



Republic of the Philippines  
Department of Health  
**OFFICE OF THE SECRETARY**

JAN 14 2021

**ADMINISTRATIVE ORDER**

No. 2020-*mc* 0012  
2021

**SUBJECT: Implementing Guidelines on the Medicine Access Program for Mental Health (MAP-MH)**

**I. RATIONALE**

Mental health (MH) issues can adversely affect one's well-being, behavior, personal relationships, contributions to society, and overall quality of life. Mental disorders account for 10% of the global burden of disease (GBD) and 30% of the non-fatal burden of disease. In the Philippines, 3.3% of the population suffer from depressive disorders and 3.1% suffer from anxiety disorders (WHO Mental Health Atlas, 2017). The World Economic Forum (WEF) estimated in 2013 that the cumulative global impact of mental disorders alone in terms of economic output will amount to US\$ 16 trillion over the next 20 years. Yet on average, governments spend less than 2% of their health budget on mental health, with most low- and middle-income countries spending less than 1%. To address the looming mental health crisis, it is crucial for governments to invest in mental health initiatives.

Recognizing the role of mental health and well-being in national development, the Department of Health (DOH) released Administrative Order (AO) No. 8 series of 2001 entitled "National Mental Health Policy". This policy set forth the guidelines for the establishment of a sustainable mental health program in the Philippines. The program was supported by the issuance of AO 2016-0039 "Revised Operational Framework for a Comprehensive National Mental Health Program (NMHP)" which provided among others, equitable access to the rational use of a wide range of pharmacologic interventions in the treatment and management of mental, neurologic, and substance use (MNS) disorders. Moreover, mental health is included as a priority agenda of the current administration as articulated in Republic Act (RA) No. 11223 "Universal Health Care (UHC) Act", as well as in RA 11036 "Mental Health Act" — which also mandated the improvement of MH services delivery nationwide.

The Medicine Access Program for Mental Health (MAP-MH), started in 2012 by the DOH Pharmaceutical Division (PD) and operationalized by the National Center for Mental Health (NCMH), was designed to ensure availability of mental health drugs in the community. Since then, 207 access sites have been opened with around 39,000 service user beneficiaries. With the transfer of MAP-MH to the National Mental Health Program (NMHP) under the DOH Disease Prevention and Control Bureau (DPCB) and the goal of expanding coverage of beneficiaries and medicines being provided, there is a need to establish standards and guidelines to aid in the proper implementation of MAP-MH nationwide.

**II. OBJECTIVES**

This Order aims to set the overall guidelines on the implementation of MAP-MH in access sites such as DOH hospitals, Centers for Health Development (CHDs), Ministry of Health - Bangsamoro Autonomous Region in Muslim Mindanao (MOH-BARMM), Treatment and Rehabilitation Centers (TRCs), and other health facilities. Specifically, this Order aims to:

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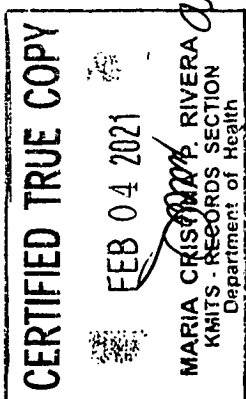
1. Increase service user's access to quality essential medicines in the treatment of various mental, neurologic, and substance use (MNS) disorders, taking into consideration rational drug use and availability up to the grassroots level.
2. Establish a functional electronic information management system for MAP-MH.
3. Improve primary health care in the poorest communities by addressing the needs of the population for essential medicines as part of primary and secondary prevention of MNS disorders.
4. Conduct efficient monitoring and evaluation of the utilization of essential medicines for MNS disorders.

### III. SCOPE AND COVERAGE

This Order shall apply to DOH hospitals, CHDs, TRCs, local government units (LGUs), rural health units (RHUs), Department of Social Welfare and Development (DSWD), Bureau of Jail Management and Penology (BJMP), and other institutions and agencies that will qualify as access sites, for an increased access to quality essential medicines for MNS disorders for the benefit of the Filipino people, especially the marginalized sector. This Order shall include MOH-BARMM pursuant to RA 11054 "Organic Law for the Bangsamoro Autonomous Region in Muslim Mindanao (BARMM)".

### IV. DEFINITION OF TERMS

1. Access site - refers to a health facility where needed essential medicines for MNS disorders are being provided for enrolled service users.
2. Enrolled service user – refers to a service user with any MNS disorder who is in the community and is seeking regular consultation in an identified access site as a beneficiary of the MAP-MH.
3. Essential medicines – refers to a list of medicines for treating MNS disorders identified by a Therapeutic Committee that will be organized for the purpose.
4. Medicine Access Program for Mental Health (MAP-MH) – refers to a medicine access program designed to provide needed essential medicines for all enrolled service users with MNS disorders who are in the community and are seeking regular consultation in an identified access site.
5. Mental Health Gap Action Programme (mhGAP) – refers to a training program developed by the World Health Organization (WHO) for primary care practitioners in non-specialized settings as an intervention guide in the treatment and management of MNS disorders and adapted for use in the Philippine context.
6. National Drug Policy Compliance Officer (NDPCO) – refers to pharmacists under CHDs or MOH-BARMM that are designated to oversee the implementation of all programs and activities of the DOH Pharmaceutical Division (PD).
7. National Mental Health Program (NMHP) – refers to a program offering a wide range of promotive, preventive, curative, and rehabilitative services for persons who suffer from MNS disorders. It has five (5) components: Wellness of Daily Living, Extreme Life Experience, Mental Disorders, Neurologic Disorders, and Substance Abuse and other Forms of Addiction.

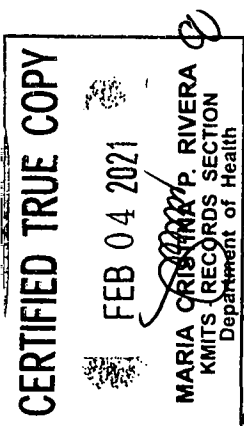


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8. Near expiry medicine – refers to a medicine that is six (6) months prior to expiration date.
9. Starter kit – refers to a set of essential medicines provided initially to a health facility whose primary care physician has been newly trained in mhGAP.

## V. GENERAL GUIDELINES

1. The Technical Working Group (TWG) created through a Department Personnel Order (DPO) shall be regularly convened to identify essential medicines for MNS disorders that shall be procured for the MAP-MH. The TWG may change or add medicines based on their assessment of the current needs and situations such as cost-effectiveness, treatment guidelines, most prescribed and fast-moving medicines, in accordance with the latest version of the Philippine National Formulary (PNF).
2. Essential medicines for MNS disorders shall be subjected to periodic review by the Health Technology Assessment Council (HTAC). Investment on any health technology or development of any benefit package by the DOH and the Philippine Health Insurance Corporation (PhilHealth) shall be based on positive recommendation of the HTAC.
3. Essential medicines for MNS disorders are classified as individual-based health services. The DOH shall finance the procurement until such time that essential mental health services are included in PhilHealth's primary care service package as stipulated in the Implementing Rules and Regulations (IRR) of RA 11223 "Universal Health Care Act".
4. Procurement of medicines shall follow the existing rules and regulations provided for in RA 9184 "Government Procurement Reform Act".
5. Quality analysis for samples of the MAP-MH shall be conducted by the Food and Drug Administration (FDA) before delivery to the access sites.
6. The MAP-MH medicines shall be packed using FDA-approved packaging materials for the purpose of promoting and advocating the program.
7. The MAP-MH shall be implemented in identified access sites by the DOH-NMHP.
8. The MAP-MH medicines shall be prescribed, dispensed, and used following existing standard treatment guidelines recognized by DOH.
9. The Pharmacotherapeutic Guidelines for the MAP-MH shall serve as the basis for clinical intervention in the primary and secondary health facilities (see Annex A).



## VI. SPECIFIC GUIDELINES

### A. Access Sites

1. The CHD Regional Coordinators shall recommend inclusion of access sites to the DOH-NMHP for approval based on the following criteria:
  - a. A licensed health facility where service users with MNS disorders are consulted, diagnosed, treated, managed, and regularly followed up in a specialty care setting (e.g. mental hospital, acute care psychiatric facility, chronic care psychiatric

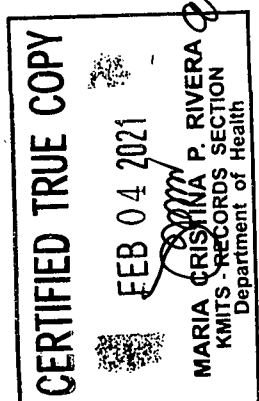
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facility, treatment and rehabilitation center (TRC), neuroscience/neurology departments and clinics, and the like).

- b. An outpatient or primary care clinic/health facility where there is an mhGAP trained nonspecialist medical personnel, or other trained primary care physician recognized by DOH e.g. rural health units (RHU).
2. Identified access sites shall be provided with essential medicines according to the needs of the service users. To this end, the access site shall be responsible for implementing MAP-MH by procuring essential medicines through a Requisition Issuance Slip (RIS) with a coverage of one (1) year. This shall allow new enrolled service users to avail of the medicines. Submission of this request form shall be in the first week of November of the previous year, and first week of May of the current year. See Annex B for the template of the RIS Form.
  3. Access sites shall regularly submit utilization reports. Reports shall be submitted quarterly on the first weeks of April, July, October, and January accordingly. See Annex C for the template of the Reporting Form.
  4. Access sites shall ensure that medicines are stored properly. It is a must for every access site to ensure that a dedicated cabinet storage with functional lock is provided for the purpose in compliance with the Guide to Good Storage Practices (GSP) for Pharmaceuticals discussed in Annex 9 of the WHO Technical Report Series No. 908, 2003.
  5. In case there is a shortage or stock-out of medicines in access sites, requests shall be made to the DOH-NMHP for augmentation purposes. However, requests shall be made known three (3) months prior to allow for processes to be completed.
  6. Near expiry medicines shall be reported to the nearest CHDs or MOH-BARMM while expired medicines shall be disposed in accordance with the Joint Department of Environment and Natural Resources (DENR)-DOH AO No. 02, s. of 2005 and its amendments. A witness from the CHD or MOH-BARMM, FDA, and Commission on Audit (COA) shall be present whenever disposal of expired drugs is conducted.
  7. Access sites shall inform and coordinate with the DOH Central Office regarding slow moving drugs and inventories, and other issues and concerns regarding the program.
  8. Access sites shall diligently enforce the mechanism of stock transfer of medicines among access sites to prevent wastage in coordination with the CHD Regional Coordinators and NDPCO.

#### **B. Enrolled Service Users**

1. Service user shall visit an identified access site and follow the process below:
  - a. Register in the access site
  - b. Undergo assessment by a physician to receive a clinical diagnosis
  - c. Present a valid prescription from a physician to avail the essential medicines for MNS disorders
  - d. Adhere to the treatment given and comply with the follow-up schedules as advised by the physician



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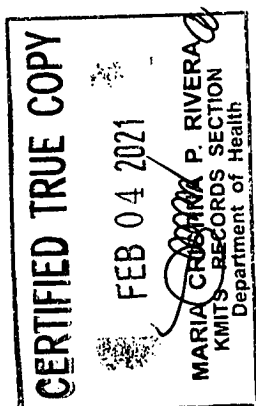
2. Enrolled service users shall be registered in the electronic information management system developed by the DOH Knowledge Management and Information Technology Service (KMITS).
3. In case of change of address, the enrolled service user shall have options to re-enroll to another access site that is more accessible to him/her and shall be properly endorsed by the previous access site including all pertinent records of the service user.
4. In cases wherein the service user was not endorsed by a previous access site, the new access site shall determine the needs of the service user and enroll him/her to the program.

## VII. MONITORING AND EVALUATION

1. Access sites shall be monitored and evaluated regularly, either by announced or unannounced visits. To this end, a Monitoring and Evaluation Committee shall be organized for this purpose. This Committee shall include, among others, representatives from the NMHP, NCMH, PD, and CHD following the provisions stated in Department Order (DO) No. 2016-0269 "Guidelines on Planning, Monitoring and Evaluation of Programs, Activities, and Projects in the DOH" and its amendments.
2. The Committee shall identify training and mentoring needs of access sites particularly in the proper dispensing of essential medicines procured for MAP-MH.

## VIII. ROLES AND RESPONSIBILITIES

1. The **National Mental Health Program (NMHP)** shall:
  - a. Lead the implementation of MAP-MH nationwide through identified access sites for all enrolled service users.
  - b. Ensure funding support for the procurement of essential medicines until such time that PhilHealth can develop and implement a benefit package for the purpose.
2. The **Pharmaceutical Division (PD) and National Drug Policy Compliance Officer (NDPCO)** shall provide technical assistance and monitoring support to NMHP in the procurement, distribution, and utilization of procured essential medicines for MAP-MH.
3. The **Knowledge Management and Information Technology Service (KMITS)** in collaboration with the NMHP shall develop a functional electronic information management system for MAP-MH.
4. The **Philippine Health Insurance Corporation (PhilHealth)** shall develop and implement an outpatient benefit package for MNS disorders.
5. The **Centers for Health Development (CHDs)** shall:
  - a. Identify health facilities to be identified as access sites for MAP-MH.
  - b. Monitor and supervise the implementation of MAP-MH in the identified access sites in their regions.
  - c. Collect, consolidate, and analyze the reports from access sites.
  - d. Prepare a summary of reports collected from access sites and submit this to NMHP with recommendations on improving the implementation.



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- e. Resolve issues and other concerns needing actions on the operationalization of the program.
- f. Enforce a mechanism of moving stocks of medicines among access sites with low levels of utilization in coordination with other access sites.

6. The **Supply Chain Management Service (SCMS)** shall:

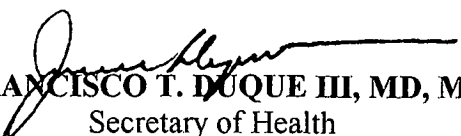
- a. Receive the goods from the local suppliers according to the quantity and specification stated in the Purchase Order.
- b. Prepare reports such as Arrival Report to End-user, Request of Inspection and Acceptance to End-User, Notice of Delivery to COA, Request of Inspection to FDA, and Request of Inspection.
- c. Oversee the inspection of medicines together with the end-user.
- d. Manage the warehousing, packaging, and distribution of medicines to the identified access sites.

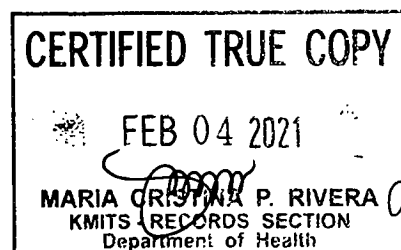
**IX. REPEALING CLAUSE**

Provisions of previous Orders and other related issuances inconsistent or contrary to the provision of this Administrative Order (AO) are hereby revised, modified, repealed, or rescinded accordingly. All provisions of existing issuances which are not affected by this Order shall remain valid and in effect.

**X. EFFECTIVITY**

This Order shall take effect fifteen (15) days after following its publication in a newspaper of general circulation and upon filing with the University of the Philippines Law Center (UPLC) of three (3) certified copies of this Order.

  
**FRANCISCO T. DUQUE III, MD, MSc.**  
Secretary of Health





Republic of the Philippines  
Department of Health  
**OFFICE OF THE SECRETARY**

**ANNEX A**

# **PHARMACOTHERAPEUTIC GUIDELINES FOR THE MEDICINE ACCESS PROGRAM FOR MENTAL HEALTH (MAP-MH)**

For Primary and Secondary Care Facilities

Technical Working Group  
Essential Non-Communicable Disease Division  
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## INTRODUCTION

Mental health and well-being are intertwined with personal well-being, family relationships, and contributions to society. Problems with mental health and well-being can adversely compromise learning, creativity, productivity, contribution to family and society and overall quality of life. The value of investing in mental health is well established. The World Economic Forum estimated in 2013 that the cumulative global impact of mental disorders alone in terms of economic output will amount to US\$ 16 trillion over the next 20 years.

Recognizing the role of mental health and well-being in national development, the Department of Health articulated a National Mental Health Policy in 2001, DOH AO No. 8 s. 2001 that provided for the establishment of a sustainable mental health program. Since then a viable mental health program has been established and is currently strengthening its implementation as mandated by DOH AO No. 2016-0039 which provided among others, the equitable access to the rationale use of a wide range of pharmacologic interventions in the treatment and management of mental, neurologic and substance use disorders and improvement in the quality of life. This mandate is further strengthened by the inclusion of mental health among the priority agenda of the current administration as articulated in the Philippine Health Agenda 2016-2022.

The Medicine Access Program for Mental Health (MAP-MH), started in 2012 by the Pharmaceutical Division and operationalized by the National Center for Mental Health was designed to ensure availability of mental health drugs in the community. Since then 138 access sites have been opened with around 20,000 patient beneficiaries. With the transfer of the Medicine Access Program for Mental Health to the National Mental Health Program under the Disease Prevention and Control Bureau of the Department of Health and the goal of expanding coverage of beneficiaries and medicines being provided, there is a need to establish standards and guidelines to aid in the proper implementation of the MAP-MH nationwide. Thus, the issuance of this Pharmacotherapeutic Guidelines on the Medicine Access Program for Mental Health.

The Pharmacotherapeutic Guidelines will serve as the basis for clinical intervention in the primary and secondary health facilities in the community. It can be utilized in conjunction with other community guidelines such as the Mental Health Gap Action Program (MHGAP) from the World Health Organization (WHO). The guideline is focuses on 6 mental health disorders, namely: Anxiety Disorders, Mood Disorders, Psychosis, Dementia, Epilepsy and Substance Abuse Disorders. All these diseases presented within the guideline is given a brief description of its clinical criteria and preferred regimen to be utilized for treatment.

This guideline was made from the collective efforts of various members of the Technical Working Group and various other stakeholders who aim for the improvement of health service provision in mental health and strengthening the implementation of the R.A. 11036 otherwise known as the Mental Health Act for the community.

# CONSENSUS TREATMENT GUIDELINES ON ANXIETY DISORDERS

# I. ANXIETY DISORDERS

Anxiety disorder reflect disorders that share a general feature of excessive fear (i.e. anticipation of emotional response to perceived or real threat) and/ or anxiety (anticipation of future threat) and demonstrate behavioral, physiologic and functional disturbance as a result. Panic attacks are a feature that can occur in the context of many anxiety disorders and reflect a type of fear response. There are several types of anxiety disorders.

## A. PANIC DISORDER

Panic disorder refers to recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches peak within minutes, and during which time four or more of a list of 13 physical and cognitive symptoms occur. The term *recurrent* literally means more than one unexpected panic attack. The term *unexpected* refers to a panic attack for which there is no obvious cue or trigger at the time of occurrence – that is, the attack appears to occur from out of the blue, such as when the individual is relaxing or emerging from sleep (nocturnal panic attack) (Philippine Psychiatric Association, 2017).

**CLINICAL CRITERIA:**

**Recurrent unexpected panic attacks** – Palpitations, sweating, trembling/shaking, sensations of shortness of breath/smothering, feelings of choking, chest pain/discomfort, nausea or abdominal distress, feeling dizzy/faint, chills/heat sensations, paresthesias, de-realization or depersonalization, fear of losing control, fear of dying (PPA, 2017).

## B. GENERALIZED ANXIETY DISORDER

The essential feature of generalized anxiety disorder (GAD) is excessive anxiety and worry about several events or activities. The intensity, duration, or frequency of the anxiety and worry is disproportionate to the actual likelihood or impact of the anticipated event. An individual with GAD finds it difficult to control the worry and to keep worrisome thoughts from interfering with attention to tasks at hand (PPA, 2017).

**CLINICAL CRITERIA:**

Should have a duration of more than 6 months that affects his/her social or occupational functioning, excessive anxiety and worry, difficulty in controlling worry, 3 or more of the following: restlessness, easily fatigued, difficulty, irritability, muscle tension, sleep disturbance (PPA, 2017).

## C. SOCIAL ANXIETY DISORDER

The essential feature of social anxiety disorder (SAD) is a marked or intense fear, or anxiety of social situations in which the individual may be scrutinized by others (PPA, 2017).

**CLINICAL CRITERIA:**

Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others. The fear, anxiety or avoidance is persistent, typically 6 months or more.

## II. PREFERRED REGIMEN

| Treatment Choice |  |   |
|------------------|--|---|
| First-Line       | <b>Selective Serotonin Reuptake Inhibitors (SSRIs)</b> <ul style="list-style-type: none"> <li>- SSRIs are effective in reducing frequency and intensity of panic attacks, anticipatory anxiety, and in improving associated depressive mood. No difference in efficacy is seen in different types of SSRIs in dealing with panic disorder. Due to the relatively favorable safety and side effect profile of SSRIs, they are recommended as the best initial choice for patients with panic disorder (PPA, 2017).</li> <li>- <i>Avoid abrupt withdrawal</i></li> </ul> |   |
|                  | <b>Medication</b>  | <b>Side Effects</b>   |
|                  | <b>Sertraline</b><br><br><i>Avoid use when driving, operating machineries, etc. (due to sedation)</i><br><br><b>Drug-lab interaction:</b><br>Sertraline can cause a false positive urine drug screen for benzodiazepines   | <b>Common:</b><br>Erectile dysfunction in men, decreased sexual desires in women, gastrointestinal disturbances (decreased appetite, nausea, diarrhea, and constipation), insomnia, sedation, agitation, tremors, headache, dizziness. May cause prolonged erection and delayed ejaculation<br><br><b>Serious:</b><br>Bruising and rare bleeding, rare hyponatremia, rare hypotension |
|                  | <b>Fluoxetine</b><br><br><i>Caution in persons with history of seizure (can lower the seizure threshold)</i><br><br><b>Drug-drug interactions:</b> Avoid combination with warfarin (may increase bleeding risk). May increase levels of TCAs, antipsychotics, and beta-blockers.<br><br>Caution in combination with tamoxifen, codeine, and tramadol (reduces the effect of these drugs).  | <b>Common:</b><br>Insomnia, headache, dizziness, gastrointestinal disturbances, changes in appetite, and sexual dysfunction.<br><br><b>Serious:</b><br>Bleeding abnormalities in those who use aspirin or other non-steroidal anti-inflammatory drugs, low sodium levels.   |
|                  | <b>Escitalopram</b><br><br><i>Use with caution among elderly. (Elderly are more prone to SSRI/SNRI induced hyponatremia)</i>   | <b>Common:</b><br>Nausea, sweating, somnolence, dizziness, insomnia, constipation, diarrhea, appetite decrease, sexual dysfunction, fatigue, pyrexia.   |

|             |  |  |   |
|-------------|--|--|---|
|             |  | Used with caution in patient using medication that will affect clotting of blood.  |   |
|             |  | Caution with other QTc-prolonging medications like some antipsychotics, macrolides, fluoroquinolones, ondansetron, and HIV protease inhibitors.  |   |
| Second-Line | <b>Atypical Antipsychotics</b><br>- There has been enough evidence recently that points to efficacy of quetiapine in the treatment of GAD and being equally efficacious as antidepressants. However, quetiapine use is associated with more metabolic and sedative effects as compared to placebo or antidepressants. As this might affect the patient's adherence, quetiapine is recommended as a second line treatment for GAD for those who cannot tolerate the use of SSRIs (PPA, 2017). |  |   |
|             | <b>Medication</b>  | <b>Caution</b>   | <b>Side Effects</b>   |
|             | <b>Quetiapine</b>  | <i>Use with caution among elderly. (Elderly are more prone to SSRI/SNRI induced hyponatremia)</i><br><br>Caution with other QT-prolonging medications like fluoroquinolones, macrolides, ondansetron, and HIV protease inhibitors.<br><br>Monitor weight, BP, Fasting Blood Sugar (FBS), and Lipid Profile, if possible. | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal pain, diarrhea, constipation, weight gain), Endocrine – diabetes mellitus (increased cholesterol and FBS) |

### III. TREATMENT DOSE

| Disorder              | Dosages   |   |  |   |
|-----------------------|---|---|--|---|
|                       | 1 <sup>st</sup> Line  |   |  | 2 <sup>nd</sup> Line  |
|                       | Sertraline  | Fluoxetine  | Escitalopram   | Quetiapine  |
| <b>Panic Disorder</b> | <b>Initial dose:</b><br>12.5 mg (Oral)<br><br><b>Maximum dose:</b><br>150-200 mg (Oral) | <b>Initial dose:</b><br>20 mg capsule (Oral)<br><br><b>Maximum dose:</b><br>80 mg daily* (Oral)<br><br>*Total Daily dose >20 mg/day should be divided in two (2) separate doses, each given every 12 hours. | <b>Initial dose:</b><br>10 mg (Oral)<br><br><b>Maximum dose:</b><br>20 mg/day (Oral) | <b>Not recommended as second line. May be used as third line.</b> |

|   |  |  |  |   |
|---|--|--|--|---|
| <b>Generalized<br/>Anxiety<br/>Disorder<br/>(GAD)</b> | <b>Initial dose:</b><br>12.5 mg (Oral)<br><br><b>Maximum<br/>dose:</b><br>150-200 mg<br>(Oral) | <b>Initial dose:</b><br>20 mg (Oral)<br><br><b>Maximum dose:</b><br>80 mg daily* (Oral)<br><br>*Total Daily dose >20<br>mg/day should be divided in<br>two (2) separate doses, each<br>given every 12 hours. | <b>Initial dose:</b><br>10 mg (Oral)<br><br><b>Maximum dose:</b><br>20 mg/day (Oral) | <b>Initial dose:</b><br>25 mg (Oral)<br><br><b>Maximum dose:</b><br>150 mg (Oral) |
| <b>Social<br/>Anxiety<br/>Disorder</b>                | <b>Initial dose:</b><br>12.5 mg (Oral)<br><br><b>Maximum<br/>dose:</b><br>150-200 mg<br>(Oral) | <b>Initial dose:</b><br>10 mg (Oral)<br><br><b>Maximum dose:</b><br>80 mg daily* (Oral)<br><br>*Total Daily dose >20<br>mg/day should be divided in<br>two (2) separate doses, each<br>given every 12 hours. | <b>Initial dose:</b><br>10 mg (Oral)<br><br><b>Maximum dose:</b><br>20 mg/day (Oral) | <b>Initial dose:</b><br>25 mg (Oral)<br><br><b>Maximum dose:</b><br>150 mg (Oral) |

# CONSENSUS TREATMENT GUIDELINES ON PSYCHOSIS



# I. PSYCHOSIS

Psychosis is characterized by distorted thoughts and perceptions, as well as disturbed emotions and behaviors. Incoherent or irrelevant speech may also be present. Symptoms such as hallucinations-fixed, false belief; severe abnormalities of behavior-disorganized behavior, agitation, excitement, inactivity or hyperactivity; disturbance in emotions-marked apathy, or disconnect between reported emotion and observed affect, such as facial expression and body language, may also be detected. The most common disorder is schizophrenia.

## A. SCHIZOPHRENIA

Schizophrenia is characterized by delusions, hallucinations, disorganized speech and behavior, and other symptoms that cause social or occupational dysfunction. For diagnosis to be made, symptoms must have been present for six months with at least one month of active symptoms.

### **CLINICAL CRITERIA:**

Two or more of the following, each present for a significant portion of time during a 1-month period: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, negative symptoms (diminished emotional expression or avolition). Continuous signs of disturbance persist for at least 6 months.

The course of treatment and management of schizophrenia can be divided into three phases, each with corresponding goals: (1) acute phase, (2) stabilization phase, (3) maintenance phase.

### 1. ACUTE PHASE

The Acute Phase is defined as the period of an acute psychotic episode. This phase begins with a new onset or acute exacerbation of symptoms and lasts until symptoms are reduced to a level considered to be the patient's expected "baseline". Before administration of medications, simple interventions such as reorientation and de-escalation techniques may be done to assist in defusing the situation (Castle et al., 2017). The patient's Advance Directive should also be taken into consideration.

For patient in the acute phase, Rapid Neuroleptization can be performed which is a common method to calm an agitated patient with Schizophrenia (Battaglia, 1997). It is defined further as a method of administering repeated doses of medication under close clinical supervision that provides rapid control of acute functional psychotic symptoms (Donion, 1979).

### 2. STABILIZATION PHASE

The stabilization period follows the acute phase and constitutes a time-limited transition to continuing treatment in the stable phase (APA Guidelines, 2010). The stabilization phase will be defined as the phase occurring from the 3<sup>rd</sup> to 6<sup>th</sup> months. Recommendation to Pharmacotherapy is to continue the same dose of antipsychotic medication which produced an adequate response for at least 6 months.



### 3. MAINTENANCE PHASE

The maintenance phase aims to sustain the patient's control of symptoms and remission.

## B. PSYCHOSIS DUE TO OTHER MENTAL DISORDERS

Psychoses could be seen in several mental disorder-like severe cases of depression. They can also be seen in substance use disorder, seizure, dementia, etc.

#### CLINICAL CRITERIA:

Patient who present with psychosis and was diagnosed of having mental disorder aside from Schizophrenia like major depression, substance use disorder, seizure, dementia, HIV, etc.

Psychosis having marked Behavioral Changes; neglecting usual responsibilities related to work, school, domestic or social activities, agitated and aggressive behavior with decreased or increased activity, fixed false beliefs not shared by others in the person's culture, hearing voices or seeing things that are not there.

## II. PREFERRED REGIMEN

| Treatment Choice |   |   |  |
|------------------|---|---|--|
| First Line       | <b>Atypical Antipsychotic</b> <ul style="list-style-type: none"> <li>Atypical agents are associated with lower risk of medication change, medication gaps and re-hospitalization. Both conventional and atypical agents are associated with improvement of positive symptoms at follow-up, but only subjects of atypical agents at follow-up experienced a significant improvement in negative symptoms. (Serra-Arain, et.al 2015)</li> </ul> |   |  |
|                  | <b>Medication</b>   | <b>Cautions</b>   | <b>Side Effects</b>  |
|                  | <b>Risperidone</b><br>(tablet or ODT*)<br><br><i>*ODT is used for extremely agitated patients</i>   | <i>Use with caution in patients with cardiac disease.</i><br><br>For elderly patients: start with 1 mg/day<br><br><b>Drug-drug interactions:</b><br>Carbamazepine can reduce levels of risperidone, whereas fluoxetine can increase levels.<br><br>Monitor weight, BP, FBS, and lipid profile, if possible. | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal cramps, diarrhea, constipation), other effects (dyspepsia, epistaxis, abnormal vision), cardiac dysrhythmia – QT Prolongation, endocrine – diabetes mellitus (increased cholesterol and FBS) |

|             |  |  |   |
|-------------|--|--|---|
|             | <b>Olanzapine</b><br>(tablet or ODT*)<br><br><i>*ODT is used for extremely agitated patients</i>   | <i>Use with caution in patients with diabetes mellitus (DM), seizures, benign prostatic hyperplasia (BPH), narrow angle glaucoma, and hepatic Disease</i><br><br>Decreased serum concentrations up to 50% with cigarette smoke<br><br>Monitor weight, BP, FBS, and lipid profile, if possible. | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal pain, diarrhea, constipation), hepatic (increase in alanine aminotransferase / ALT – 3 times greater), endocrine – diabetes mellitus (increased cholesterol and FBS)  |
|             | <b>Quetiapine</b>  | <i>Use with caution for elderly patients.</i><br><br>Caution with other QT-prolonging medications like fluoroquinolones, macrolides, ondansetron, and HIV protease inhibitors.<br><br>Monitor weight, BP, FBS, and lipid profile, if possible.   | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal pain, diarrhea, constipation, weight gain), endocrine – diabetes mellitus (increased cholesterol and FBS)   |
| Second Line | <b>Typical Antipsychotic</b><br>- Typical antipsychotic medications may be considered since the risks and benefits of various treatments for each patient change over time. It can improve positive symptoms of patients with schizophrenia (PPA, 2017). |  |   |
|             | <b>Medication</b>  | <b>Cautions</b>  | <b>Side Effects</b>   |
|             | <b>Haloperidol</b>   | <b>Watch out for orthostatic hypotension, increase water intake, regular eye exams recommended</b><br><br>Sedative effects are most marked during the few days of administration   | <b>Common:</b><br>Sedation, anticholinergic effect (dry mouth, urinary retention, tachycardia, constipation, blurred vision), extrapyramidal symptoms (EPS), Weight Gain, tardive dyskinesia, photosensitivity, EEG abnormalities, neuroleptic malignant syndrome, increased susceptibility to developing EPS |
|             | <b>Chlorpromazine</b>  | <i>Use with caution for elderly patients.</i><br><br><b>Contraindications:<sup>1</sup></b><br>Bone marrow suppression, pheochromocytoma, lactation   | <b>Common:</b><br>Tardive dyskinesia (on long-term therapy). Involuntary movements of extremities may also occur. Dry mouth, constipation, urinary retention, mydriasis, agitation, insomnia, depression and convulsions; postural hypotension, ECG changes. Allergic   |

<sup>1</sup> MIMS Philippines (n.d.): Chlorpromazine, retrieved from:  
<https://www.mims.com/philippines/drug/info/chlorpromazine/?type=brief&mtype=generic>

|  |  |   |  |
|--|--|---|--|
|  |  | <b>Drug-lab interaction:</b><br>Chlorpromazine can cause a false positive in urine drug screening for amphetamines. | skin reaction, amenorrhea, gynecomastia, hyperglycemia, and raised serum cholesterol.<br><br><b>Fatal:</b><br>Agranulocytosis, neuroleptic malignant syndrome, extrapyramidal dysfunction. |
|--|--|---|--|

### III. TREATMENT DOSE

| Disorder                                       | Dosages   |  |  |   |  |
|--|---|--|--|---|--|
|  | 1 <sup>st</sup> Line  |  |  | 2 <sup>nd</sup> Line  |  |
|  | Risperidone   | Olanzapine   | Quetiapine   | Haloperidol   | Chlorpromazine   |
| <b>Schizophrenia</b>                           |   |  |  |   |  |
| <b>a. Acute Phase*</b>                         | <b>Initial dose:</b><br>1-2 mg/day (Oral)<br><br><b>Maximum dose:</b><br>6 mg/day (Oral)<br><br><i>*For elderly start with 1 mg/day</i> | <b>Initial dose:</b><br>10 mg/day (Oral)<br><br><b>Maximum dose:</b><br>20 mg/day (Oral) | <b>Initial dose:</b><br>200 mg/day (Oral)<br><br><b>Maximum dose:</b><br>800 mg/day (Oral)     | <b>Initial dose:</b><br>5 mg/day (Oral)<br><br><b>Maximum dose:</b><br>20 mg/day (Oral)           | <b>Initial dose:</b><br>75-100 mg / day (Oral)<br><br><b>Maximum dose:</b><br>400 mg/day (Oral)  |
| <b>b. Stabilization Phase</b>                  | <b>Initial dose:</b><br>1 mg/day (Oral)<br><br><b>Maximum dose:</b><br>4 mg/day (Oral)  | <b>Initial dose:</b><br>10 mg/day (Oral)<br><br><b>Maximum dose:</b><br>20 mg/day (Oral) | <b>Initial dose:</b><br>300-400 mg/day (Oral)<br><br><b>Maximum dose:</b><br>800 mg/day (Oral) | <b>Initial dose:</b><br>1.5 – 3 mg daily (Oral)<br><br><b>Maximum dose:</b><br>20 mg daily (Oral) | <b>Initial dose:</b><br>25-50 mg daily (Oral)<br><br><b>Maximum dose:</b><br>300 mg daily (up to 1000 mg may be necessary for severe cases) (Oral) |
| <b>c. Maintenance Phase</b>                    | Same as above   |  |  |   |  |
| <b>Psychosis Due to Other Mental Disorders</b> | <b>Initial dose:</b><br>0.5 mg/day (Oral)   | <b>Initial dose:</b><br>2.5 mg/day (Oral)  | <b>Initial dose:</b><br>300-800 mg/day (Oral)  | <b>Initial dose:</b><br>20-60 mg/day (Oral)   | <b>Initial dose:</b><br>300-1000 mg / day (Oral)   |

Special Considerations:

- In women with psychosis who are planning pregnancy or pregnant or breastfeeding, low-dose oral haloperidol or chlorpromazine may be considered.
- In adolescent with psychotic or bipolar disorder, risperidone can be offered as a treatment option only under supervision of a specialist, if treatment with risperidone is not feasible, haloperidol or chlorpromazine may be used only under supervision of a specialist.
- Antipsychotics carry an increased risk of cerebrovascular events and death in older adults with dementia-related psychosis.
- In those with Parkinson's disease psychosis, clozapine may be less likely to worsen Parkinson's symptoms (given proper monitoring is done) and quetiapine may be useful.
- Try the medication at a typically effective dose for at least 4-6 weeks with adherence and interactions noted before considering it ineffective.

## C. MANAGEMENT FOR TREATMENT- RESISTANCE AND/OR NON- ADHERENCE

Due to the extensive treatment and monitoring of the treatment phase, existence of treatment resistance and non-adherence. The efficient treatment course for such incidences involves the use of Long Acting Injectable (LAI) and other anti-psychotics.

### I. PREFERRED REGIMEN

| Treatment Choice |   |  |  |  |
|------------------|---|--|--|--|
| First Line       | <b>Long Acting Injectable</b>   |  |  |  |
|                  | <ul style="list-style-type: none"> <li>- They are also considered for patients with a history of non-adherence with oral medications. It provides a steady level of the antipsychotics in the body and minimizes fluctuations in blood levels.</li> </ul> |  |  |  |
|                  | <b>Medication</b>   | <b>Dosage and Frequency</b>            | <b>Cautions</b>  | <b>Side Effects</b>  |
|                  | <b>Fluphenazine decanoate 25 mg, 1 ml Ampule (Intramuscular)*</b>   | <b>12.5 mg – 50 mg every 2-4 weeks</b> | <b>Contraindications:</b><br>Impaired Consciousness, Parkinsonism<br><br><b>Cautions in patients with:</b><br>Cardiac Disease, Kidney Disease, Liver Disease. Use with caution in older adults | <b>Common:</b><br>Sedation, dizziness, blurred vision, dry mouth, urinary retention, constipation, tachycardia<br><br><b>Serious:</b><br>Orthostatic hypotension, syncope, extrapyramidal symptoms, photosensitivity, weight gain, galactorrhea, |

|  |  |  |   |  |
|--|--|--|---|--|
|  |  |  | <p><b>Drug to Drug Interactions:</b><br/>Increases effects to blood pressure lowering medications<br/>Can lower blood pressure if used with epinephrine</p>   | <p>amenorrhea, sexual dysfunction, priapism, neuroleptic malignant syndrome (NMS), agranulocytosis, jaundice</p>   |
|  | <p><b>Flupenthixol decanoate 20mg/mL, amplus (Intramuscularly)</b></p> | <p>20mg-40mg every 2 to 4 weeks</p> <p>(Initial dose of 20mg for patients who have not been exposed to long-acting depot antipsychotics, 40mg for patients who have previously demonstrated tolerance to long-acting depot antipsychotics; after 4-10 days can give additional 20mg dose; maximum of 200mg every 1-4 weeks.)</p> | <p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>• diminished consciousness due to any cause</li> <li>• collapse due to very low blood pressure</li> <li>• brain damage</li> <li>• diseases of the blood with a reduced number of red or white blood cells or platelets</li> <li>• phaeochromocytoma, a rare tumour of the adrenal gland which sits near the kidney.</li> <li>• Do not give Fluanxol to anyone who currently has alcohol poisoning, or poisoning with medicines used to produce calmness or to help you sleep, or medicines used to treat epilepsy or strong pain.</li> <li>• Do not give Fluanxol to anyone who is unconscious or in a coma.</li> <li>• Do not give Fluanxol to a child or adolescent or in pregnant women.</li> </ul> <p><b>Cautions in patients with:</b></p> <ul style="list-style-type: none"> <li>• Renal impairment, hepatic impairment, cardiac impairment, and elderly.</li> </ul> <p><b>Drug to Drug Interactions:</b></p> | <p><b>Common and serious:</b><br/>Neuroleptic-induced deficit syndrome<br/>Extrapyramidal symptoms (more common at the start of treatment), parkinsonism<br/>Insomnia, restlessness, agitation, sedation<br/>Tardive dyskinesia (risk increases with duration of treatment and with dose)<br/>Galactorrhea, amenorrhea</p> |

|  |  |  |  |  |
|--|--|--|--|--|
|  |  |  | <ul style="list-style-type: none"> <li>• may decrease the effects of levodopa, dopamine agonist</li> <li>• may increase the effects of antihypertensive drugs except for guanethidine, whose antihypertensive actions flupenthixol may antagonize</li> <li>• CNS effects may be increased if used with other CNS depressants</li> <li>• combined with epinephrine may lower blood pressure</li> <li>• Ritonavir may increase plasma levels of flupenthixol</li> <li>• May increase carbamazepine plasma levels</li> <li>• Some patients taking a neuroleptic and lithium have developed an encephalopathic syndrome similar to neuroleptic malignant syndrome</li> </ul> |  |
|  | <b>Paliperidone palmitate</b><br>78, 117, 156, 234 mg prefilled syringes | <p>Starting dose: 150 mg (day 1) + 100mg (day 8)</p> <p>Maintenance dose: 75 mg (25 – 100 mg)</p> <p>No need for oral supplementation</p> <p>Some elderly patients may tolerate lower doses better</p> | <p>LAI paliperidone is not recommended for patients who have not first demonstrated tolerability to oral paliperidone or risperidone</p> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>• Use with caution in patients with conditions that predispose to hypotension (dehydration, overheating)</li> <li>• Dysphagia has been associated with antipsychotic use, and paliperidone should be used cautiously in patients at risk for</li> </ul>   | <p><b>Notable Side Effects:</b></p> <ul style="list-style-type: none"> <li>• Dose-dependent extrapyramidal symptoms</li> <li>• Hyperprolactinemia</li> <li>• May increase risk for diabetes and dyslipidemia</li> <li>• Rare tardive dyskinesia (much reduced risk compared to conventional antipsychotics)</li> <li>• Sedation, hypersalivation</li> <li>• Dose-dependent orthostatic hypotension</li> <li>• Tachycardia</li> <li>• Injection site reactions</li> <li>• Weight gain and/or sedation may be experienced and/or can be significant amount, may be dose dependent, may be less than for some antipsychotics, more than for others</li> </ul> |

|  |  |  |  |   |
|--|--|--|--|---|
|  |  |  | <p>aspiration pneumonia</p> <ul style="list-style-type: none"> <li>• Paliperidone prolongs QTc interval more than some other antipsychotics</li> <li>• Priapism has been reported with other antipsychotics, including risperidone</li> </ul> <p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>• If patient is taking agents capable of significantly prolonging QTc interval (eg. pimozide, thioridazine, selected antiarrhythmics, moxifloxacin, sparfloxacin)</li> <li>• If there is a history of QTc prolongation or cardiac arrhythmia, recent acute myocardial infarction, uncompensated heart failure</li> <li>• If patient has a preexisting severe gastrointestinal narrowing</li> <li>• If there is a proven allergy to paliperidone or risperidone</li> </ul> <p><b>Drug Interactions:</b></p> <ul style="list-style-type: none"> <li>• May increase effects of antihypertensive agents</li> <li>• May antagonize levodopa, dopamine agonists</li> </ul> <p>May enhance QTc prolongation of other drugs capable of prolonging QTc interval</p> | <p><b>Life-threatening or Dangerous side effects</b></p> <ul style="list-style-type: none"> <li>• Hyperglycemia, in some extreme cases and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients taking atypical antipsychotics</li> <li>• Increased risk of death and cerebrovascular events in elderly patients with dementia-related psychosis</li> <li>• Rare neuroleptic malignant syndrome (much reduced risk compared to conventional antipsychotics)</li> <li>• Rare seizure</li> </ul> |
|--|--|--|--|---|



|  |                                   |                   |   |  |
|--|-----------------------------------|-------------------|---|--|
|  | <b>Clozapine 100 mg tablet PO</b> | 12.5 mg to 100 mg | <b>Contraindications:<sup>2</sup></b><br>Impaired bone marrow function, uncontrolled epilepsy, CNS depression, severe cardiac disorder, severe renal and hepatic impairment<br><br><b>Drug to Drug Interactions:</b> <ul style="list-style-type: none"> <li>- Increased risk of neuroleptic malignant syndrome with lithium</li> <li>- Increased risk of seizures with valproic acid</li> <li>- Increased risk of myelosuppression with long-acting depot antipsychotics</li> </ul> | <b>Common:</b><br>Decreased gastrointestinal motility, urinary retention, dyslipidemia, extrapyramidal symptoms, deep vein thrombosis<br><br><b>Serious:</b><br>Orthostatic Hypotension, bradycardia, Severe agranulocytosis/neutropenia, myocarditis and cardiomyopathy, hepatotoxicity including hepatic failure, hepatic necrosis and hepatitis, torsade de pointes, cardiac arrest, neuroleptic malignant syndrome, respiratory depression or failure, paralytic ileus, intestinal obstruction |
|--|-----------------------------------|-------------------|---|--|

## II. TREATMENT DOSE

| Disorder                                    | Dosages  |   |
|---|--|---|
|   | 1 <sup>st</sup> Line   | 2 <sup>nd</sup> Line  |
|   | Fluphenazine decanoate   | Clozapine   |
| <b>Treatment Resistance / Non-Adherence</b> | <b>Initial dose:</b> 12.5 mg every 2-4 weeks (Intramuscular in the gluteal muscle)<br><br><b>Maximum dose:</b> 50 mg every 2-4 weeks (Intramuscular in the gluteal muscle) | <b>Initial dose:</b> 12.5 mg/day (Oral)<br><br><b>Maximum dose:</b> 450 mg/day (up to 900 mg may be necessary for severe cases) (Oral) in divided doses |

<sup>2</sup> MIMS Philippines (n.d.): Clozapine, retrieved from:  
<https://www.mims.com/philippines/drug/info/clozapine?mtype=generic>

# **CONSENSUS TREATMENT GUIDELINES ON MOOD DISORDERS**

# I. MOOD DISORDERS

## A. MAJOR DEPRESSIVE DISORDER

Major Depressive Disorder (MDD) is a chronic, brain disorder characterized by low mood and loss of interest that can affect a person's thoughts, behavior, feelings, and social functioning. As such, depression poses a great impact to a person's relationships and productivity. It may also complicate existing medical conditions adding to the burden of chronic diseases and may lead to possible suicide.

### CLINICAL FEATURES:

MDD is characterized by either a depressed mood or loss of interest or pleasure as the core symptoms, persisting for at least 2 weeks and associated with a change from previous functioning.

There must have a significant effect on the individual's functioning and must have at least five other symptoms of depression: Depressed mood, markedly diminished interest or pleasure in almost all activities, significant weight loss, insomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to think or concentrate or indecisiveness.

An adequate trial of an anti-depressant should be a minimum of three weeks at the recommended therapeutic dose. If there is no improvement at 2 to 4 weeks of adequate antidepressant dose, it is recommended to increase dose or to switch to another antidepressant if the patient experiences intolerable side effects (Kennedy et al, 2016). Once remission sets in, maintenance antidepressant treatment for at least six months up to one year is recommended.

## II. PREFERRED REGIMEN

| Treatment Choice |   |   |  |  |
|------------------|---|---|--|--|
| First Line       | <b>Selective Serotonin Reuptake Inhibitors (SSRIs)</b>  |   |  |  |
|                  | - These are the first-line treatment recommendations for adult MDD (e.g. escitalopram, sertraline, fluoxetine). |   |  |  |
|                  | <b>Medication</b>   | <b>Dosage and Frequency</b>   | <b>Cautions</b>  | <b>Side Effects</b>  |
|                  | <b>Escitalopram</b>   | 20 – 60 mg/day<br><br><i>Elderly/Medically Ill: Preferred Choice, Start 10 mg daily, then increase to 20 mg</i> | Elderly are more prone to SSRI induced Hyponatremia<br><br>Used with caution in patient medication that will affect clotting of blood. | *Adverse effects are usually transient:<br><br>Nausea, Sweating, Somnolence, Dizziness, Insomnia, Constipation, Diarrhea, Appetite Increase, |

|                      |   |  |   |   |
|----------------------|---|--|---|---|
|                      |   |  | Do not take at night unless sedation occurs.  | Sexual Dysfunction, Fatigue, Pyrexia, Yawning   |
|                      | <b>Fluoxetine</b>   | Adult:<br>Start 10 mg daily for one week then 20 mg daily. If no response in 6 weeks, increase to 40 mg (maximum of 80 mg) | Elderly are more prone to SSRI induced Hyponatremia<br><br>Combination with Tamoxifen, codeine and tramadol can lead to treatment failure | Headache, Nausea, Insomnia, Anorexia, Anxiety, Asthenia, Diarrhea, Nervousness, Somnolence<br><br><b>Less Common:</b><br>Dizziness, Dry mouth, dyspepsia, sweating, tremor, decreased libido, abnormal taste, agitation, chest pain, sleep disorder |
|                      |   | Adolescent:<br>Start 10 mg daily. Increase 20 mg daily if no response in 6 weeks (maximum 40 mg)                           | Do not take at night unless sedation occurs<br><br>Cautions in persons with history of seizure.   | <b>Serious:</b><br>Bleeding abnormalities in those who use aspirin or other non-steroidal anti-inflammatory drugs, low sodium levels  |
|                      |   | Elderly/Medically Ill: Preferred Choice, Start 10 mg daily, then increase to 20 mg (maximum of 40 mg)                      | <b>Drug-Drug Interactions:</b><br>Avoid combination with warfarin (may increase levels of TCAs, anti-psychotics and beta-blockers.        |   |
|                      | <b>Sertraline</b>   | Initial Dose: 12.5 mg<br><br>Maximum Dose: 150-200 mg<br><br>Elderly: maximum dose = 50 mg/day                             | Elderly are more prone to SSRI induced Hyponatremia<br><br>Do not take at night unless sedation occurs                                    | Headache, Somnolence, drowsiness, fatigue, dizziness, insomnia, tremor, anxiety, paresthesia, agitation, sexual dysfunction, nausea, dry mouth, diarrhea, constipation, abnormal vision   |
| <b>Second - Line</b> | <b>Atypical antipsychotic</b><br>The conventional and atypical antipsychotics show modest efficacy in the treatment of psychosis, agitation, and aggression in patient with depression. |  |   |   |
|                      | <b>Quetiapine</b>   | 150-300mg  | Special Instructions:<br>Metabolic Effects<br>Monitoring (need specificity)   | <b>Common:</b><br>CNS (dizziness, ataxia, headache), GI (dry mouth, abdominal pain, diarrhea, constipation, weight gain), Endocrine (increased cholesterol and FBS)   |

### III. TREATMENT DOSE

| Disorder                         | Dosages  |   |  |                      |
|----------------------------------|--|---|--|----------------------|
|                                  | 1 <sup>st</sup> Line   |   |  | 2 <sup>nd</sup> Line |
|                                  | Escitalopram   | Fluoxetine  | Sertraline   | Quetiapine           |
| <b>Major Depressive Disorder</b> | <p>Initial dose: 10-20 mg/day (Oral)</p> <p><i>Elderly/Medically Ill: Start 10 mg once daily, then increase to 20 mg</i></p> | <p><b>Adult:</b><br/>Start 10 mg once daily for one week then increase to 20 mg once daily. If no response in 6 weeks, increase to 40 mg once daily (Maximum dose: 80 mg/day)</p> <p><b>Adolescent:</b><br/>Start 10 mg once daily for one week then increase to 20 mg once daily if no response in 6 weeks (Maximum dose: 40 mg/day)</p> <p><b>Elderly:</b><br/>Start 10 mg once daily then increase to 20 mg once daily (Maximum dose: 40 mg/day)</p> | <p>Initial dose: 12.5 mg once daily (Oral)</p> <p>Maximum dose: 150 – 200 mg once daily</p> <p><i>*Elderly maximum dose: 50 mg/day</i></p> | 150-300 mg/day       |

#### Special Considerations:

- Antidepressant medications usually need to be continued for at least 9 – 12 months after resolution of symptoms
- If the person develops a manic episode – stop the antidepressant immediately, it may trigger a manic episode in untreated bipolar disorder
- Do not combine with other depressants and serotonergic agents (e.g. tramadol, ginseng, St. John's wort, etc.), this may cause serotonin syndrome (these conditions consist of a combination of mental status changes, neuromuscular hyperactivity and autonomic hyperactivity)<sup>3</sup>
- Antidepressants may increase suicidal ideation, especially in adolescents and young adults of aged 24 and below, however the effect decreases amongst adults ages 25 and above.
- If symptoms persist or worsen despite interventions, consider FLUOXETINE. Ask adolescent to return weekly for the first 4 weeks to monitor thoughts or plans of suicide.
- If the woman is breastfeeding, avoid long acting anti-depressant medication such as Fluoxetine.
- For adults with thoughts or plans of suicide – SSRIs are the first choice.

<sup>3</sup> Volpi-Abadie, J., et al (2013): Serotonin Syndrome, National Institute of Health, The Oshner Journal Vol 13(4) pp 553-540, retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3865832/>

## B. BIPOLAR DISORDER<sup>4</sup>

Bipolar Mood Disorder is a chronic mental health condition characterized by manic and/or hypomanic episodes, either with or without depressive episodes, which cause significant impairment in social, occupational and/or academic functioning. It is often co-morbid with other psychiatric conditions such as anxiety disorders, substance use disorders, personality disorders, and attention deficit hyperactivity disorder.

### 1. BIPOLAR I DISORDER

#### **CLINICAL CRITERIA:**

The DSM-5 criteria for Bipolar I disorder require at least one episode of mania. In most cases, the manic episode may be preceded or followed by a hypomanic or depressive episode.

### 2. BIPOLAR MOOD DISORDER WITH MIXED FEATURES

#### **CLINICAL CRITERIA:**

Manic or Hypomanic Episodes with mixed features are characterized by episodes that meet all criteria for mania or hypomania, with at least three of the following symptoms during most days of the episode: Depressed mood, Diminished interest or pleasure in most activities, Psychomotor Retardation, Low Energy, Excessive Guilt or Thoughts of Worthlessness, Recurrent thoughts about death or suicide, or suicide attempt.

\*The purpose of the treatment is similar and thus treated with same medications

### 3. HYPOMANIA

#### **CLINICAL CRITERIA:**

This is associated with unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic. It is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization.

*\*Clinical practice suggests that Mood Stabilizers used in acute mania are also effective in hypomanic episodes.*

### 4. RAPID CYCLING BIPOLAR MOOD DISORDER

#### **CLINICAL CRITERIA:**

At least four mood episodes in a 12-month period, the episodes meet both the symptom and duration criteria for mania, hypomania, or major depression; the episodes that occur as part of a rapid cycling pattern are no different from episodes that occur as part of a non-rapid cycling pattern; the episodes are demarcated by a period of partial or full remission for at least two months, or by a switch to an episode of opposite polarity.

<sup>4</sup> PPA (February 2017): Consensus Treatment Guidelines on Bipolar Mood Disorder.

The treatment of manic and hypomanic episodes in patients with rapid cycling bipolar disorder is comparable to the treatment of mania or hypomania in general. The choice of treatment for rapid cycling is governed by current mood state and the need to prevent depressive state. The treatment options include valproate, lithium, olanzapine, and lamotrigine. Quetiapine has also been shown to be effective.

## I. PREFERRED REGIMEN

| Treatment Choice |   |   |  |   |
|------------------|---|---|--|---|
| First Line       | <b>Mood Stabilizers + Anti-Psychotics</b> <ul style="list-style-type: none"> <li>- The goal of treatment is to control the mood and psychotic symptoms, that is why management of Bipolar Mood Disorder is preferably a combination of Mood Stabilizers and Anti-Psychotics.</li> <li>- Atypical Antipsychotics have been shown to be more efficacious than Lithium in the dysphoric, mixed, and psychotic manic episodes.</li> </ul> |   |  |   |
|                  | <b>Medication</b>   | <b>Dosage and Frequency</b>   | <b>Cautions</b>  | <b>Side Effects</b>   |
|                  | <b>Divalproex Sodium ER Tablet</b>  | 600 – 750 mg/day in divided doses.<br>Increase dose by 200 – 500 mg/day at 3 day intervals until desired response.<br><br>Or<br><br>Administer loading dose of 20 /mg/kg/day in divided doses | Contraindicated in patients with liver disease or severe liver dysfunction; take with large amount of water or food to avoid GI upset; caution on Pregnant women, Monitor liver function during the 1 <sup>st</sup> six months of therapy and monitor platelet function before major surgery.<br><br><b>Drug to Drug Interactions:</b> Valproate levels decreased by Carbamazepine | <b>Common:</b><br>Sedation, Headache, tremor, ataxia, nausea, vomiting, diarrhea, weight gain, transient hair loss.<br><br><i>*Caution on pregnant women / breastfeeding women</i><br><br><b>Serious:</b><br>Impaired hepatic function, thrombocytopenia, leucopenia, drowsiness/confusion, liver failure, hemorrhagic pancreatitis |
|                  | <b>+ Risperidone</b>  | 0.5 mg  | Special Instructions:<br>Fasting Blood Sugar (GBS) and lipid profile monitoring<br><br><i>Avoid abrupt withdrawal</i><br><br>Cautions in patients with cardiac disease.  | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal cramps, diarrhea, constipation), Other effects (Dyspepsia, epistaxis, abnormal vision)  |

|             |                          |   |   |   |
|-------------|--------------------------|---|---|---|
|             |                          |   | <b>Drug-Drug Interactions:</b><br>Carbamazepine can reduce levels of risperidone, whereas fluoxetine can increase levels.   |   |
|             | <b>+ Olanzapine</b>      | 5 mg  | Use with caution in patients with Diabetes Mellitus (DM), seizures, Benign Prostatic Hyperplasia (BPH), Narrow Angle Glaucoma   | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal pain, diarrhea, constipation), Hepatic (increase in Alanine Aminotransferase – ALT – 3 times greater)   |
| Second-Line | <b>Lithium Carbonate</b> | In Acute Mania:<br>450 – 2000 mg in divided doses in 5-7 days | Severe cardiac or kidney disease. Dehydration can increase lithium levels.<br><br><b>Drug-Drug Interactions:</b><br>Nonsteroidal Anti-inflammatory Drugs (NSAIDs), Angiotensin-Converting Enzyme Inhibitor (ACE Inhibitor), thiazide diuretics, Metronidazole, and Tetracycline can increase lithium levels.<br><br><b>Lithium toxicity can cause seizures, delirium, coma and death.</b> | <b>Common:</b><br>Sedation, cognitive problems, tremor, impaired coordination, hypotension, leukocytosis, polyuria, polydipsia, nausea, diarrhea, weight gain, hair loss, rash.<br><br><b>Serious:</b><br>Diabetes insipidus, hypothyroidism, ECG changes (arrhythmia, sick sinus syndrome, t-wave changes) |
|             | <b>+ Haloperidol</b>     | 0.5 – 2 mg  | Watch out for orthostatic hypotension, increase water intake, regular eye exams recommended, Sedative effects are most marked during the few days of administration   | Sedation, anticholinergic effect (dry mouth, urinary retention. Tachycardia, constipation. Blurred vision), EPS, Weight Gain, Tardive dyskinesia, photosensitivity, EEG Abnormalities   |



|  |                         |   |  |  |
|--|-------------------------|---|--|--|
|  |                         |   | Caution in patients with kidney disease, liver disease, cardiac disease, long QT syndrome or taking QT-prolonging medications. Monitor ECG if possible.  |  |
|  | <b>+ Chlropromazine</b> | 10 – 25 mg<br><br>May increase to 25-100 mg to maintenance dose of 100-300 mg | <p>Watch out for orthostatic hypotension, increase water intake</p> <p>Regular eye exams recommended</p> <p>Sedative effects are most marked during the few days of administration</p> <p>Contraindications:<br/>impaired consciousness, bone marrow depression, pheochromocytoma</p> <p>Caution in Patients with respiratory disease, kidney disease, liver disease, glaucoma, urinary retention, cardiac disease, long QT syndrome or taking QT-prolonging medications. Monitor ECG if possible.</p> <p><b>Drug-Drug Interactions:</b></p> <ul style="list-style-type: none"> <li>- Increases effects of blood pressure lowering medications</li> <li>- Lowers blood pressure if combined with epinephrine</li> </ul> <p>Levels may be increased by antimalarial including quinine</p> | <p>Sedation, Anticholinergic effect (dry mouth, urinary retention, tachycardia, constipation, blurred vision), EPS, Weight Gain, Tardive Dyskinesia, Photosensitivity, EEG abnormalities</p> |

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## II. TREATMENT DOSE

| Disorder   | Dosages  |               |  |   |
|--|--|---------------|--|---|
|  | 1 <sup>st</sup> Line   |               | 2 <sup>nd</sup> Line   |   |
|  | Divalproex Sodium  |               | Lithium Carbonate  |   |
| <b>Bipolar I</b>                                 | 600 – 750 mg/day in divided dose. Increase dose by 200 – 500 mg/day at 3-day intervals until desired response. (Oral)<br><b>OR</b><br>Administer loading dose of 20 mg/kg/day in divided doses |               | In Acute Mania: 450 – 2000 mg/day in divided doses in 5-7 days |   |
| <b>Bipolar Mood Disorder with Mixed Features</b> |  |               |  |   |
| <b>Hypomania</b>                                 | + Risperidone  | + Olanzapine  | + Haloperidol  | + Chlorpromazine  |
|  | 0.5 – 2mg/day  | 5 – 10 mg/day | 0.5-2 mg/day   | 10-25 mg/day<br><br>May increase to 25-100 mg/day to maintenance dose of 100-300 mg/day |

## A. BIPOLAR II

Bipolar II is characterized by the predominance of depressive episodes, its treatment mirrors the treatment of bipolar I depression.

In Bipolar II Disorder, both hypomanic episode and major depressive episode must be present to meet the criteria.

## I. PREFERRED REGIMEN

| Treatment Choice  |  |  |   |
|-------------------|--|--|---|
| <b>First Line</b> | Treatment for acute depressive episode of Bipolar II disorder is almost the same as that of Bipolar I. <i>Quetiapine</i> and <i>Lamotrigine</i> are the most favored agents in clinical practice (PPA, 2017) |  |   |
|                   | <b>Medication</b>  | <b>Cautions</b>  | <b>Side Effects</b>   |
|                   | <b>Quetiapine</b>  | <i>Use with caution for elderly patients.</i><br><br>Caution with other QT-prolonging medications like macrolides, fluoroquinolones, ondansetron, and HIV protease inhibitors.<br><br>Monitor weight, BP, FBS, and Lipid Profile, if possible. | <b>Common:</b><br>CNS (dizziness, drowsiness, ataxia, headache), GI (dry mouth, abdominal pain, diarrhea, constipation, weight gain), Endocrine – diabetes mellitus (increased cholesterol and FBS) |

|                    |                    |  |  |
|--------------------|--------------------|--|--|
| <b>Second Line</b> | <b>Lamotrigine</b> | <p><i>Caution in patients with renal, hepatic, and cardiac impairment and elderly.</i></p> <p>Life-threatening rashes have developed in association with lamotrigine use; it should generally be discontinued at the first signs of serious rash</p> <p><b>Drug-Lab interaction:</b><br/>Lamotrigine can cause a false positive urine drug screen for phencyclidine and synthetic cannabinoids</p> | <p><b>Common:</b><br/>Benign rash (approximately 10%)</p> <p>Dose dependent: Blurred or double vision, dizziness, ataxia, sedation, headache, tremor, insomnia, poor coordination, fatigue, nausea, vomiting, dyspepsia, rhinitis,</p> <p>Additional effects in pediatric patients with epilepsy: infection, pharyngitis, asthenia</p> <p><b>Serious:</b><br/>Rare serious rash, rare multi-organ failure associated with Stevens-Johnson syndrome, toxic epidermal necrolysis, or drug hypersensitivity syndrome, rare blood dyscrasias, rare aseptic meningitis, rare activation of suicidal ideation and behavior</p> |
|--------------------|--------------------|--|--|

## II. TREATMENT DOSE

| Disorder                | Dosages   |  |   |
|-------------------------|---|--|---|
|                         | 1 <sup>st</sup> Line  |  | 2 <sup>nd</sup> Line  |
|                         | Quetiapine  | Lamotrigine  | Lamotrigine   |
| <b>Acute Depression</b> | <p>Initial dose: 50mg/day at bedtime.</p> <p>Increase to 100 mg/day on day 2 and increase dose by 50-100mg/day until desired response, maximum dose generally 300 mg once daily</p> | <b>Not recommended as first line medication</b>  | <p>As monotherapy (without phenytoin, phenobarbital, carbamazepine, rifampicin, or lopinavir/ritonavir):</p> <ul style="list-style-type: none"> <li>- For the first 2 weeks: 25mg/day</li> <li>- At week 3: increase to 50mg/day</li> <li>- At week 5: increase to 100mg/day</li> <li>- At week 6: increase to 200mg/day, maximum dose generally 200mg/day</li> </ul> <p>As monotherapy (<u>with</u> phenytoin, phenobarbital, carbamazepine, rifampicin, lopinavir/ritonavir)</p> <ul style="list-style-type: none"> <li>- For the first 2 weeks: 50mg/day</li> <li>- At week 3: increase to 100mg/day</li> <li>- At week 5: increase to 200mg/day in divided doses</li> <li>- At week 6: increase to 300mg/day in divided doses, maximum dose generally 400mg/day</li> </ul> <p>Adjunct to Valproate:</p> |
| <b>Maintenance</b>      | 300 mg once daily   | <p>As monotherapy (<u>without</u> phenytoin, phenobarbital, carbamazepine, rifampicin, or lopinavir/ritonavir):</p> <ul style="list-style-type: none"> <li>- For the first 2 weeks: 25mg/day</li> <li>- At week 3: increase to 50mg/day</li> <li>- At week 5: increase to 100mg/day</li> </ul> |   |

|  |  |  |   |
|--|--|--|---|
|  |  | <ul style="list-style-type: none"> <li>- At week 6: increase to 200mg/day, maximum dose generally 200mg/day</li> </ul> <p>As monotherapy (<u>with</u> phenytoin, phenobarbital, carbamazepine, rifampicin, lopinavir/ritonavir)</p> <ul style="list-style-type: none"> <li>- For the first 2 weeks: 50mg/day</li> <li>- At week 3: increase to 100mg/day</li> <li>- At week 5: increase to 200mg/day in divided doses</li> <li>- At week 6: increase to 300mg/day in divided doses, maximum dose generally 400mg/day</li> </ul> <p>Adjunct to Valproate:</p> <ul style="list-style-type: none"> <li>- For the first 2 weeks: 25mg/day every other day</li> <li>- At week 3: increase to 25mg/day</li> <li>- At week 5: increase to 50mg/day</li> <li>- At week 6: increase to 100mg/day; maximum dose generally 100mg/day</li> </ul> | <ul style="list-style-type: none"> <li>- For the first 2 weeks: 25mg/day every other day</li> <li>- At week 3: increase to 25mg/day</li> <li>- At week 5: increase to 50mg/day</li> <li>- At week 6: increase to 100mg/day; maximum dose generally 100mg/day</li> </ul> |
|--|--|--|---|

# CONSENSUS TREATMENT GUIDELINES ON DEMENTIA

# DEMENTIA<sup>6</sup>

Dementia is a term used to describe a large group of conditions affecting the brain which cause a progressive decline in a person's ability to function. It is NOT considered as a normal part of aging.

## CLINICAL CRITERIA:

Decline or problems with memory (severe forgetfulness) and orientation (awareness of time, place and person), Mood or Behavioral Problems such as apathy (appearing uninterested) or irritability, loss of emotional control (easily upset, irritable or tearful), difficulties in carrying out usual work, domestic or social activities.

EMERGENCY PRESENTATION: Agitated and/or aggressive disorder

## I. STAGES OF DEMENTIA:

*\*These are general descriptions. Behaviors may vary.*

### A. EARLY STAGE

Forgetfulness; word-finding difficulty; lost and confused in familiar places; misplaces objects; losing track of time; difficulty handling finances; possible mood changes such as anxiety or depression.

### B. MIDDLE STAGE

Very forgetful especially of recent events and names; more confused with time and place; needs help with personal care (ex. toileting, dressing); unable to live alone safely; disturbed sleep; hallucinations; inappropriate behavior.

### C. LATE STAGE

Unaware of time, place and events; unable to recognize family and friends; unable to eat without assistance; may be confined to wheelchair or bed and unable to walk; may have aggressive behavior.

## II. PRINCIPLE GOALS FOR DEMENTIA CARE:

- Early diagnosis in order to promote early and optimal management
- Optimizing physical health, cognition, activity, and well-being
- Identifying and treating accompanying physical illness

<sup>6</sup> WHO (2016): MhGAP Intervention Guide for Mental, Neurological and Substance Abuse Disorders in non-specialized Health Settings, Version 2.0.

- Detecting and treating challenging behavioral and psychological symptoms
- Providing information and long-term support to carers.
- Psychosocial intervention is always first line. Provide support to carers.

### III. TYPES OF DEMENTIA

#### A. ALZHEIMER'S DISEASE

It is the most common cause of dementia. It is a progressive disease marked by neuropathologic changes which include neuritic plaques and neurofibrillary tangles.

#### B. VASCULAR DEMENTIA

Vascular dementia is the second most common cause of dementia after Alzheimer's disease. It can occur when blood flow to the brain becomes reduced. Vascular dementia can also be called vascular cognitive impairment and is sometimes split into more specific types. (Alzheimer's Research UK, 2018). Examples include: /

- Stroke-related dementia. This includes multi-infarct dementia (MID), which happens after a series of small strokes. It also includes dementia which happens after a stroke (called post-stroke dementia). /
- Subcortical vascular dementia (also called Binswanger's disease, small vessel disease-related dementia or lacunar state). This is caused by changes to very small blood vessels in the brain.

### IV. PREFERRED REGIMEN

| Treatment Choice                                |  |   |  |
|---|--|---|--|
| Alzheimer's Disease<br>and<br>Vascular Dementia | Acetylcholinesterase (ACE) Inhibitors<br>- These are recommended first-line therapy, although combination therapy with ACE Inhibitors and Memantine is likewise recommended since the two classes of drugs have different mechanisms of action. Monotherapy may also be a treatment option. (ADAP, 2014) |   |  |
|   | Medication   | Cautions  | Side Effects   |
| - Early Stage                                   | Donepezil  | Monitor for cardiac dysrhythmias, especially in those with preexisting cardiovascular disease.<br><br>Watch out for respiratory exacerbation in those with asthma or COPD. This medication is contraindicated during pregnancy. | GI upset, headache, fatigue, pain, common cold, anorexia, psychiatric disturbances, syncope, dizziness, insomnia, rash, pruritus, muscle cramps, urinary incontinence, accident. |

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|                |  |   |   |
|----------------|--|---|---|
|                |  |   | Reports of seizures, bradycardia, raised creatinine kinase, EPS, NMS. <sup>7</sup>  |
| - Middle Stage | <b>Donepezil</b>   | <i>See above</i>  | <i>See above</i>  |
|                | <b>Memantine</b>   | Use with caution in those with impaired kidney function.<br><br><u>Renal Adjustment for Memantine:</u><br>CrCl 5-29 mL/min: max 10 mg per day<br>(CrCl <5 mL/min not defined) | Headache, dizziness, constipation, HTN, somnolence, anxiety, confusion, hallucinations, fatigue, abnormal gait, hypertonia, vomiting, fungal infections, cystitis, thromboembolism, increased libido, psychotic reactions, pancreatitis, agranulocytosis, leucopenia (including neutropenia), thrombocytopenia, pancytopenia, thrombotic thrombocytopenic purpura, CHF, hepatitis, suicidal ideation, acute renal failure (including increased creatinine and renal impairment), Stevens-Johnson syndrome. <sup>8</sup> |
| - Late Stage   | May consider discontinuation if patient is no longer communicative and completely dependent. |   |   |

## V. TREATMENT DOSE

| Dosages           |                                     |  |  |
|-------------------|-------------------------------------|--|--|
| Stage of Dementia | Alzheimer's Disease                 | Vascular Dementia  | Notes  |
| Early Stage       | <b>Donepezil</b> 5-10 mg/day (Oral) | <b>Memantine</b> 10 mg/day (gradually increase to 20 mg / day) | <b>Memantine titration</b> - (10mg/tablet) titrate accordingly:<br><br>Week 1: 5 mg (1/2 tablet) once daily before bedtime |
|                   |                                     | <b>OR</b><br><br><b>Donepezil</b> 5-10 mg/day                  |  |

<sup>7</sup> MIMS UK (n.d.): Donepezil, retrieved from: <https://www.mims.co.uk/drugs/central-nervous-system/alzheimer-s-dementia/donepezil>

<sup>8</sup> MIMS Philippines (2018): Memantine, retrieved from: <https://www.mims.com/philippines/drug/info/memantine/?type=brief&mtype=generic#AdverseReactions>



|              |  |  |   |
|--------------|--|--|---|
| Middle Stage | <p><b>Donepezil</b> 5 mg/day (Oral)</p> <p><b>OR</b></p> <p>(<b>Donepezil</b> 5-10 mg/day) + (<b>Memantine*</b> 10 mg/day) (Oral)</p> <p>Gradually increase to 20 mg/day</p> | Continue Memantine. May add <b>Donepezil</b> 5-10 mg per tab | <p>Week 2: 5 mg (1/2 tablet) twice daily</p> <p>Week 3: 5 mg (1/2 tablet) twice daily</p> <p>Week 4 onwards: 10 mg (1 tablet) twice daily</p> |
| Late Stage   | May consider discontinuation if patient is no longer communicative and completely dependent.   |  |   |

**Special Considerations:**

- Antipsychotic should only be considered **IF**
  - a. Psychotic symptoms persist (i.e. violent behavior, hallucinations, persecutory delusions)
  - b. You assess that there is imminent risk for the person and/or carer
  - c. "Start slow, go slow" titrate and review the need regularly
  - d. Use the lowest effective dose
  - e. Monitor the person for side effects such as extrapyramidal symptoms and oversedation
- Avoid anticholinergics/antihistamines for sedations (hydroxyzine, diphenhydramine)
- Avoid haloperidol (I.V.)
- Avoid diazepam
- Medications should not be routinely considered in all cases.
- Adequate supervision and monitoring of side effects are important.
- Follow up should be every 3 months at a minimum. Discontinue drugs if confusion and behavioral changes worsen.

# CONSENSUS TREATMENT GUIDELINES ON EPILEPSY

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# I. EPILEPSY

Epilepsy is a disease of the brain defined by any of the following conditions:<sup>9</sup>

1. At least two unprovoked (or reflex) seizures occurring >24 hours apart.
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years.
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.

## A. EPILEPTIC SEIZURE<sup>10</sup>

Manifestation (s) of epileptic (excessive and/or hypersynchronous) usually self-limited activity of neurons in the brain.

### CLINICAL CRITERIA:

Sudden and transitory abnormal phenomena which may include alterations of consciousness, motor, sensory, automatic, or psychic events perceived by the patient or an observer.

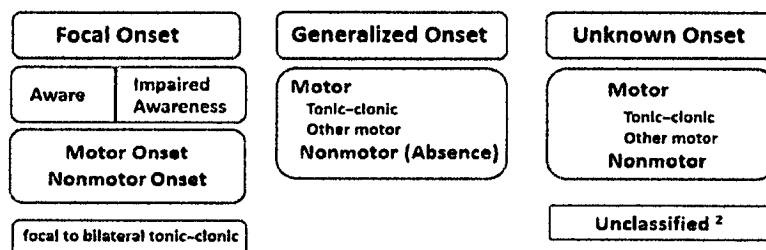
*Source: ILAE 1993,1997*

### A. Classification of Seizure Types:

International League Against Epilepsy (ILAE) Classification of Seizure Types is based on 3 key features: where seizures begin in the brain, the level of awareness during a seizure and other features of seizures. The seizure types are based on the seizure onset and how the seizures spread.<sup>11</sup>

The type of seizure onset (seizure type) is important because it affects choice of antiepileptic drugs, may relate to possible etiologies and prognosis in different age groups and other treatment possibilities.

### ILAE 2017 CLASSIFICATION OF SEIZURE TYPES BASIC VERSION<sup>12</sup>



Philippine League Against Epilepsy (PLAE) References:

<sup>9</sup> Fisher et al. (n.d.): ILAE Official Report: A Practical Clinical Definition of Epilepsy. *Epilepsia* 55 (4), 475-482.

<sup>10</sup> ILAE Classification on Task Force and Terminology, 2001

<sup>11</sup> Fisher et al. (2017): operational Classification of Seizure Types by International League Against Epilepsy – Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia*, 58 (4): 522-530.

1. **Focal Seizures** – start in an area or network of cells on one side of the brain. **Focal to Bilateral Seizure** – a seizure that starts in one side or part of the brain and spreads to both sides has been called a secondary generalized seizure.
2. **Generalized Seizures** – engage or involve networks on both sides of the brain at the onset.
3. **Unknown Onset** – if the onset of seizure is unknown.

## II. ANTIEPILEPTIC DRUG (AED) SELECTION:

1. **1<sup>ST</sup> Line Antiepileptic Drug** - AED of first choice for specific seizure types and group selected epilepsy syndromes.
2. **2<sup>ND</sup> Line Antiepileptic Drug** - AED of next choice when seizures are not controlled with an appropriately chosen and adequately dosed 1st line AED or development of adverse drug reactions with the use of the 1st line AED. May also be used as an alternative AED when there is a contraindication to the use of the 1st line AED or the inability to screen for the HLAB1502 allele in cases where carbamazepine is indicated for first time users.

Patients currently on phenobarbital with good seizure control should continue to be maintained on phenobarbital, since switching to another antiepileptic drug will not ensure seizure control. Switching from one antiepileptic drug to another should be done gradually, with transient overlap of the two drugs based on their respective half-lives to prevent withdrawal seizures.

### III. PREFERRED REGIMEN<sup>12</sup>:

| Antiepileptic Drugs for Specific Seizure Types and Age Group                     |                            |                                |   |                                      |   |
|--|----------------------------|--------------------------------|---|--------------------------------------|---|
| Seizure Type   |                            | Children (<18 years old)       | Girls and Women of Child Bearing Age          | Adults                               | Elderly (>60 years old)                       |
| Focal Onset Seizure with or without Evolution to Bilateral Tonic, Clonic, Tonic- | <b>1<sup>st</sup> Line</b> | Oxcarbazepine                  | Lamotrigine <sup>17***</sup><br>Levetiracetam | Carbamazepine <sup>16</sup><br>1718* | Lamotrigine***<br>Levetiracetam <sup>14</sup> |
|  | <b>2<sup>nd</sup> Line</b> | Levetiracetam<br>Valproic Acid | Oxcarbazepine <sup>17*</sup>                  | Levetiracetam<br>Valproic Acid*      | Carbamazepine*<br>Valproic Acid **            |

<sup>12</sup> Philippine League Against Epilepsy (PLAE) mhGAP Task Force on Epilepsy

<sup>16</sup> MIMS (n.d.): Tegretol Drug Information, retrieved from:

<https://www.mims.com/philippines/drug/info/tegretol/special-precautions?selectedTab=precautions>

<sup>17</sup> Pharma US (n.d.): Tegretol, retrieved from:

<https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/tegretol.pdf>

<sup>18</sup> Ferrell and Mcleod (2018): Carbamazepine, HLA-B\*1502 and Risk of Stevens – Johnson Syndrome and Toxic Epidermal Necrolysis – USFDA Recommendations, Pharmacogenomics 9 (10): 1543-1546

|  |                      |  |                             |                 |                                 |
|--|----------------------|--|-----------------------------|-----------------|---------------------------------|
| Clonic Seizures <sup>13</sup><br>14 15         |                      |  |                             |                 |                                 |
| Generalized Onset Seizures <sup>13</sup><br>15 | 1 <sup>st</sup> Line | Valproic Acid **                       | Levetiracetam <sup>17</sup> | Valproic Acid** | Lamotrigine<br>Levetiracetam    |
|  | 2 <sup>nd</sup> Line | Levetiracetam                          | Lamotrigine <sup>17</sup>   | Levetiracetam   | Valproic Acid**                 |
| Unknown Onset Seizure                          | 1 <sup>st</sup> Line | Valproic Acid <sup>19 20</sup><br>21** | Levetiracetam               | Valproic Acid** | Lamotrigine***<br>Levetiracetam |
|  | 2 <sup>nd</sup> Line | Levetiracetam                          | Lamotrigine***              | Levetiracetam   | Valproic Acid**                 |

*\*Screening for HLAB1502 required for first time users*

*\*\* Avoid in girls and women of childbearing potential, unless there is no other treatment option. When used in girls and women of child bearing potential, should be prescribed at lowest effective dose (DO NOT exceed 500 – 600 mg/day). There may be patients who will require higher doses to attain seizure control.*

*\*\*\*Lamotrigine may worsen myoclonic seizures*

| Antiepileptic Drugs for Selected Epilepsy Syndromes in Primary Care |                      |                                     |
|---|----------------------|-------------------------------------|
| Seizure Type  |                      |                                     |
| Child Absence Epilepsy (CAE) <sup>13 15</sup>                       | 1 <sup>st</sup> Line | Valproic Acid <sup>19 20 21**</sup> |
|   | 2 <sup>nd</sup> Line | Lamotrigine***                      |
| Rolandic Epilepsy <sup>13 15</sup>                                  | 1 <sup>st</sup> Line | Oxcarbazepine                       |
|   | 2 <sup>nd</sup> Line | Levetiracetam                       |
| Juvenile Myoclonic Epilepsy (JME) <sup>13 15</sup>                  | 1 <sup>st</sup> Line | Valproic Acid**                     |
|   | 2 <sup>nd</sup> Line | Levetiracetam                       |

*\*\*All girls and women with epilepsy on antiepileptic drugs of child bearing potential should receive folic acid supplementation at 400 micrograms to 5 milligrams per day.*

PLAE References:

<sup>13</sup> Glauser et al. (2013): Updated ILAE Evidence Review of Antiepileptic Drug Efficacy and Effectiveness as Initial Monotherapy for Epileptic Seizures and Syndromes. *Epilepsia*, 54 (3): 551-563.

<sup>14</sup> Werhahn et al (2015): A Randomized, Double Bind Comparison of Antiepileptic Drug Treatment in the Elderly with New-onset Focal Epilepsy, *Epilepsia*, 56 (3): 450-459.

<sup>15</sup> National Institute of Clinical Experience (NICE) Guidelines 2012, retrieved from:

<http://www.nice.org.uk/guidance/cg137/chaoter/1-Guidance#pharmacological-treatment>

<sup>19</sup> Tomson et al (2015): Valproate in the Treatment of Epilepsy in Girls and Women of Childbearing Potential, *Epilepsia*, 56 (7): 1006-1019

<sup>20</sup> Tomson et al (2018): Comparative Risk of Major Congenital Malformations with Eight Different Anti-Epileptic Drugs: A Prospective Cohort Study of the EURAP Registry, *Lancet Neurology*, 17 (6): 530-538

<sup>21</sup> European Medicines Agency (EMA), 2018

## IV. TREATMENT DOSE

| Medication                             | Patient Group | Dosage and Frequency  | Maintenance  | Maximum Dose   | Cautions  | Side Effects   |
|--|---------------|---|--|--|---|--|
| <b>Carbamazepine</b>                   | Adult         | Initial:<br>100-200 mg/day in 2-3 divided doses. <sup>22</sup><br><br>Increase by 100 – 200 mg each week, until a dose of 400 mg/day is reached | 10 – 20 mg/kg/day                                    | 1400 mg/day <sup>22</sup>  | Caution in patients with history of blood disorders, kidney, liver or cardiac disease <sup>22</sup><br><br>Dose may need to be adjusted after 2 weeks, due to induction of its own metabolism <sup>22</sup> | <b>Common:</b><br>Sedation, confusion, dizziness, ataxia, double vision, nausea, diarrhea, benign leukopenia <sup>22</sup><br><br><b>Serious:</b><br>Hepatotoxicity, cardiac conduction delay, low sodium levels <sup>22</sup> |
|  | Child         | Initial:<br>5 mg/kg/day divided 2-4 times per day.<br><br>Titration:<br>10-20 mg/kg/day over 2-4 weeks.   | 5 – 30 mg/kg/day<br><br>*Infants:<br>10-40 mg/kg/day | < 6 y/o: 35 mg/kg/day<br><br>6-15 y/o: 1000 mg/day<br><br>>15 y/o: 1200 mg/day | Screening for HLAB1502 required for first time users to prevent serious allergic reaction (Stevens-Johnson syndrome/Toxic Epidermal Necrolysis) <sup>23 24</sup>  |  |
| <b>Sodium Valproate/ Valproic Acid</b> | Adult         | Initial:<br>500 mg/day in 2 divided doses.<br><br>Increase by 500 mg/day each week  |  | 3000 mg/day  | Use with caution with underlying or suspected hepatic disease <sup>25</sup><br><br><b>*If ER tablet is used DO NOT SPLIT TABLET</b>   | <b>Common:</b><br>Sedation, headache, tremor, ataxia, nausea, vomiting, diarrhea, weight gain, transient hair loss   |

PLAE References:

<sup>22</sup> MhGAP Base Course – Version 2.0 (2016)

PLAE References:

<sup>23</sup> US FDA (2008): Safety Alerts for Drugs, Biologics, Medical Devices and Dietary Supplements – 2007

<sup>24</sup> Ferrel and Mcleod (October 2008): Carbamazepine, HLAB-1502 and risk of Steven-Johnson Syndrome and Toxic Epidermal Necrolysis, US FDA Recommendations Pharmacogenomics, 2008 Octoberr: 9(10): 1543-1546.

Doi: 10.2217/14622416.9.10.1543

<sup>25</sup> MhGAP Base Course – Version 2.0 (2016)

|                    |                     |  |  |   |  |   |
|--------------------|---------------------|--|--|---|--|---|
|                    | Child               | Initial:<br>10-15<br>mg/kg/day<br>divided twice a<br>day or thrice a<br>day<br>*Extended<br>Release – once a<br>day  | Children<br><20 kg:<br>20-40<br>mg/kg/day<br><br>Children<br>>20 kg:<br>20-30<br>mg/kg/day | 60<br>mg/kg/day   | <b>Drug-drug<br/>interactions:</b><br>Valproic levels<br>decreased by<br>carbamazepine,<br>increase by aspirin <sup>12</sup><br><br>AVOID in girls and<br>women of child<br>bearing potential,<br>unless there is no<br>other treatment<br>option <sup>26 27</sup><br>f. When used in<br>girls and women<br>of Childbearing<br>potential, should<br>be prescribed at<br>lowest effective<br>dose, not exceed<br>500-600 mg/day.<br>There may be<br>patients who will<br>require higher<br>doses to attain<br>seizure control. <sup>26<br/>27</sup> | <b>Serious:</b><br>Impaired hepatic<br>function,<br>thrombocytopenia,<br>leukopenia,<br>drowsiness,<br>confusion<br>(valproate-induced<br>hyperammonemic<br>encephalopathy, a<br>sign of toxicity),<br>liver failure,<br>hemorrhagic<br>pancreatitis. |
| <b>Lamotrigine</b> | Adult <sup>28</sup> | a. Monotherapy<br>:<br>First 2 weeks:<br>25mg/day<br><br>Week 3:<br>50mg/day<br><br>Week 5:<br>100mg/day<br><br>Week 6:<br>200mg/day,<br>maximum dose<br>generally<br>200mg/day<br><br>b. If with<br>valproic<br>acid: |  | Monotherapy<br>: 200 mg/day<br><br>With<br>valproic<br>acid: 100<br>mg/day<br><br>With<br>enzyme<br>inducer: 400<br>mg/day in<br>divided<br>doses | Very slow titration to<br>prevent serious<br>idiosyncratic rash.<br>Strictly adhere to<br>very slow titration<br>recommendation.<br>(Very slow titration<br>precludes in patients<br>with frequent<br>seizures recurring<br>several times daily,<br>weekly, or monthly)<br><br><b>Drug-lab<br/>interaction:</b><br>Lamotrigine can<br>cause a false<br>positive urine drug<br>screen for   | <b>Common:</b><br>Dizziness,<br>diplopia,<br>insomnia, ataxia <sup>22</sup><br><br><b>Serious:</b><br>Idiosyncratic<br>rash <sup>22</sup>   |

<sup>26</sup> Tomson, et. Al (2015): Valproate in the treatment of Epilepsy in Girls and Women of Childbearing Potential, *Epilepsia*, 56(7): 1006-1019, doi: 10.1111/epi.13201

<sup>27</sup> European Medicines Agency (EMA), 2018

<sup>28</sup> Continuum, American Academy of Neurology – February 2016

|  |                     |   |   |  |  |  |
|--|---------------------|---|---|--|--|--|
|  |                     | <p>First 2 weeks:<br/>25mg/day every<br/>other day</p> <p>Week 3:<br/>25mg/day</p> <p>Week 5:<br/>50mg/day</p> <p>Week 6:<br/>100mg/day;<br/>maximum dose<br/>generally<br/>100mg/day</p> <p>c. If with<br/>enzyme-<br/>inducer (as<br/>noted in<br/>above<br/>dosing):</p> <p>First 2 weeks:<br/>50mg/day</p> <p>Week 3:<br/>100mg/day</p> <p>Week 5:<br/>200mg/day in<br/>divided doses</p> <p>Week 6:<br/>300mg/day in<br/>divided doses,<br/>maximum dose<br/>generally<br/>400mg/day</p> |   |  | phencyclidine and<br>synthetic<br>cannabinoids |  |
|  | Child <sup>28</sup> | <p>Initial:<br/>monotherapy –<br/>(for weeks 1 and<br/>2) 0.3<br/>mg/kg/day</p> <p>With valproate:<br/>0.15 mg/kg/day</p> <p>If with enzyme-<br/>inducer:<br/>0.6 mg/kg/day</p> <p><b>Titration dose:</b></p>   | <p>Mono-<br/>therapy:<br/>4.5-7.5<br/>mg/kg/day</p> <p>With<br/>valproate:<br/>1-5<br/>mg/kg/day</p> <p>With<br/>enzyme<br/>inducer:<br/>5-15<br/>mg/kg/day</p> |  |  |  |



|                      |                     |   |  |                            |   |  |
|----------------------|---------------------|---|--|----------------------------|---|--|
|                      |                     | <p>a. Monotherapy –<br/>Week 3-4: 0.6 mg/kg/day</p> <p>Week 5 onwards:<br/>increase by 0.6 mg/kg/day</p> <p>b. With valproate:<br/>Weeks 3-4:<br/>0.3 mg/kg/day<br/>Week 5 onwards:<br/>increase 0.3 mg/kg/day every 1-2 weeks</p> <p>c. With enzyme inducer:<br/>Weeks 3-4: 1.2 mg/kg/day<br/>Week 5 onwards: increase dose by not more than 1.2 mg/kg/day every 1-2 weeks</p> |  |                            |   |  |
| <b>Levetiracetam</b> | Adult <sup>29</sup> | Initial:<br>250 mg a day and increase by 250 mg every 2 weeks to 500 mg twice a day   |  | 3000 mg/day                | AVOID in patients with psychosis, irritability, aggressive behavior, unless there is no other treatment option. | <p><b>Common:</b><br/>Irritability, aggressiveness, behavioral changes, hallucinations, dizziness<sup>30</sup></p> <p><b>Serious:</b><br/>None reported<sup>30</sup></p> |
|                      | Child               | 10-20 mg/kg/day and adjusted, according to response by increments of 10-20 mg/kg/day every 2 weeks  |  | 60mg/kg/day or 3000 mg/day |   |  |

<sup>29</sup> Product Insert, Levetiracetam. Version Number NCDS v.07, June 15 016

<sup>30</sup> Perucca and Engel (2017): Treatment of Epilepsy, 3<sup>rd</sup> Edition, Medscape Drug Reference, Blackwell Publishing Ltd.

|               |       |  |   |   |  |  |
|---------------|-------|--|---|---|--|--|
| Oxcarbazepine | Adult | Initial: 300mg<br>twice daily <sup>31 32</sup><br><br>Titration:<br>300mg per week<br>based on<br>response <sup>27</sup>       | 600 –<br>1200<br>mg/day   | 2400<br>mg/day                                | Cross-reactivity with<br>carbamazepine has<br>been reported, with<br>25.5% of patients<br>who had a history of<br>skin rashes on<br>carbamazepine also<br>developing a rash<br>when they were<br>converted to<br>oxcarbazepine. A<br>few cases of<br>Stevens–Johnson<br>syndrome have been<br>reported.<br><br>Avoid in patients<br>with history of skin<br>rash with<br>antiepileptic<br>medications. | CNS: Headache,<br>somnolence<br>dizziness<br>GI: nausea<br>Skin: rash<br>Endo: reduces<br>serum vitamin D<br>GU: hyponatremia<br>usually<br>asymptomatic, but<br>could cause an<br>increase in<br>seizures and other<br>adverse effects<br>when serum levels<br>fall below 125<br>mEq/L. |
|               | Child | Initial: 8-10<br>mg/kg/d <sup>27</sup><br><br>Titration:<br>5-10mg/k/d<br>every 3-7 days<br>based on<br>response <sup>27</sup> | 20-40<br>mg/kg/d <sup>27</sup><br><br>Dose for<br>child 2-16<br>years old<br>and 4-16<br>years old,<br>please see<br>PNF<br>chapter on<br>Nervous<br>system | <60 mg/kg/d<br>or<br>2100mg/day <sup>27</sup> |  |  |

## V. SPECIALTY REFERRAL

### When to refer to a specialist:

- In cases where the physician is in doubt of the diagnosis
- Uncontrolled seizures despite being on adequate doses of appropriately chosen AED: One monotherapy failure in children, Two sequential monotherapy failure in adults
- Children with epilepsy below age 2
- Children with epilepsy with developmental delay or regression in development

<sup>31</sup> Abou-Khalil, B. W. (2016). Antiepileptic Drugs. CONTINUUM: Lifelong Learning in Neurology, 22(1, Epilepsy), 132–156. doi:10.1212/con.0000000000000289

<sup>32</sup> Shorvon, S., Perucca, E., Engel, J. The Treatment of Epilepsy 4th ed. November 2015 p.575

- Patients presenting with recurrent seizures with focal neurologic deficits or suggestion of a progressive neurologic condition
- Patients with psychiatric comorbidity or other neurologic comorbidities.
- Women who are planning pregnancy or pregnant women with epilepsy
- Patients who develop adverse drug reactions
- Patients who are considered for tapering of AEDs.
- When in doubt, for pre-employment clearance

# CONSENSUS TREATMENT GUIDELINES ON SUBSTANCE USE DISORDERS

# I. SUBSTANCE USE DISORDERS

## A. ALCOHOL USE AND ALCOHOL USE DISORDERS

Conditions resulting from different patterns of alcohol consumption include acute alcohol intoxication, harmful alcohol use, the alcohol dependence syndrome, and the alcohol withdrawal state. Acute Intoxication is a transient condition following intake of alcohol resulting in disturbances of consciousness, cognition, perception, affect or behavior. Harmful use of alcohol is a pattern of alcohol consumption that is causing damage to health. The damage may be physical (e.g. liver disease) or mental (e.g. episodes of depressive disorder). It is often associated with social consequences (e.g. family problems, or problems at work).

Alcohol dependence is a cluster of physiological, behavioral and cognitive phenomena in which the use of alcohol takes on a much higher priority for a given individual than other behaviors that once had greater value. The alcohol withdrawal state refers to a group of symptoms that may occur upon cessation of alcohol after its prolonged daily use.<sup>33</sup>

The course of treatment and management of a person with Alcohol Use Disorders undergoes 3 phases: (1) Detoxification and Withdrawal Management, (2) Rehabilitation Program, (3) After-Care and Follow-Up.

### A.1 ACUTE ALCOHOL INTOXICATION

Acute Alcohol Intoxication is a transient condition following the administration of alcohol or resulting in disturbances in level of consciousness, cognition, perception, affect or behavior, or other psychophysiological functions and responses. Alcohol intoxication is usually closely related to dose levels. Alcohol intoxication is a transient phenomenon. Intensity of intoxication lessens with time, and effects eventually disappear in the absence of further use of the substance.<sup>34</sup>

|  |   |
|--|---|
| <b>Look for:</b> <ul style="list-style-type: none"> <li>➤ Smell of alcohol on the breath</li> <li>➤ Slurred speech</li> <li>➤ Uninhibited behavior</li> </ul>                                | <b>Assess:</b> <ul style="list-style-type: none"> <li>➤ Level of Consciousness</li> <li>➤ Cognition and Perception</li> </ul> |
| <b>If Intoxication is likely:</b> <ul style="list-style-type: none"> <li>➤ Assess airway and breathing</li> <li>➤ Put person on the side to prevent aspiration in case they vomit</li> </ul> |   |
| <b>Refer to hospital if necessary or observe until effects of alcohol have worn off</b><br><b>If methanol poisoning is suspected, refer to hospital for emergency management</b>             |   |

<sup>33</sup> mhGAP Intervention Guide Ver. 2.0, World Health Organization, 2016

<sup>34</sup> International Classification of Diseases 10, World Health Organization, 1996

## A.2 ALCOHOL WITHDRAWAL

Alcohol withdrawal state is a group of symptoms of variable clustering and severity occurring on absolute or relative withdrawal of a substance after repeated, and usually prolonged and/or high dose, use of that substance. Onset and course of withdrawal state are time-limited and are related to the type of substance and the dose being used immediately before abstinence. The withdrawal state may be complicated by convulsions.<sup>35</sup>

**Alcohol Withdrawal is best treated under a medical setting.**

|  |  |
|--|--|
| Alcohol withdrawal occurs following cessation of heavy alcohol consumption, typically between 6 hours and 6 days after the last drink  |  |
| <b>Look for:</b> <ul style="list-style-type: none"> <li>➤ Tremor in the hands</li> <li>➤ Sweating</li> <li>➤ Vomiting</li> <li>➤ Increased pulse and blood pressure</li> <li>➤ Agitation</li> </ul>  | <b>Ask about:</b> <ul style="list-style-type: none"> <li>➤ Headache</li> <li>➤ Nausea</li> <li>➤ Anxiety</li> </ul> <b>Note: Seizure and confusion may occur in severe cases</b> |
| <b>Refer to a Specialist/Hospital:</b> <ol style="list-style-type: none"> <li>1. <b>If withdrawal likely to be SEVERE:</b> <ol style="list-style-type: none"> <li>a. <b>Look for:</b> <ol style="list-style-type: none"> <li>i. Past episodes of severe alcohol withdrawal including delirium and seizures</li> <li>ii. Other medical or psychiatric problems or Benzodiazepine dependence</li> <li>iii. Severe withdrawal symptoms already present only a few hours after stopping drinking</li> </ol> </li> </ol> </li> <li>2. <b>If withdrawal is complicated by Delirium</b></li> <li>3. <b>If withdrawal is complicated by a Seizure</b></li> </ol> |  |

## B. DRUG USE AND DRUG USE DISORDERS

Conditions resulting from different patterns of drug use include acute sedative overdose, acute stimulant intoxication or overdose, harmful or hazardous use, cannabis dependence, opioid dependence, stimulant dependence, benzodiazepine dependence, and their corresponding withdrawal states. Harmful use of drugs is a pattern of drug consumption that is causing damage to health. The damage may be physical (as in cases of infection related to drug use) or mental (e.g. episodes of depressive disorders) and is often associated with damage to social functioning (e.g. family problems, legal problems, or work-related problems) Drug Dependence is a cluster of psychological, behavioral and cognitive phenomena in which drug use takes higher priority for a given individual than

<sup>35</sup> mhGAP Intervention Guide Ver. 2.0, World Health Organization, 2016

other behaviors that once had greater value. The drug withdrawal state refers to a group of symptoms occurring upon the cessation of a drug after its prolonged daily use.<sup>36</sup>

|  |
|--|
| <p><b>Opioid Overdose or other sedative overdose or mixed drug with or without alcohol overdose</b></p> <p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>➤ Unresponsiveness or minimally responsive</li> <li>➤ Slow respiratory rate</li> <li>➤ Pinpoint pupils (Opioid Overdose)</li> </ul>   |
| <p><b>Acute Opioid Withdrawal</b></p> <p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>➤ History of Opioid Dependence, recent heavy use ceasing in the last days</li> <li>➤ Muscle aches and pains, abdominal cramps, headaches</li> <li>➤ Nausea, vomiting, diarrhea</li> <li>➤ Dilated pupils</li> <li>➤ Raised pulse and blood pressure</li> <li>➤ Yawning, runny eyes and nose, pilo-erection (“gooseflesh”)</li> <li>➤ Anxiety, restlessness</li> </ul> |
| <p><b>Acute stimulant intoxication or overdose</b></p> <p><b>Look for:</b></p> <ul style="list-style-type: none"> <li>➤ Dilated pupils</li> <li>➤ Excited, racing thoughts, disordered thinking, paranoia</li> <li>➤ Recent use of stimulants (Methamphetamine, Cocaine, Ecstasy, etc.)</li> <li>➤ Raised blood pressure</li> <li>➤ Aggressive, erratic or violent behavior</li> </ul>   |
| <p><b>Refer to a Specialist/Hospital</b></p>   |

## C. MENTALLY ILL CHEMICAL ABUSE (MICA)

Adults with severe mental illness have high rates of co-occurring substance use disorders which adversely affect their current adjustment, course, and outcome. Separate and parallel mental health and substance abuse treatment systems do not offer interventions that are accessible, integrated, and tailored for the presence of co-occurrence. Recent integrated interventions for this population have the specific goal of ameliorating substance use disorder and the general goal of improving adjustment and quality of life.<sup>37</sup>

Pharmacological management of both psychiatric and the substance use disorder is an important foundation of the treatment of clients with co-occurring severe mental illness and substance use disorders.<sup>28</sup>

<sup>36</sup> mhGAP Intervention Guide Ver. 2.0, World Health Organization, 2016

<sup>37</sup> International Classification of Diseases 10, World Health Organization, 1996

**Mentally Ill Chemical Abuser (MICA)**

**Pharmacological Interventions**

- Medications shown to be effective for the treatment of substance use disorders are probably effective also in patients with serious mental illness
- Antidepressants reduce not only symptoms of depression but also substance abuse in clients with both mental disorder and substance use disorder
- Mood stabilizers are active not only in common mania but also on substance use in clients with bipolar disorders and co-morbid substance dependence
- Typical Antipsychotics improve the symptoms of schizophrenia but have little effect on co-morbid substance dependence
- Atypical Antipsychotics are equally effective as the typical antipsychotics in improving schizophrenia symptoms and may offer some benefit in reducing craving or substance use, but research is preliminary

**Recommendations:**

- Use protocols for management of Mental Disorders
- Integrated management/Multidisciplinary approach is recommended

**Refer to Specialist/Hospital for initial management and complicated cases**



# **CONSENSUS TREATMENT GUIDELINES ON EXTRAPYRAMIDAL SYMPTOMS (EPS)**

# I. EXTRAPYRAMIDAL SYMPTOMS (EPS)

Antipsychotics induced extra pyramidal symptoms include a variety of movement disorders. Acute extrapyramidal symptoms are like acute dystonia, akathisia and parkinsonism develop within hours or weeks after initiating or increasing doses of antipsychotics. Tardive dyskinesia and tardive dystonia are delayed onset syndromes and usually develop after a prolonged use of antipsychotics.

1. Dystonia are characterized by intermittent or sustained muscle action.
2. Akathisia manifests as the feeling of restlessness and irresistible urge to move.
3. Drug--induced Parkinsonism is characterized by a triad of bradykinesia, muscle rigidity and tremor
4. Tardive dyskinesia is manifested by involuntary choreoathetoid movements of the orofacial region, extremities, trunk and respiratory muscles.
5. Neuroleptic malignant syndrome (NMS) is marked by rigidity, fever, changes in the mental status and the autonomic dysfunction. (Kirgaval et al., 2017)

# II. PREFERRED REGIMEN

| Treatment Choice | Preferred Regimen   |   |  |   |
|------------------|---|---|--|---|
| First Line       | <b>Anticholinergic</b> <ul style="list-style-type: none"> <li>Short-term use of anticholinergics may be considered only in individuals with significant extrapyramidal side-effects when dose reduction and switching strategies have proven ineffective, or when these side-effects are acute or severe.<sup>40</sup></li> </ul> |   |  |   |
|                  | <b>Medication</b>   | <b>Dosage and Frequency</b>                     | <b>Cautions</b>  | <b>Side Effects</b>   |
|                  | <b>Biperiden</b>  | 1 mg twice daily<br>(Increase to 3-12 mg daily) | Caution in patients with cardiac, liver, or kidney disease.<br><br><b>Drug-Drug Interactions:</b><br>Caution when combining with other anticholinergic medications | <b>Common:</b><br>Sedation, Confusion and memory imbalance (especially in older adults), tachycardia, dry mouth, urinary retention and constipation |
|                  | <b>Diphenhydramine<sup>41</sup></b>   | 0.5 to 1 ml (IM/IV)                             | Caution in: Patient w/ glaucoma,   | Chest tightness, extrasystoles, hypotension, palpitations,  |

<sup>40</sup> World Health Organization (n.d.): Mental Health - Role of anticholinergic medications in patients requiring long-term antipsychotic treatment for psychotic disorders, retrieved from:

[https://www.who.int/mental\\_health/mhgap/evidence/psychosis/q6/en/](https://www.who.int/mental_health/mhgap/evidence/psychosis/q6/en/)

<sup>41</sup> MIMS Philippines (2018): Diphenhydramine, retrieved from:

<https://www.mims.com/philippines/drug/info/diphenhydramine?mtype=generic>

|  |                    |  |   |   |
|--|--------------------|--|---|---|
|  | 50 mg/ml, 1 ml amp |  | urinary retention, myasthenia gravis, epilepsy or seizure disorders, bronchitis or COPD, CV disease, thyroid dysfunction. Hepatic and moderate to severe renal impairment. Pregnancy. | tachycardia; ataxia, chills, confusion, dizziness, drowsiness, euphoria, excitement, fatigue, headache, insomnia, irritability, nervousness, neuritis, paraesthesia, paradoxical excitation, restlessness, sedation, seizure, vertigo; diaphoresis; menstrual disease; GI disturbances (e.g. anorexia, constipation, diarrhoea); difficulty in micturition, urinary frequency, urinary retention; agranulocytosis, haemolytic anaemia, thrombocytopenia; anaphylactic shock; tremor; blurred vision, diplopia; acute labyrinthitis, tinnitus; constriction of pharynx, nasal congestion, thickening of bronchial secretions, wheezing; photosensitivity, rash, urticaria (topical). |
|--|--------------------|--|---|---|

# APPENDICES

**APPENDIX A**  
**GLOSSARY (mbGAP Intervention Guide Version 2.0)**

| <b>TERMS</b>                    | <b>DEFINITION</b>  |
|---------------------------------|--|
| Agitation                       | Marked restlessness and excessive motor activity, accompanied by anxiety   |
| Agranulocytosis                 | A blood disorder in which there is an absence of granulocytes (a type of white blood cell). It is an acute condition involving a severe and dangerous leukopenia, also known as drug-induced secondary agranulocytosis.  |
| Akathisia                       | A subjective sense of restlessness, often accompanied by observed excessive movements (e.g. fidgety movements of the legs, rocking from foot to foot, pacing, inability to sit or stand still).  |
| Akinesia                        | The absence or lack of voluntary movement. A state of difficulty in initiating movements or changing from one motor pattern to another that is associated with Parkinson's disease.  |
| Altered Mental Status           | A changed level of awareness or mental state that falls short of unconsciousness which is often induced by substance intake or other mental or neurological conditions. Examples include confusion and disorientation. See delirium and confusional state.   |
| Alzheimer's Disease             | A primary degenerative cerebral disease of unknown etiology in the majority of cases with characteristic neuropathological and neurochemical features. The disorder is usually insidious in onset and develops slowly but steadily over a period of several years.   |
| Anticholinergic Side-effects    | Anticholinergic medicines block the effects of acetylcholine at muscarinic receptors. Anticholinergic effects include dryness of the mouth, urinary frequency or retention, palpitations and sinus tachycardia.  |
| Ataxia                          | Failure of muscular coordination. People with ataxia have problems with coordination because parts of the nervous system that control movement and balance are affected. Ataxia may affect the fingers, hands, arms, legs, body, speech, and eye movements.  |
| Cerebrovascular Accident        | A sudden disturbance of cerebral function attributable to vascular disease, principally thrombosis, hemorrhage, or embolism. See stroke  |
| Cognitive                       | Mental processes associated with thinking. These include reasoning, remembering, judgement, problem-solving and planning.  |
| Comorbid, Comorbidity           | Describing diseases or disorders that exist simultaneously   |
| Confusion, Confusional State    | A state of impaired consciousness associated with acute or chronic cerebral organic disease. Clinically it is characterized by disorientation, slowness of mental processes with scanty association of ideas, apathy, lack of initiative, fatigue, and poor attention. In mild confusional states, rational responses and behavior may be provoked by examination but more severe degrees of the disorder render the individual unable to retain contact with the environment. |
| Convulsion, Convulsive Movement | Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells (see seizure). Clinical manifestations include abnormal motor, sensory and psychic phenomena.  |

|  |   |
|--|---|
| Delirium                                   | Transient fluctuating mental state characterized by disturbed attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (i.e., reduced orientation to the environment) that develops over a short period of time and tends to fluctuate during the course of a day. It is accompanied by (other) disturbances of perception, memory, thinking, emotions or psychomotor functions. It may result from acute organic causes such as infections, medication, metabolic abnormalities, substance intoxication or substance withdrawal. |
| Delusion                                   | Fixed belief that is contrary to available evidence. It cannot be changed by rational argument and is not accepted by other members of the person's culture or subculture (i.e., it is not an aspect of religious faith).   |
| Detoxification                             | The process by which an individual is withdrawn from the effects of a psychoactive substance. Also referring to a clinical procedure, the withdrawal process is carried out in a safe and effective manner, such that withdrawal symptoms are minimized.  |
| Disability                                 | Any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner, or within the range, considered to be normal for a human being. The term disability reflects the consequences of impairment in terms of functional performance and activity by the individual.  |
| Disorganized / Disordered Thinking         | A disturbance in the associative thought process typically manifested in speech in which the person shifts suddenly from one topic to another that is unrelated or minimally related to the first. The individual gives no indication of being aware of the disconnectedness or illogicality of his or her thinking.  |
| Disorganized Behavior                      | Behavior including posture, gait, and other activity that is unpredictable or not goal-directed (e.g., shouting at strangers on the street).  |
| Dystonia                                   | Sustained muscle contraction or involuntary movements that can lead to fixed abnormal postures. See tardive dyskinesia.   |
| Extrapyramidal Side-effects/Symptoms (EPS) | Abnormalities in muscle movement, mostly caused by antipsychotic medication. These include muscle tremors, stiffness, spasms and/or akathisia.  |
| Hallucination                              | False perception of reality: seeing, hearing, feeling, smelling or tasting things that are not real.  |
| Hypersensitivity Reaction                  | Hypersensitivity reactions are the adverse effects of pharmaceutical formulations (including active drugs and excipients) that clinically resemble allergy. It belongs to type B adverse drug reactions, which are defined by the WHO as the dose-independent, unpredictable, noxious, and unintended response to a medicine taken at a dose normally used in humans. It covers many different clinical phenotypes with variable onset and severity.  |
| Irritability, Irritable Mood               | A mood state characterized by being easily annoyed and provoked to anger, out of proportion to the circumstances  |
| Motor Twitching                            | See convulsion  |
| Neuroleptic Malignant Syndrome             | A rare but life-threatening condition caused by antipsychotic medications, which is characterized by fever, delirium, muscular rigidity and high blood pressure   |

|                            |   |
|----------------------------|---|
| Orthostatic Hypotension    | Sudden drop of blood pressure that can occur when one changes position from lying to sitting or standing up, usually leading to feelings of light-headedness or dizziness. It is not life-threatening   |
| Pruritus                   | Itching; an intense sensation that produces the urge to rub or scratch the skin to obtain relief.   |
| QT Prolongation            | A potential medication induced side-effect of ventricular myocardial repolarization characterized by a prolonged QT interval on the electrocardiogram (ECG) that can lead to symptomatic ventricular arrhythmias and an increased risk of sudden cardiac death.   |
| Relapse                    | A return to drinking or other drug use after a period, of abstinence, often accompanied by reinstatement of dependence symptoms. The term is also used to indicate return of symptoms of MNS disorder after a period of recovery.   |
| Rigidity                   | Resistance to the passive movement of a limb that persists throughout its range. It is a symptom of Parkinsonism.   |
| Seizure                    | Episode of brain malfunction due to disturbances of cortical function resulting in sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena.   |
| Self-Harm                  | Intentional self-inflicted poisoning or injury to oneself, which may or may not have a fatal intent or outcome.   |
| Slurred Speech             | Speech with indistinctive pronunciation   |
| Status Epilepticus         | Defined as 5 min or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery (returning to baseline) between seizures; it can be convulsive or non-convulsive.   |
| Stevens-Johnson Syndrome   | Life-threatening skin condition characterized by painful skin peeling, ulcers, blisters and crusting of mucocutaneous tissues such as mouth, lips, throat, tongue, eyes and genitals, sometimes associated with fever. It is most often caused by severe reaction to medications, especially antiepileptic medicines. |
| Stigma                     | A distinguishing mark establishing a demarcation between the stigmatized person and others attributing negative characteristics to this person. The stigma attached to mental illness often leads to social exclusion and discrimination and creates an additional burden for the affected individual.                |
| Stroke                     | See cerebrovascular accident (CVA).   |
| Suicidal Thoughts/Ideation | Thoughts, ideas, or ruminations about the possibility of ending one's life, ranging from thinking that one would be better off dead to formulation of elaborate plans.  |
| Tardive Dyskinesia         | This is dystonia characterized by twisting and sustained muscle spasms that affect regions of the head, neck, and occasionally, the back. It may not improve after stopping the antipsychotic medicine.   |
| Thrombocytopenia           | Abnormally low number of platelets in the blood. This disease may present with increased bruising or hemorrhaging. Confirmation is by identification of decreased platelet count in a blood sample.   |
| Tremor                     | Trembling or shaking movements, usually of the fingers, that is an involuntary oscillation of a body part   |

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Republic of the Philippines  
Department of Health

ANNEX B

FORM 1

REQUISITION AND ISSUANCE SLIP (RIS)

MENTAL HEALTH MEDICINES ACCESS PROGRAM

Name of Health Facility: \_\_\_\_\_  
Address: \_\_\_\_\_

Contact No: \_\_\_\_\_

| Psychotropic Medicines |  | Quantity for<br>1 year<br>consumption<br>+ 3-month<br>buffer stock | Total<br>*Number<br>of<br>Patients<br>using the<br>medicine | Target<br>Number of<br>Patients for<br>the year<br>_____ |
|------------------------|--|--|---|--|
| 1.                     | Carbamazepine 200 mg Tablet                      |  |   |  |
| 2.                     | Lithium Carbonate 450 mg MR Tablet               |  |   |  |
| 3.                     | Valproate Disodium + Valproic Acid 250 mg tablet |  |   |  |
| 4.                     | Sodium Valproate 250 mg/5 ml Syrup               |  |   |  |
| 5.                     | Valproic Acid + Sodium Valproate 500 mg (MR)     |  |   |  |
| 6.                     | Biperiden Hydrochloride 2 mg Tablet              |  |   |  |
| 7.                     | Chlorpromazine 200 mg Tablet                     |  |   |  |
| 8.                     | Clozapine 100 mg Tablet                          |  |   |  |
| 9.                     | Fluphenazine Decanoate 25 mg/mL, 1 mL Ampoule    |  |   |  |
| 10.                    | Diphenhydramine 50 mg/mL, 1 mL Ampoule           |  |   |  |
| 11.                    | Haloperidol 5 mg Tablet                          |  |   |  |
| 12.                    | Haloperidol 5 mg/mL, 1 mL Ampoule                |  |   |  |
| 13.                    | Olanzapine 10 mg Tablet                          |  |   |  |
| 14.                    | Olanzapine 10 mg Oro-Dispersible Tablet (ODT)    |  |   |  |
| 15.                    | Quetiapine 200 mg Tablet                         |  |   |  |
| 16.                    | Risperidone 2 mg Tablet                          |  |   |  |
| 17.                    | Risperidone 2 mg Oro-dispersible Tablet (ODT)    |  |   |  |
| 18.                    | Escitalopram 10 mg Tablet                        |  |   |  |
| 19.                    | Fluoxetine 20 mg Capsule                         |  |   |  |
| 20.                    | Sertraline 50 mg Tablet                          |  |   |  |
| 21.                    | Lamotrigine 100 mg Tablet                        |  |   |  |
| 22.                    | Donepezil 10 mg Tablet                           |  |   |  |
| 23.                    | Flupenthixol 20 mg/ml                            |  |   |  |
| 24.                    | Paliperidone Palmitate 150 mg prefilled syringes |  |   |  |
| 25.                    | Paliperidone Palmitate 100 mg prefilled syringes |  |   |  |

|  |              |                    |
|--|--------------|--------------------|
| .....  |              |                    |
| Previously number of patients served with the following mental health conditions (2018): |              |                    |
| Mental Health Conditions   |              | Number of patients |
| Psychosis (Schizophrenia)  |              |                    |
| Anxiety Disorders  |              |                    |
| Mood Disorders   |              |                    |
| Dementia   |              |                    |
| Epilepsy   |              |                    |
| Substance Abuse Disorders  |              |                    |
| Other diagnosis (please specify):  |              |                    |
| *****  |              |                    |
|  | Prepared by: | Approved by:       |
| Signature:   |              |                    |
| Name:  |              |                    |
| Designation:   |              |                    |
| Contact No.:   |              |                    |
| Email Address:   |              |                    |



[illegible]

Yours truly,

