
# PMB definition guidelines for bipolar mood disorder

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*Disclaimer:*

*The bipolar disorder benefit definition has been developed for the majority of standard patients. These benefits may not be sufficient for outlier patients. Therefore, regulation 15h and 15I may be applied for patients who are inadequately managed by the stated benefits.*

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Abbreviations

| | |
|---|---|
| ALT | Alanine aminotransferase |
| APA | American Psychiatry Association |
| AST | Aspartate transaminase |
| BD | Bipolar Disorder |
| CMS | Council for Medical Schemes |
| CT | Computed tomographic |
| DSM | Diagnostic and Statistical Manual |
| DTPs | Diagnosis Treatment Pairs |
| ECG | Electrocardiogram |
| EEG | Electroencephalogram |
| EUC | Electrolytes, urea and creatinine |
| GGT | Gamma glutamyl transferase |
| GP | General Practitioner |
| HDL | High-density lipoprotein |
| HIV | Human Immunodeficiency virus |
| ICD | International Classification of Diseases |
| IM | Intramuscular |
| ISBD | International Society for Bipolar Disorder |
| LDL | Low-density lipoprotein |
| MDD | Major Depressive Disorder |
| MRI | Magnetic resonance imaging |
| PMB | Prescribed minimum benefit |
| SADAG | South African Depression and Anxiety Support Group |
| SNRIs | Serotonin and Noradrenaline Reuptake Inhibitors |
| SSRIs | Selective Serotonin Reuptake Inhibitors |
| TCAs | Tricyclic antidepressants |
| Trig | Triglycerides |
| TSH | Thyroid stimulating hormone |
| U&E | Urea and electrolytes |
| UD | Unipolar Depression |

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## Introduction

1.1. The legislation governing the provision of the prescribed minimum benefits (PMBs) is contained in the regulations enacted under the Medical Schemes Act, 1998 (Act No. 131 of 1998). In respect of some of the diagnosis treatment pairs (DTPs), medical scheme beneficiaries find it difficult to know their entitlements in advance. In addition, medical schemes interpret these benefits differently, resulting in a lack of uniformity of benefit entitlements.

1.2. The benefit definition project is coordinated by the CMS, with the aim to define the PMB package; and to guide the interpretation of the PMB provisions by relevant stakeholders. The guidelines are based on the available evidence of clinical and cost effectiveness, taking into consideration affordability constraints and financial viability of medical schemes in South Africa.

## 2. Scope and Purpose

2.1. This is a recommendation for the diagnosis, treatment and care of individuals with bipolar mood disorder in any clinically appropriate setting as outlined in the Medical Schemes Act.

2.2. The purpose of this guide is to improve clarity in respect of funding decisions by medical schemes, taking into consideration evidence-based medicine, affordability and in some instances, cost-effectiveness.

Table 1: Applicable PMB code for bipolar mood disorder

| *PMB Code* | *PMB Description* | *Treatment Component* |
|---|---|---|
| 902T | Major affective disorders, including unipolar and bipolar depression. | Hospital-based management up to 3 weeks/year (including inpatient electro-convulsive therapy and inpatient psychotherapy) or outpatient psychotherapy of up to 15 contacts. |

Bipolar Mood Disorder is also included in the Chronic Disease List (CDL).

Table 2: Applicable ICD 10 codes for bipolar mood disorder

| ICD10 code | WHO description |
|---|---|
| F31.0 | Bipolar affective disorder, current episode hypomanic |
| F31.1 | Bipolar affective disorder, current episode manic without psychotic symptoms |
| F31.2 | Bipolar affective disorder, current episode manic with psychotic symptoms |
| F31.3 | Bipolar affective disorder, current episode mild or moderate depression |
| F31.4 | Bipolar affective disorder, current episode severe depression without psychotic symptoms |
| F31.5 | Bipolar affective disorder, current episode severe depression with psychotic symptoms |
| F31.6 | Bipolar affective disorder, current episode mixed |
| F31.7 | Bipolar affective disorder, currently in remission |
| F31.8 | Other bipolar affective disorders |
| F31.9 | Bipolar affective disorder, unspecified |

## 3. Defining bipolar disorder

3.1. Bipolar disorder (BD) is a brain disorder that causes changes in a person's mood, energy levels and ability to function. Bipolar disorder is characterised by episodes of mania, hypomania or depression. A person living with bipolar disorder will have severe mood swings which can last several weeks, months or a long period of time. The Royal College of Psychiatrists states that feelings include severe depression, feelings of extreme happiness or a combination of depression with restlessness (Scott et al., 2016).

3.2. A manic episode is an emotional state where a person is unusually irritable in an extreme way, most of the day for most days, has more energy than usual for at least one week. The change in mood is uncharacteristic of the person's usual state or behaviour. Changes in mood is severe enough to cause difficulties or impairment in the person's ability to function at work, with friends or family or other important areas in their life.

3.3. A hypomanic episode is similar to a manic episode; however, the symptoms are less severe and may only last four consecutive days.

3.4. A major depressive episode is a period of two weeks in which a person has at least five or more of the following symptoms: (Thakur, 2015; Scott et al., 2016);

- Depressed mood, such as feeling sad, empty, hopeless or tearful
- Loss of interest in activities
- Feeling worthless or inappropriate guilt
- Sleeping problems (Insomnia or sleeping too much)
- Feeling restless or agitated or slowed behaviour
- Changes in appetite
- Loss of energy or fatigue
- Difficulty concentrating, or indecisiveness
- Frequent thoughts of death or suicide

3.5. Bipolar disorder is widely cited as one of the most severe psychiatric disorders and is among the most disabling and economically catastrophic medical disorders (Ayano, 2016). According to Ferrari et al (2016), despite being relatively rare, bipolar disorder is a disabling illness due to its early onset, severity and chronicity.

## 4. Classification of bipolar disorder

The most recent Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classification recognises seven categories of bipolar disorder, namely: bipolar I disorder, bipolar II disorder, cyclothymic disorder, substance/medication induced bipolar and related disorder, bipolar and related disorder due to another medical condition, other specified bipolar and related disorder, and unspecified bipolar and related disorder (Jeste et al., 2013).

Bipolar I disorder is diagnosed when a person has had at least one manic episode that may be preceded or followed by hypomanic or major depressive episodes (SASOP, 2013).

Bipolar II disorder involves a person having at least one major depressive episode and at least one hypomanic episode, however, without a manic episode (SASOP, 2013).

Cyclothymic disorder is a milder form of bipolar disorder involving many mood swings, with hypomania and depressive symptoms that occur often and constantly but do not meet the criteria for major depressive disorder (SASOP, 2013).

## 5. Epidemiology

5.1. According to the Royal College of Psychiatrists (quoted in WPA, 2016), 1 in every 100 adults has bipolar disorder at some point in their life. The International Society for Bipolar Disorder (ISBD) works on a premise that the disease affects over 60 million people worldwide, a figure provided by the World Health Organisation (WHO) (2017). According to the Depression and Anxiety Support Group (SADAG, 2019), 3-4% of South Africans have Bipolar Disorder.

5.2. The South African Society of Psychiatrists reported the mean age of the first mood episode of bipolar 1 to be 18.2 years with a lifetime prevalence is 1%. For bipolar II disorder, the mean reported age of first mood episode is 20.3 years, while the lifetime prevalence is 1.1%. Bipolar I disorder affects men and women equally, while bipolar II disorder is more common in women (Emsley et al., 2013).

5.3. Bipolar disorder in children under 12 years is very rare (NICE,2014). For this reason, the NICE guideline recommends that the 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

5.4. Culpepper (2014) is of the view that age at onset appears to be decreasing, with the current median age at onset likely to be during the teenage years. Also, in the youth, manic and mixed states are more common, but, in adulthood, depression becomes more predominant. He further states that new-onset bipolar disorder is unusual in the elderly, so suspicion of this diagnosis in older patients should stimulate an investigation for a possible primary central nervous system disorder.

## 6. Comorbidities and other associated factors for patients with bipolar mood disorder

6.1. In patients with bipolar disorder, comorbidity is the rule rather than the exception (Culpepper, 2010; Das, 2013). This was concluded from a US general population survey data which found that 100% of patients with bipolar I disorder reported at least 1 other psychiatric disorder in their lifetimes, and 95.5% reported 3 or more. From that study, anxiety disorders were present in 92.9% of patients with bipolar I disorder, 71.0%, in substance use disorders, 59.4% in conduct disorders and 29% in adult antisocial behaviours.

6.2. According to Jann (2014), substantial challenges facing patients with bipolar disorder, in addition to their severe mood symptoms, include frequent incidence of psychiatric and general medical comorbidities. Common comorbities include anxiety disorders, alcohol or drug dependence (Culpepper, 2010), diabetes, cardiovascular disease, obesity, migraine, and hepatitis C virus infection. Both SASOP guidelines (Emsley et al. 2013) and the APA guidelines (Reus et al. 2017) corroborate the comorbid psychiatric disorders cited.

6.3. The risk of suicide is significantly higher among people with bipolar disorder than among the general population (Jeste et al. 2013). Bipolar disorder is almost always recurrent and can be associated with severe illness-related morbidity and increased medical mortality, with about 10 to 20 percent of patients with the condition dying of their illness by suicide (Ayano, 2016).

## 7. Diagnosis of bipolar mood disorder

Bipolar disorder diagnosis should be made over time as the full spectrum of the disorder does not present itself at one point in time (SASOP, 2013). According to Scott and Leboyer (2011), over 60% of individuals with bipolar disorders are reported to have received between 1-4 prior diagnoses, with delay in diagnosis being a problem in females with bipolar II disorders. This can be attributed to the fact that unipolar depression (UD) is more common than bipolar depression, and because bipolar depression lacks pathognomonic features, bipolar disorder is often incorrectly identified as major depressive disorder (MDD). Among patients who are eventually diagnosed with bipolar disorder, approximately 70% reportedly had an initial misdiagnosis and more than 33% remained misdiagnosed for 10 years or more (Jann,2014).

### 7.1. Differential diagnosis

7.1.1. Bipolar disorders must be differentiated from other psychiatric and medical illnesses, as well as from disorders such as heavy metal toxicity, adverse effects of drugs, and vitamin deficiencies (Jeste et al. 2013; Ayano, 2016). The NICE guidelines (2014) recommend considering 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/hyperthyroidism. The depressive manifestation in both unipolar and bipolar disorder is identical, however, the two require different psychopharmacological treatments. For this reason, it is beneficial to establish a diagnosis of bipolar depression prior to the expression of a manic episode (Heymann and Bonne, 2011).

7.1.2. Differentiating bipolar disorder (BD) from recurrent unipolar depression (UD) is a major clinical challenge. Main reasons for this include the higher prevalence of depressive relative to hypo/manic symptoms during the course of BD illness, and the high prevalence of subthreshold manic symptoms in both BD and UD depression (NICE, 2014).

7.1.3. Emsley et al. (2013) confirmed that separating major depressive disorder (MDD) and BD, particularly BD II, can be a challenge. This has reportedly been established from several reports that have found that BD is associated with:

- A significantly earlier age of onset
- More recurrences
- Atypical and mixed depressions

- A family history of BD or completed suicide.

7.1.4. According to Ayano (2016) only one manic/hypomanic episode is required to diagnose bipolar rather than unipolar disorder.

## 7.2. Criteria for Diagnosis

Diagnostic categories and criteria for bipolar disorders show some concordance between the internationally and widely used Tenth Edition of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) and the DSM 5 as they share many commonalities regarding diagnostic categorisation of bipolar and related disorders, and they both acknowledge the existence of a distinct bipolar disorder, which more or less represents a modern view of the classic manic-depressive disorder.

However, there are also major differences that are worth highlighting, as shown in tables below.

Table 3: Difference between ICD-10 and DSM-5 regarding bipolar and related disorders

| | ICD-10 | DSM-5 |
|---|---|---|
| Taxonomy | Bipolar disorders appear in the chapters of mood (affective) disorders, behavioural disorders due to psychoactive substance use, and organic mood (affective) disorder | Bipolar and related disorders are summarised in a distinct chapter between "Schizophrenia Spectrum and Other Psychotic Disorders" and "Depressive Disorders." |
| Criteria for a manic episode | Mood must be Predominantly elevated expansive, or irritable for at least 1 week, plus at least 3 of 9 other symptoms are required. | Features of both elevated, Expansive or irritable mood AND increased goal-directed- activity or energy for at least 1 week plus 3 or 7 other symptoms are required. |
| Single manic episode sufficient for diagnosis of bipolar disorder | No | Yes |
| Distinction between bipolar I and bipolar II | Not explicitly | Yes |
| Use of specifiers | No | Yes |

| | | |
|---|---|---|
| Mixed affective episode | Distinct diagnosis: Bipolar affective disorder, current episode mixed. | Distinct specifiers: With mixed features.<br><br>This specifier is also applicable for patients with (unipolar) major depressive disorder. |
| Consideration of concurrent anxiety | No | Distinct specifier: With anxious distress |
| Date of release | 1992 | 2013 |

*Source: Kaltenboeck, Winkler, and Kasper (2016)*

In terms of the differences, the following areas are worth pointing out: nosology, criteria for manic episodes and bipolar disorders, distinction of types of bipolar disorders, and the degree of details in categorization.

- Nosologies used within the diagnostic systems: Both classifications discriminate between bipolar disorder and unipolar depression but represent this in different ways. However, none considers the occurrence of unipolar mania, which is seen as a major shortcoming in both systems, given the growing scientific evidence for the existence of unipolar mania.
- Criteria for manic episode and bipolar disorders: DSM-5 has more restrictive criteria for a manic episode than ICD-10. This may have important implications for clinical practice and scientific investigation. This, according to Severus and Bauer (2013) might have the advantage of lowering the probability of false positive diagnoses and therefore help to avoid unnecessary psychopharmacological treatment. On the other hand, however, it leads to the problem that there might be patients who are diagnosed with mania or bipolar disorder in ICD-10 but must be allocated to a subthreshold group in DSM-5.
- Distinction of types of bipolar disorders: DSM-5 allows for the diagnoses of bipolar I disorder and bipolar II disorder, while ICD-10 does not make such an explicit distinction. This appears to be a major shortcoming in the classification of bipolar disorders in ICD-10, as it does not take into account the spectrum of clinical symptomatology in patients with bipolar disorders. As a result, patients who present with their first episode of mood (affective) disorder can be diagnosed with a distinct category in ICD-10, such as (hypo)manic episode or depressive episode; DSM-5 does not make this distinction, meaning that a manic episode is sufficient to warrant a diagnosis of bipolar I disorder under this classification.
- Details of a patient's clinical presentation: DSM-5 allows for the use of specifiers, which intends to allow better categorisation and easier communication among clinicians. ICD-10 takes into account some features that might be present in patients with bipolar disorders, such as psychosis or episodes with mixed features. However, this is far less extensive than the specifiers in DSM-5.

All the critiques of these classification systems pointed out that there are more than 20 years between the release of ICD-10 and DSM-5, and therefore some of the differences described might resolve when the new issue of the ICD (ICD-11) is

published. An international survey of psychiatrists in 66 countries back in 2002, comparing use of the ICD-10 and DSM-IV, found that the former was more often used for clinical diagnosis while the latter was more valued for research (Mezzich, 2002). The ICD is the official system, although many mental health professionals do not realize this due to the dominance of the DSM.

The ICD-11 version for preparing implementation in Member States, including translations, was released on 18 June 2018 and accepted at the Seventy-second World Health Assembly for endorsement by Member States in May 2019. ICD-11 will come into effect on 1 January 2022 (WHO, 2019).

## 7.3. Diagnostic basket

The recommended PMB level of care diagnostic basket for bipolar disorder describes the professional disciplines that may make a diagnosis, as well as the investigations needed to make a definite diagnosis.

### 7.3.1. Consultations and disciplines for diagnosis

Many patients with bipolar disorder seek treatment in primary care practices, therefore, clinicians in these settings need to be able to diagnose bipolar disorder and common psychiatric and medical comorbidities; and to initiate and manage treatment (Culpepper, 2010).

According to the Mental Health Care Act No, 2002 (Act No. 17 of 2002), "a mental health practitioner" means a psychiatrist or registered medical practitioner or a nurse, occupational therapist, psychologist or social worker who has been trained to provide prescribed mental health care, treatment and rehabilitation services. A "mental health care provider" means a person providing mental health services to mental health care users and includes mental health practitioners (Mental health Act, 2002).

In view of the definitions of a mental health provider and / or practitioner, table 3 gives the recommended providers for diagnosis and the supportive allied providers.

Table 4: Recommended disciplines for diagnosis of bipolar disorder

| Discipline | Comment |
|---|---|
| General Practitioner | A GP can do the initial diagnosis and can initiate treatment. However, the patient should be referred to a psychiatrist within 6 months to confirm the diagnosis. Stable patients can be managed by the GP. |
| Psychiatrist | Preferred provider for diagnosis |
| Other supportive providers only upon referral from GP or psychiatrist | |
| Clinical psychologist<br>Occupational therapist | |

| |
|---|
| Social worker |

According to Deckersbach (2010) two-thirds of patients with bipolar disorder experience a moderate to severe impact of the illness on occupational functioning. Occupational therapists (OT) work with these individuals to assist them in all capacities of their daily living. OT's can see not only to their mental well-being, but their physical well-being and safety (Covington, 2018). Through the application of different therapies, OTs can intervene in different occupational areas of life in people with mental disorders. The treatment produces more effect to drug treatments combined with cognitive or behavioural therapies (Rodríguez Martínez, M., & Montero Sánchez, R. (2017). In addition, Fast (2019), advises that Occupational therapy can be a great way to cope with bipolar disorder symptoms as it allows an individual to get their mind off negative thoughts and create something.

The National Alliance on Mental Illness asserts that Social workers help people overcome life's most difficult challenges; they help prevent crises and counsel individuals, families and communities to cope more effectively with the stresses of everyday life. Social workers focus on improving individual well-being in the context of family and other social structures, such as work and community (McLain, 2014).

### 7.3.2. Recommended baseline lab investigations for diagnostic workup

According to Soreff (2018), several reasons exist for obtaining selected laboratory studies in patients with bipolar disorder, or manic-depressive illness. An extensive range of tests is indicated, because bipolar disorder encompasses both depression and mania; also, because a significant number of medical causes for each state exists.

Table 5: Laboratory/ point of care baseline investigations for diagnostic work-up of bipolar disorder recommended as PMB level of care

| Investigation |
|---|
| Full blood count |
| Urea and electrolytes including serum creatinine |
| Fasting blood sugar and/ or random blood glucose |
| Fasting lipogram<br>• triglycerides,<br>• high-density lipoprotein (HDL),<br>• low-density lipoprotein (LDL) |
| Thyroid stimulating hormone |

| |
|---|
| Treponema pallidum hemagglutination |
| HIV |
| Liver function test<br>• Aspartate aminotransferase (AST)<br>• Alanine aminotransferase (ALT)<br>• Gamma glutamyl transferase (GGT) |
| Toxic drug screen |
| Pregnancy test |
| Vitamin B 12 - for patients above 60 years or when indicated |

### 7.3.3. Other baseline investigations for diagnostic work up of bipolar mood disorder

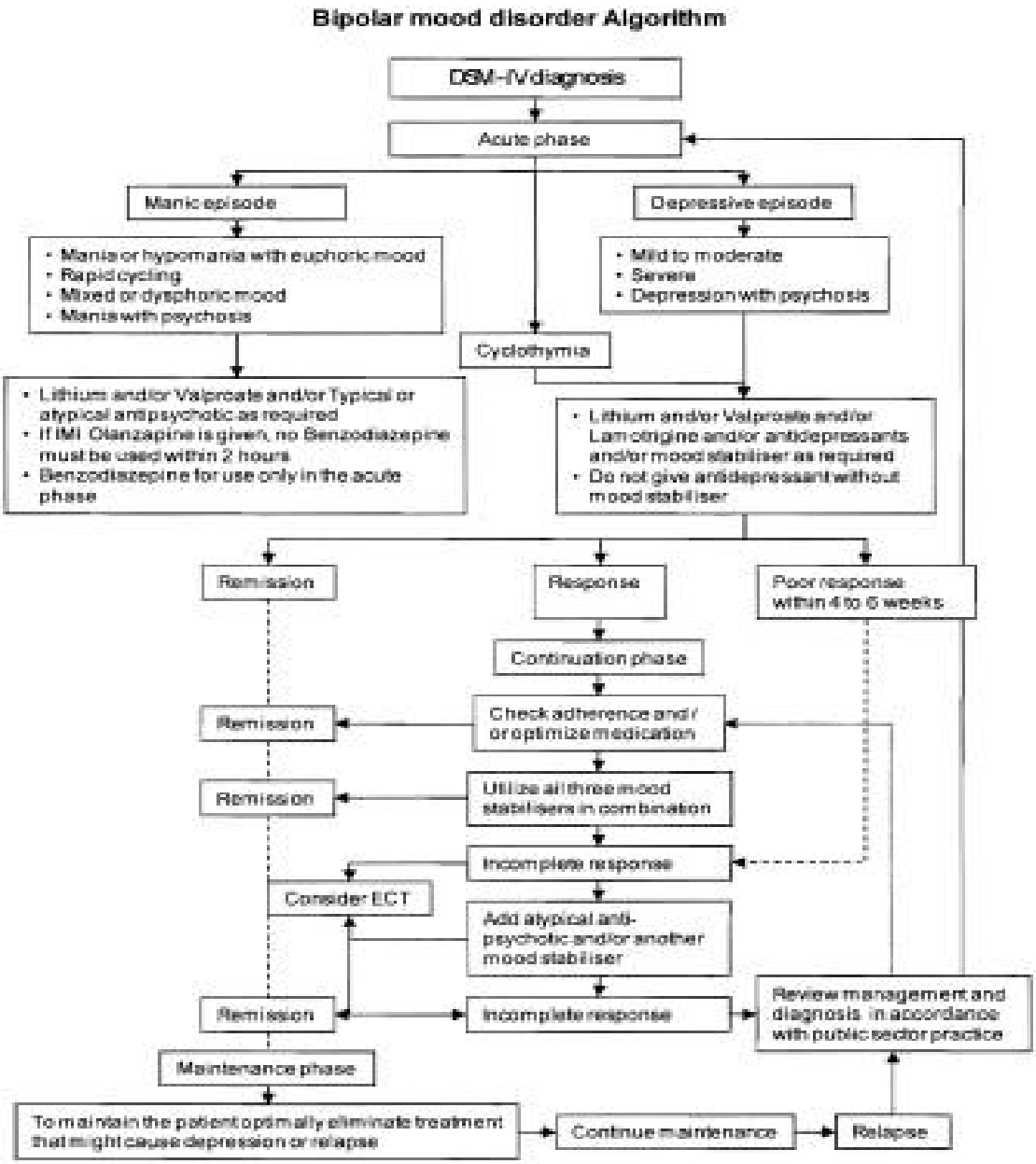
Table 6: Other investigations for diagnosis of bipolar disorder recommended as PMB level of care (SASOP, 2013)

| Investigation | Comment |
|---|---|
| 24-hour EEG | Only if there is any clinical suspicion of temporary lobe epilepsy |
| Computed tomography (CT) | Clinically indicated for 1st episode patients and ALL late onset |
| Brain MRI | Only on motivation as CT is usually adequate |
| ECG with QTc calculation | Baseline ECG should be performed as most medication prolongs the QT interval. |

## 8. Management of bipolar mood disorder

There is currently no cure for bipolar disorder, but treatment can help control symptoms (NIMH, 2015). People with bipolar disorder can be adequately managed and subsequently lead a very full and productive life (Scott et al. 2016).

Figure 1: Treatment algorithm for bipolar mood disorder as outlined in the Medical Schemes Act Chronic Disease List

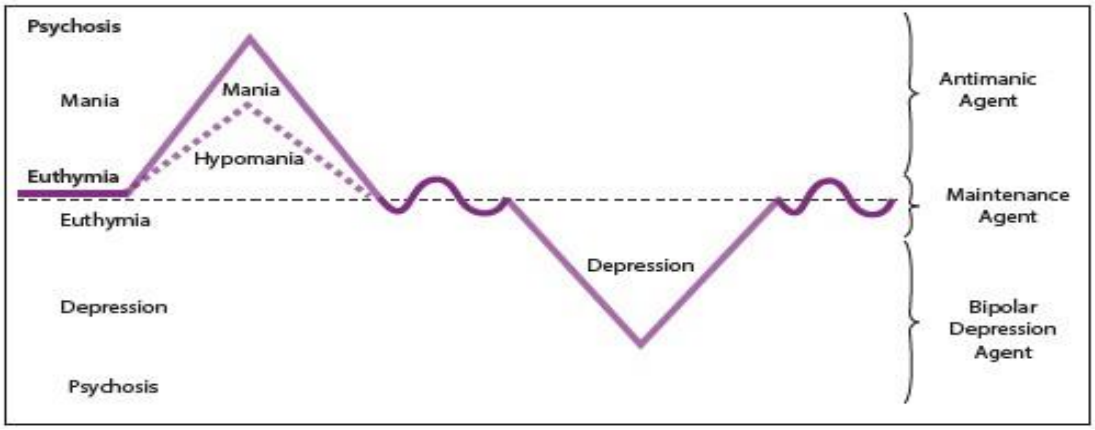



8.1. Pharmacological management of bipolar disorder in and out-of-hospital

The CMS reviewed international and local guidelines; a phase-based treatment of bipolar disorder, as indicated in figure 4 is recommended (Emsley et al. 2013). The CMS recommends that medical management out-of-hospital (maintenance phase) should be a continuation of medicines already initiated in-hospital, except for medicines used for agitation. The

selection of maintenance medicines should be on an individual basis, taking into consideration efficacy and tolerability profiles. In addition, consideration needs to be given to individual patient factors (preference, past response, safety).

Figure 2: *Phases of bipolar illness with matching treatment terminology (Emsley et al. 2013)*




The above approach mainly recommends the use of the following agents:

- Anti-manic agent
- Bipolar depression agent
- Maintenance agent

8.1.1. Anti-manic agents

8.1.1.1. Anti-manic agents include anticonvulsants (e.g. sodium valproate, carbamazepine and lamotrigine), lithium and antipsychotics.

8.1.1.2. Based on randomised clinical trials, lithium occupies a particularly important role in the prevention of relapse to mania and depression. Valproate and lithium are used in the manic episode as monotherapy or in combination with atypical antipsychotics. Valproate should be used with extreme caution in women of childbearing age due to the risk of foetal malformations and adverse neurodevelopmental outcomes after any exposure in pregnancy (NICE, 2014). Lamotrigine is used in the maintenance mainly for the prevention of depressive episodes (SASOP, 2013). There is no consensus of the role of carbamazepine, it is however listed as a second line maintenance agent in the SASOP guidelines (SASOP, 2013).

8.1.1.3. Antipsychotics are classified as typical (first generation antipsychotics) or atypical (second generation antipsychotics). Atypical antipsychotics are the newer drugs which are generally well tolerated with less side effects when compared to the older drugs. Medicines in this class are recommended as 1st line agents.

8.1.1.4. Typical antipsychotics are the older drugs with generally more serious side effects and are recommended as 2nd line agents.

8.1.2. Bipolar depression agent

8.1.2.1. Lamotrigine, valproate and lithium are also recommended in the depressive phase of bipolar mood disorder.

8.1.2.2. Atypical antipsychotics, e.g. quetiapine and olanzapine are recommended as PMB level of care.

8.1.2.3. Antidepressants are the most commonly prescribed drug class for treating depression. The benefits of conventional antidepressants such as the tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin and noradrenaline reuptake inhibitors (SNRIs) in the treatment of bipolar depression is currently unclear. If a conventional antidepressant is employed for bipolar depression, it should be concurrently administered with an anti-manic maintenance agent to diminish the possibility of switching (SASOP, 2013). SSRIs (e.g. fluoxetine, citalopram, escitalopram) are recommended as 1st line antidepressants in combination with mood stabilisers.

8.1.3. Maintenance therapy

8.1.3.1. There is limited evidence for combining treatments hence monotherapy is preferred.

Table 7: Summary of therapeutic classes and examples of medicines recommended as PMB level of care for bipolar depression[2]

| Medicine class | Examples of medicines |
|---|---|
| Manic/ hypomanic episode | |
| Mood stabilisers | Lithium carbonate |
| | Anticonvulsants<br>- Sodium valproate (PO and IMI)<br>- Carbamazepine<br>- Lamotrigine |
| Second generation antipsychotics/ Atypical antipsychotics | - Quetiapine<br>- Olanzapine (PO and IMI)<br>- Risperidone<br>- Aripiprazole[3] |
| First generation antipsychotics/ Typical antipsychotics | - Haloperidol – when other options have failed as it lacks efficacy in maintenance treatment |
| Depressive episode | |

[2]Schemes can develop their own formularies which should include medicines from all classes recommended

[3] Indicated for children and for cardiovascular unstable patients.

| | |
|---|---|
| Mood stabilisers | - Lithium carbonate<br>- Sodium valproate<br>- Lamotrigine |
| Atypical antipsychotics | - Quetiapine<br>- Olanzapine |
| Typical antipsychotics | Not recommended for depression phase |
| Antidepressants<br>(only in combination with mood stabilisers) | Ø SSRI's (1st line)<br>- Fluoxetine<br>- Citalopram<br>Ø Norepinephrine- Dopamine Reuptake Inhibitors (2nd line)<br>- Bupropion<br>Ø SNRIs are not recommended |
| Agitation in mania and/ or depression | |
| | - Lorazepam IM<br>- Olanzapine IM<br>- Ziprasidone IMI[4]<br>- Haloperidol<br>- Zuclopenthixol<br>- Clonazepam IMI<br>- Clothiapine IMI |
| Maintenance | |
| Mood stabilisers | - Lithium carbonate - mainly for preventing manic episodes<br>- Lamotrigine- mainly for preventing depressive episodes<br>- Sodium valproate<br>- Carbamazepine – 2nd line |
| Atypical antipsychotics | - Quetiapine<br>- Olanzapine<br>- Risperidone<br>- Aripiprazole |

## 8.2 Non-pharmacological management in and out-of-hospital

8.2.1. Ayano (2016) and Goodwin et al (2016) agree that the complexity of bipolar disorders usually renders any single therapeutic approach inadequate to deal with the multifaceted disorder, and therefore psychosocial modalities, including psychoeducation and behaviour change, should be integrated into the drug treatment regimen. Adjunctive psychosocial therapies should also be considered early in the course of illness to improve medication adherence, identify prodromes of relapse, decrease residual symptoms

[4] For sedation

(particularly depressive) and suicidal behaviour, and help move patients towards a comprehensive functional recovery.

8.2.2. There is strong evidence for non-pharmacological management to compliment pharmacotherapy in the holistic management of bipolar disorder (Scott et al., 2016; Jeste et al., 2013; NICE, 2014). These interventions should include the entire multidisciplinary team. In psychotherapy, the individual works alongside a mental health professional to decide a treatment plan, better understand the illness and to help rebuild relationships. Helping the person cope with the stress of the illness, especially as it affects relationships and ability to work, is often very important. According to Connolly and Thase (2011) psychoeducation focusing on recognition of early warning signs of relapse is an effective adjunct to medication management and should be offered to all patients with bipolar disorder. More intensive psychotherapies (cognitive-behavioural therapy, family focused therapy, interpersonal and social rhythm therapy) have also demonstrated benefit as adjuncts to improve both symptoms and function and should be considered.

8.2.3. The current Medical Schemes Act stipulates 15 psychotherapy sessions out hospital. The CMS recommends that a care plan should be submitted to the funder/ administrator when a patient is diagnosed with bipolar mood disorder. The case coordinator will be able to assist and ensure the optimal utilisation of the 15 sessions currently prescribed. Patients should also get appropriate referral from the treating doctor to the most appropriate allied health professional. It is also important that all benefits especially for allied health professionals are individualised and not bundled as family benefits. The social workers and psychologists are recommended for patients with bipolar mood disorder when referred by the treating provider.

8.2.4. Other allied healthcare professionals who may play a role in selected patients when clinically indicated include occupational therapists, physiotherapists and dieticians.

8.2.5. Follow-up consultations are included in the PMB level of care under the “care” component for bipolar mood disorder and may not form part of the 15 psychotherapy sessions.

## 9. Lab investigations out-of-hospital

Maintenance of euthymia is the primary goal in the long-term treatment of bipolar disorder and is best achieved using long-term medication (Conolly and Thase, 2011). The long-term use of some of the medication warrants ongoing monitoring of the patient. The table below provides guidance on the drugs which need to be monitored.

Table 8: Recommended drug specific laboratory investigations

| Patient Is Maintained on: | Check | Monitor for: |
|---|---|---|
| Lithium | Drug serum level: once therapeutic level is achieved, every 3–6 months | Sub-therapeutic or toxic level |
| | Electrolytes, urea and creatinine (EUC): every 3–6 months | Renal insufficiency, nephrogenic diabetes insipidus |
| | Calcium, TSH, weight: after 6 months and then annually | Thyroid/parathyroid dysfunction |
| Valproate | Serum level: during initial therapy and then as clinically indicated | Sub therapeutic or toxic level |
| | Weight, complete blood count, menstrual history, liver function tests every 3 months for the first year and then annually | Weight gain, thrombocytopenia, dysmenorrhea, liver failure |
| | Blood pressure, fasting blood glucose, lipid profile, bone densitometry (if risk factors) | Metabolic syndrome, anticonvulsant-related osteopenia |
| Carbamazepine | Serum level: during initial therapy and then as clinically indicated | Sub therapeutic or toxic level |
| | Complete blood count, liver function tests, EUC monthly for 3 months then annually Bone densitometry | Blood dyscrasias, liver failure, hyponatremia, monitor for rash, anticonvulsant-related osteopenia, Stevens-Johnson Syndrome |
| Lamotrigine | | Stevens-Johnson Syndrome Monitor for rash |
| Second-generation antipsychotics | Weight monthly for 3 months and then every 3 months | Weight gain |
| | Blood pressure, fasting blood glucose, lipid profile every 3 months and then annually | Metabolic syndrome |
| | Abnormal movements | Acute dystonias, drug-induced parkinsonism, tardive dyskinesia |
| | Electrocardiogram, prolactin as clinically indicated | QTc prolongation/dysrhythmias, hyperprolactinemia |

Table 9: Other lab investigations recommended as PMB level of care out-of-hospital

| Investigation | Frequency | Comment |
|---|---|---|
| Glucose | Twice yearly and thereafter annually | Co-morbid diabetes may be exacerbated by antipsychotic medication hence medical monitoring is advocated in addition to education about lifestyle modification (Owen, Sawa & Mortensen, 2016; De Hert et al., 2011). |
| Lipogram | Annually | All individuals with bipolar disorder should be under active care and be screened for cardiometabolic risk at least annually if they have normal baseline values. Those who already present with cardiovascular risk factors should be monitored more frequently (Owen, Sawa & Mortensen, 2016; De Hert et al., 2011). |
| AST, ALT and GGT | Annually | Asymptomatic increases in ALT, AST, GGT and serum bilirubin levels in the first month of the study. |
| | | These results were in accordance with previous studies that asymptomatic increase of liver enzymes are common but significant liver enzyme elevations are rare during atypical antipsychotic treatment. We suggest that obtaining baseline liver enzyme tests before atypical antipsychotic therapy and monitoring regularly specifically in patients with risk factors for liver damage during therapy (Atasoy et al., 2007). |
| Prolactin | Annually | Antipsychotic-induced hyperprolactinaemia has been estimated to occur in up to 70% of patients with bipolar disorder depending on the choice of antipsychotic agent (Barnes & Paton, 2011). |

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