



**PMB Definition Guideline for Schizophrenia**

**Disclaimer:**

*This schizophrenia benefit definition guideline has been developed for most patients who require standard care. These benefits may not be applicable to all patients, especially those with complex presentations or comorbidities. Section 15(H) and 15(I) should be applied to beneficiaries who are inadequately managed by the defined benefits.*

## Introduction

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. 31 of 1998). It has become clear that medical scheme beneficiaries find it difficult to be fully aware of their entitlements in advance. In addition, medical schemes interpret these benefits differently, resulting in a lack of uniformity of benefit entitlements. The guideline covers the assessment, diagnosis, treatment, and management of schizophrenia. It aims to define the prescribed minimum benefits (PMBs) for the management of schizophrenia and to make recommendations and suggestions to enhance the overall care of individuals with schizophrenia. The primary objective of the PMB definition guideline is to:

- Provide clear, comprehensive descriptions of the benefits, in terms of the provisions of the PMB regulations of the Medical Schemes Act, No. 131 of 1998.
- Improve clarity in the funding decisions by medical schemes; and
- Ensure protocols and algorithms developed by medical schemes are developed on best available clinical practice guidelines.

This guideline is based on the best available evidence (*safety, efficacy, effectiveness, and economic aspects*) and clinical practice knowledge of schizophrenia.

Our recommendations are put together by technical experts, healthcare professionals and the medical schemes industry. This Guideline should be read in conjunction with the supplementary information included as [Annexure A](#) to this guideline.

This PMB Definition guideline was developed as a policy prescript in line with Section 15 (A) to (I) of the Medical Schemes Act, 131 of 1998, for the development of protocols and formularies, and should be viewed as such.

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## **GUIDANCE FOR THE ASSESSMENT AND MANAGEMENT OF SCHIZOPHRENIA**

**This guideline provides recommendations for the:**

- Assessment and diagnosis of schizophrenia.
- Treatment and care in schizophrenia.
- Monitoring and evaluation of patients with schizophrenia; and
- Rehabilitation and reintegration of mental health care users with schizophrenia.

### **1. ASSESSMENT AND DIAGNOSIS**

#### **1.1. Diagnosis in primary care**

- 1.1.2. In primary health care, the diagnosis of schizophrenia involves ruling out other mental health disorders and determining that the symptoms are not due to substance use, medication, or another medical condition.
- 1.1.3. The diagnosis of schizophrenia must be confirmed by two mental health care practitioners, one of whom should be qualified to do physical examinations i.e., a medical practitioner (GP or psychiatrist). In primary care, one mental health care practitioner (MHCP) may make a provisional diagnosis for schizophrenia, but this must be confirmed by a medical practitioner (*see Table 1*).
- 1.1.4. Stable patients can receive maintenance treatment by the GP or any MHCP whose scope of practice incorporates care, treatment, and rehabilitation of mental health care users.
- 1.1.5. Those patients with a poor response to antipsychotic treatment, non-or poor adherence to medication, or who require psychological intervention that is not available in primary care, or who are a danger to self, others, or property, should be referred to secondary care without delay.

#### **1.2. History and examination**

- 1.2.1. A comprehensive multidisciplinary assessment should be conducted.
- 1.2.2. The assessment (*see Table 1*) should include a:
- psychiatric history
  - medical history
  - physical examination
  - mental state examination
  - psychosocial assessment (psychological assessment is a component of the psychosocial assessment)
  - the psychosocial assessment must include a:
    - Neurocognitive assessment (social, cognitive, and motor development); and
    - Social skills assessment (routines, roles, values, interests, environment, attitudes, motivation, activities of daily living (ADL), family and relationships).

- occupational functioning or educational assessment; and
- an assessment of socioeconomic status.

### 1.3. Base-line investigations

1.3.2. The following baseline investigations (**see Table 2**) should be performed before initiating treatment and for monitoring the adverse effects of medication:

- weight (plotted on a chart)
- height
- waist circumference
- pulse and blood pressure
- fasting blood glucose or glycosylated haemoglobin (HbA1c)
- Liver Function Tests (LFT)
- Thyroid Function Test (TFT)
- blood lipid profile
- Treponema Pallidum Haemagglutination (TPHA)
- pregnancy test (females of childbearing age)
- Human Immunodeficiency Virus (HIV) Test, with consent
- computerised tomography (CT) scan

1.3.3. An electrocardiogram (ECG) if:

- this is specified in the medicine authorisation package insert.
- a physical examination has identified specific cardiovascular risk factors e.g., diagnosis of hypertension.
- there is a personal history of cardiovascular disease; or
- the service user is being admitted as an inpatient.

## 2. TREATMENT AND CARE

### 2.1. *Early intervention services for psychosis*

2.1.1. A patient presenting with a first episode of psychosis may present with brief or attenuated psychotic symptoms, and other experiences or behaviours that are suggestive of a psychotic disorder.

2.1.2. The first-contact healthcare professional must refer such patients for assessment without delay to a MHCP or secondary care service that incorporates an early psychosis intervention service, because they may be at increased risk of developing schizophrenia.

2.1.3. These individuals must be assessed by MHCPs in terms of Chapter V of the Mental Health Care Act.

2.1.4. Early intervention services for psychosis should be accessible to all patients with a first episode of

psychosis, irrespective of the person's age or the duration of untreated psychosis (DUP).

- 2.1.5. Patients should be assessed without delay. If the resources to manage patients with a first episode of psychosis are inadequate at the primary care level, such a patient must be referred to a secondary care level of care.
- 2.1.6. Early intervention in psychosis services should aim to provide a comprehensive package of care that includes the assessment and management of patients with schizophrenia.
- 2.1.7. The management of schizophrenia must include pharmacological, psychosocial, occupational, and educational interventions for people with psychosis, consistent with this guideline.
- 2.1.8. The first-contact professional must initiate emergency antipsychotic treatment. Long-term antipsychotic treatment must only be initiated at the primary care level in consultation with a psychiatrist.

## **2.2. Treatment and care in secondary care (in-hospital)**

- 2.2.1. A care plan must be developed following the assessment based on a psychiatric and psychosocial assessment, as well as a full assessment of physical health. A copy of the care plan must be provided to the primary healthcare professional who made the referral, and the patient.
- 2.2.2. For people with first episode psychosis, offer:
  - psychoeducation
  - oral antipsychotic medication
  - psychological intervention, including individual Cognitive Behavioural Therapy (CBT); and
  - advice on the effectiveness of psychological interventions in conjunction with antipsychotic medication.
- 2.2.3. The recommended maximum hospital stay is 21 days.
- 2.2.4. Patients with symptoms and behaviour that suggest an affective psychosis or disorder including bipolar disorder and psychotic depression, follow the recommendations in the major affective disorders, including unipolar and bipolar depression (**PMB code 902T**).
- 2.2.5. Assess for post-traumatic stress disorder and other reactions to trauma because people with schizophrenia are likely to have experienced previous adverse events. For people who show signs of post-traumatic stress accompanied by recent significant trauma, including physical or sexual abuse, refer to the PMB definition guideline on acute mental health conditions (**PMB Code 901T**).

## **2.3. Return to primary care.**

- 2.3.1. For patients who have responded effectively to treatment and remain stable, consider the option to return to primary care for further management by a GP and other MHCPs.
- 2.3.2. GPs and other primary healthcare professionals should monitor the physical health of people with schizophrenia when providing maintenance treatment in line with the recommended care plan.

2.3.3. Patients with schizophrenia who have high blood pressure, abnormal lipid levels, diabetes or pre-diabetes (as indicated by abnormal blood glucose levels in baseline assessment) or are physically inactive must be identified and monitored at primary care level in line with the best available guidelines in line with PMB Chronic Disease List for Hypertension and Diabetes respectively.

2.3.4. A Case Manager should be assigned for all mental health patient care users diagnosed with schizophrenia. A detailed care plan should be submitted to Case Management to coordinate optimal care for the patient both in and out-of-hospital.

#### **2.4. Relapse and re-referral to secondary care**

2.4.1. If a patient with an established diagnosis of schizophrenia presents with a suspected relapse (*for example, with increased psychotic symptoms or a significant increase in the use of alcohol or other substances*) to a primary healthcare professional i.e., GP, that patient should be referred to secondary care and a psychiatrist through the case manager without delay.

2.4.2. A patient being managed in primary care with poor response to treatment; non-adherence to medication, intolerable side effects from medication; comorbid substance use and/or who is a risk to self and others should be re-referred to secondary care.

#### **2.5. General considerations for treatment and care**

2.5.1. The treatment of schizophrenia is symptomatic and includes treatment for the primary symptom domains viz, positive symptoms (*delusions and hallucinations*) negative symptoms (*impaired motivation, poverty of speech, and social withdrawal*) and cognitive symptoms (*memory impairment*).

2.5.2. Antipsychotics are effective mainly for the positive symptoms of schizophrenia and is the cornerstone of acute exacerbation or recurrence of schizophrenia; hence effective therapy necessitates new oral antipsychotic medication or a review of existing medication.

2.5.3. The negative and cognitive symptoms do not respond as well as the positive symptoms to currently available antipsychotic medication. Significant occupational and social dysfunction are associated with schizophrenia. Hence, psychosocial interventions are an essential component of the management plan.

2.5.4. Duration of untreated psychosis (*DUP*) i.e., manifestation of the first psychotic symptom to initiation of adequate antipsychotic drug treatment is associated with poorer overall outcome. Hence, patients should be initiated on antipsychotics as soon as possible after a first diagnosis of schizophrenia.

2.5.5. Intermittent long-acting injectable antipsychotic (*LAI-AP*) maintenance strategies (*use of antipsychotic medication only during periods of incipient relapse or symptom exacerbation*) is not recommended for routine use.

2.5.6. Pharmacological therapy should be tailored to the individual patient's needs. Due consideration must be given to:

- metabolic risk factors (*including weight gain and diabetes*).
- sensitivity to extrapyramidal side effects (*including akathisia, dyskinesia, and dystonia*).
- cardiovascular risk factors (*including prolonging the QT interval*).
- hormonal factors (*including increasing plasma prolactin*).
- other factors (*including unpleasant subjective experiences*); and
- if a generic formulation is available, generic substitution is recommended.

## **2.6. Pharmacological treatment**

### *2.6.1. Choice of first-line oral antipsychotic*

2.6.1.1. Antipsychotics consist of various classes of medicine based on their pharmacological action (see *Table 3*).

2.6.1.2. To promote individualised therapy, clinicians should:

- Discuss treatment options with the MHCU and family if available.
- Record the indication, expected benefits, potential risks of oral antipsychotic medication, and the expected time for a change in symptoms and appearance of side effects.
- At the initiation of treatment, prescribe a dose at the lower end of the licensed dose range and slowly titrate upwards within the given dose range as per the South African Medicines Formulary of Medicines Package Insert.
- Justify and record reasons for dosages that are prescribed outside of the recommended range.
- Accurately record the rationale for continuing, changing, or stopping medication, and the effects of any such changes.
- Carry out a trial of the medication therapy at optimum dosage for 4 to 6 weeks, monitoring the patient continuously.

2.6.1.3. The choice of medicine must be in line with the criteria listed in **2.5.6**

- It is recommended that monotherapy oral therapy is initiated at the lowest dose and slowly titrated upwards to the highest effective dose.
- The monotherapy treatment initiated should continue for at least 4-6 weeks to evaluate response to the first-line antipsychotic.

### *2.6.2. Choice of second-line oral antipsychotic*

2.6.2.1. For patients with an acute exacerbation or recurrence of schizophrenia, a review of the existing medication regimen must be conducted.

- Consider errors in diagnoses, medical co-morbidity as well as non-adherence to anti-psychotic medication before concluding that a patient is resistant to a specific antipsychotic.

- The clinical response and side effects of the patient's current and previous medication should be considered.

2.6.2.2. Second-line antipsychotics are required when patients experience exacerbations of symptoms and/or poor response to adequate treatment with a first line antipsychotic.

### 2.6.3. *Choice of third-line antipsychotics*

2.6.3.1. Clozapine is the only antipsychotic with established efficacy in reducing symptoms and the risk of relapse for adults with treatment-resistant schizophrenia.

2.6.3.2. Clozapine should be prescribed for those patients who have not adequately responded to treatment with the chronological use of adequate doses of at least two different antipsychotic medicines for 6-8 weeks.

### 2.6.4. *Use of depot/long-acting injectable antipsychotics*

2.6.4.1. Depot/ LAI-AP with market authorisation in South Africa for intramuscular formulations should be considered:

- to avoid covert non-adherence (*either intentional or unintentional*) to oral antipsychotic medication
- when it is a clinical priority within the treatment plan
- when patients are unwilling to accept a continuous oral antipsychotic maintenance regimen LAI-APs are a feasible alternative to oral antipsychotic (OAP) treatment; and
- in the early stages of schizophrenia, LAI -APs may prevent relapse and recurrence in patients with a first episode of schizophrenia.
- patient preferences and attitudes towards regular intramuscular injections, and access to outpatient mental health services must be taken into consideration when prescribing LAI-APs.

## 2.7. **Non-pharmacological treatment**

### 2.7.1. *Electro-convulsive therapy*

2.7.1.1. ECT is a safe and effective treatment for schizophrenia. The clinical indications for ECT in schizophrenia include:

- treatment resistant schizophrenia
- catatonia

- suicidal behaviour with command type hallucinations
- severe agitation
- clozapine-resistant schizophrenia

2.7.1.2. Prolonged courses of ECT without measured improvement are not recommended for people with schizophrenia. A maximum of 12 treatments per cycle is recommended.

2.7.1.3. Longer courses may be required if progressive improvement occurs with each session.

#### 2.7.2. *Physiotherapy*

- Physical health is integral to health promotion efforts in patients with schizophrenia.
- Encouraging healthier lifestyle choices and higher levels of habitual physical activity is recommended.
- A Physiotherapist serves to assess any movement disorders, level of physical activity and develops a physical therapy care plan as part of the MDT at secondary level e.g.,

#### 2.7.3. *Dieticians*

- Play an important role in improving the physical health of patients with schizophrenia.
- Assess the nutritional status of a patient and recommend an appropriate diet.
- Develop a care plan in line with the base-line assessment.

### 2.8. **Psychosocial interventions**

2.8.1. Psychosocial interventions should be delivered by qualified, trained therapists with the appropriate level of competence and duly registered to provide such services.

2.8.2. psychosocial interventions are recommended as adjunctive therapy to pharmacological therapy.

2.8.3. Psychosocial interventions can be classified into behavioural, cognitive, psychodynamic, humanistic, systemic, motivational, social, occupational, and environmental interventions.

2.8.4. Psychosocial interventions such as Individual CBT, cognitive remediation therapy and programmes for family intervention for patients with schizophrenia are recommended.

2.8.5. Psychosocial interventions should be delivered on an individual basis (*one-to-one*) over at least 16-21 sessions for patients with schizophrenia.

2.8.6. Interventions can also be applicable in group form, namely social skills training, cognitive remediation, psychoeducation, and multi-family groups, synergising the already known benefits with newer therapy

models.

2.8.7. A treatment plan should be followed and developed so that:

- patients with schizophrenia can establish links between their thoughts, feelings, or actions and their current or past symptoms and/or functioning; and
- perceptions, beliefs, or reasoning related to target symptoms can be re-evaluated.

2.8.8. The sessions should include:

- patients monitoring their own thoughts, feelings, or behaviours with respect to their symptoms or recurrence of symptoms; and
- reducing distress.

2.8.9. The role of the multi-professional team is critical in the management of patients with schizophrenia. Therefore, psychosocial interventions are recommended for full recovery.

2.8.10. Family interventions should:

- include the person diagnosed with schizophrenia if practical.
- be carried out for between 12 weeks and one year.
- include at least 10 planned sessions; and
- take account of the whole family's preference for either single-family intervention or multi-family group intervention.

2.8.11. Art Therapy i.e., the use of artistic methods to treat psychological disorders and enhance mental health, is a technique rooted in the idea that creative expression can foster healing and mental well-being.

2.8.12. The following can be considered - art therapies e.g., dance movement, music or art therapy or drama therapy are recommended for people with schizophrenia, particularly for the alleviation of negative symptoms, during the acute phase or later, including in inpatient hospital settings.

### **3. MONITORING**

#### **3.1. *General considerations for monitoring therapy***

3.1.1. Monitoring the response to pharmacological and psychosocial therapy ensures that the effectiveness of therapy can be assessed and adjusted if needed. It also provides an opportunity for MHCPs to monitor other outcomes, such as the effects on any long-term conditions and the patient's ability to continue or return to employment.

#### **3.2. *Monitoring of pharmacological treatment***

3.2.1. Pharmacological therapy must be monitored regularly and systematically throughout treatment

period. Special attention must be paid to periods of up and cross-titration of antipsychotics. To ensure quality of care, regular monitoring must include:

- response to treatment, including changes in symptoms and behaviour.
- side effects of treatment, considering the overlap between certain side effects and clinical features of schizophrenia
- the appearance of movement disorders
- weight, weekly for the first six weeks, then at 12 weeks, at one year and then annually, because some antipsychotics increase the risk of metabolic syndrome (the statement regarding SGAs is not correct)
- waist circumference annually (*plotted on a chart*)
- pulse and blood pressure at 12 weeks, at one year and then annually.
- fasting blood glucose or HbA1c, and blood lipid levels at 12 weeks, at one year and then annually.
- Adherence to oral antipsychotics; and
- overall physical health.

### **3.3. Monitoring of psychosocial interventions**

3.3.1. Within the MDT, a lead professional should monitor and review access to and decisions about what psychosocial interventions to offer.

3.3.2. Psychosocial interventions should be monitored for a range of outcomes across relevant areas, including patient satisfaction and, if appropriate, family satisfaction routinely and systematically.

## **4. REHABILITATION AND REINTEGRATION**

### **4.1. General considerations for rehabilitation and reintegration**

4.1.1. The importance of case management is to co-ordinate integrated health and social care services of severely mentally ill people in the community. The end goal for rehabilitation is re-establishing social connections and getting back to social and vocational roles for successful reintegration, reintegration into society.

4.1.2. Only one out of seven patients recover after a first episode of psychosis despite mental health care and treatment.

4.1.3. The role of rehabilitation in schizophrenia is to complement psychotherapy and psychopharmacological treatments to improve functional outcomes and to promote recovery.

4.1.4. Psychosocial rehabilitation interventions should typically start from in-patient level if the patient had

been admitted and continue into the long-term.

- 4.1.5. Various factors need to be assessed to establish an individual “functional diagnosis.”, which mostly definitely helps to determine an individualized intervention plan and to define life goals in collaboration with the patient.

## **4.2. MDT role in rehabilitation and reintegration**

### *4.2.1. Role of Occupational Therapist*

- Occupational therapy interventions improve, maintain performance and occupational participation for people with serious mental illness.
- Occupational therapists work in both hospital and community settings using a combination of individual and group interventions to enable skill development and building of their confidence in the execution of everyday tasks.
- Interventions may include practical self-care; domestic skills, such as cooking and budgeting; work skills; leisure activities; development of social skills and carer support.

### *4.2.2. Role of Social Worker*

- Social Work practitioners have postulated that the psychosocial functioning or dysfunction in severe mental illness was mostly determined by the interaction between the individual needs, aspirations, and functional capacities on one side, and environmental (*situations*) expectations, opportunities, and resources on the other.
- Interventions in this category may include family psychoeducation and support, family-aided ACT, and case management.

### *4.2.3. Role of Mental Health Nurse*

- Mental Health nurses prioritize person-centered care, therapeutic relationships, and collaboration with peer support workers to enhance treatment effectiveness.
- Their interventions focus on improving medication adherence, providing coping support, and promoting social capabilities, ultimately improving individuals' quality of life.



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## **APPENDICES**

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### Appendix A

**Table 1: Assessment And Management of Patients with Schizophrenia at Primary and Secondary care**

### Appendix B

**Table 2: Base-Line Investigations and Monitoring**

### Appendix C

**Table 3: Table 3. Pharmacological Therapy in Schizophrenia**

**Table 1: Assessment and Management of Schizophrenia in Primary and Secondary Care**

Primary Care Level	Role	Benefit/Service
<b>Medical Practitioner</b>	<ul style="list-style-type: none"> <li>Assessment and baseline investigations</li> <li>Diagnosis and confirmation of MHCP diagnosis</li> <li>Treatment initiation</li> <li>Monitor for 4-8 weeks.</li> <li>Stable patients continue treatment (referral to psychiatrist when required)</li> <li>Risk assessment and referral</li> </ul>	<ul style="list-style-type: none"> <li>First consultation</li> <li>Monitoring</li> </ul>
<b>Mental Health Specialist Nurse</b>	<ul style="list-style-type: none"> <li>Assessment and baseline investigations</li> <li>Diagnosis</li> <li>Stable patients' continuation of treatment</li> <li>Risk assessment and referral</li> </ul>	<ul style="list-style-type: none"> <li>First consultation</li> <li>Monitoring</li> </ul>
<b>Secondary Care Level</b>		
<b>Out-patient care</b>		
<b>Psychiatrist</b>	<ul style="list-style-type: none"> <li>Assessment and baseline investigations</li> <li>Diagnosis and confirmation of MHCP</li> <li>Psychosocial interventions</li> <li>Treatment and review</li> </ul>	<ul style="list-style-type: none"> <li>Monitoring</li> <li>Psychosocial therapy</li> </ul>
<b>Psychologist (Clinical /Counselling)</b>	<ul style="list-style-type: none"> <li>Psychosocial interventions</li> </ul>	<ul style="list-style-type: none"> <li>Psychosocial therapy</li> </ul>
<b>In-patient care</b>		
<b>Multidisciplinary Mental Health Team</b> <ul style="list-style-type: none"> <li>Psychiatrist</li> <li>MH Specialist Nurse</li> <li>Psychologist (Clinical/Counselling)</li> <li>Clinical Social Worker</li> <li>Occupational therapists</li> </ul> <b>Other healthcare professionals as part of MDT</b> <ul style="list-style-type: none"> <li>Dieticians</li> <li>Physiotherapist</li> <li>Art and music therapists</li> </ul>	<ul style="list-style-type: none"> <li>Assessment and baseline investigations</li> <li>Diagnosis</li> <li>Pharmacological treatment</li> <li>Development of treatment plan</li> <li>Psychosocial intervention</li> <li>Rehabilitation and reintegration</li> <li>Nutritional assesment and treatment</li> <li>Physical therapy</li> <li>Art therapy</li> </ul>	<ul style="list-style-type: none"> <li>21 Days in hospital (max)</li> <li>Psychosocial therapy</li> <li>Services specified in the treatment plan.</li> </ul>

**Table 2: Base-Line Investigations and Monitoring**

<b>RECOMMENDED INVESTIGATIONS</b>				
<b>INVESTIGATION</b>	<b>BASELINE SCREENING</b>	<b>3 MONTHS</b>	<b>6 MONTHS</b>	<b>ANNUALY</b>
Anthropometry-height, weight, WC, WHP ratio	X	X	X	X
Blood Pressure	X	X	X	X
Full Blood Count (FBC)	X			
Urea and Electrolytes (U &E)	X			
Fasting Blood Glucose (FBG) or HbA1c	X	X		X
Liver Function Tests (LFT)	X			
Thyroid Function Test (TFT)	X			
Lipogram	X			X
Treponema Pallidum Hemagglutination (TPHA)	X			
Pregnancy Test (females of childbearing age)	X			
HIV with consent	X			
ECG	X			
CT Scan	X			
<b>When clinically indicated:</b>				
Toxic drug screen (urine or blood) - Suspected substance abuse				
24 hr EEG- Suspect Temporal Lobe Epilepsy				

**Table 3. Pharmacological Therapy in Schizophrenia**

	<b>ANTIPSYCHOTIC</b>	<b>CLASS</b>	<b>INN</b>	<b>Defined Daily Dosage (DDD)</b>
<b>ATC Class</b>	<b>FIRST LINE ORAL ANTIPSYCHOTIC</b>			
<b>N05AD</b>	Butyrophenone derivatives	<b>FGA</b>	Haloperidol	8 mg
<b>N05AA</b>	Phenothiazines with aliphatic sidechain	<b>FGA</b>	Chlorpromazine	0.3 g
<b>N05AX</b>	Other antipsychotics	<b>SGA</b>	Risperidone	5 mg
<b>N05AH</b>	Diazepines, oxazepines, thiazepines and oxepines	<b>SGA</b>	Olanzapine	10 mg
<b>N05AH</b>	Indole derivatives	<b>SGA</b>	Quetiapine	0.4 g
<b>N05AL</b>	Benzamides	<b>SGA</b>	Amisulpride	0.4 g
<b>N05AX</b>	Other antipsychotics	<b>SGA</b>	Aripiprazole	15 mg
<b>N05AE</b>	Indole derivatives	<b>SGA</b>	Ziprasidone	80 mg
<b>SECOND LINE ANTIPSYCHOTIC</b> Different antipsychotic (different MOA or different class) to one used as first-line				
<b>THIRD LINE ANTIPSYCHOTIC</b> Clozapine				
<b>FOURTH LINE</b> Antipsychotics Combination OR Antipsychotic + anticonvulsant				
<b>DEPOT/LONG-ACTING INJECTABLE ANTIPSYCHOTICS (LAI -AP)</b>				
<b>N05AF</b>	Thioxanthene derivatives	<b>FGA</b>	Flupentixol	4 mg
<b>N05AF</b>	Thioxanthene derivatives	<b>FGA</b>	Zuclopenthixol	15mg
<b>ADDITIONAL ORAL ANTIPSYCHOTICS IN SOUTH AFRICA</b>				
<b>N05AX</b>	Other antipsychotics	<b>SGA</b>	Brexpiprazole	3 mg
<b>ADDITIONAL DEPOT/LONG-ACTING ANTIPSYCHOTIC IN SOUTH AFRICA</b>				
<b>N05AX</b>	Other antipsychotics	<b>SGA</b>	Aripiprazole	13.3 mg
<b>N05AX</b>	Other antipsychotics	<b>SGA</b>	Paliperidone	2.5 mg
<b>N05AX</b>	Other antipsychotics	<b>SGA</b>	Risperidone	2.7 mg

## **ANNEXURE A: Supplementary Information on the PMB Definition Guideline on Schizophrenia**