

Bipolar Disorder – Medication Pathway for Adults

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Quick Reference Guide

This Pathway provides guidance on the safe and appropriate use of medications for bipolar disorder. It is not a substitute for sound clinical decision making and should be viewed in line with national and BNF guidance.

Click on the 'buttons' on this page to navigate the document.
Use "Ctrl+F" and type in keywords to quickly search the document.

Any drug marked with an **(N)** is recommended by NICE guidelines. As you move through the steps, some choices may be off-label (see Licensed Indications).

Related Guidance

Starting Medication

The Prescribing and Initiation of Medicines policy covers all the key aspects to consider before prescribing

Communication and Transfer of Prescribing

The Safe Transfer of Prescribing Guidance covers key aspects of communication with GPs and broad rules of transfer of Specialist Initiation and Shared Care medicines

Further guidance

Links to the trust policies and guidance: [Medicines Optimisation Interactive Guide](#)
[A bespoke version is available for primary care - here](#)

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Key Prescribing Considerations

- Consider non-pharmacological options at all steps
- Utilise HIE (Health Information Exchange) viewer to view medical problems and medication by the GP (request this from the GP if not available). Consider comorbid physical health issues before prescribing
- Be aware of potential drug interactions when prescribing combination therapy.
- Ensure pre-treatment and ongoing monitoring is carried out per [Trust psychotropic medication monitoring guidance](#), including annual physical health review as per [LESTER tool](#).
- Ensure prescribing decisions account for advance directives, the person's preference and clinical context (including physical comorbidity, previous response to treatment and side effects) where possible. Ensure the person is included in decisions around their medication. [[Psymatik](#); [Choice and Medication](#) (TEWV staff only)]
- Bipolar disorder is a lifelong condition. Consider the teratogenicity of medication before prescribing to patients of childbearing potential (see also [perinatal prescribing guideline](#))
- Note [BNF warning](#) re: antiepileptics and risk of suicidal thoughts and behaviour
- Consider toxicity in overdose when prescribing during periods of high suicide risk. Assess the need to limit the quantity of medication prescribed (e.g. 7-day prescriptions) to reduce the risk. [See Medication Safety Bulletin](#) for further guidance

People aged over 65 years

Any doses stated in this guidance refer to adult dosing. The prescriber should consult the BNF for dose advice for older patient groups. This patient group has an increased risk of drug-drug interactions and increased sensitivity to anticholinergic effects (which can decrease cognitive function and increase risk of falls). Ensure comorbidities are recognised & treated.

- Refer to [MHRA advice](#) and [Trust guidance](#) around the use of **Valproate in anyone under 55**. Valproate must not be started unless two independent specialists agree that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply. The appropriate risk acknowledgement forms must be completed with the patient prior to prescribing. NB Valproate is **AMBER shared care** in those of childbearing potential including women and those assigned female at birth.
- Please refer to relevant local [Lithium shared care](#) to support Lithium prescribing and transfer to primary care. [A further supplement to support lithium prescribing can be found - here](#)
- Please note that for bipolar disorder, Cariprazine is **BLACK** (non formulary) as per the safe transfer of prescribing guidelines. This requires an application which must be approved by a panel, and prescribing cannot be transferred to primary care.
- TEWV Level 1 & 2 NMPs cannot initiate lithium or clozapine. Level 2 NMPs may adjust clozapine and lithium doses if this is specified in their scope of practice and the consultant is aware of dose changes.

Deprescribing

If stopping long-term pharmacological treatment:

- Discuss how to recognise early signs of relapse and what to do if symptoms recur
- Stop treatment gradually and monitor for signs of relapse
- Discontinuation of any medicines should normally be tapered over at least 4 weeks, preferably longer
- The risk of relapse remains even after years of sustained remission, and may be increased upon stopping lithium

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Bipolar Disorder – Mania/Hypomania Acute Management

FIRST LINE OPTIONS

If appropriate:

- **STOP ANTIDEPRESSANT**
- **OPTIMISE MOOD STABILISER**

THEN:

Consider (in any order, based on patient preference/past history of response/non-response):

- **OLANZAPINE (N)** Initially 10-15mg OD; max 20mg/day
- **QUETIAPINE (IMMEDIATE RELEASE) (N)** Initiate 50mg BD; ↑ by 50mg BD until day 4, then ↑ by 200mg/day according to response. Max 800mg/day
- **QUETIAPINE MR (N)** if faster titration/response required 300 mg OD for day 1, 600 mg OD for day 2. Then adjust according to response, usual dose 400–800 mg OD
- **RISPERIDONE (N)** 2mg daily; ↑ steps of 1mg/day if required. Max 6mg/day
- **HALOPERIDOL (N)** 2-10mg/daily (1-2 divided doses); adjust every 1-3 days; max 15mg/day
- **ARIPIPRAZOLE** 15mg/day; increased to 30mg/day if required; consider if limited by comorbidities

IF FIRST ANTIPSYCHOTIC POORLY TOLERATED (at any dose) OR INEFFECTIVE (at max. licensed dose) OFFER AN ALTERNATIVE FROM THE LIST ABOVE (N)

SECOND LINE OPTIONS

LITHIUM (N)

- **ADD** if alternative antipsychotic insufficient at max dose
- Adjust dose to serum lithium concentration
- Target: 0.8-1.0mmol/L

THIRD LINE OPTIONS

VALPROATE (N) 750mg/day (2-3 divided doses); usual dose 1-2g/day
Only when there is no other effective or tolerated treatment. Requires independent review and signed agreement by two specialists for initiation in those <55 years old
CONTRAINDICATED IN PATIENTS OF CHILDBEARING POTENTIAL

ECT (N) severe or treatment-resistant mania, severe mania in pregnancy or expressed preference

ADJUNCT MEDICINES – SHORT TERM ONLY

See [Oral PRN guidelines](#) and [Rapid Tranquilisation policy](#) for further details

Aim to calm agitated and overactive patients, help promote sleep

Discontinue as soon as symptoms improve

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BAP (2016)	CANMAT (2023) Bipolar I*	
<u>Highest efficacy:</u> Haloperidol – EPSEs limit use Olanzapine Quetiapine Risperidone (Dopamine antagonists most effective short-term)	<u>First line (Hierarchical):</u> MONOTHERAPY: Lithium Quetiapine Valproate Aripiprazole Risperidone Cariprazine**	COMBINATIONS: Quetiapine + Lithium/Valproate Aripiprazole + Li/Val Risperidone + Li/Val
Lithium and Valproate (Augmentation if appropriate) Start if considering longer term	<u>Second line (Hierarchical):</u> Olanzapine Carbamazepine Olanzapine + Li/Val	Li + Val Haloperidol ECT
	<u>Third line:</u> Carbamazepine + Li/Val Chlorpromazine Clozapine Haloperidol + Li/Val	rTMS Tamoxifen** Tamoxifen** + Li/Val
	<u>Not recommended:</u> Allopurinol Eslicarbazepine Gabapentin Lamotrigine	Omega-3 Fatty Acids Topiramate Zonisamide

*NB medications which are not commercially available in the UK have been removed from this chart

**Would require SAF prior to prescribing

Medication-specific advice

- Note that most of the evidence which forms national and international guidelines generally relates to treatment of Bipolar I . The treatment of Bipolar II and hypomania has been less well-studied.
- UK guidelines have not been updated recently, as British Association of Psychopharmacology bipolar disorder guideline were last updated in 2016 and NICE guidelines for bipolar disorder were last fully updated in 2014.
- Therefore, CANMAT guidelines have been included because these have been most recently updated (2023) and reflect the latest evidence and network meta-analyses.
- NB CANMAT guidelines consider efficacy alongside long-term tolerability in its ranking of medications, which may explain some discrepancies between UK and these guidelines. First and second-line treatments are ranked hierarchically
- Haloperidol is superior in efficacy to other agents, but there is an increased risk of adverse events including EPSE compared to use in schizophrenia. Haloperidol can also cause a switch to depression from mania unlike lithium and valproate – this leads to downgrading of its place in therapy in other guidelines compared with NICE/BAP.

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Acute Manic Episode

Prescribing Considerations

- Choice of medication should be balanced between the benefits of medication efficacy and the risks of adverse effects.
- Consider any advance statements, person's preferences and clinical context (including physical comorbidities, previous response to treatment, side effects and family plans)
- Consider the need for prophylactic treatment after the acute phase has ended when selecting an anti-manic drug
- Combination therapy may be considered in a severe manic episode
- Assess the contribution of substance use to a manic/hypomanic episode and consider if medically assisted withdrawal is required

Hypomania

- Most standard antimanic agents have not been studied in hypomania. However, clinical experience suggests that antimanic agents can be effective.

Use of other medications

- Short-term parenteral administration of antipsychotics and benzodiazepines may be necessary in the early stages of treatment. Switch to oral at the earliest possible opportunity.
- Short-term benzodiazepine/hypnotic use may be required to promote sleep for agitated, overactive patients
- Antidepressant drugs (drugs approved for treatment of unipolar depression) should be tapered and discontinued during a manic episode
- Support people to discontinue substances such as stimulants (including caffeine) and alcohol. Any medicine used as an adjunct to promote sleep or sedation should be discontinued as soon as symptoms improve

If already taking long-term treatment

- If current presentation is due to inadequate symptom control, ensure that treatment doses are optimised
- If current episode is due to poor adherence, establish and address reasons for this.
- If non-adherence is deliberate, long-term treatment with lithium may not be appropriate due to increased relapse risk upon abrupt withdrawal

Mixed Affective State

- Follow mania recommendations if the person is presenting with both manic and depressive symptoms. Monitor closely for the emergence of depression. Do not offer lamotrigine monotherapy to treat mania, because this lacks anti-manic properties.

Refractory/Difficult to Treat Mania

- Clozapine has been used in refractory mania; this is an off-label indication. It is pre-approved in certain patient groups – please check the unlicensed/off-label policy prior to prescribing
- ECT should only be considered if the mania is severe, difficult to treat, if this is the person's preference or they are pregnant
- LAI such as risperidone, paliperidone, haloperidol and aripiprazole are unsuitable for the acute treatment of mania, as there is a time lag (weeks to months) for the full therapeutic effect.

Ongoing Treatment following Symptom Resolution

- Drug discontinuation should be planned in relation to the need for long-term maintenance treatment (i.e. with a mood stabiliser).
- Discuss with the person (and their carers if appropriate) whether to continue their current antipsychotic treatment for mania or to start a long-term mood stabiliser within 4 weeks of symptom resolution.
- If the person decides to continue their previous treatment for mania, offer it for a further 3-6 months then review

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Bipolar Disorder – Depression Acute Management

FIRST LINE OPTIONS

If appropriate:

- **OPTIMISE MOOD STABILISER**

Then consider any of the following based on patient preference (*listed in hierarchical order based on level of evidence in Bipolar I*):

- **QUETIAPINE (N) (IMMEDIATE RELEASE)**
Titrate to 300mg over 4 days, then adjust according to response. Max 600mg/day
- **QUETIAPINE (MR) (N)** if faster titration/response required 300 mg OD for day 1, 600 mg OD for day 2. Then adjust according to response, usual dose 400–800 mg OD
- **OLANZAPINE** 5-20mg/day; Max 20mg/day + **FLUOXETINE (N)** 20mg daily; Max 60mg/day
- **OLANZAPINE (N)** 10mg daily; max 20mg daily

SECOND LINE OPTIONS

IF INEFFECTIVE/NOT TOLERATED, CONSIDER

- **LURASIDONE** 37mg daily for a month, then increase to 74mg daily
Must be taken with a meal (>350kcal) for optimal absorption
- **LAMOTRIGINE (N)** Slow titration as per BNF/SmPC to 200mg/day due to risk of rash/SJS; max 400mg/day; **unsuitable if rapid response required**
NB lower dose needed if prescribed valproate.
CAN BE USED FIRST LINE IF PATIENT PREFERS
- Take a one-off Lamotrigine level for women and birthing people (of childbearing age) when at a stable dose as a baseline.
 - NICE recommends monitoring levels throughout pregnancy. NB Lamotrigine levels decrease from first trimester; effect most pronounced in second and third trimester

THIRD LINE OPTIONS

IF INEFFECTIVE/ NOT TOLERATED CONSIDER

CARIPRAZINE – could be applied for if clinically appropriate; requires panel approval

ECT

- Poor oral intake, high suicide risk or patient preference

Prescribing antidepressants in bipolar depression

- Avoid antidepressants without a mood stabiliser as there is a risk of “switching” to mania and inducing rapid cycling, particularly in bipolar I
- Studies suggest mood stabilisers alone are as effective as a mood-stabiliser-antidepressant combination; evidence for antidepressants in bipolar depression is not as conclusive as in unipolar
- SSRIs preferred over TCA’s, MAOIs and SNRIs (dual action antidepressants are more likely to induce a manic switch)

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Supporting Information – Acute Depressive Episode

BAP (2016)	CANMAT (2023) Bipolar I*		CANMAT (2023) Bipolar II*	
QUETIAPINE has best evidence. Then OLANZAPINE + FLUOXETINE (monotherapy less so) And LURASIDONE	<u>First line - Hierarchical</u> Quetiapine Lurasidone + li/dvp Lithium		<u>First line - Hierarchical</u> Quetiapine	
Antidepressants may be effective but evidence base is poor, and prescription of an antimanic is also required Increased risk of manic switch with a TCA/SNRI compared to SSRI	<u>Second line - Hierarchical</u> Valproate SSRI/Bupropion** (adj) ECT Olanzapine + fluoxetine		<u>Second line - Hierarchical</u> Lithium Lamotrigine Bupropion* (adj) ECT Sertraline Venlafaxine	
LAMOTRIGINE has evidence in acute depression; best when combined with an anti-manic ECT	<u>Third line</u> Aripiprazole (adj) Carbamazepine Levothyroxine** (adj) Light therapy with or without sleep deprivation (adj)	Modafinil** (adj) N-acetylcysteine** (adj) Olanzapine Pramipexole** (adj) rTMS (adj) SNRI/MAOI (adj)	<u>Third line</u> Agomelatine** (adj) Bupropion** (adj) Valproate N-Acetylcysteine**	Pramipexole** (adj) T3** and T4** (adj) Tranylcypromine**
Poor evidence: LITHIUM, VALPROATE, CARBAMAZEPINE	<u>Not recommended</u> Antidepressant monotherapy Aripiprazole	Lamotrigine + folic acid Mifepristone		

*NB medications which are not commercially available in the UK have been removed from this chart

**Medication requires approval prior to prescribing

Medication-specific advice

- Note that most of the evidence which forms national and international guidelines generally relates to treatment of Bipolar I. The treatment of Bipolar II has been less well-studied.
- UK guidelines have not been updated recently, as BAP was last updated in 2016 and NICE guidelines for bipolar disorder were last fully updated in 2014.
- Therefore, CANMAT guidelines have been included because these have been most recently updated (2023) and reflect the latest evidence and network meta-analyses.
- NB CANMAT guidelines consider efficacy alongside long-term tolerability in its ranking of medications, which may explain some discrepancies between UK and these guidelines. First and second-line treatments are ranked hierarchically.

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Acute Depressive Episode

- Note that most of the evidence which forms national and international guidelines generally relates to treatment of Bipolar I depression. The treatment of Bipolar II has been less well-studied.
- There is a risk of a switch to mania or mood instability during treatment for depression. Whilst this will often reflect the natural history of the disorder; it may be increased by monotherapy with antidepressants.

Medication-specific advice:

- Please see [here](#) for ranking of evidence for medication use in bipolar depression.

Antidepressants in Bipolar depression

- Although NICE does not differentiate between bipolar I and II, there is more evidence regarding use of antidepressant drugs in bipolar II. In clinical practice, antidepressant drugs are used more often in this population.
- Dual action monoamine reuptake inhibitors such as SNRIs and TCAs carry a greater risk of manic switch than single action drugs such as SSRIs.
- Antidepressants may be continued longer term for those who have previously relapsed upon withdrawal of antidepressants.

Lithium

- Lithium may be considered when depressive symptoms are less severe with a view to long-term treatment
- Avoid sudden dose changes and switches

Depressive Relapse on previous treatment

- If a patient experiences an acute depressive episode whilst taking long-term treatment:
 - Check current medication choice protects against manic relapse
 - Check adherence (including lithium levels if prescribed)
 - Check dose is optimised

Following this, consider initiation of additional treatment per guidance.

Difficult to treat Bipolar Depression

- When symptoms have failed to remit after 8 weeks of at least either two different monotherapy trials or a monotherapy and combination trial, consider augmentation strategies with treatments that have evidence in bipolar depression before considering unipolar strategies.
- Common augmentation strategies include lithium + quetiapine. Thyroid augmentation is uncommon.
- Consider ECT for patients with high suicidal risk, treatment resistance, psychosis, severe depression during pregnancy or life-threatening inanition. See NICE guidance for ECT.

Long term Treatment Plan

- Drug discontinuation should be planned in relation to the need for long term maintenance treatment. Within four weeks of resolution of symptoms, discuss with the person, and their carers if appropriate, whether to continue with current treatment for bipolar depression or start long-term treatment. If the person decides to continue treatment for bipolar depression, offer it for a further 3-6 months then review.

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Bipolar Disorder – Maintenance Treatment

FIRST LINE/GOLD STANDARD

LITHIUM

- Refer to relevant [Lithium shared care](#) prior to prescribing and throughout treatment
 - A further supplement to support lithium prescribing can be found [here](#)
- Consider long-term adherence. May be less suitable for patients with ongoing adherence issues due to increased risk of relapse when stopped abruptly.
- Offer MHRA purple lithium book
- Consider if the person is of childbearing potential; will require preconception advice and discussion prior to pregnancy. Lithium in pregnancy pathway [\[link\]](#)
- Levels 0.4-0.8mmol/L optimal for prophylaxis; 0.6-0.8mmol/L for mania prophylaxis

IF POORLY TOLERATED/UNSUITABLE CONSIDER:

OLANZAPINE if previously effective; may be better for mania prophylaxis

or

QUETIAPINE if previously effective; evidence for prophylaxis of manic and depressive episodes

or

LURASIDONE if previously effective for bipolar depressive symptoms

or

ARIPIPRAZOLE if previously effective

or

RISPERIDONE if previously effective

or

ANTIPSYCHOTIC LAIs if patient preference

IF LITHIUM INEFFECTIVE ADD:

ATYPICAL ANTIPSYCHOTIC

Choice based on previous response in acute phase (*clozapine may be considered in refractory rapid cycling*)

IF ADHERENCE IS A CONCERN:

Consider **PALIPERIDONE LAI**, **ARIPIPRAZOLE LAI** or **HALOPERIDOL LAI** according to previous treatment and symptom profile if adherence to oral medication is erratic or injection preferred

IF ALL OTHER OPTIONS INEFFECTIVE/POORLY TOLERATED/UNSUITABLE, REPLACE WITH:

VALPROATE *Use only if all other options ineffective/not tolerated; requires independent agreement and signature by two specialists for initiation in those <55 years old*

CONTRAINDICATED IN PATIENTS OF CHILDBEARING POTENTIAL (including women and those assigned female at birth) [\[MSS13\]](#)

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Supporting Information – Long-term Management

BAP (2016) (no particular order)	CANMAT (2023) Bipolar I*	CANMAT (2023) Bipolar II
LITHIUM – maintain a concentration of 0.6-0.8mmol/L for mania prophylaxis LAMOTRIGINE – consider if predominantly depressive burden	<u>First line - Hierarchical</u> Lithium Quetiapine Valproate Lamotrigine Quetiapine + Li/Val Aripiprazole + Li/Val Aripiprazole Aripiprazole LAI	<u>First line - Hierarchical</u> Quetiapine Lithium Lamotrigine
DOPAMINE RECEPTOR ANTAGONISTS – Effect predicted response in acute treatment VALPROATE – less effective for relapse prevention	<u>Second line - Hierarchical</u> Olanzapine Risperidone LAI Risperidone LAI (adj) Carbamazepine Paliperidone** >6mg Lurasidone + Li/Val	<u>Second line</u> Venlafaxine
ANTIDEPRESSANTS may be continued long-term when risk of severe depressive relapse is high. Use in combination with an antimanic drug	<u>Third line</u> Aripiprazole + Lamotrigine (adj) Clozapine** (adj) Gabapentin** (adj) Olanzapine + Fluoxetine	<u>Third line</u> Carbamazepine Valproate Escitalopram Fluoxetine Other antidepressants Risperidone
CARBAMAZEPINE – less effective for relapse prevention, interferes with drug metabolism	<u>Not recommended</u> Perphenazine TCA's	

Medication-specific advice

- Note that most of the evidence which forms national and international guidelines generally relates to treatment of Bipolar I . The treatment of Bipolar II has been less well-studied.
- UK guidelines have not been updated recently, as BAP was last updated in 2016 and NICE guidelines for bipolar disorder were last fully updated in 2014.
- Therefore, CANMAT guidelines have been included because these have been most recently updated (2023) and reflect the latest evidence and network meta-analyses.
- NB CANMAT guidelines consider efficacy alongside long-term tolerability in its ranking of medications, which may explain some discrepancies between UK and these guidelines. First and second-line treatments are ranked hierarchically.

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**Would require SAF prior to prescribing

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Long-term Bipolar Management

Maintenance treatment should be considered in most people, especially if they have frequent episodes associated with significant dysfunction and risks. Continuous rather than intermittent treatment with medications is recommended to prevent new mood episodes.

Preventing Relapse/Early Warning Signs

Short-term add-ons may be needed when an acute stressor is imminent or present, early symptoms of relapse (especially insomnia) are present or anxiety becomes prominent. Consider supplying these prospectively with instructions on how and when to use. Higher doses of long-term treatments may also be effective instead of add-ons.

Adjunctive psychotherapy should be considered to address subthreshold symptoms.

Lithium

Lithium should be considered as the first line medication for prevention because in addition to relapse prophylaxis, it can reduce the risk of suicide and is the only medication to reduce the risk of Alzheimer's dementia.

If a medicine leads to prompt remission from a recent mood episode, it may be favoured as long-term monotherapy. However, this may lead to preferential use of antipsychotics due to their short-term efficacy. Lithium should be actively considered as a better alternative due to its additional long-term actions.

Refer to relevant [Lithium shared care](#) for information around initiation, including baseline monitoring, counselling and transfer to primary care when stable. Patients should be added to relevant lithium register and provided with a purple lithium book upon initiation. Further prescribing advice can be found [here](#).

When Lithium is unsuitable

Consider alternative treatment when lithium is ineffective, poorly tolerated or patients have poor oral and/or monitoring adherence. Note that valproate monotherapy is less effective than lithium and the lithium and valproate combination.

Consider antipsychotic depots if anti-manic prophylaxis is required and oral adherence is erratic. Avoid LAIs which can raise prolactin in patients (particularly female/AFAB) who have not reached their peak bone density.

If clozapine was effective in refractory mania, consider long-term continuation. Clozapine may have some significant mood stabilising effects in treatment-resistant bipolar or schizoaffective patients.

Poor response to long-term monotherapy

If a patient continues to experience sub-threshold depressive symptoms or relapses despite adequate medication adherence, consider long term combination treatment.

- Where the burden of disease is mania, combine two anti manic drugs e.g. Lithium, antipsychotic or valproate (prescribing as per MHRA guidance)
- Where the burden of disease is depressive, a combination of lithium, lamotrigine, quetiapine, lurasidone or olanzapine may be more appropriate.

The role of antidepressants in long term treatment is not established, but they appear to be effective in a minority of patients in the long term.

Maintenance ECT may be considered for patients who respond to ECT during an acute episode but respond poorly to all oral agents.

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Rapid Cycling Classification

Rapid cycling Bipolar Disorder is defined as four (or more) clear switches in polarity of mood in a 12-month period (i.e. [hypo]mania and depression). It is generally less responsive to pharmacological treatment than non-rapid cycling bipolar illness, and higher doses of medications are often seen.

Initial Steps

If the person's bipolar course is rapid cycling, the following steps are suggested:

- Identify and treat/manage conditions that may contribute to cycling
 - Hypothyroidism (including thyroid antibodies)
 - Alcohol
 - Substance use
 - External stressors
 - Menstrual cycle/hormonal component
- Consider tapering and stopping antidepressants and stimulants that may contribute to cycling

Medication treatment options

There is no formal first-line recommendation or combination for rapid cycling bipolar; continued prescribing depends on how the person has responded to treatments for previous mood episodes. Many patients require combinations of medications.

e.g. Lithium + valproate;
Lithium + Lamotrigine;
Lithium/Valproate + quetiapine/olanzapine/aripiprazole

Quetiapine has the best supporting data for use in rapid cycling but there is no evidence of superiority over aripiprazole or olanzapine.

Other tips:

- Anti-cycling effects of medications should be evaluated over periods of 6 months or more
- Discontinue ineffective treatments to avoid unnecessary polypharmacy
- Minimise adverse drug reactions to improve adherence
- Clozapine is approved for off-label use in TEWV treatment of refractory rapid cycling bipolar disorder.

NB response to treatment may be idiosyncratic

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Supporting Information – Guidelines for Quetiapine XL use

Quetiapine is available as immediate-release (standard) and modified-release (XL) tablets.

The drug tariff price of generic immediate-release quetiapine tablets is considerably lower than modified-release quetiapine tablets (Seroquel® XL, Biquelle XL, etc). Therefore, the modified-release tablets should only be used when they offer a **clear clinical benefit** over the standard tablets.

This may be the case in:

- Patients who would benefit from a faster titration before switching to immediate-release tablets (see table)
- Patients at high risk of adverse events that are related to peak blood levels (e.g. orthostatic hypotension) – the modified-release formulation may be the preferred option for initiation of therapy (see table)
- Patients on treatment who are experiencing side-effects that are related to peak blood levels
- Patients who are poorly adherent to treatment and would benefit from once-daily dosing

N.B. quetiapine XL is not suitable for covert administration to adherent. The modified-release nature of the formulation is completely dependent upon the tablet being swallowed whole. If tablets need to be crushed, then immediate-release tablets should be used.

	Using immediate-release tablets				Using modified-release tablets
	Schizophrenia		Acute Mania		Schizophrenia or acute mania
	AM	PM	AM	PM	Once daily
Day 1	25mg	25mg	50mg	50mg	300mg XL
Day 2	50mg	50mg	100mg	100mg	600mg XL
Day 3	100mg	100mg	150mg	150mg	Switch to twice daily immediate release tablets and adjust dose according to response
Day 4	150mg	150mg	200mg	200mg	As above
Day 5 onwards	Adjust dose according to response; usual range 300-450mg daily in two divided doses. Max 750mg daily		Adjust dose according to response (max 200mg increments); usual range 400-800mg daily in two divided doses. Max 800mg daily		As above

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