statutory right to a formal carer's assessment provided by social care services and explain how to access this.[2]

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

When providing information, offer the carer support if necessary.[1]

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.[1]

Review regularly how information is shared, especially if there are communication and collaboration difficulties between the person and their carer.[2]

Include carers in decision-making if the person agrees.[1]

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[1]

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.

Recognising and Managing Bipolar Disorder in Adults in Primary Care

Recognising Bipolar Disorder in Primary Care and Referral

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.

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.

Do not use questionnaires in primary care to identify bipolar disorder in adults.

Managing Bipolar Disorder in Primary Care

When working with people with bipolar disorder in primary care:

- Engage with and develop an ongoing relationship with them and their carers.
- 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.

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 high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with recommendations in the NICE guideline Depression. The treatment and management of depression in adults (NICE clinical guideline 90).

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.

Psychological therapists working with people with bipolar depression in primary care should have training in and experience of working with people with bipolar disorder.

Do not start lithium to treat bipolar disorder in primary care for people who have not taken lithium before, except under shared-care arrangements.

Do not start valproate in primary care to treat bipolar disorder.

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

Monitoring Physical Health

Develop and use practice case registers to monitor the physical and mental health of people with bipolar disorder in primary care.[1]

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 below 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.[1]

Ensure that the physical health check for people with bipolar disorder, performed at least annually, includes:

- Weight or body mass index (BMI), diet, nutritional status and level of physical activity
- Cardiovascular status, including pulse and blood pressure
- Metabolic status, including fasting blood glucose, glycosylated haemoglobin (HbA_{1c}) and blood lipid profile
- Liver function
- Renal and thyroid function, and calcium levels, for people taking long-term lithium

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 the NGC summaries of the NICE guidelines Hypertension. Clinical management of primary hypertension in adults (NICE clinical guideline 127) and Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (NICE clinical guideline 181) and follow the NICE guidelines Prevention of cardiovascular disease (NICE public health guideline 25); Obesity: Guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children (NICE clinical guideline 43); Physical activity: brief advice for adults in primary care (NICE public health guideline 44); and Preventing type 2 diabetes: risk identification and interventions for individuals at high risk (NICE public health guideline 38).[1]

Offer treatment to people with bipolar disorder who have diabetes and/or cardiovascular disease in primary care in line with the NICE guidelines Type 1 diabetes: Diagnosis and management of type 1 diabetes in children, young people and adults (NICE clinical guideline 15), Type 2 diabetes. The management of type 2 diabetes (NICE clinical guideline 87) and the NGC summary of the NICE guideline Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (NICE clinical guideline 181).[1]

Assessing Suspected Bipolar Disorder in Adults in Secondary Care

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.
- Provide treatment and care in the least restrictive and stigmatising environment possible, and in an atmosphere of hope and optimism in line with the NICE guideline Service user experience in adult mental health: improving the experience of care for people using adult NHS mental health services (NICE clinical guideline 136).

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

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.

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.

If bipolar disorder is diagnosed, develop a care plan in collaboration with the person with bipolar disorder based on the assessment carried out in a recommendation above 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.[1]

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 next section.

Managing Crisis, Risk and Behaviour That Challenges in Adults with Bipolar Disorder in Secondary Care

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

Offer crisis services to support people with bipolar disorder who are in crisis, in line with recommendations in the NGC summary of the NICE guideline Psychosis and schizophrenia in adults: treatment and management (NICE clinical guideline 178).

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

- Violence: The short-term management of disturbed/violent behaviour in in-patient psychiatric settings and emergency departments (NICE clinical guideline 25) and Service user experience in adult mental health: improving the experience of care for people using adult NHS mental health services (NICE clinical guideline 136) for advice on managing agitation, challenging behaviour and imminent violence, and on rapid tranquillisation **or**
- Self-harm: The short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care (NICE clinical guideline 16) for advice on managing acts of self-harm and suicide risk

Managing Mania or Hypomania in Adults in Secondary Care

Support and Advice

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.

Pharmacological Interventions

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 the recommendation below, regardless of whether the antidepressant is stopped.

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 the section "How to Use Medication" below.

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 the recommendation above, taking into account any advance statements, the person's preference and clinical context (including physical comorbidity, previous response to treatment and side effects).

If an alternative antipsychotic is not sufficiently effective at the maximum licensed dose, consider adding lithium.[3] 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[4] instead.

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.

If the person is already taking lithium, check plasma lithium levels to optimise treatment (see the section "How to Use Medication" below). Consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment.

If the person is already taking valproate or another 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 "How to Use Medication" below.

If the clinical presentation is of a mixed affective state, characterised by both manic and depressive symptoms, follow the recommendations above for the treatment of mania, and monitor closely for the emergence of depression.

Do not offer lamotrigine to treat mania.

Electroconvulsive Therapy

For the treatment of severe mania that has not responded to other interventions, see the NICE guideline Guidance on the use of electroconvulsive therapy (NICE technology appraisal guidance 59).

Reviewing Treatment for Mania

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 "Managing Bipolar Disorder in Adults in the Longer Term in Secondary Care" below). Explain the potential benefits of long-term treatment and the risks, including side effects of medication used for long-term treatment.

If the person decides to continue treatment for mania, offer it for a further 3 to 6 months, and then review.

Managing Bipolar Depression in Adults in Secondary Care

Psychological Interventions

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 high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with recommendations in the NICE guideline Depression. The treatment and management of depression in adults (NICE clinical guideline 90).
- 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

Psychological therapists working with people with bipolar depression should have training in, and experience of, working with people with bipolar disorder.

Pharmacological Interventions

If a person develops moderate or severe bipolar depression and is not taking a drug to treat their bipolar disorder, offer fluoxetine[5] combined with olanzapine[6], 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[7] 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 "How to Use Medication" below.

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[5] combined with olanzapine[6] or add quetiapine, depending on the person's preference and previous response to treatment.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine[7] 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 on using lithium, antipsychotics and lamotrigine in the section "How to Use Medication" below.

If a person develops moderate or severe bipolar depression and is already taking valproate, consider increasing the dose within the therapeutic range. If the maximum tolerated dose, or the top of the therapeutic range, has been reached and there is a limited response to valproate, add fluoxetine[5] combined with olanzapine[6] or add quetiapine, depending on the person's preference and previous response to treatment.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine[7] to valproate.
- If there is no response to adding fluoxetine combined with olanzapine, or adding quetiapine, stop the additional treatment and consider adding lamotrigine to valproate.

Follow the recommendations on using valproate, antipsychotics and lamotrigine in the section "How to Use Medication" below.

Follow the recommendations on using antipsychotics in the section "How to Use Medication" below and be aware of the potential interactions between valproate and fluoxetine, lamotrigine and olanzapine.

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.

Reviewing Treatment for Bipolar Depression

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 "Managing Bipolar Disorder in Adults in the Longer Term in Secondary Care," below). Explain the potential benefits of long-term treatment and the risks, including side effects of medication used for long-term treatment.

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.

Managing Bipolar Disorder in Adults in the Longer Term in Secondary Care

Discussing Long-term Treatment

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.

Psychological Interventions

Offer a family intervention to people with bipolar disorder who are living, or in close contact, with their family in line with the recommendations in the NGC summary of the NICE guideline Psychosis and schizophrenia in adults: treatment and management (NICE clinical guideline 178).

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.

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.

Pharmacological Interventions

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.

Offer lithium as a first-line, long-term pharmacological treatment for bipolar disorder and:

- If lithium is ineffective, consider adding valproate.[8]
- If lithium is poorly tolerated, or is not suitable (for example, because the person does not agree to routine blood monitoring), consider valproate or olanzapine[9] instead or, if it has been effective during an episode of mania or bipolar depression, quetiapine.

Discuss with the person the possible benefits and risks of each drug for them.

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 "How to Use Medication" below) and monitor the person for signs of relapse.

Continue monitoring symptoms, mood and mental state for 2 years after medication has stopped entirely. This may be undertaken in primary care (see "Return to Primary Care," below).

Monitoring Physical Health in Secondary Care

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 above under "Monitoring Physical Health" after responsibility for monitoring has been transferred from secondary care.[1]

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.[1]

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 and offer interventions in line with the NICE guideline Obesity: Guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children (NICE clinical guideline 43); the NGC summary of the NICE guideline Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (NICE clinical guideline 181); or the NICE guideline Preventing type 2 diabetes: risk identification and interventions for individuals at high risk (NICE public health guidance 38).[1]

Routinely monitor weight and cardiovascular and metabolic indicators of morbidity in people with bipolar disorder. These should be audited in the annual team report.[1]

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.[1]

Promoting Recovery and Return to Primary Care

Continuing Treatment in Secondary Care

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 above.

Consider intensive case management for people with bipolar disorder who are likely to disengage from treatment or services.[1]

Return to Primary Care

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.[1]

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.

Encourage and support the person to visit their GP and discuss the care plan before discharge and transfer.

Employment, Education and Occupational Activities

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.[1]

How to Use Medication

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

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.[1]

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.

Do not offer gabapentin or topiramate to treat bipolar disorder.

Using Antipsychotic Medication

Starting Antipsychotic Medication

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

- Weight or BMI
- Pulse
- Blood pressure
- Fasting blood glucose or HbA_{1c}
- Blood lipid profile[1]

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[1]

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.[1]

Monitoring Antipsychotic Medication

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
- Blood glucose or HbA_{1c} 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[1]

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.[1]

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.

'As required' (p.r.n.) prescriptions of antipsychotic medication should be made as described above. 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.[1]

Do not start regular combined antipsychotic medication, except for short periods (for example, when changing medication).[2]

Stopping Antipsychotic Drugs

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

Using Lithium

Starting Lithium

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

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.

Consider maintaining plasma lithium levels at 0.8–1.0 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

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

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.

Monitoring Lithium

Measure the person's plasma lithium level every 3 months for the first year.

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

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.

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 the NGC summaries of the NICE guidelines Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care (NICE clinical guideline 182) and Acute kidney injury. Prevention, detection and management of acute kidney injury up to the point of renal replacement therapy (NICE clinical guideline 169).

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.

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.

Stopping Lithium

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.

During dose reduction and for 3 months after lithium treatment is stopped, monitor the person closely for early signs of mania and depression.

Using Valproate

Starting Valproate

When starting valproate, measure the person's weight or BMI and carry out a full blood count and liver function tests.

Do not offer valproate to women of childbearing potential for long-term treatment or to treat an acute episode.

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[10] or blood dyscrasia is detected.

When prescribing valproate, be aware of its interactions with other anticonvulsants (particularly carbamazepine and lamotrigine) and with olanzapine and smoking.

Monitoring Valproate

Do not routinely measure plasma valproate levels unless there is evidence of ineffectiveness, poor adherence or toxicity.

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.

Monitor sedation, tremor and gait disturbance carefully in older people.

Stopping Valproate

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

Using Lamotrigine

Starting Lamotrigine

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.

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.

Monitoring Lamotrigine

Do not routinely measure plasma lamotrigine levels unless there is evidence of ineffectiveness, poor adherence or toxicity.

Stopping Lamotrigine

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

Recognising, Diagnosing and Managing Bipolar Disorder in Children and Young People

Recognition and Referral

Do not use questionnaires in primary care to identify bipolar disorder in children or young people.

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).

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

Diagnosis and Assessment

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.

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.

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.

When assessing suspected bipolar disorder in children or young people, follow recommendations above for adults, but involve parents or carers routinely and take into account the child or young person's educational and social functioning.

Management in Young People

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 above.

Mania

To treat mania or hypomania in young people see the NGC summary of the NICE guideline Aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder (NICE technology appraisal guidance 292)[11] and also consider the recommendations for adults above.[12] 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.

Do not offer valproate to girls or young women of childbearing potential.

Bipolar Depression

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.

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.

If there is a risk of suicide or self-harm or any other risk outlined above, carry out an urgent review and develop a risk management plan.

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

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 above[14] but refer to the BNF for children to modify drug treatments, and 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.

Long-Term Management

After the multidisciplinary review, consider a structured individual or family psychological intervention for managing bipolar disorder in young people in the longer term.

Footnotes

[1]Adapted from Psychosis and schizophrenia in adults (NICE clinical guideline 178) (see the NGC summary of the NICE guideline Psychosis and schizophrenia in adults: treatment and management).

[2]From Psychosis and schizophrenia in adults (NICE clinical guideline 178) (see the NGC summary of the NICE guideline Psychosis and schizophrenia in adults: treatment and management).

[3]Although its use is common in UK clinical practice, at the time of publication (September 2014) lithium did not have a UK marketing authorisation for this indication, although its use is common in UK clinical practice. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and

documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4]At the time of publication (September 2014) semi-sodium valproate had a UK marketing authorisation for the treatment of mania if lithium is not tolerated or is contraindicated. Sodium valproate did not have a UK marketing authorisation for this indication, although its use is common in UK clinical practice. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[5]Although its use is common in UK clinical practice, at the time of publication (September 2014), fluoxetine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[6]At the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[7]Although its use is common in UK clinical practice, at the time of publication (September 2014), lamotrigine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[8]At the time of publication (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. Sodium valproate did not have a UK marketing authorisation for this indication, although its use is common in UK clinical practice. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[9]Although its use is common in UK clinical practice, at the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[10]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.

[11]At the time of publication (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.

[12]At the time of publication (September 2014), olanzapine, risperidone, haloperidol, quetiapine, lamotrigine, lithium and valproate did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[13]At the time of publication (September 2014), olanzapine, quetiapine and lamotrigine did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Definitions:

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) pathway titled "Bipolar Disorder Overview" is available from the NICE Web site.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate assessment and management of bipolar disorder

See the "Trade-off between clinical benefits and harms" sections in the full version of the original guideline document (see the "Availability of Companion Documents" field) for benefits of specific interventions.

Potential Harms

Antipsychotics

- Antipsychotic drugs are variably associated with a range of side effects, the most problematic of which is probably weight gain. Other side effects include dry mouth, blurred vision, sedation, sexual dysfunction, extrapyramidal side effects (tremor, stiffness, restlessness, and abnormal movements) and dizziness.
- Recently, there has been increasing concern about the possible metabolic side effects of second generation antipsychotics including elevation of glucose, cholesterol and triglycerides.

Anticonvulsants

- Valproate is associated with a number of side effects including tremor, weight gain, and rarely, liver damage. It can interact with a number of commonly prescribed medicines and notably is known to decrease plasma levels of olanzapine, an antipsychotic drug that is commonly prescribed in people with bipolar disorder. Valproate is a known major human teratogen. There are significant risks associated with taking valproate during pregnancy for the unborn child, including risk of autism and its use is

best avoided completely in women of child-bearing age. Treatment with lithium and possibly valproate should not be stopped abruptly as this has been associated with early relapse.

- The main side effects associated with carbamazepine are dizziness, drowsiness, nausea and headaches, and it can cause a low white blood count, hyponatraemia (low level of sodium in the blood) and rarely, liver damage. Carbamazepine is a potent inducer of hepatic cytochrome enzymes and this can lead to increased metabolism so lower plasma levels of a number of commonly prescribed medicines. For example standard dose combined oral contraceptives can be rendered ineffective due to the increased metabolism of oestrogen. Carbamazepine is also a known human teratogen.
- Lamotrigine is associated with rash which can be serious and to minimise the risk of this occurring, the dose of lamotrigine has to be increased very slowly at the start of treatment. Lamotrigine can also cause drowsiness, dizziness and blurred vision and it can depress the bone marrow. Lamotrigine too is a known human teratogen, although it is considerably safer in pregnancy than valproate.
- Anticonvulsant drugs can interact with each other and if more than one of these drugs is prescribed, the British National Formulary (BNF) should be checked to ensure doses are adjusted if required.

Antidepressants

The selective serotonin reuptake inhibitors (SSRIs) are the most frequently prescribed antidepressants. These drugs are generally well tolerated although they can cause headache, gastrointestinal upset and sexual dysfunction. SSRIs can also cause hyponatraemia (low blood sodium) and they increase the risk of bleeds, particularly in the gastrointestinal tract.

Lithium

- Lithium has adverse effects on the kidneys, thyroid and parathyroid. Lithium is a known human teratogen, that is, it is potentially harmful to an unborn child.
- Lithium may be associated with an increased risk of reduced urinary concentrating ability (extent to which the kidneys are able to manufacture urine rich in dissolved wastes yet low in water), hormone disorders, and weight gain. Lithium has a narrow therapeutic range meaning that there is a small difference between a dose that is too low to be effective and one that is known to be toxic. Toxic levels of lithium cause a range of symptoms including confusion, neurological disorders, cardiac arrhythmias (irregular heartbeat), and, as levels rise, further convulsions, coma and death. A number of commonly used medicines can increase the concentration in the blood and potentially lead to lithium toxicity.
- Treatment with lithium and possibly valproate should not be stopped abruptly as this has been associated with early relapse.

See the "Trade-off between clinical benefits and harms" sections in the full version of the original guideline document (see the "Availability of Companion Documents" field) for harms of specific interventions.

Contraindications

Contraindications

- Valproate should not be offered to girls of child-bearing potential because of the risk of polycystic ovary syndrome and risks to the unborn child.
- The Guideline Development Group (GDG) determined that the long-term use of medication was more likely to cause harm than do good for most children and young people. They therefore determined that pharmacological interventions should not be used for the long-term management of bipolar disorder in children and young people.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.
- Patients and healthcare professionals in England have rights and responsibilities as set out in the National Health Service (NHS) Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make in for med decisions about their care and treatment, in partnership with their healthcare professionals. If someone does not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent, the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards.
- NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in Patient experience in adult NHS services (NICE clinical guideline 138).
- NICE has also produced guidance on the components of good service user experience. All healthcare professionals and social care practitioners working with people using adult NHS mental health services should follow the recommendations in Service user experience in adult mental health (NICE clinical guideline 136).
- If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's Transition: getting it right for young people.
- Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with bipolar disorder. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Implementation of the Guideline

Description of Implementation Strategy

Implementation tools and resources to help users put the guideline into practice are also available on the National Institute for Health and Care Excellence (NICE) Web site (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Care for Adults, Children and Young People Across All Phases of Bipolar Disorder

Support for Carers of People with Bipolar Disorder

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.[1]

Recognising and Managing Bipolar Disorder in Adults in Primary Care

Managing Bipolar Disorder in Primary Care

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 high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with recommendations in the NICE guideline Depression. The treatment and management of depression in adults (NICE clinical guideline 90).
- 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.

Managing Mania or Hypomania in Adults in Secondary Care

Pharmacological Interventions

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.

If the person is already taking lithium, check plasma lithium levels to optimise treatment. Consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person's preference and previous response to treatment.

Managing Bipolar Depression in Adults in Secondary Care

Psychological Interventions

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 high-intensity psychological intervention (cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy) in line with recommendations in the NICE guideline Depression. The treatment and management of depression in adults (NICE clinical guideline 90).
- 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.

Pharmacological Interventions

If a person develops moderate or severe bipolar depression and is not taking a drug to treat their bipolar disorder, offer fluoxetine[2] combined with olanzapine[3], 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[4] 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 "Major Recommendations" field.

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[2] combined with olanzapine[3] or add quetiapine, depending on the person's preference and previous response to treatment.

- If the person prefers, consider adding olanzapine (without fluoxetine) or lamotrigine[4] 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 on using lithium, antipsychotics and lamotrigine.

Managing Bipolar Disorder in Adults in the Longer Term in Secondary Care

Psychological Interventions

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.

Pharmacological Interventions

Offer lithium as a first-line, long-term pharmacological treatment for bipolar disorder and:

- If lithium is ineffective, consider adding valproate.[5]
- If lithium is poorly tolerated, or is not suitable (for example, because the person does not agree to routine blood monitoring), consider valproate or olanzapine[6] instead or, if it has been effective during an episode of mania or bipolar depression, quetiapine.
- Discuss with the person the possible benefits and risks of each drug for them.

Recognising, Diagnosing and Managing Bipolar Disorder in Children and Young People

Recognition and Referral

Diagnosis and Assessment

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.

Management in Young People

Mania

To treat mania or hypomania in young people see the NGC summary of the NICE guideline Aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder (NICE technology appraisal guidance 292)[7] and also consider the recommendations for adults[8]. 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.

Do not offer valproate to girls or young women of childbearing potential.

Bipolar Depression

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.

Footnotes

[1]Adapted from Psychosis and schizophrenia in adults (NICE clinical guideline 178) (see the NGC summary of the NICE guideline Psychosis and schizophrenia in adults: treatment and management).

[2]Although its use is common in UK clinical practice, at the time of publication (September 2014), fluoxetine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[3]At the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4]Although its use is common in UK clinical practice, at the time of publication (September 2014), lamotrigine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[5]At the time of publication (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. Sodium valproate did not have a UK marketing authorisation for this indication, although its use is common in UK clinical practice. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[6]Although its use is common in UK clinical practice, at the time of publication (September 2014), olanzapine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[7]At the time of publication (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.

[8]At the time of publication (September 2014), olanzapine, risperidone, haloperidol, quetiapine, lamotrigine, lithium and valproate did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Mental Health. Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Sep. 58 p. (Clinical guideline; no. 185).

Adaptation

The Guideline Development Group (GDG) adapted recommendations from Psychosis and Schizophrenia in Adults where appropriate:

- NICE. Psychosis and schizophrenia in adults. NICE Clinical Guideline 178. 2014. Available from: http://guidance.nice.org.uk/CG178.

Date Released

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Guideline Developer(s)

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Financial Disclosures/Conflicts of Interest

To minimise and manage any potential conflicts of interest, and to avoid any public concern that commercial or other financial interests have affected the work of the Guideline Development Group (GDG) and influenced guidance, members of the GDG must declare as a matter of public record any interests held by themselves or their families which fall under specified categories. These categories include any relationships they have with the healthcare industries, professional organisations and organisations for people with bipolar disorder and their families/carers.

Individuals invited to join the GDG were asked to declare their interests before being appointed. To allow the management of any potential conflicts of interest that might arise during the development of the guideline, GDG members were also asked to declare their interests at each GDG meeting throughout the guideline development process. The interests of all the members of the GDG are listed in Appendix 2 in the full version of the original guideline document (see the "Availability of Companion Documents" field), including interests declared prior to appointment and during the guideline development process.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Mental Health. Bipolar disorder: the management of bipolar disorder in adults, children, and adolescents, in primary and secondary care. Leicester (UK): British Psychological Society, Royal College of Psychiatrists; 2006. 592 p.

This guideline meets NGC's 2013 (revised) criteria.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site.

Availability of Companion Documents

The following are available:

- Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. Full guideline. London (UK): National Institute for Health and Care Excellence; 2014 Apr. 363 p. (Clinical guideline; no. 185). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site.
- Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. Appendices. London (UK): National Institute for Health and Care Excellence; 2014 Apr. 70 p. (Clinical guideline; no. 185). Electronic copies: Available from the NICE Web site.
- Bipolar disorder. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2014 Sep. (Clinical guideline; no. 185). Electronic copies: Available from the NICE Web site.
- Bipolar disorder. Clinical audit tool. London (UK): National Institute for Health and Care Excellence; 2014 Sep. (Clinical guideline; no. 185). Electronic copies: Available from the NICE Web site.
- Bipolar disorder. Costing statement. London (UK): National Institute for Health and Care Excellence; 2014 Sep. 7 p. (Clinical guideline; no. 185). Electronic copies: Available from the NICE Web site.
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Electronic copies: Available from the NICE Web site.

Patient Resources

The following is available:

- Bipolar disorder. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Sep. 21 p. Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download as a Kindle or EPUB ebook from the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on June 19, 2006. This NGC summary was updated by ECRI Institute on April 1, 2009. This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on January 8, 2010 following the U.S. Food and Drug Administration advisory on Valproate sodium. This summary was updated by ECRI Institute on March 18, 2010, following the U.S. Food and Drug Administration advisory on Zyprexa (olanzapine). This summary was updated by ECRI Institute on September 15, 2010 following the U.S. Food and Drug Administration advisory on Lamictal (lamotrigine). This summary was updated by ECRI Institute on May 20, 2011 following the U.S. Food and Drug Administration advisory on antipsychotic drugs. This summary was updated by ECRI Institute on September 12, 2011 following the U.S. Food and Drug Administration advisory on Celexa (citalopram hydrobromide). This summary was updated by ECRI Institute on October 31, 2014.

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