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MOH Protocol for the Management of Adult Obsessive-Compulsive Disorder (OCD)

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- **Introduction**

Obsessive-compulsive disorder (OCD) is a chronic disease with a waxing and waning course in clinical practice. It is marked by repeated and persistent obsessions or compulsions that the person feels compelled to carry out (DSM5) [1]. In the adult, OCD affects both men and women equally, with a lifetime prevalence of (1.1 % –1.8 %) worldwide [1]. According to the Saudi National Health and Stress Survey, the lifetime prevalence of OCD is 4.1 % in Saudi Arabia [2].

Obsessions and/or compulsions are required for a diagnosis of OCD in DSM-5. Compulsions are described as repetitive behaviors or mental acts that the patient feels driven to execute to relieve obsession-related anxiety, and obsessions are described as recurring, persistent, and intrusive thoughts, images, or desires that create noticeable anxiety. Obsessions or compulsions consume a lot of time and interfere with social or vocational functioning [1].

OCD has been transferred from the category of "anxiety disorders" to a new one called "obsessive-compulsive and related disorders" in the DSM-5. In addition to OCD, diagnostic criteria for body dysmorphic disorder, hoarding disorder, hair-pulling disorder (trichotillomania), and skin picking disorder are included in this new category [1,3].

Treatment-seeking rates have been estimated to be between 14 and 56 % of patients, implying that OCD is under-recognized and under-treated [4,5]. Negative emotionality, social isolation, and a history of physical abuse are all risk factors for the development of OCD [6].

A. Purpose

Obsessive-compulsive disorder (OCD) has effective evidence-based therapies; nonetheless, several studies show that the approach to this disease is still less than ideal, and that seeking therapy is typically delayed, which is linked to a worse outcome [7, 8]. Less than 40% of patients receiving treatment receive OCD-specific treatment, and less than 10% receive evidence-based treatment [9, 10].

B. Aim & Scope

The protocol is considered to be a useful resource for health professionals working in settings where they will be caring for people with OCD. The general goal of these protocols is to deliver evidence-based recommendations on the pharmacological and non-pharmacological management in patients with OCD. This protocol also aimed to propose updated decision-making algorithms for practitioners involved in the treatment of these patients. Having a MOH protocol for managing OCD on hand could aid in the management of the disease in our environment and lessen the disease's burden on the patient.

C. Targeted Population

This consensus applies to adults (18 years and older) who have been diagnosed with OCD, as well as their relatives/caregivers and all healthcare professionals who provide them with aid, treatment, or care at the level of specialized mental health care.

D. Setting

- Iradah Complex / Hospital and Mental Health.
- Psychiatric clinics in MOH General Hospitals.

E. End Users

Psychiatry Consultants, Specialists and Residents, primary care physicians, Psychiatry clinical pharmacists, Pharmacists, Nurses.

Primary Care physicians Role:

1- initially, primary care physician assess the case for mental health disorders, if he provisionally diagnoses the case with Obsessive-compulsive disorder (OCD) he should refer the case to specialized psychiatry clinic.

2- After the case of Obsessive-compulsive disorder (OCD) has been stabilized, and proper care was provided by the treating psychiatrist, who can refer back the case to primary care physician for regular follow up and continuing the psychiatric Management plan.

3- During follow up of a Known case of Obsessive-compulsive disorder (OCD) in the primary care clinic, once the case showed any signs or symptoms of disorder relapse or any safety issues (e.g. suicidality or homicidally), primary care physician should refer the case to specialized psychiatry clinic for stabilization and management.

4- primary care physician should commit to this guideline in regard to all steps of assessment, Management, prescription of psychotropic medications and required routine investigations.

F. Methodology

Given the extensive range of expertise, disciplines, and positions of employees at the MOH, it's impossible to capture the whole scope of specialist practice used by experienced practitioners across different disciplines and settings. As a result, this Handbook can be applied in a wide range of situations. It provides an overview of fundamental principles and practical resources for less experienced employees, which they may implement and discuss with their supervisors. Multidisciplinary teams can utilize it as a common reference point to aid in coordinated treatment, and more experienced employees can use it as a refresher or training resource. The protocol should be used in conjunction with local rules and procedures.

This is the first version of the Saudi practical protocol on the management of the obsessive-compulsive disorder. This protocol development is completed through 2 phases:

Phase 1: A committee of professional psychiatrists examined numerous published recommendations for OCD management and created an appropriate protocol for MOH health care providers as part of a Saudi Arabian Ministry of Health initiative. Started with literature review and the MOH formulary along with reviewing multiple published protocols by the teamwork of a group of psychiatric consultants and Specialized Pharmacist. The published protocols were evaluated using the Appraisal of protocols, Research and Evaluation II (AGREE II) scale. A total of 4 protocols were reviewed, including the 2005 United Kingdom protocol of the National Institute for Health and Care Excellence (NICE) and its 2013 update, the 2007 United States American Psychiatric Association (APA) protocol and its 2013 update, Canadian clinical practice guidelines for the

management of anxiety, posttraumatic stress and obsessive-compulsive disorders, and the British Association for Psychopharmacology (BAP) protocol. The Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders were meet the criteria for use in the development of this protocol. In addition, we added some clinically relevant information from the APA protocol that does not contradict the management concept of Canadian protocols.

Phase 2: The protocol was sent to a group of experts in adult psychiatry to put their input and provide their review. Their input was collected over 3 weeks. Followed by Further meeting and assessment for the feedback by the committee.

G. Updating

The first version of this guidance was created in 2021. The guidance will be updated every 3 years or if any changes or updates are released by international/national protocols, pharmacotherapy references, or MOH formulary.

H. Conflict of Interest

This guidance was developed based on valid scientific evidence. No financial relationships with pharmaceutical, medical device, and biotechnology companies.

I. Funding

No fund was provided.

J. DISCLAIMER

This Clinical protocol is an evidence-based decision-making tool for managing health conditions. It is based on the best information that is available at the time of writing and is to be updated regularly. This protocol is not intended to be followed as a rigid treatment protocol. It is also not meant to replace clinical judgment of practicing physicians but is the only tool to help manage patients with OCD. Treatment decisions must always be made on an individual basis, and prescribing physicians must customize care and tailor treatment regimens to patients' unique situations and health histories. For dosage, special warnings

and precautions for usage, contraindications, and monitoring of side effects and potential risks, physicians should check the approved product monographs within their institution's formulary. When choosing treatment options, take into account any constraints imposed by the institution's formulary. During the decision-making process for picking specific drugs within a recommended specialized class, prescribing physicians should consult their institution's formularies.

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• Protocol Overview (Summary)

- Assessment and diagnosis of Obsessive-compulsive disorder.
- Consider assessing the symptoms severity and level of functioning of the patients by (Y-BOCS)
- Determine the presence of comorbidities and make a differential diagnosis.
- Improve the patient's and others' safety.

- ✓ The initial treatment modality selected is based on a variety of factors.
- ✓ (CBT), (SSRIs), or a combination of the two are the first-line treatments for OCD.
- ✓ The combination looks a lot better than pharmacotherapy alone, but not than CBT alone.

- Examine the patient's response to the 1ST LINE therapy.
- After 8–12 weeks (4–6 weeks at a maximally acceptable dose), assess pharmacotherapy progress.
- Continue effective medication for 1–2 years, then try gradual taper month-by-month.
- After 13–20 weekly sessions, assess CBT (ERP) progress.
- Continue effective CBT through monthly booster sessions for 3–6 months after acute treatment.

If there is a partial response or no response:

- ✓ Examine commitment and treatment adherence.
- ✓ Examine therapy goals and expectations, and rule out medication related effect.
- ✓ Ensure that the treatment given was in accordance with the protocol.
- ✓ Re-evaluate comorbidity (depression, substance abuse).

- ✓ Consider continuing, modifying, or enhancing the management plan based of the treatment line of choices listed below.
- ✓ Consider changing to another 1st-line treatment before trying 2nd-line medications (If the response to appropriate doses of 1st line (SSRI) is insufficient or the drug is not tolerated).
- ✓ Consider adjunctive methods to retain any therapeutic advantages (for partial or insufficient response to SSRI) and for patients with treatment-resistant OCD.

1st line drug options:

SSRI

Fluoxetine 40-80 mg/day (up to 120 mg/day)
Escitalopram 20-40 mg/day (up to 60 mg/day)
Fluvoxamine 200-300 mg/day (up to 450 mg/day)

2nd line drug options:

Clomipramine 100-250 mg/day
Venlafaxine XR Up to 375 mg /day
Mirtazapine 30-60mg/day

Adjunctive Therapy +

1st line*

Risperidone (.5-4mg/day)
Aripiprazole (5-20 mg/day)

2nd line*

Quetiapine 25-400 mg/day
Topiramate Up to 400 mg added to SSRI

3rd line*

Olanzapine 5-20 mg/day
Amisulpride200-600 mg/day
Haloperidol 2-10mg/day
Mirtazapine 15-30 mg/day
Lamotrigine 100 mg/day added to SSRI
Clomipramine (Clomipramine + Fluoxetine (≤75 and ≤40 mg/d)

*Not FDA approved (off label). However, those pharmacological agents supported by evidence as adjunctive therapy.

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- **General principles in Assessment and Management of OCD**

A. Assessment:

- To diagnose OCD, use DSM-5 criteria [1].

Table DSM-5 diagnosis of OCD:

- Presence of either obsessions, compulsions, or both
  - Obsessions are defined by the following:
    - Recurrent and persistent thoughts, urges, or images that are experienced as intrusive and unwanted and that cause marked anxiety or distress.
    - The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with other thoughts or actions.
  - Compulsions are defined by the following:
    - Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rigid rules.
    - Compulsions are aimed preventing or reducing anxiety or preventing some dreaded situation or event; however, they are not connected in a realistic way with what they are designed to neutralize or are clearly excessive.
- The obsessions or compulsions are time-consuming (e.g., take >1 h/day) or cause clinically significant distress or functional impairment.
- Specify patient's degree of insight as to reality of OCD beliefs:
  - Good or fair insight (i.e., definitely or probably not true)
  - Poor insight (i.e., probably true)
  - Absent insight (i.e., completely convinced beliefs are true)
- Specify if "tic-related" OCD

Adapted from DSM-5.

- Consider assessing the symptoms severity and the level of functioning of the patients [13]
    - Keeping track of baseline severity helps in tracking how well the patient is responding to treatment.
    - The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is an effective symptom scale.
- Evaluate the comorbidity and execute differential diagnosis with differentiating OCD obsessions, compulsions, and rituals from similar symptoms found in other disorders (Bipolar disorder, Depressive disorders, Schizophrenia, Generalized anxiety disorder, somatic symptoms disorders, Posttraumatic stress disorder, Obsessive-compulsive personality disorder (OCPD), Paraphilias and Tourette's disorder) [13].
- Assess the patient's and others' safety [13].

B. Management:

Psychological and pharmaceutical treatments are available for OCD. Patient preference and motivation, ability to engage in therapy, degree of sickness, doctors' expertise and skills, availability of psychological treatments, patient's prior reaction to treatment, and the presence of concomitant medical or psychiatric disorders all influence treatment selection [14].

All patients should be educated on their disorder, the efficacy (including the expected time for therapeutic effects to appear) and tolerability of treatment options, aggravating factors, and relapse symptoms. Self-help resources, such as books or websites, may also be beneficial [14].

- **Psychological Treatment**

Meta-analyses show that psychological treatment for OCD, especially CBT, which includes exposure with response prevention (ERP), is useful [15-23]. CBT is comparable to, if not superior to, pharmacotherapy [20,24-26]. **The combination of psychotherapy and pharmacotherapy looks a lot better than pharmacotherapy alone, but not than CBT alone** [24,27-30].

A. Individual CBT Efficiency VS Group for OCD:

According to several meta-analyses, there are no substantial differences in efficiency between group and individual CBT [15,17,31]. Individual therapy can allow the therapist to be more aware of the patient's dysfunctional beliefs; however, group therapy may provide the benefits of group encouragement, mutual support, imitation, and interpersonal learning, which can lead to increased motivation and reduced treatment discontinuation [17].

B. Telephone, Self-Help or Face-to-Face ERP:

ERP delivered by telephone is equal to face-to-face ERP [32]. In addition, self-help instructions sent to patients through email showed considerably better reductions in OCD symptoms than wait-list control groups in two RCTs [33,34].

C. Internet-Delivered CBT (ICBT) for OCD:

ICBT programs have been shown to be considerably more helpful than supportive therapy or relaxation control methods for OCD in several RCTs [35-37]. When ICBT incorporated quick, scheduled, therapist-initiated telephone support, it achieved much better outcomes than on-demand phone support [38].

D. Other Effective Therapies:

Other treatments that may be effective include acceptance and commitment therapy (ACT) [39] and mindfulness training [40].

E. Psychological Treatment's Long-Term Effects:

The effectiveness of CBT has been shown to last for one to five years of monitoring in follow-up studies [30,41-44].

- **Pharmacological treatment**

	Drugs options	*Comment*
First-line agents.	**SSRIs** **Fluoxetine** 40-80 mg/day (up to 120 mg/day) **Escitalopram** 20-40 mg/day (up to 60 mg/day) **Fluvoxamine** 200-300 mg/day (up to 450mg/day)	• The use of SSRIs is supported by evidence from RCTs and meta-analyses [25, 26] [45-63]. • An alternative SSRI may be used if the first SSRI is either has a poor response or not tolerated [64]. • These highest doses are occasionally used for rapid metabolizers or those who have no or minor side effects but have not had a satisfactory therapeutic response after eight weeks or more at the typical maximum dose [13]. • The use of SSRI with reversible non-selective MAOIs is contraindicated [56]. • If the daily fluvoxamine dose is more than 150 mg, divide it into two or three doses and take them at different times [56]. • Keep a close eye on patients taking SSRIs to monitor suicidal thoughts and self-harming behaviors, especially at the beginning of treatment and after dosage increases. [66,67]. • The majority of SSRI or SNRI adverse effects occur during the first two weeks of treatment and are temporary, but others, such as sexual dysfunction and excess weight, may last for the duration of treatment [68-70]. • Educate the patient about the discontinuation syndrome that occurs when SSRIs or SNRIs are abruptly stopped [68,71].

Second-line agents	**Clomipramine** 100–250 mg/day [24,51-58,62,76,77] **Mirtazapine** [78] 30-60 mg **Venlafaxine XR** Up to 375 mg /day [59]	• Clomipramine has equal efficiency as SSRIs. However, SSRIs are often better tolerated. • Anticholinergic effects are one of Clomipramine's most common side effects. Cardiac arrhythmias, convulsions, medication interactions, and overdose toxicity are the main safety concerns [72,73]. • The half-life of venlafaxine is very short. It is recommended that the patient be educated about the discontinuation symptoms [68,71].
Adjunctive therapy	*First-line adjunctive therapies* ○ **Aripiprazole** (5-20 mg/day) [79-83] ○ **Risperidone** (.5-4mg/day) [84-86] *Second -line adjunctive therapies* ○ **Quetiapine** (25-400 mg/day) [87-89] ○ **Topiramate** Up to 400 mg added to SSRI [90,91] *Third -line adjunctive therapies*	• Adjunctive therapy is for patients who have had an insufficient or partial response to SSRI medication, as well as those with treatment-resistant OCD [72]. • Treatment-resistance OCD is defined by non-response to two adequate trials of 12 weeks SRI or Clomipramine at full therapeutic dose [117]. • Atypical antipsychotic augmentation should be reserved for patients with treatment-resistant OCD due to concerns about atypical antipsychotics' tolerability.

	○ **Olanzapine** (5-20mg/day) [94-96] ○ **Amisulpride** 200-600 mg/day [97]	• Some studies are available to suggest they may be useful but there is conflicting or inadequate evidence to warrant stronger recommendations. These agents may be useful for some patients, but more data are needed.
	○ **Haloperidol** (2-10 mg/day)	• Haloperidol may be as effective as adjunctive risperidone; nonetheless, it is a third-line option due to its poor tolerability [98,99].
	○ **Adjunctive Mirtazapine** 15-30 mg	• The adjunctive mirtazapine resulted in a quicker onset of response to OCD symptoms.
	○ **Adjunctive Clomipramine** ○ **Lamotrigine** 100 mg added to SSRI [102]	• Adjunctive clomipramine was not found to be more effective than SSRI treatment. Some patients may benefit from the addition of adjunctive clomipramine to fluoxetine (≤75 and ≤40 mg/d, respectively); nevertheless, plasma levels should be monitored due to the potential of medication interactions with SSRIs [103]. • Buspirone, Clonazepam, Lithium, Morphine, Gabapentin, or Minocycline ***are not recommended as adjuncts*** [109].

- **Maintenance pharmacological treatment**

In order to avoid relapse:

- Over six to twelve months, SSRI treatment demonstrated a substantial decrease in relapse rates when compared to placebo [110].
- Escitalopram [111], and high-dose fluoxetine [113] have all been shown to decrease relapse rates in RCTs.
- Mirtazapine [78] and clomipramine [114] have shown maintained improvement over six to twelve months in RCT discontinuation studies as compared to placebo.
- Over six to 24 months, more evidence supports the effectiveness of fluoxetine, and fluvoxamine XR [50,115-117].

• Appendix 1 (Drug Dosage and Monitoring)

This is adapted from:

- Lexicomp Online, Lexi-Drugs Online. https://online.lexi.com. Accessed August 23, 2021. [118]
- Taylor, David M., Thomas R. E. Barnes, and Allan H. Young. 2018. The Maudsley Prescribing Guidelines in Psychiatry. 13th ed. New York, NY: John Wiley & Sons. [119]

Drug Name	MOH formulary	Dose Range	Monitoring
Fluoxetine	Available	**Initial:** 10 to 20 mg once daily; may increase by 20 mg increments at intervals ≥1 week. **Dose range:** 40 to 80 mg/day. **Maximum dose:** 80 mg/day *(Higher doses up to ~120mg/day occasionally used for rapid metabolizers or those who have no or minor side effects but have not had a satisfactory therapeutic response after eight weeks or more at the typical maximum dose)*	Serum sodium in at-risk populations; blood glucose for diabetic patients; liver and renal function; ECG in patients who suffer from risk factors for QT prolongation and ventricular arrhythmia; closely monitor patients for depression, clinical worsening, suicidality, or unusual changes in behavior; signs/symptoms of serotonin syndrome, autonomic instability, neuromuscular changes, GI symptoms, and/or seizures; akathisia; sleep status
Escitalopram	Available	**Initial:** 10 mg once daily; may be increased by 10 mg at intervals ≥1 week. **Dose range:** 10–20 mg/day **Maximum dose:** 40 mg once daily. *(Higher doses up to ~60 mg/day occasionally used for rapid metabolizers or those who have no or minor side effects but have not had a satisfactory therapeutic response after eight weeks or more at the typical maximum dose)*	ECG; electrolytes (potassium and magnesium); liver and renal function tests; serum sodium in at-risk populations; CBC; examine all patients for any personal or family history of bipolar disorder, hypomania, or mania (prior to initiating therapy); closely monitor patients for depression, clinical worsening, suicidality, psychosis, or unusual changes in behavior; signs/symptoms of serotonin syndrome, autonomic instability, neuromuscular changes, GI, and/or seizures.
Fluvoxamine	Available	**Immediate release:** **Initial:** 50 mg once daily at bedtime. may be increased by 50 mg at 4- to 7-day intervals **Dose range:** 100 to 300 mg daily; **Maximum dose:** 300 mg/day. *(Higher doses up to ~450 mg/day occasionally used for rapid metabolizers or those who have no or minor side effects but have not had a satisfactory therapeutic response after eight weeks or more*	Evaluate mental status, suicide ideation, anxiety, social functioning, mania, panic attacks or other unusual changes in behavior; signs/symptoms of serotonin syndrome; akathisia; weight and BMI; hepatic function.

		at the typical maximum dose) (Daily doses >150 mg is given in 2 divided doses, with the larger dose administered at bedtime.)	
Clomipramine	Available	**Initial:** 25 mg daily. may increase over the first 2 weeks to ~100 mg daily in divided dose THEN may increase further to 250 **Dose range:** 100–200 mg/day **Maximum dose:** 250 mg/day as a single once daily dose at bedtime	Serum sodium in at-risk populations; pulse rate and blood pressure; ECG/cardiac status in older adults and patients with cardiac disease; suicidal ideation; signs/symptoms of serotonin syndrome; hepatic transaminases.
Venlafaxine	Available	**(Off-label use):** **Initial:** 75 mg once daily for extended release (75 mg/day in 3 divided doses for immediate release) Increase by 75 mg every 2 weeks to 225 mg/day. Increase further up to 375 mg/day **Dose range:** 75–375mg/day **Maximum dose:** 375 mg/day	BP; lipid panel; closely monitor patients for depression, clinical worsening, suicidality, psychosis, or unusual changes in behavior, signs/symptoms of serotonin syndrome, autonomic instability, neuromuscular changes, GI symptoms, and/or seizures; hyponatremia, discontinuation symptoms; children's height and weight should be monitored; intraocular pressure and mydriasis (in patients with high ocular pressure or who are at risk of acute narrow angle glaucoma)
Mirtazapine	Available	**Initial:** 30 mg/day titrated over 2 weeks to 60 mg/day. **Dose range:** 30–60 mg at night **Maximum dose:** 60 mg/day [78]	signs of agranulocytosis or extreme neutropenia such as sore throat, stomatitis or other indications of infection or a low WBC; renal and hepatic function; indications/symptoms of serotonin syndrome; mental status for depression, suicidal thoughts , anxiety, mania, social functioning, panic attacks; lipid profile; gaining weight.
Risperidone	Available	**(Off-label use):** **Initial:** 0.25 to 0.5 mg/day. may increase by 0.5 to 1 mg/day every 3 to 7 days. **Dose range:** 0.5 to 4 mg/day. **Maximum dose:** 4 mg/day	Mental status and alertness; vital ; blood pressure ; weight, height, BMI, waist circumference ; CBC ; electrolytes, renal and liver function; obesity, diabetes, dyslipidemia, hypertension, or cardiovascular disease in the family or personal history ; fasting plasma glucose level/HbA1c ; fasting lipid panel; changes in menstruation, libido, development of galactorrhea, erectile and ejaculatory function ; abnormal involuntary movements or parkinsonian signs ; tardive dyskinesia ; ocular examination; fall risk; signs and symptoms of neuroleptic malignant syndrome, autonomic instability

Aripiprazole	Available	**(Off-label use):** **Initial:** 5 mg once daily. may increase gradually by 5 mg at intervals ≥1 week **Dose range:**5-20 mg/day **Maximum dose:** 20 mg/day	Patients should be continuously monitored for symptoms of depression, clinical worsening, suicidality, psychosis, or unusual changes in behavior; vital signs ; BP; weight, height, BMI, waist; CBC; electrolytes and liver function; obesity, diabetes, dyslipidemia, hypertension, or cardiovascular disease in the family or personal history; fasting plasma glucose level/HbA1c; fasting lipid panel; changes in menstruation, libido, development of galactorrhea, erectile and ejaculatory function; abnormal involuntary movements or parkinsonian; tardive dyskinesia; ocular examination; fall risk, signs and symptoms of neuroleptic malignant syndrome.
Quetiapine	Available	**(Off-label use):** Immediate release: **Initial:** 25 to 50 mg once daily; increase by 25 to 100 mg every 2 to 3 weeks **Dose range:**25-400 mg/day **Maximum dose:** 400 mg/day	Mental status and alertness; Patients should be continuously monitored for symptoms of clinical worsening, psychosis, suicidality, or unusual changes in behavior; vital signs; BP; weight, height, BMI, waist circumference; CBC ; signs and symptoms of infection or fever ; electrolytes and liver function; TSH, free T4, and thyroid clinical assessment; fasting plasma glucose level/HbA1c ; symptoms of hyperglycemia ; fasting lipid panel; changes in menstruation, libido, development of galactorrhea, erectile and ejaculatory function; abnormal involuntary movements or parkinsonian signs , tardive; lens examination, examinations ,fall risk; signs and symptoms of neuroleptic malignant syndrome.
Topiramate	Available	**Initial:** 50 mg once daily. increase by 25 to 100 mg at intervals ≥1 week. **Dose range**:50-400mg/day **Maximum dose:** 400 mg/day [90]	Hydration status, signs and symptoms of oligohidrosis and hyperthermia during strenuous exercise, exposure to high external temperature, or in patients using other carbonic anhydrase inhibitors and drugs with anticholinergic activity; electrolytes (serum bicarbonate), serum creatinine; monitor for symptoms of acute acidosis and complications of long-term acidosis ; ammonia level in patients with unexplained lethargy, vomiting, or mental status changes; intraocular pressure, visual acuity and/or ocular pain, symptoms of secondary angle closure glaucoma; suicidality ; sedation and mental alertness.
Olanzapine	Available	**Initial:** 2.5 mg once daily. may increase by 2.5 mg every 1 to 2 weeks **Dose range**:2.5 - 20 mg/d	Mental status and alertness; vital signs; BP ; weight, height, BMI, waist circumference (for a weight gain of ≥ 5% of initial weight, try switching to a different antipsychotic); CBC; electrolytes and liver function; obesity, diabetes, dyslipidemia, hypertension, or

		Maximum dose: 20mg/day [94,96]	cardiovascular disease in the family or personal history; fasting plasma glucose level/HbA1c; fasting lipid panel ; changes in menstruation, libido, development of galactorrhea, erectile and ejaculatory function ; abnormal involuntary movements or parkinsonian; tardive dyskinesia; ocular examination; fall risk ; signs and symptoms of NMS.
Amisulpride	Available	**Initial:** 200 mg/day given once daily or in 2 divided doses titrated up to 600mg/day **Dose range**: 200-600mg/day **Maximum dose:** 600 mg/day [97]	Mental status; vital signs; BP; ECG; weight, height, BMI, waist circumference; CBC; electrolytes, renal and liver function; personal and family history of obesity, diabetes, dyslipidemia, hypertension, or cardiovascular; fasting plasma glucose level/hemoglobin A1c; changes in menstruation, libido, development of galactorrhea, erectile and ejaculatory function; abnormal involuntary movements or parkinsonian signs; tardive dyskinesia; fall risk.
Haloperidol	Available	**Initial:2mg/day** May increase by ≤5 mg at an interval of 2 days **Dose range**: 2-10 mg/day **Maximum dose:**10mg/day [98,99]	Mental status; vital signs; ECG; weight, height, BMI, waist circumference; CBC ; electrolytes and liver function; fasting plasma glucose level/ HbA1c ; lipid panel ; changes in menstruation, libido, development of galactorrhea, erectile and ejaculatory function ; abnormal involuntary movements or parkinsonian signs ; tardive dyskinesia ; visual changes ; ocular examination ; fall risk; signs and symptoms of NMS.
Lamotrigine	Available	**Dose range**: 100 mg/day [102]	LFTs, renal function, hypersensitivity reactions; ECG; clinical worsening in bipolar disorder; signs/symptoms of aseptic meningitis; signs and symptoms of blood dyscrasias.

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