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GUIDE FOR THE RATIONAL PRESCRIPTION OF MEDICATIONS FOR PRIORITY MENTAL AND NEUROLOGICAL CONDITIONS

FOR SPECIALISTS IN THE PUBLIC HEALTH SYSTEM



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Guide for the Rational Prescription of Medications for Priority Mental and Neurological Conditions for Specialists in the Public Health System

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A second edition of this guide is expected to be published in 2020. Comments and suggestions for improving content and/or format of this guide are welcome at: mentalhealth@moph.gov.lb or emwroleb@who.int



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FOREWORD

Psychotropic and neurological medications constitute a pillar of the holistic person-centred care. It is essential that these medications are effective, safe, prescribed rationally, and made accessible to everyone. In this regard, the Ministry of Public Health (MOPH), through its National Mental Health Programme (NMHP), has conceived the “National List of Psychotropic and Neurological Medications for Humanitarian Response”, covering priority conditions.

This “Guide for the Rational Prescription of Medications for Priority Mental and Neurological Conditions for Specialists in the Public Health System” is aligned with the aforementioned medication list and constitutes a reference document for evidence-based and culturally appropriate decision-making. In line with the continuum of care, this guide advocates for the rational medication prescription based on the national list and highlights the importance of the psychosocial component in the treatment of mental and neurological conditions as part of the holistic person-centred care.

This guide was made possible through the fruitful collaboration between the MOPH and the World Health Organization (WHO) in addition to local and international technical experts from different local and international organizations and UN agencies.

We hope that specialists working in the public health system and humanitarian response would embrace this document as a key tool for rationalizing the prescription of medication for priority mental and neurological conditions.



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LIST OF ACRONYMS

ECG	Electrocardiogram
EEG	Electroencephalogram
EMDR	Eye Movement Desensitization and Reprocessing
FBC	Full Blood Count
IM	Intramuscular
IV	Intravenous
LFT	Liver Function Tests
mhGAP	mental health Gap Action Programme
MOPH	Ministry of Public Health
NMHP	National Mental Health Programme
OCD	Obsessive Compulsive Disorder
PRN	Pro re nata (as needed or as required)
NSAID	Non Steroidal Anti-Inflammatory Drug
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	Tricyclic Antidepressant
TSH	Thyroid Stimulating Hormone
WHO	World Health Organization

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INTRODUCTION

Since the launch of the National Mental Health and Substance Use Strategy (2015-2020), the Ministry of Public Health (MOPH) has been prioritizing the integration of mental health into primary healthcare in order to increase access to quality care for people with mental conditions.

In addition, and since the start of the Syrian crisis, local and international non-governmental organizations have initiated specialized mental health services using different lists of psychotropic and neurological medications. The main trend of prescription has been skewed towards high cost medication at start of treatment – a practice that is not necessarily in line with latest evidence. In few instances, prescription relies on in-kind donation of high cost psychotropic medications, hindering the continuum of care for persons with mental conditions. Sustaining this trend, especially in economically vulnerable settings, puts the person at increased economic hardship, induces risk of interruption in treatment, and increases risk of relapse.

In order to harmonize the procurement and provision of medications amongst all actors, and to reinforce continuum of care, the MOPH established a national list of psychotropic and neurological medications for the humanitarian response (*Appendix A*) in 2016, integrating the national essential one and adding medications used at specialized level. It is of utmost importance to ensure the uninterrupted availability of these medications, thus preventing the risk of deterioration of the person's condition and avoiding enduring financial hardship. In addition, a summarized list of medical tests needed to monitor the side effects of these medications can be found in *Appendix B*.

This guide is for pharmacological treatment of mental and neurological conditions; it is based on the national list of psychotropic and neurological medications which covers the following priority conditions mostly seen at outpatient level: (1) major depressive disorder; (2) bipolar affective disorder; (3) schizophrenia and other psychotic disorders; (4) obsessive compulsive disorder; (5) anxiety disorders; (6) epilepsy; (7) alcohol withdrawal management; and (8) other disorders (dementia, behavioural disorders in children with developmental disorders, and insomnia).

This guide provides simple and evidence-based information for rational pharmacological ambulatory treatment¹ to persons with mental and neurological conditions. It does not provide information for diagnosis. It is intended to be used by specialists in the public health system, namely psychiatrists and neurologists, to inform practice and ensure economic viability of the public health system.

¹ Another guide for the management of psychiatric emergencies at emergency department is available at the MOPH. For more information, kindly contact mentalhealth@moph.gov.lb

GUIDING PRINCIPLES

This guide was conceptualized, developed, and revised with the following guiding principles in mind:

Continuum of care	Adopting a comprehensive approach (including promotion, prevention, treatment, and recovery) and ensuring continuous care at different levels (community, primary and secondary). Continuum of care is facilitated by adopting the most cost-effective interventions and promoting referral between the different levels of care.
Quality of care	Adopting interventions based on scientific evidence and/or best practice, taking cultural considerations into account.
Person-centred approach	Placing people at the centre of the care they receive, including participatory and equal decision-making on all aspects of their lives, without discrimination, thus promoting their empowerment and respecting their human rights.
Bio-psychosocial approach	Coordinating the care within the mental health multidisciplinary team and with other sectors following the bio-psychosocial approach and the recovery-oriented practice. Adopting a holistic approach to the condition, taking into consideration the biological, psychological, and social factors and their interactions and setting the care and recovery plan while considering that each person is unique and thus promoting their active engagement in life.
Recovery-oriented approach	Working in partnership with the person and their family/carer and acknowledging that every person is an expert in their own life. Recovery is not synonymous with cure. It aims at gaining and retaining hope, understanding one's abilities and disabilities, engaging in an active life, gaining personal autonomy, social identity, meaning and purpose in life, and a positive sense of self.

PSYCHOSOCIAL INTERVENTIONS

Guidance on psychosocial support and interventions can be found at the beginning of each chapter, as they are effective in reducing the psychological sources of dysfunction, improving functioning and wellbeing, and facilitating social reintegration.

Psychosocial support and interventions address the ongoing psychological and social problems of persons, their families and their carers, targeting basic needs (i.e. food, clothes, housing), safety and security (i.e. vocational training, employment, financial stability), and family and community support. As per the mental health Gap Action Programme (mhGAP), psychosocial interventions encompass activities such as psychoeducation, problem solving techniques, behavioural activation, psychotherapies, etc. More details on evidence-based psychotherapies can be found in [Appendix C](#). A glossary of terms for psychotherapy used in this guide can be found in [Appendix D](#).



CHAPTER 1: MAJOR DEPRESSIVE DISORDER

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CHAPTER 1: MAJOR DEPRESSIVE DISORDER

GENERAL CONSIDERATIONS

- Rule out:
 - » Medical conditions (in particular, hypothyroidism and anemia; tests conducted as needed and not systematically).
 - » The use of medications that can induce depressive symptoms e.g. isotretinoin for acne, levetiracetam² for epilepsy, calcium-channel blockers, estrogens, interferon alpha, etc.
 - » Other mental conditions (history of mania/hypomania).
 - » Normal reactions to recent major loss.
- Consider psychosocial interventions as first line treatment, before medication use.
- Offer psychoeducation to the person and family/carer (where applicable), behavioural activation, relaxation techniques and breathing exercises, social network reactivation, addressing psychosocial stressors (by discussing methods such as problem solving techniques) and strengthening social support.
- Refer to psychotherapy as needed such as cognitive and behavioural therapy, interpersonal psychotherapy, group interpersonal psychotherapy, and family focused therapy.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

INDICATION FOR PHARMACOLOGICAL TREATMENT

- Moderate to severe depression.

CHOICE OF FIRST LINE MEDICATION

- Consider:
 - » The person's preferences.
 - » The previous personal and family member's responses to antidepressants.
 - » The side effect profile of each antidepressant.
 - » The presence of comorbidities.
 - » The potential interactions with other medications.
- Prescribe only one medication, at the lowest starting dose.
- It is recommended to start with selective serotonin reuptake inhibitors (SSRIs) since they are equally effective as tricyclic antidepressants (TCAs) and have a favourable risk-benefit ratio.
- For psychotic depression, augment the antidepressant with an antipsychotic in the acute phase of treatment. Discontinue the antipsychotic gradually thereafter.
- *Table 1* summarizes the dosing, side effects and cautions of medications used for major depressive disorder.

²This medication is recommended for use only under supervision of a specialist.

Table 1: Medications for major depressive disorder

		Dosing	Side effects	! Main cautions
SSRIs	Sertraline (tablets 50 mg)	<p>Start: 25 mg daily.</p> <p>Minimum effective dose: 50 mg.</p> <p>Increase: by 25–50 mg per week (maximum dose: 200 mg).</p> <p>Given once or divided each 12 hours if side effects.</p>	<p>Common: gastrointestinal symptoms, sweating, agitation, anxiety, headache, sedation, insomnia, sexual dysfunction, increased appetite. Most side effects subside after a few days.</p> <p>Serious: hyponatremia (<i>see box 1</i>), rare bleeding risk (in those who use aspirin or other non steroidal anti-inflammatory drugs).</p>	<p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • Inhibits CYP2D6. • Increases blood levels of some antipsychotics and TCAs. • Avoid combination with warfarin and NSAID like aspirin (may rarely increase bleeding risk).
	Fluoxetine (tablets 20 mg)	<p>Start: 20 mg in the morning.</p> <p>Minimum effective dose: 20 mg.</p> <p>Increase: by 20 mg per month (maximum dose: 80 mg).</p>	<p>As for sertraline, but insomnia and agitation* possibly more common and less likely to increase appetite.</p> <p>* if insomnia and/or agitation present, consider prescribing a benzodiazepine (<i>see box 2</i>), preferably diazepam, for a maximum of 2 weeks.</p>	<p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • Inhibits CYP2D6, CYP3A4. • Increases blood levels of some antipsychotics, some benzodiazepines, carbamazepine, cyclosporine, phenytoin, and TCAs. • Reduces the effect of tamoxifen, codeine, and tramadol. • Avoid combination with warfarin and NSAID like aspirin (may rarely increase bleeding risk).
TCAs	Amitriptyline (tablets 25 mg)	<p>Start: 25 mg at bedtime.</p> <p>Minimum effective dose: 75–100 mg.</p> <p>Increase: by 25–50 mg per week (maximum dose: 300 mg).</p> <p>Given once at bedtime or divided each 8–12 hours, with the larger dose at bedtime.</p>	<p>Common: sedation, orthostatic hypotension (risk of fall), blurred vision, dry mouth, constipation, urinary retention, nausea, weight gain, sexual dysfunction.</p> <p>Serious: ECG changes (e.g. QTc prolongation), cardiac arrhythmia, increased risk of seizure.</p>	<p>Avoid in persons with cardiac disease, history of seizure, hyperthyroidism, urinary retention, narrow angle-closure glaucoma, and bipolar disorder (higher risk of manic switch than SSRIs) (<i>see box 3</i>).</p> <p>Avoid in persons with high risk of suicide: overdose can lead to seizures, cardiac arrhythmias, hypotension, coma, or death.</p> <p>Drug-drug interactions: SSRIs, phenothiazines, alcohol, antimuscarinics, antipsychotics, antiarrhythmics.</p>
	Clomipramine (tablets 75 mg)	<p>Start: 37.5 mg at bedtime.</p> <p>Minimum effective dose: 75–112.5 mg (divided each 8–12 hours), with the larger dose at bedtime.</p> <p>Increase: by 37.5–75 mg per week (maximum dose: 225 mg).</p> <p>May be given as single dose at bedtime once tolerated.</p>	<p>Same as amitriptyline.</p>	<p>Same as amitriptyline.</p>

Box 1: Hyponatremia

Symptoms: nausea, lethargy, muscle cramps/weakness, confusion, seizures, coma. 

Treatment: withdraw the causative antidepressant, monitor sodium level daily, fluid restriction.

If sodium level <125 mmol/l, hospital admission is warranted.

After sodium levels are back to normal, consider another antidepressant medication, preferably from a different class, with close monitoring.

Box 2: Role of benzodiazepines in the treatment of depression

Benzodiazepines are not a treatment for depression and should not be prescribed systematically. In rare cases, they can be prescribed if anxiety symptoms, irritability or insomnia are present during the first 2 weeks of treatment with SSRIs (SSRIs need at least 2 weeks to become effective and can cause these side effects themselves). They should be discontinued after 2 weeks because of their addictive potential. Other mild anxiolytics/sedatives, such as hydroxyzine can be used as alternatives to benzodiazepines.

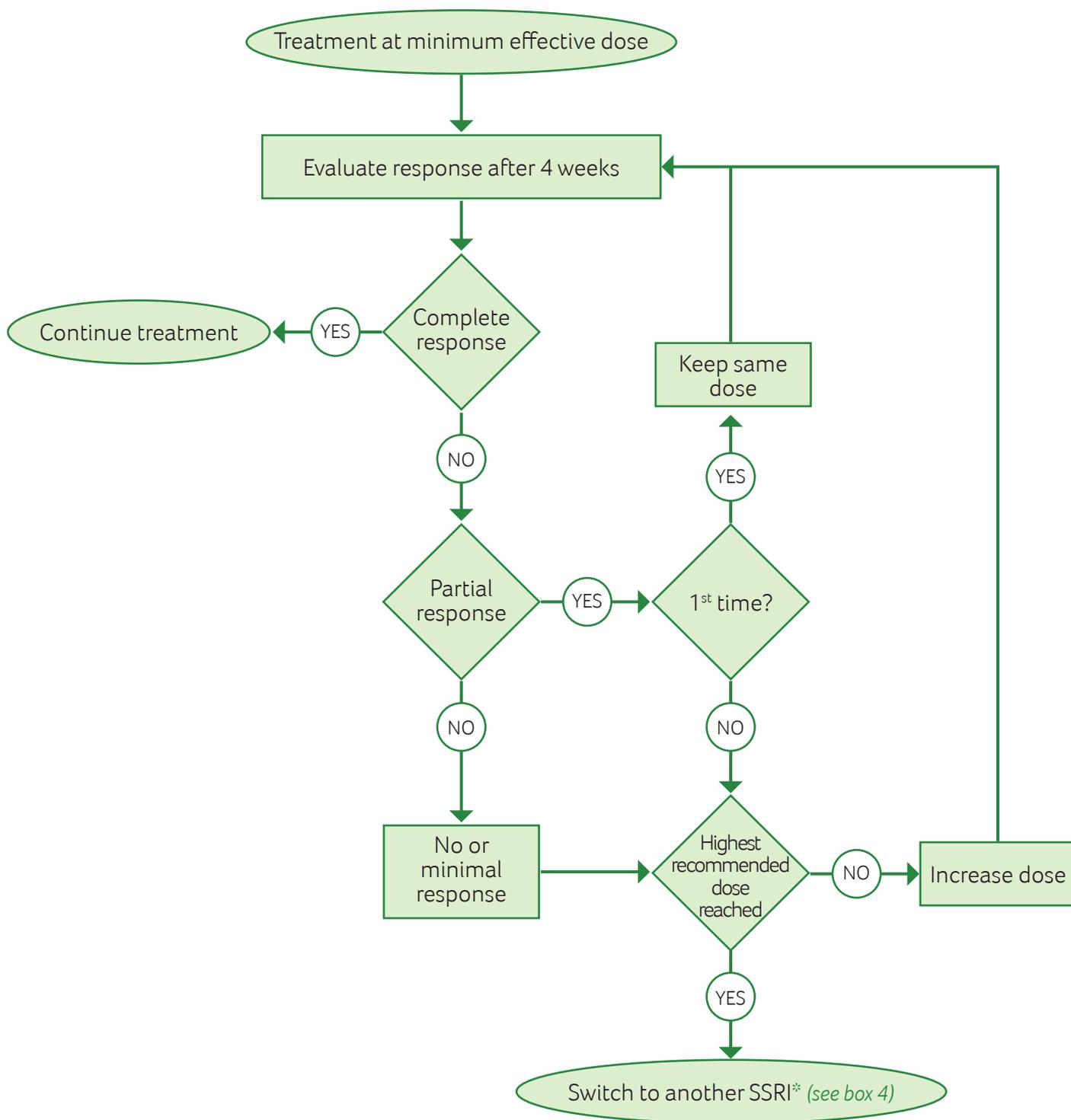
Box 3: Manic switch

If a person develops hypomania/mania secondary to an antidepressant, stop the antidepressant immediately and if symptoms persist, treat like a usual manic episode. For subsequent depressive episode, consider the use of mood stabilizers for this person, applying the bipolar depression treatment recommendations (*see chapter 2*).

MONITORING TESTS

No specific tests are routinely needed before starting treatment with antidepressants or for monitoring purposes, unless clinically indicated such as sodium levels if symptoms of hyponatremia (*see box 1*), ECG if TCAs used in a person at risk of cardiac diseases, weight in an overweight person, etc.

TREATMENT FOLLOW-UP



* Preferably, TCAs should only be prescribed after failure of 2 trials of SSRIs, at the maximum effective dose, and for an appropriate period of treatment.

Box 4: Switching antidepressants

When changing from one antidepressant to another, abrupt withdrawal should usually be avoided. Cross-tapering is preferred, in which the dose of the ineffective or poorly tolerated drug is slowly reduced while the new drug is slowly introduced. The speed of cross-tapering is best judged by monitoring person tolerability.

In some cases abrupt switch may be possible, as is the case when switching from other SSRIs to fluoxetine.

! **Caution** when switching from fluoxetine (long half-life) to other antidepressants: after stopping the fluoxetine, wait 2 weeks before starting the new antidepressant to avoid serotonin syndrome (*see box 5*).

! **Caution** when switching from fluoxetine or paroxetine to a TCA (both inhibit the metabolism of TCAs): a lower starting dose of the TCA is required.

Box 5: Serotonin syndrome

Symptoms: restlessness, hyperreflexia, myoclonus, peripheral hypertonicity, shivering, tachycardia, increased blood pressure, diaphoresis, increased bowel sounds, diarrhea, agitation, convulsions, fever, mydriasis, and delirium. **Risk of death.** !

Treatment: stop the antidepressants immediately. Consider benzodiazepines to control agitation, seizures and muscle stiffness. Consider serotonin-blocking agents like cyproheptadine. Severe forms will require hospital admission.

Once the syndrome is resolved, reintroduce an antidepressant at the lowest dose and taper it up very gradually while monitoring for re-emergence of symptoms. Do not give more than one antidepressant at a time.

TREATMENT OF RESISTANT CASES

If the person is still unresponsive to monotherapy with 2 SSRIs and 1 TCA successively, consider augmenting an antidepressant with lithium³ or a second generation antipsychotic like risperidone (0.5 to 2 mg per day).

SPECIAL POPULATIONS

- **Children (<12 years old):** antidepressants are not advised.
- **Adolescents (12 to 18 years old):** after failure of adequate psychosocial interventions, fluoxetine is the drug of choice, combined with continued psychotherapy. TCAs are contraindicated. Provide psychoeducation to the family/carer and monitor closely for risk of treatment-emergent suicidal thoughts and acts (*see box 6*).

³ This medication is recommended for use only under supervision of a specialist.

- **Older persons (> 65 years old):** SSRIs are the drugs of choice at the same doses as in adults. Beware as older persons are more prone to develop bleeding with SSRIs. Therapeutic response may be delayed (6 to 12 weeks). TCAs are best avoided (hypotension and risk of falls, constipation and urinary retention, delirium).
- **Pregnant women:** antidepressants are best avoided, especially in the first trimester. When needed, sertraline or fluoxetine at the lowest effective doses are the drugs of choice. Paroxetine is the least safe of SSRIs. Beware of discontinuation symptoms of the neonate. Contact a gynecologist.
- **Breastfeeding women:** antidepressants are best avoided. If necessary, sertraline is the drug of choice. Fluoxetine is not recommended.

Box 6: Suicidal ideations with SSRIs

SSRIs might increase the risk of suicidal thoughts and behaviours in the short term, especially in youth (adolescents and young adults up to 24 years of age). However, reduction in the prescription of SSRIs is associated with increased rates of suicide; therefore, they should be prescribed when needed, after explaining the risks to the person and family/carer and while maintaining close monitoring.

DURATION OF TREATMENT

- Continue treatment for 9 to 12 months after symptom resolution.
- Continue treatment for at least two years if:
 - » The person has had more than two major depressive episodes.
 - » The person is at increased risk of relapse (residual symptoms, history of severe episodes).
 - » The consequences of relapse are likely to be severe (suicide attempts, severe life disruption, and inability to work).
- Discontinuation should be over at least 4 weeks, except for fluoxetine (longer half-life, can be discontinued faster). If discontinuation symptoms (*see box 7*) are severe, consider reintroducing the original antidepressant and taper it more gradually while monitoring symptoms.

Box 7: Discontinuation symptoms

Antidepressants are not addictive, but they may produce some symptoms when stopped after being taken continuously for at least 6 weeks. Paroxetine, venlafaxine and amitriptyline are the most associated with discontinuation symptoms.

Symptoms: flu-like (myalgia, chills), “shock-like” sensations, headache, nausea, insomnia, irritability, movement disorders.

Usually symptoms are mild and self-limiting, but occasionally may be severe and prolonged.



CHAPTER 2: BIPOLAR AFFECTIVE DISORDER

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20	Indication for pharmacological treatment
20	Choice of first line medication
23	Monitoring tests
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CHAPTER 2: BIPOLAR AFFECTIVE DISORDER

GENERAL CONSIDERATIONS

- Rule out:
 - » Medical conditions (in particular delirium).
 - » Medication side effects (corticoids, hormonal treatments, acne treatment, etc.).
 - » Other mental conditions (alcohol and drug use disorders).
- Offer psychoeducation to the person and family/carer (where applicable), social network reactivation, maintaining social rhythm, addressing psychosocial stressors (by discussing methods such as problem solving techniques) and strengthening social support.
- Refer to psychotherapy as needed such as cognitive behavioural therapy, interpersonal psychotherapy, and family focused therapy.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

INDICATION FOR PHARMACOLOGICAL TREATMENT

- Bipolar mania.
(*This chapter mainly focuses on bipolar mania, for information on bipolar depression see box 8*).

CHOICE OF FIRST LINE MEDICATION

- Discontinue antidepressant medication if present.
- Consider:
 - » The person's preferences.
 - » The side effect profile of each medication.
 - » The presence of comorbidities.
 - » The potential interactions with other medications.
- Initiate treatment with antipsychotics (haloperidol or risperidone; *see table 4* for dosage) or sodium valproate, for a more rapid response. Lithium⁴ is also a first line treatment for acute mania, but it has a slower onset of action and it should only be prescribed when laboratory tests are available and affordable. Carbamazepine could also be a choice for treatment of mania, but its efficacy is backed up with less evidence.
- Consider benzodiazepines like diazepam for agitation (for 2-4 weeks maximum).

⁴ This medication is recommended for use only under supervision of a specialist; avoid using lithium as a first line treatment in case the person is unable to comply with the routine blood tests or is moving destination.

- If already on lithium, sodium valproate, or carbamazepine, optimize the dose then add an antipsychotic if needed. If already on an antipsychotic, optimize the dose and add sodium valproate or lithium if needed.
- *Table 2* summarizes the dosing, side effects and cautions of medications used for bipolar affective disorder.

Box 8: Pharmacological treatment of bipolar depression

Treatment of an acute depressive episode:

- Use mood stabilizers (lithium, sodium valproate, carbamazepine, lamotrigine or an antipsychotic) alone or in combination with an antidepressant (preferably an SSRI - *see table 2*).
- **Antidepressants should never be prescribed alone in bipolar depression, as they can induce a manic switch (*see box 3*).**
- If symptoms of mania develop, stop the antidepressant immediately.

For long term prophylaxis:

- Long term use of antidepressants is best avoided.
- Lithium or lamotrigine are probably the best options among mood stabilizers for prevention of depressive relapses. Lamotrigine is probably more effective for prevention of relapses than for acute treatment of depression.

Table 2: Medications for bipolar affective disorder

	Dosing	Side effects	! Main cautions
Lithium⁵ (tablets 400 mg)	<p>Start: 400 mg (in divided doses each 12 hours).</p> <p>Increase: by increments of 200 mg.</p> <p>Lithium titration: Measure blood level of lithium 7 days after every dose. Change until target blood level reached:</p> <ul style="list-style-type: none"> • Acute manic episode: 0.8-1.2 mEq/l. • Maintenance treatment: 0.6-0.8 mEq/l. 	<p>Common: sedation, cognitive problems, tremor, impaired coordination, hypotension, leukocytosis, polyuria, polydipsia, nausea, diarrhea, weight gain, hair loss, rash.</p> <p>Serious: nephrogenic diabetes insipidus, hypothyroidism, hyperparathyroidism, ECG changes (arrhythmia, sick sinus syndrome, T-wave changes), reduction in the Glomerular Filtration Rate that may lead to kidney failure and dialysis.</p>	<p>Use only if clinical and laboratory monitoring are available. Contraindicated in persons with severe cardiac or kidney disease. May exacerbate psoriasis and acne. Dehydration can increase lithium levels.</p> <p>Beware of lithium toxicity (<i>see box 9</i>).</p> <p>Risk of teratogenicity.</p> <p>Drug-drug interactions: NSAID, Angiotensin-converting-enzyme inhibitor (ACE inhibitor), thiazide diuretics, metronidazole, and tetracycline can increase lithium levels.</p>

⁵ This medication is recommended for use only under supervision of a specialist.

Table 2: Medications for bipolar affective disorder (continued)

	Dosing	Side effects	! Main cautions
Sodium valproate (tablets 500 mg immediate release or controlled release)	<p>Start: 500 mg.</p> <p>Increase: gradually against response and side effects.</p> <p>Average effective dose: 1000-2000 mg daily (maximum dose: 60 mg/kg/day).</p> <p>Target blood level: 50-100 mg/l.</p> <ul style="list-style-type: none"> Acute manic episode: 100 mg/l. Maintenance treatment: 50 mg/l. <p>Immediate release: at least twice daily.</p> <p>Controlled release: once daily.</p>	<p>Common: sedation, headache, tremor, ataxia, nausea, vomiting, diarrhea, weight gain, transient hair loss, benign increase in Liver Function Tests (LFT).</p> <p>Serious: liver failure, thrombocytopenia, leucopenia, drowsiness/confusion, hemorrhagic pancreatitis, hyperammonaemia, peripheral oedema, hyperandrogenism and polycystic ovaries in women.</p>	<p>Caution in persons with underlying or suspected hepatic disease.</p> <p>Risk of teratogenicity and impaired cognitive function in children exposed in utero: not recommended in women of child-bearing age.</p> <p>Drug-drug interactions:</p> <ul style="list-style-type: none"> Sodium valproate levels decreased by carbamazepine, increased by aspirin. Sodium valproate increases dose of lamotrigine.
Carbamazepine (tablet 200 mg and 400 mg)	<p>Start: 200 mg (in divided doses each 12 hours).</p> <p>Increase: gradually against response and side effects.</p> <p>Average effective dose: 600-800 mg (maximum dose: 1200 mg daily) (in divided doses each 8 hours).</p> <p>Target blood level: 7-12 mg/l.</p> <p>Dose may need to be adjusted after 2 weeks due to induction of its own metabolism.</p>	<p>Common: sedation, confusion, dizziness, ataxia, double vision, nausea, diarrhea, benign leucopenia, benign increase in LFT.</p> <p>Serious: hepatotoxicity, cardiac conduction delay, low sodium levels, severe rash.</p>	<p>Contraindicated in persons with history of blood disorders, kidney, liver, or cardiac disease.</p> <p>Risk of teratogenicity.</p> <p>Drug-drug interactions:</p> <ul style="list-style-type: none"> May reduce the effects of hormonal birth control, immunosuppressants, antiepileptics, antipsychotics, methadone and some antiretrovirals. Levels can be increased by certain antifungals and antibiotics.
Lamotrigine⁶ (tablets 100 mg)	<p>Start: 25 mg daily for 2 weeks, then give in divided doses each 12 hours: 50 mg/day for 2 weeks, then 100 mg/day for 1-2 weeks, then 150 mg/day for 1-2 weeks, then 200 mg/day.</p> <p>If given with sodium valproate: start 25 mg every other day for 2 weeks, then follow the same titration regimen.</p> <p>Rapid titration increases risk of Stevens Johnson syndrome.</p>	<p>Common: benign rash, sedation, blurred or double vision, dizziness, ataxia, headache, tremor, insomnia, fatigue, nausea, abdominal pain, constipation, rhinitis.</p> <p>Serious: Stevens Johnson syndrome (rash and multi-organ failure), rare blood dyscrasias.</p>	<p>Caution in persons with renal, hepatic or cardiac diseases.</p> <p>Drug-drug interactions:</p> <ul style="list-style-type: none"> Sodium valproate increases blood levels of lamotrigine, requiring lower doses of lamotrigine. Carbamazepine may increase the clearance of lamotrigine and lower its blood levels.

⁶ This medication is recommended for use only under supervision of a specialist.

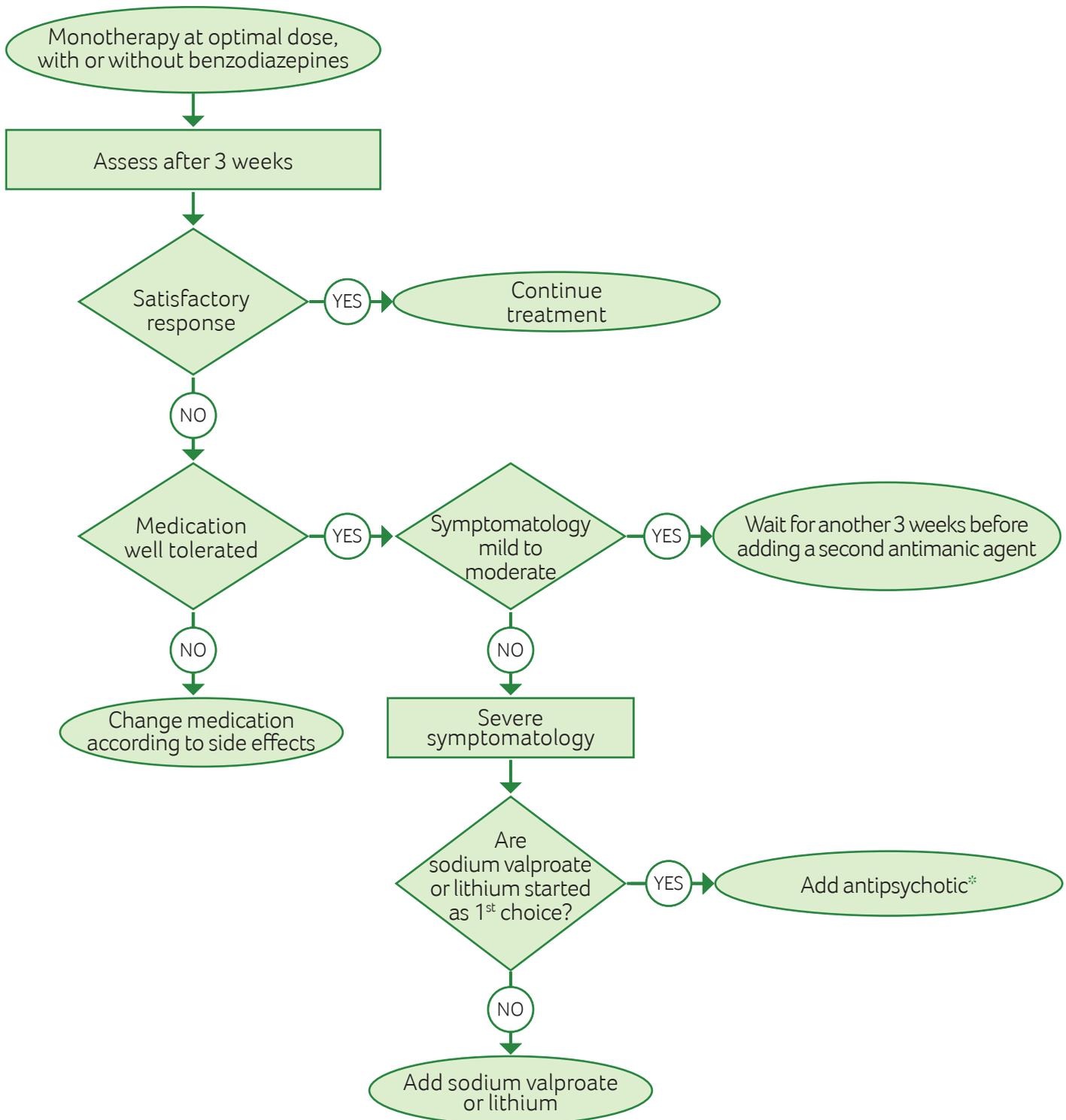
MONITORING TESTS

The recommended monitoring tests for medications with their frequency and proposed interventions if results are not within normal range can be found in *table 3*.

Table 3: Recommended monitoring tests for medications related to bipolar affective disorder

Medication	Monitoring tests	Frequency	Proposed interventions if results not within normal range
Lithium <i>(do not start lithium if tests are not feasible)</i>	Lithium level (before the morning dose and 12 hours after the evening dose)	For every dose change in the first weeks, then every 3 months for the first year then every 6 months.	<ul style="list-style-type: none"> Elevated TSH: reversible after stopping lithium. Not an indication to stop lithium. Consider thyroid hormone supplementation. Elevated creatinine levels: refer to specialist care for more investigations and consider stopping lithium.
	Weight, FBC, urea, creatinine, TSH	Before starting, then every 6 months.	
	ECG	Before starting, if clinically indicated.	
	Pregnancy test	Before starting (where applicable).	
Sodium valproate	Sodium valproate level	Until dose stabilization in the first weeks of treatment. No need for continuous monitoring unless evidence of ineffectiveness, non-adherence, or toxicity.	<ul style="list-style-type: none"> Elevation of liver enzymes up to 2–3 times the normal levels: probably benign, repeat tests and if no further deterioration, no need to stop sodium valproate. Liver enzymes >3 times the normal levels: refer to specialist care for further evaluation to rule out acute hepatic and pancreatic toxicity. Stop sodium valproate. Thrombocytopenia: if moderate (100,000–150,000/microl), repeat tests, no need to stop sodium valproate. If < 100,000/microl: refer to specialist care and stop sodium valproate. If hyperammonemia: stop sodium valproate.
	Weight, SGPT, SGOT, gammaGT, FBC	Before starting, then at 6 months, 1 year and then annually.	
	Pregnancy test	Before starting (where applicable).	
	Blood ammonia level	If signs of hyperammonemia (confusion, lethargy, vomiting, seizures).	
Carbamazepine	Weight, urea, electrolytes, SGPT, SGOT, gammaGT, FBC	Before starting. Repeat annually or if clinically indicated.	<ul style="list-style-type: none"> Elevation of liver enzymes up to 2–3 times the normal levels: probably benign, repeat tests and if no further deterioration, no need to stop carbamazepine. Liver enzymes >3 times the normal levels: refer to specialist care for further evaluation to rule out acute hepatic and pancreatic toxicity. Stop carbamazepine. Hyponatremia (<i>see box 1</i>): stop carbamazepine, treat as usual. Leucopenia: usually benign, repeat tests, do not stop carbamazepine unless severe deterioration (neutrophils count < 1500/mm³). The combination of carbamazepine and clozapine increases the risk of agranulocytosis. 
Lamotrigine	No need for baseline or monitoring tests.		
Antipsychotics	See tests under schizophrenia chapter (<i>chapter 3</i>).		

TREATMENT FOLLOW-UP



* Clozapine is reserved for resistant cases: after failure of multiple combinations.

SPECIAL POPULATIONS

- **Adolescents (12 to 18 years old):** among the available medications on the national list of psychotropic and neurological medications, risperidone is one of the best options for the treatment of acute mania, followed by lithium, sodium valproate and haloperidol.
- **! Sodium valproate is contraindicated in adolescent girls.**
- **Older persons (> 65 years old):** use lower doses of medication. Anticipate an increased risk of drug-drug interactions.
- **Pregnant and breastfeeding women:** avoid sodium valproate, lithium, and carbamazepine during pregnancy due to the **risk of birth defects**. Antipsychotics are relatively safe during pregnancy, so consider low dose haloperidol or risperidone. Consider lamotrigine in bipolar depression. Discuss with the person the risk of bipolar relapse during pregnancy if not treated and the risks of each medication.

Antiepileptic medications and lithium are best avoided during breastfeeding as their side effects potential increases in infants. It is best to switch to antipsychotics (risperidone, haloperidol). Sodium valproate could be used if an adequate contraceptive method is in place (alongside breastfeeding), and if infants are monitored for possible hepatotoxicity.

DURATION OF TREATMENT

- After remission from a first episode of mania, continue treatment for at least 2 years to prevent relapses (prophylactic treatment phase).
- After a second episode, treatment is usually continued for 5 years and sometimes more.
- If more than one medication was used to control the acute manic episode, it is recommended to keep only one of them for prophylactic treatment (as monotherapy is always safer than polytherapy).
- It is usually recommended to keep the effective dosage of acute treatment of mania for prophylactic treatment. However, if this dose is high, one can try to decrease it to the minimum effective dose to reduce the risk of side effects during the prophylactic treatment phase. This should be decided on a case by case basis, and balanced against the risk of relapse.
- Lithium has the best evidence for long term prophylaxis, followed by sodium valproate, antipsychotics, and carbamazepine. Therefore, in case of frequent relapses, lithium might be the preferred option as prophylactic treatment, if laboratory tests are available and affordable.
- In case of non adherence to long term prophylactic treatment: discuss reasons for non adherence with the person and family/carer and provide information regarding the importance of medication in prevention of relapses.
- For discontinuation of treatment:
 - » Discontinuation of antipsychotics, sodium valproate and carbamazepine should be over at least 4 weeks.
 - » Discontinuation of lithium should be over at least 4 weeks and preferably over 3 months (increased risk of relapse after sudden discontinuation).

Box 9: Lithium toxicity

Lithium has a safety factor and therapeutic index that are extremely low, hence the importance of adhering to the prescribed dose.

Symptoms:

- When lithium levels > 1.5 mmol/l: anorexia, nausea, diarrhea, muscle weakness, drowsiness, ataxia, coarse tremor and muscle twitching.
- When lithium levels > 2 mmol/l: disorientation, seizures, **coma and death.** 

Risk factors: dehydration, low sodium diet, drug-drug interactions (*see table 2*).

Treatment: stop lithium, hydration, and close monitoring of lithium levels. Might need hospital admission with osmotic or forced alkaline diuresis (not thiazide or loop diuretics), or even peritoneal dialysis or hemodialysis.

Psychoeducation of the person and family/carer about symptoms and risk factors of toxicity is mandatory.

 **Persons at risk of suicidal attempts with overdose should not have unsupervised access to their lithium tablets.**



CHAPTER 3: SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS

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CHAPTER 3: SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS

GENERAL CONSIDERATIONS

- Rule out:
 - » Medical conditions (in particular delirium, medication side effects e.g. steroids and some antimalarial).
 - » Other mental disorders (e.g. alcohol and drug use disorders, dementia).
- Offer psychoeducation to the person and family/carer (where applicable), social network reactivation, addressing psychosocial stressors (by discussing methods such as problem solving techniques) and strengthening social support. Promote functioning in daily living and social activities and promote independence. Assess family/carer who may present a mental condition associated with providing care.
- Refer to psychotherapy as needed such as family focused therapy, and cognitive remediation therapy.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

INDICATION FOR PHARMACOLOGICAL TREATMENT

- Schizophrenia.
- Schizoaffective disorder.
- Delusional disorder.

CHOICE OF FIRST LINE MEDICATION

- When psychosis is identified, start antipsychotic medication immediately, prescribe one antipsychotic at a time, start at lowest dose and titrate up as quickly as tolerated.
- First-generation antipsychotics and non-clozapine second-generation antipsychotics have similar efficacy in treating psychosis but different side effect profiles. Choice of medication is guided by the person's preferences, their level of adherence to the treatment plan, previous treatment response and tolerability, the side effect profile of each antipsychotic, the presence of comorbidities and potential interactions with other medications.
- Clozapine⁷ is reserved for resistant cases because of the risk of **agranulocytosis** and the need for repeated blood tests (*see box 10*). It is superior in efficacy to all other antipsychotics.
- *Table 4* summarizes the dosing, side effects and cautions of medications used for schizophrenia and other psychotic disorders.

⁷ This medication is recommended for use only under supervision of a specialist.

Table 4: Medications for schizophrenia and other psychotic disorders

	Dosing	Side effects	! Main cautions
First-generation antipsychotics	Haloperidol (tablets 5 mg) Start: 2.5 mg to 5 mg. Minimum effective dose: 5 mg to 10 mg. Increase: gradually over 2 weeks; maximum dose: 30 mg in divided doses each 8 hours.	Common: sedation, dizziness, blurred vision, dry mouth, urinary retention, constipation, tachycardia, weight gain, galactorrhea, amenorrhea, sexual dysfunction. Serious: orthostatic hypotension, extrapyramidal symptoms (<i>see box 11</i>), ECG changes (prolonged QT interval) (<i>see box 12</i>), neuroleptic malignant syndrome (<i>see box 13</i>).	Caution in persons with kidney disease, liver disease, cardiac disease, epilepsy, long QT syndrome or taking QT-prolonging medications. Monitor ECG if possible.
	Chlorpromazine (tablets 100 mg) Start: 25 to 50 mg. Minimum effective dose for antipsychotic effect: 300 mg. Maximum dose for antipsychotic effect: 1000 mg (in divided doses each 8 hours). Minimum effective dose for sedation: 50 mg. Maximum dose for sedation: 300 mg (in divided doses each 8 hours).	Same as haloperidol. More risk of: sedation, orthostatic hypotension, syncope, photosensitivity, jaundice.	Same as haloperidol. Additional caution in persons with respiratory disease, glaucoma, urinary retention. Contraindications: impaired consciousness, bone marrow depression, pheochromocytoma. Drug-drug interactions: <ul style="list-style-type: none"> Increases effects of blood pressure lowering medications. Lowers blood pressure if combined with epinephrine.
	Zuclophenthixol decanoate⁸ (IM 200 mg/ml) Test dose: 100 mg. Give a second injection (200 mg) after 1 to 4 weeks according to response. Adjust dose and frequency of injections according to response and tolerability. Minimum effective dose: 200 mg every 4 weeks. Maximum dose: 200 mg every week. Keep the person on their previous oral antipsychotic for the first week after the initial injection then taper it down and stop it over another week. Conversion equivalences: 100 mg/week of zuclophenthixol IM is equivalent to a daily dose of 25 to 50 mg of oral zuclophenthixol, 1 to 5 mg of oral haloperidol, 0.5 to 3 mg of oral risperidone. Wait 2–3 months to evaluate full therapeutic effect.	Same as haloperidol.	Same as haloperidol. Contraindications: hypersensitivity, circulatory collapse, depressed level of consciousness of any cause. Not recommended for those who never had oral antipsychotics. Avoid in persons who previously developed neuroleptic malignant syndrome following antipsychotics treatment.

⁸ This medication is recommended for use only under supervision of a specialist.

Table 4: Medications for schizophrenia and other psychotic disorders (continued)

	Dosing	Side effects	 Main cautions
Second-generation antipsychotics	<p>Risperidone (tablets 2 mg, syrup 1 mg/ml)</p> <p><u>Tablets:</u> Start: 1 mg.</p> <p>Minimum effective dose: 2 mg.</p> <p>Maximum dose: 8 mg* (once daily or divided each 12 hours).</p> <p>* if well tolerated and no optimal response, can go up to 10 mg.</p> <p><u>Syrup in children and older persons:</u> from 0.25 to 2 mg per day.</p> <p>Syrup can be mixed with water, coffee, orange juice, and low-fat milk, but not with cola or tea.</p>	<p>Common: sedation, dizziness, tachycardia.</p> <p>Serious: orthostatic hypotension, metabolic effects (elevated lipids, insulin resistance, weight gain), extrapyramidal symptoms, elevated prolactin, sexual dysfunction, neuroleptic malignant syndrome.</p>	<p>Caution in persons with cardiac disease.</p> <p>Increased cardiovascular accident risk in older persons.</p> <p>Drug-drug interactions: carbamazepine can reduce levels of risperidone, whereas fluoxetine can increase its levels.</p>
	<p>Clozapine⁹ (tablets 100 mg)</p> <p>Start: 25 mg.</p> <p>Increase: slowly by 25 mg every 1–2 days, divided each 12 hours.</p> <p>Average effective dose: 300 to 450 mg (can be given once at night when efficacy reached and well tolerated).</p> <p>Maximum dose: 900 mg.</p> <p>If treatment stopped for more than 2 days and less than a week, titrate up quickly over at least 3 days, starting at half the previous dose.</p> <p>If stopped for more than a week re-titrate as if new person.</p>	<p>Common: sedation, hypersalivation, nausea, gastro-oesophageal reflux, orthostatic hypotension, tachycardia, fever, enuresis.</p> <p>Serious: important metabolic effects (elevated lipids, insulin resistance, weight gain), seizures (at doses > 500 mg/day; consider adding prophylactic valproic acid), agranulocytosis/neutropenia, eosinophilia, myocarditis, pneumonia, severe constipation.</p>	<p>Caution in persons with cardiac disease, metabolic syndrome, epilepsy.</p> <p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • Dose may need to be reduced if given in conjunction with fluvoxamine. • Dose may need to be raised if given in conjunction with cigarette smoking (in case of smoking cessation, consider decreasing the dose of clozapine).
Anticholinergic agents	<p>Biperiden (tablets 4 mg)</p> <p>Start: 2 mg.</p> <p>Maximum dose: 12 mg (in divided doses each 6 to 12 hours).</p>	<p>Common: sedation, confusion, agitation and memory disturbance (especially in older persons), tachycardia, dry mouth, urinary retention and constipation.</p> <p>Serious: angle-closure glaucoma, myasthenia gravis and gastro-intestinal obstruction.</p>	<p>Caution in persons with cardiac, liver, or kidney disease.</p> <p>Do not use anticholinergics on a routine basis in persons taking antipsychotics.</p> <p>Drug-drug interactions: caution when combining with other anticholinergic medications.</p>
	<p>Trihexyphenidyl (tablets 5 mg)</p> <p>Start: 2.5 mg</p> <p>Maximum dose: 15 mg (in divided doses each 6 to 12 hours).</p>		

⁹ This medication is recommended for use only under supervision of a specialist.

MONITORING TESTS

- It is recommended to check weight, pulse and blood pressure, before starting antipsychotics and then once monthly during the first 3 months, at 1 year and then annually thereafter.
 - An electrocardiogram is recommended if clinically indicated (high blood pressure) or if personal history of cardiac disease. It can be done before starting antipsychotics, after 3 months, at 1 year then annually thereafter.
 - If possible, do blood lipids and fasting glucose, after 6 months of starting antipsychotics, then at 1 year and yearly thereafter. This is especially important when risk factors are present and second generation antipsychotics used.
 - In clozapine users, full blood count should be done weekly for 18 weeks, then every 2 weeks until a year, and monthly thereafter.
- !** If these regular checks are not feasible, clozapine should not be prescribed, due to the risk of life-threatening agranulocytosis.

TREATMENT FOLLOW-UP

- During the first weeks, monitor response to treatment and tolerability and take action guided by *table 5*.
- Medication should generally be given at an effective dose for at least 6 to 8 weeks before considering switching to another antipsychotic. However, consider earlier switch (at 2–3 weeks) if symptoms are severe and unresponsive to treatment.
- Switching should happen slowly through cross-tapering.
- If adherence to treatment is unsatisfactory, discuss reasons for non adherence with the person and family/carer, provide information regarding importance of medication, and consider depot/long-acting injectable antipsychotics.

Table 5: Treatment response and tolerability

	Tolerance +	Tolerance -
Response +	Continue same treatment.	<ul style="list-style-type: none"> • Decrease the dose. • Add treatment for side effects (anticholinergic medication, etc.). • Switch to another antipsychotic, preferably of a different class and side effect profile.
Response -	Increase to the maximum recommended dose.	<ul style="list-style-type: none"> • Switch to another antipsychotic, preferably of a different class.

TREATMENT OF RESISTANT CASES

Persons who fail to respond to 2 trials of antipsychotics (one of them being a non-clozapine second-generation antipsychotic), at an optimal dose and duration, should be treated with clozapine, if blood tests can be performed as recommended. Treatment effectiveness for clozapine should be assessed over 6 months.

SPECIAL POPULATIONS

- **Adolescents (12 to 18 years old):** preferably start with risperidone, followed by haloperidol. Beware of increased risk of extrapyramidal symptoms in youth.
- **Older persons (> 65 years old):** use a third to a half of the usual dose of medication. Anticipate an increased risk of drug-drug interactions.
- **⚠ Caution: antipsychotics carry an increased risk of cerebrovascular events and death in older persons with dementia-related psychosis.**
- **Pregnant and breastfeeding women:** in women with psychosis who are planning a pregnancy or are pregnant or breastfeeding, low dose haloperidol or risperidone may be considered.
- **⚠ Beware of extrapyramidal symptoms risk in the neonate.** Anticholinergics should not be prescribed in pregnancy, except in cases of acute, short term use (days to weeks). Benzodiazepines can only be given in acute situations (days to weeks), and carry a risk of floppy baby syndrome near delivery.

Box 10: Neutropenia/Agranulocytosis

Rare side effect of clozapine treatment: 0.8%.

Risk is highest during the first 18 weeks of treatment.

Severe neutropenia, defined as an absolute neutrophil count $< 500/\text{mm}^3$ can lead to infection and **death**: advise persons to immediately report fever and signs of infection.

A baseline of absolute neutrophil count must be $> 1500/\text{mm}^3$ to initiate clozapine treatment and treatment should be suspended if absolute neutrophil count falls below $1000/\text{mm}^3$.

Box 11: Extrapyramidal symptoms

Symptoms: acute dystonic reaction, pseudo-parkinsonism (tremor, bradykinesia, cog-wheeling), akathisia, tardive dyskinesia.

Treatment: reduce the antipsychotic dose, add anticholinergic medications (except for tardive dyskinesia, where they should be stopped), switch to antipsychotic with lower potential for extrapyramidal symptoms (clozapine).

Promethazine (25-75 mg) can also reduce acute extrapyramidal symptoms, especially acute dystonic reaction.

Propranolol (30-80 mg/day) can be used for akathisia.

Box 12: QT prolongation

Antipsychotics (especially haloperidol and chlorpromazine) can prolong the QT interval.

QTc (QT corrected for heart rate) is normal when < 440 msec for men, < 470 msec for women.

High risk of arrhythmia (especially torsade de pointes) when > 500 msec: stop suspected drug, switch to drug of lower effect (e.g. switch from haloperidol to risperidone or clozapine, monitor ECG closely).

Between normal limits and 500 msec: consider reducing the dose or switching, monitor ECG closely.

Risk factors for QT prolongation: cardiac diseases, hypokalemia, hypomagnesaemia, hypocalcaemia.

Non-psychotropic drugs associated with QT prolongation: erythromycin, ampicillin, quinine, quinidine, amiodarone, amantadine, cyclosporine, diphenhydramine, hydroxyzine, tamoxifen, etc.

Box 13: Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but **potentially life-threatening** adverse effect of antipsychotics.

Symptoms: muscular rigidity, elevated temperature, high blood pressure, tachycardia, confusion.

Abnormal tests: elevated creatinine kinase (CPK), leucocytosis, elevated liver function tests.

Treatment: urgent hospital admission and discontinuation of antipsychotics. Consider: rehydration, benzodiazepines and bromocriptine. Artificial ventilation might be needed in severe cases.

After resolution of symptoms, re-challenge with another antipsychotic with low-dopamine affinity like clozapine. Start with low doses and monitor closely.

Box 14: Catatonia

Symptoms: stupor, mutism, waxy flexibility, negativism, posturing, echolalia, echopraxia, refusal to eat and drink.

Associated with schizophrenia, depression, mania, etc.

Rule out medical conditions.

Treatment: hospital admission is recommended. Rule out neuroleptic malignant syndrome. Consider: benzodiazepines.

DURATION OF TREATMENT

- Continue antipsychotics treatment for at least 1 to 2 years, if full remission of symptoms is attained after a first episode of psychosis.
- Discuss with person and family/carer the risks of relapse against long-term medication side effects and educate them to detect early symptoms of relapse.
- Slowly reduce the medication dose, over a few months and monitor for symptoms of relapse.
- Consider continuation treatment for several years after a second episode of psychosis.



CHAPTER 4: OBSESSIVE COMPULSIVE DISORDER

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CHAPTER 4: OBSESSIVE COMPULSIVE DISORDER

GENERAL CONSIDERATIONS

- Offer psychoeducation to the person and family/carer (where applicable), relaxation techniques and breathing exercises, addressing psychosocial stressors (by discussing methods such as problem solving techniques).
- Refer to psychotherapy as needed such as cognitive behavioural therapy.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

INDICATION FOR PHARMACOLOGICAL TREATMENT

- Severe Obsessive Compulsive Disorder (OCD).

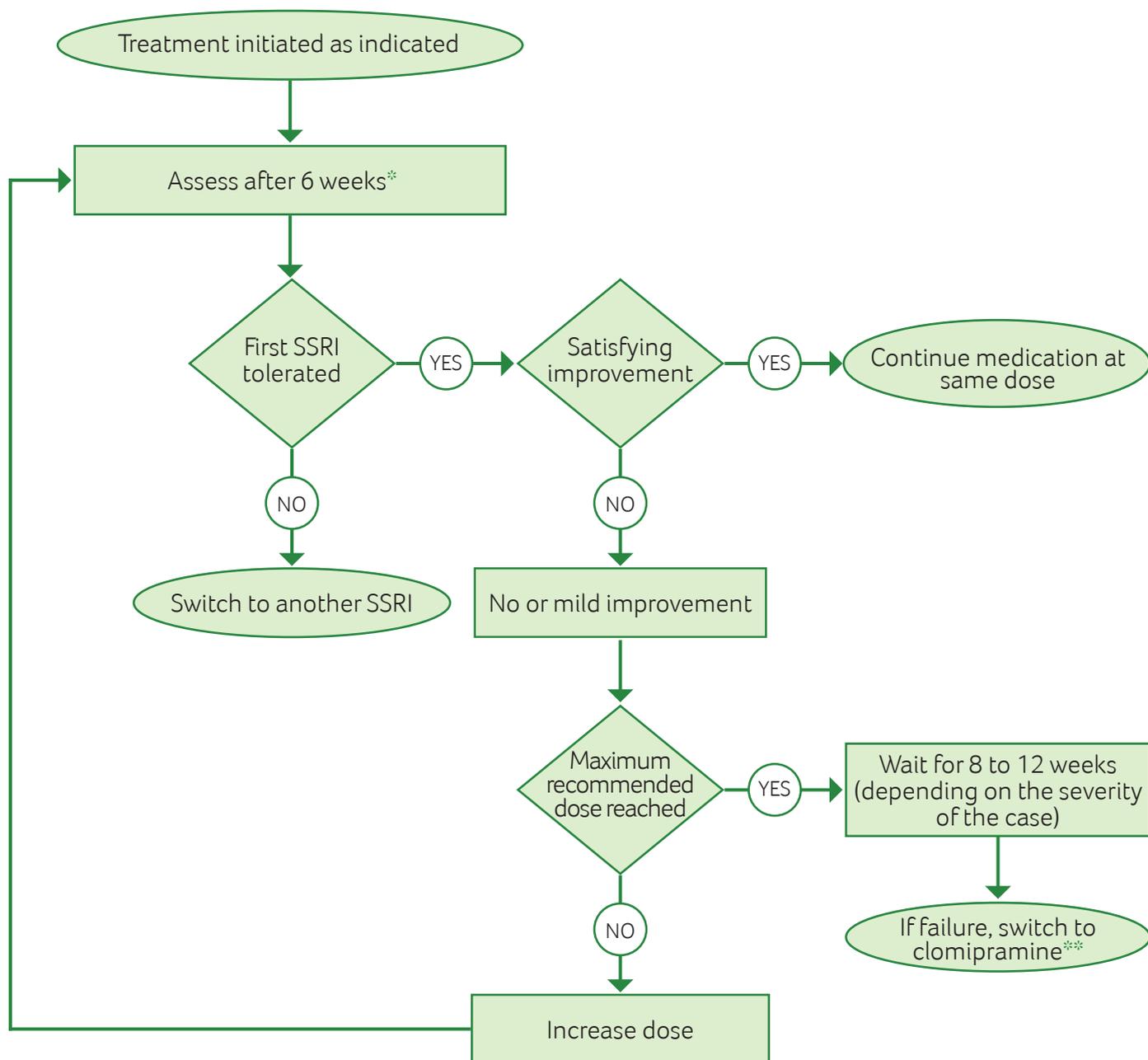
CHOICE OF FIRST LINE MEDICATION

- Severe Obsessive Compulsive Disorder (OCD) is best treated directly with a combination of medication and cognitive behavioural therapy.
- SSRIs are the treatment of choice in OCD as they are thought to be of same efficacy and are better tolerated than TCAs. Choice between fluoxetine and sertraline should be based on the person's preferences, side effect profile, comorbidities and possible interactions with other medications.
- Therapeutic effect can be delayed in OCD by comparison to depression, and might need higher doses of SSRIs.
- Benzodiazepines can be used at the beginning of treatment for no more than 2-4 weeks, in case of excessive anxiety, insomnia or agitation. Avoid long term use because of their addictive potential.
- For medications, *see table 1* under depression chapter (*chapter 1*).

MONITORING TESTS

No specific tests are routinely needed before starting pharmacological treatment or for monitoring purposes, unless clinically indicated such as sodium levels if symptoms of hyponatremia (*see box 1*), ECG if TCAs used in a person at risk of cardiac diseases, weight in an overweight person etc.

TREATMENT FOLLOW-UP



* Unless severe side effects require a psychiatric consultation before that.

** Follow same algorithm for clomipramine: first increase the dose to the average therapeutic dose and evaluate after 6 weeks, and if response is not satisfying, and medication is well tolerated, increase to the maximum dose and wait for 8 to 12 weeks.

TREATMENT OF RESISTANT CASES

If failure of clomipramine trial:

- Combine clomipramine with an SSRI (caution with fluoxetine as it increases blood levels of clomipramine).
- Or, add an antipsychotic (risperidone) to either an SSRI or clomipramine.

Beware of higher risk of side effects with combination therapy especially cardiac adverse effects and serotonin syndrome.

SPECIAL POPULATIONS

- **Adolescents (12 to 18 years old):**
 - » If OCD is mild, try at least 3 months of cognitive behavioural therapy before trying medications.
 - » If OCD is moderate to severe, decision should be made based on access to cognitive behavioural therapy and parent/adolescent preference, knowing that either cognitive behavioural therapy or medications alone are effective, and combination is best.
 - » Fluoxetine and sertraline are the drugs of choice, avoid TCAs and benzodiazepines.
 - » If failure of a trial of SSRI at the maximum dose, for an adequate duration of treatment, always switch to another SSRI, before considering clomipramine.
 - » Provide psychoeducation to the family/carer and monitor closely for risk of treatment-induced suicidal thoughts and acts.
- **Pregnant and breastfeeding women:** same considerations as in treatment of depression. Avoid benzodiazepines, especially before delivery as it induces floppy baby syndrome.
- **Older persons (> 65 years old):** avoid benzodiazepines due to increased risk of falls, confusion and paradoxical reactions. Beware of drug-drug interactions and comorbidities.

DURATION OF TREATMENT

- After remission of symptoms, treatment should be continued for at least 12 months, preferably at the same acute effective dose.
- Discontinuation is done slowly, over several weeks.
- Recurrence of symptoms might imply treatment continuation for many years.



CHAPTER 5: ANXIETY DISORDERS

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CHAPTER 5: ANXIETY DISORDERS

GENERAL CONSIDERATIONS

- Rule out medical conditions (in particular cardiovascular diseases, hyperthyroidism).
- Consider psychosocial interventions as first line treatment, before medication use.
- Offer psychoeducation for the person and family/carer (where applicable), behavioural activation, relaxation techniques and breathing exercises, addressing psychosocial stressors (by discussing methods such as problem solving techniques).
- Refer to psychotherapy as needed such as cognitive and behavioural therapy and Eye Movement Desensitization and Reprocessing (EMDR) for post-traumatic stress disorder.
- Promote full engagement of persons in their care and recovery plan.
- Do not prescribe vitamin and mineral supplements unless medically indicated.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

INDICATION FOR PHARMACOLOGICAL TREATMENT

- Panic disorder.
- Social phobia.
- Generalized anxiety disorder.
- Post-traumatic stress disorder.

CHOICE OF FIRST LINE MEDICATION

- SSRIs are the treatment of choice in anxiety disorders, and not benzodiazepines.
- All SSRIs are thought to be of the same efficacy in anxiety disorders. The choice between fluoxetine and sertraline should be based on the person's preferences, side effect profile, comorbidities and possible interactions with other medications.
- Therapeutic effect can be delayed in anxiety disorders compared to depression, and might need higher doses of SSRIs.
- Benzodiazepines can be used at the beginning of treatment for a period of 2 weeks usually, in case of excessive anxiety, insomnia or agitation. Avoid long term use because of their addictive potential and because they are not an effective treatment for anxiety disorders. *See box 15* for benzodiazepine withdrawal.
- Propranolol can sometimes be helpful as adjunct treatment to decrease somatic anxiety symptoms (hypervigilance, tachycardia, diaphoresis, akathisia, etc.) and it can be used solely on a PRN basis to control performance anxiety.
- Hydroxyzine and promethazine PRN can be used as an alternative to benzodiazepines to relieve acute anxiety symptoms, akathisia, and insomnia.
- *Table 6* summarizes the dosing, side effects and cautions of medications used for anxiety disorders.

Table 6: Medications for anxiety disorders

		Dosing	Side effects	! Main cautions
SSRI	Sertraline (tablets 50 mg)	<p>Start: 25 mg daily.</p> <p>Minimum effective dose: 50 mg.</p> <p>Increase: by 25-50 mg per week (maximum dose: 200 mg).</p> <p>Given once or divided each 12 hours if side effects.</p>	<p>Common: gastrointestinal symptoms, sweating, agitation, anxiety, headache, sedation, insomnia, sexual dysfunction, increased appetite. Most side effects subside after a few days.</p> <p>Serious: hyponatremia (<i>see box 1</i>), rare bleeding risk (in those who use aspirin or other non steroidal anti-inflammatory drugs).</p>	<p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • Inhibits CYP2D6. • Increases blood levels of some antipsychotics and TCAs. • Avoid combination with warfarin and NSAID like aspirin (may rarely increase bleeding risk).
	Fluoxetine (tablets 20 mg)	<p>Start: 20 mg in the morning.</p> <p>Minimum effective dose: 20 mg.</p> <p>Increase: by 20 mg per month (maximum dose: 80 mg).</p>	<p>As for sertraline, but insomnia and agitation* possibly more common and less likely to increase appetite.</p> <p><i>* if insomnia and/or agitation present, consider prescribing a benzodiazepine (see box 2), preferably diazepam, for a maximum of 2 weeks.</i></p>	<p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • Inhibits CYP2D6, CYP3A4. • Increases blood levels of some antipsychotics, some benzodiazepines, carbamazepine, cyclosporine, phenytoin, and TCAs. • Reduces the effect of tamoxifen, codeine, and tramadol. • Avoid combination with warfarin and NSAID like aspirin (may rarely increase bleeding risk).
Benzodiazepines	Diazepam (tablets 5 mg)	<p>Start: 2.5 mg.</p> <p>Maximum dose: 20 mg per day (divided each 6 to 12 hours).</p> <p>Can be given PRN. Use minimal effective dose, for the minimal duration possible, not to exceed 4 weeks.</p> <p>Probably less dependency potential than other benzodiazepines.</p>	<p>Common: drowsiness, sedation, vertigo, headache, muscle weakness.</p> <p>Serious: confusion, depression, dysarthria, tremor, visual disturbances, urinary retention or incontinence, gastrointestinal disturbances, amnesia, jaundice, blood disorders, hypersensitivity, respiratory depression, life threatening hypotension, paradoxical reaction (excitation, disinhibition, aggression).</p> <p>Prolonged use can lead to dependence.</p>	<p>Avoid driving.</p> <p>Do not use in persons who are sedated and avoid combining with other sedatives or alcohol.</p> <p>Duration of effect may be prolonged in severe liver disease.</p> <p>Risk of addiction with long term use.</p> <p>Supervise dosing and supply with small amounts at a time to minimize the risk of abuse and diversion (i.e. selling the medication to somebody else).</p> <p>Relatively safe in overdose, unless combined with other sedatives/ alcohol: flumazenil is the antidote to benzodiazepines intoxication (<i>see box 16</i>).</p> <p>Long term use linked to memory problems and risk of falls in older persons.</p>

Table 6: Medications for anxiety disorders (continued)

		Dosing	Side effects	! Main cautions
Benzodiazepines	Clonazepam (tablets 2 mg)	<p>Start: 0.5 mg.</p> <p>Maximum dose: 4 mg per day (divided each 8 to 12 hours).</p> <p>Can be given PRN. Use minimal effective dose, for the minimal duration possible, not to exceed 4 weeks.</p>	Same as diazepam.	Same as diazepam.
Beta-blocker	Propranolol (tablets 20 mg, 40 mg)	<p>Start: 20 mg PRN (for performance anxiety) or 10 mg each 8 hours (for somatic symptoms of anxiety, akathisia or tremors).</p> <p>Maximum dose: 40 mg PRN or 40 mg each 8 hours.</p>	<p>Common: bradycardia, hypotension, fatigue, gastro-intestinal disturbances, paresthesia.</p> <p>Serious: depression.</p>	<p>Contraindications: asthma, Chronic Obstructive Pulmonary Disease (COPD), severe bradycardia, heart block or heart failure.</p> <p>May exacerbate ischemic heart disease and angina after abrupt discontinuation: gradually reduce dose over 1-2 weeks.</p>

Box 15: Benzodiazepines withdrawal

Benzodiazepines are known to be addictive and dependence can develop after 4-6 weeks of continuous use.

Withdrawal symptoms: anxiety, insomnia, tremors, nausea/vomiting, increased heart rate and blood pressure, seizures, agitation, confusion, hallucinations. **Can be life-threatening.** !

Tapering should be done gradually over 8-12 weeks.

Recommended tapering schedule for high doses:

- First switch to an equivalent dose of diazepam (see table 7).
- Taper by no more than 5 mg diazepam equivalent/week.
- Adjust rate of taper according to symptoms.
- Slow the pace of the taper once dose is below 20 mg of diazepam equivalent (e.g., 1-2 mg/week).
- Dispense daily, twice weekly, or weekly depending on dose and person reliability.
- Note that slow tapering should ideally be associated with behavioural desensitization, particularly with persons having severe difficulties with discontinuation.

Box 16: Benzodiazepines intoxication

Symptoms: slurred speech, unsteady gait, nystagmus, impaired attention and/or memory, respiratory depression, stupor or **coma**. 

Treatment in hospital setting:

- Flumazenil 0.2 mg IV over 30 seconds, if no response after 1 minute, give 0.3 mg over 30 seconds, if no response after 1 minute, give 0.5 mg over 30 sec, and continue this way until a maximum cumulative dose of 3 mg/hour.

Flumazenil has a short half-life, so in case of re-sedation: repeat dose at 20-minute intervals, not to exceed 0.5 mg/min and no more than 3 mg/hour.

Table 7: Benzodiazepine equivalency

Diazepam	5-10 mg
Clonazepam	0.25-0.5 mg
Alprazolam	0.5-1 mg
Lorazepam	1-2 mg
Bromazepam	3-6 mg

MONITORING TESTS

No specific tests are routinely needed before starting pharmacological treatment or for monitoring purposes, unless clinically indicated such as sodium levels if symptoms of hyponatremia (*see box 1*), ECG if TCAs used in a person at risk of cardiac diseases, weight in an overweight person etc.

TREATMENT FOLLOW-UP

- Evaluation every 6 weeks: if no satisfying response, increase the dose until the maximum tolerated dose is reached.
- Wait 12 weeks at maximum dose: if no satisfying response, switch to a second SSRI.

TREATMENT OF RESISTANT CASES

- No specific recommendations are provided and the clinician should look into the latest evidence for every disorder.
- Clomipramine may be considered in panic disorder and post-traumatic stress disorder, after failure of two trials of SSRIs at maximum dose for 8 to 12 weeks.

SPECIAL POPULATIONS

- **Adolescents (12 to 18 years old):**
 - » If anxiety symptoms are mild, try at least 3 months of cognitive behavioural therapy before trying medications.
 - » If anxiety symptoms are moderate to severe, decision should be made based on availability of cognitive behavioural therapy and parent/adolescent preference, knowing that either cognitive behavioural therapy or medications alone are effective, and combination is best.
 - » Fluoxetine and sertraline are the drugs of choice, avoid TCAs, avoid benzodiazepines.
 - » If failure of a trial of SSRI at the maximum dose, for an adequate duration of treatment, always switch to another SSRI, before considering clomipramine.
 - » Provide psychoeducation to the family/carer and monitor closely for risk of treatment-induced suicidal thoughts and acts.
- **Pregnant and breastfeeding women:** same considerations as in treatment of depression. Avoid benzodiazepines, especially before delivery as it induces floppy baby syndrome.
- **Older persons (> 65 years old):** avoid benzodiazepines due to increased risk of falls, confusion and paradoxical reactions. Beware of drug-drug interactions and comorbidities.

DURATION OF TREATMENT

- After remission of symptoms, continue treatment for at least 12 months, preferably at the same acute effective dose.
- Discontinuation is done slowly, over several weeks or months, as persons with anxiety are very sensitive to discontinuation symptoms.
- Recurrence of symptoms might imply treatment continuation for many years.



CHAPTER 6: EPILEPSY

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CHAPTER 6: EPILEPSY

GENERAL CONSIDERATIONS

- Rule out:
 - » Reversible causes (metabolic disorder, medication side effects or withdrawal, etc.).
 - » Acute medical conditions (e.g. trauma, neuroinfection, cerebrovascular accidents, etc.).
 - » Other mental disorders (e.g. non-epileptic pseudoseizures).
- Offer psychoeducation to the person and family/carer (where applicable), social network reactivation. Promote functioning in daily activities and community life and assess family/carer who may present a mental condition associated with providing care.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

INDICATION FOR PHARMACOLOGICAL TREATMENT

Treatment with antiepileptic drug is generally recommended after a second epileptic seizure. However, treatment might be given in some cases after a first episode, if the risk of a second seizure is high (e.g. abnormal EEG, nocturnal seizures, abnormal brain imaging).

An EEG confirming the diagnosis is desirable but not mandatory. A normal EEG does not rule out a diagnosis of epilepsy.

Antiepileptic drug therapy in children and young persons should only be initiated by a neurologist.

CHOICE OF FIRST LINE MEDICATION

- When possible, choose which antiepileptic drug to offer on the basis of the presenting epilepsy syndrome or seizure type.
- Start with only one medication at lowest starting dose.
- Increase dose slowly until convulsions are controlled.
- Choose the antiepileptic drug according to the seizure type, the neurological and psychiatric comorbidities, the sex, the age (childbearing age, older person, pediatric), the metabolic profile (hepatic or renal abnormalities), associated medications, and the cost.
- The two subtypes of antiepileptic drugs are:
 - » Broad spectrum (all seizure types: partial onset and generalized form onset seizures): lamotrigine, levetiracetam and sodium valproate.
 - Sodium valproate can be used for absence seizures (a type of generalized seizures).
 - » Narrow spectrum (simple partial, complex partial and secondary generalized seizures): carbamazepine, phenytoin.
- *Table 8* summarizes the dosing, side effects and cautions of medications used for epilepsy.

Table 8: Medications for epilepsy

	Dosing	Side effects	! Main cautions
Sodium valproate (tablets 500 mg immediate release or controlled release, syrup 200 mg/5 ml)	<p>Adults: Start: 500 mg daily in 2 divided doses.</p> <p>Increase: by 500 mg daily each week (maximum dose: 3000 mg daily).</p> <p>Children: Start: 15-20 mg/kg daily in 2-3 divided doses.</p> <p>Increase: each week by 15 mg/kg daily (maximum dose: 15-40 mg/kg daily).</p>	<p>Common: sedation, headache, tremor, ataxia, nausea, vomiting, diarrhea, weight gain, transient hair loss, benign increase in LFT.</p> <p>Serious: liver failure, thrombocytopenia, leucopenia, drowsiness/confusion, hemorrhagic pancreatitis, hyperammonemia, peripheral edema, hyperandrogenism and polycystic ovaries in women.</p>	<p>Caution in persons with underlying or suspected hepatic disease.</p> <p>Not recommended in women of child-bearing age: risk of teratogenicity and impaired cognitive function in children exposed in utero.</p> <p>Drug-drug interactions: sodium valproate levels decreased by carbamazepine, increased by aspirin.</p> <p>Sodium valproate increases dose of lamotrigine.</p>
Carbamazepine (tablets 200 mg and 400 mg, syrup 100 mg/5 ml)	<p>Adults: Start: 200 mg daily in 2 divided doses.</p> <p>Increase: by 200 mg each week (maximum dose: 1400 mg daily).</p> <p>Children: Start: 5 mg/kg daily in 2-3 divided doses.</p> <p>Increase: by 5 mg/kg daily each week (maximum dose: 40 mg/kg daily or 1400 mg daily).</p> <p>Dose may need to be adjusted after 2 weeks due to induction of its own metabolism.</p>	<p>Common: sedation, confusion, dizziness, ataxia, double vision, nausea, diarrhea, benign leucopenia, benign increase in LFT.</p> <p>Serious: hepatotoxicity, cardiac conduction delay, low sodium levels, severe rash.</p>	<p>Contraindicated in persons with history of blood disorders, kidney, liver, or cardiac disease.</p> <p>Caution when prescribed for generalized seizures: risk of aggravation of absences and myoclonic seizures.</p> <p>Risk of teratogenicity.</p> <p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • May reduce the effects of hormonal birth control, immunosuppressants, antiepileptics, antipsychotics, methadone and some antiretrovirals. • Levels can be increased by certain antifungals and antibiotics.
Lamotrigine¹⁰ (tablets 100 mg)	<p>Start: 25 mg daily for 2 weeks, then give in divided doses each 12 hours: 50 mg/day for 2-4 weeks, then increase by 50 mg/day every 2 weeks (according to clinical response) to a maximum of 350 mg/day.</p> <p>If given with sodium valproate: start 25 mg every other day for 2 weeks, then follow the same titration regimen.</p> <p>Rapid titration increases risk of Stevens Johnson syndrome.</p>	<p>Common: benign rash, sedation, blurred or double vision, dizziness, ataxia, headache, tremor, insomnia, fatigue, nausea, abdominal pain, constipation, rhinitis.</p> <p>Serious: Stevens Johnson syndrome (rash and multi-organ failure), rare blood dyscrasias.</p>	<p>Caution in persons with renal, hepatic or cardiac diseases.</p> <p>Drug-drug interactions:</p> <ul style="list-style-type: none"> • Sodium valproate increases blood levels of lamotrigine, requiring lower doses of lamotrigine. • Carbamazepine may increase the clearance of lamotrigine and lower its blood levels.

¹⁰ This medication is recommended for use only under supervision of a specialist.

Table 8: Medications for epilepsy (continued)

	Dosing	Side effects	! Main cautions
Phenytoin¹¹ (tablets 100 mg)	<p>Adults: Start: 100 mg daily in 2 divided doses.</p> <p>Increase: by 50 mg daily every 3-4 weeks (maximum dose: 400 mg daily).</p> <p>Children: Start: 3-4 mg/kg daily in 2 divided doses.</p> <p>Increase: by 5 mg/kg daily every 3-4 weeks (maximum dose: 300 mg per day).</p>	<p>Common: sedation, confusion, dizziness, tremor, motor twitching, ataxia, double vision, nystagmus, slurred speech, nausea, vomiting, constipation.</p> <p>Serious: hematologic abnormalities, hepatitis, polyneuropathy, gum hypertrophy, acne, lymphadenopathy, increase in suicidal ideation.</p>	<p>Lower doses for persons with kidney or liver disease.</p>
Levetiracetam¹² (tablets 500 mg, syrup 100 mg/ml)	<p>Start: with 250 mg each 12 hours.</p> <p>Increase: by 500 mg/day every 2 weeks to recommended dose of 500 mg each 12 hours.</p> <p>Maximum dose: 1500 mg each 12 hours.</p>	<p>Common: fatigue, headache, drowsiness.</p> <p>Serious: increased blood pressure, infection, depression, abnormal hepatic function tests, bone marrow suppression.</p>	<p>Lower doses for persons with kidney diseases.</p> <p>Caution: may trigger depression, suicidal thoughts and behavioural disturbances.</p>

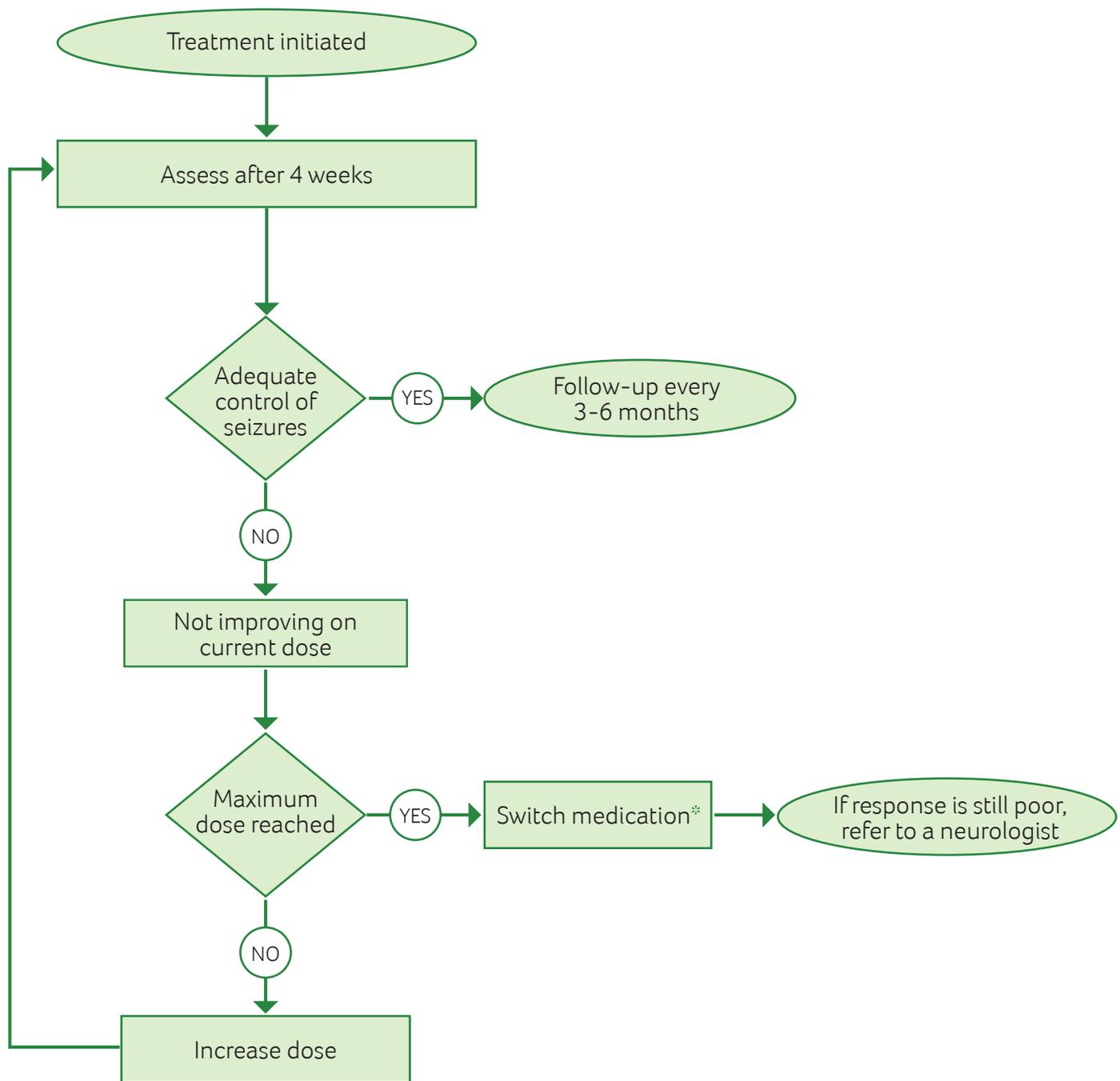
MONITORING TESTS

- EEG is desirable but not mandatory. A normal EEG does not rule out a diagnosis of epilepsy.
- Refer to bipolar affective disorder chapter (*chapter 2*) for monitoring tests required for lamotrigine, sodium valproate and carbamazepine. Phenytoin and levetiracetam follow the same monitoring tests as carbamazepine.
- Medication blood levels for sodium valproate are not required in epilepsy compared to bipolar affective disorder unless there is suspicion of non adherence, toxicity, or in case of persistence of seizures.

¹¹ Phenytoin has a safety factor and therapeutic index that are extremely low, hence the importance of adhering to the prescribed dose.

¹² This medication is recommended for use only under supervision of a specialist.

TREATMENT FOLLOW-UP



* The new medication should be at an optimum dose before slowly discontinuing the first.

P.S. Trials of combination therapy and adjunctive treatment with benzodiazepines should only be initiated by a neurologist.

SPECIAL POPULATIONS

- **Women of childbearing age:**
 - » Avoid sodium valproate.
- **Pregnant women:**
 - » Avoid sodium valproate.
 - » Avoid polytherapy: **increases the risk of teratogenicity. !**
 - » Advise folate (5 mg/day) to prevent neural tube defects in women taking sodium valproate (not fully protective; best to avoid prescribing sodium valproate).
 - » At delivery, give 1 mg vitamin K IM to the newborn to prevent hemorrhagic disease.
- **Breastfeeding women:** breastfeeding should be encouraged even if the mother is on antiepileptic drug. Carbamazepine preferred to other medication. Avoid benzodiazepines.
- **Adolescents (12 to 18 years old):** antiepileptic drug is best initiated by a neurologist.
- **! Sodium valproate should not be given to girls of reproductive age.**
- **Older persons (> 65 years old):** use lower doses.

DURATION OF TREATMENT

Generally, if the person has been convulsion free for 2 years:

- Discuss the risk of seizure occurrence with the person, family or carer (if epilepsy is due to head injury, stroke or neuroinfection, there is a higher risk of seizure recurrence if the person is taken off medication), and risks and benefits of discontinuing medications.
- If in agreement, gradually take the person off medication by reducing the doses over 2 months and monitoring closely for seizure recurrence.
- EEG is desirable but not mandatory: if abnormal, do not stop medication.



CHAPTER 7: ALCOHOL WITHDRAWAL MANAGEMENT

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CHAPTER 7: ALCOHOL WITHDRAWAL MANAGEMENT

GENERAL CONSIDERATIONS

- Rule out associated medical conditions (heart diseases, liver diseases, neurological problems). If not already done, consider the following tests in every chronic alcohol user (*see box 17* for symptoms of alcohol withdrawal):
 - » Liver function tests (elevated SGPT, SGOT and gammaGT indicate liver disease).
 - » FBC (look for macrocytic anemia and low platelets).
- Offer psychoeducation to the person and family/carer (where applicable), motivational interviews, addressing psychosocial stressors (by discussing methods such as problem solving techniques) and strengthening social support.
- Refer to psychotherapy as needed such as cognitive and behavioural therapy.
- Promote full engagement of persons in their care and recovery plan.

Box 17: Symptoms of alcohol withdrawal

- Tremors, nausea/vomiting, increased heart rate and blood pressure, agitation, confusion, seizures, hallucinations. **Can be life-threatening. !**
- Delirium tremens is the most severe complication of alcohol withdrawal: confusion, tremors/convulsions, hallucinations, autonomic hyperactivity that can progress to cardiovascular collapse. **High mortality rate. !**

OUTPATIENT ASSISTED ALCOHOL DETOXIFICATION

- Hydration: encourage oral fluid intake.
- Diazepam:
 - » Start diazepam when withdrawal symptoms of alcohol begin, not if the person is intoxicated with alcohol or still sedated.
 - » Initial dose of up to 40 mg daily (10 mg each 6 hours or 20 mg each 12 hours) for 3-7 days. Gradually decrease the dose and/or frequency as soon as symptoms improve. Benzodiazepines should not be prescribed for longer periods due to their addictive potential.
 - » If more than 40 mg daily are needed to relieve symptoms, admit the person to an inpatient setting where daily doses of diazepam can reach 120 mg.
 - » In persons with signs of liver disease or the older persons, use an initial single low dose of 5-10 mg, as benzodiazepines may have a longer duration of action in these populations.

- Thiamine (Vitamin B1):
 - » Chronic heavy users of alcohol are at risk for Wernicke's encephalopathy, a thiamine deficiency syndrome characterized by confusion, nystagmus, ophthalmoplegia (trouble with eye movements), and ataxia.
 - » To prevent this syndrome, all persons with a history of chronic alcohol use undergoing withdrawal should be given 100 mg/day of oral thiamine for 5 days, or even longer where diet is inadequate or alcohol consumption is resumed.
 - » Give thiamine prior to administering glucose to avoid precipitating Wernicke's encephalopathy.
 - » In a person with suspected or confirmed Wernicke's encephalopathy: admit to hospital, treat with IV thiamine and magnesium and observe for possible development of Wernicke-Korsakov Syndrome and cardiovascular beriberi.
- Other:
 - » Manage specific withdrawal symptoms as they emerge: treat nausea with antiemetics, pain with simple analgesics, insomnia with light sedative, depression with antidepressants.
 - » Correct electrolytes deficiency (magnesium, potassium) if present.

TREATMENT FOLLOW-UP

- Monitor the person every other day during the first week of outpatient assisted withdrawal, or even every day for up to 3 weeks if withdrawal is severe.
- Adjust the dose if severe withdrawal symptoms or over-sedation occur.
- Avoid giving large quantities of benzodiazepines to take home to prevent overdose or diversion. Do not dispense more than 2 days' medication supply at any time.
- A family member or carer should preferably oversee the administration of medication between visits.

SPECIAL POPULATIONS

- **Pregnant women:** avoid alcohol completely. Inform women that consuming even small amounts of alcohol early in pregnancy can harm the developing fetus, and that larger amounts of alcohol can result in a syndrome of severe developmental problems (Fetal Alcohol Syndrome). If a pregnant woman wants to undergo assisted alcohol detoxification, it is best done in a hospital setting (*see box 18*).
- **Breastfeeding women:** avoid alcohol completely. Given the benefits of exclusive breastfeeding (particularly in the first 6 months), if mothers continue to drink alcohol they should be advised to limit their alcohol consumption, and to minimize the alcohol content of their breast milk, such as by breastfeeding before drinking alcohol and not breastfeeding again until after blood levels fall to zero (allowing approximately 2 hours for each drink consumed, i.e. 4 hours if two drinks are consumed), or by using expressed breast milk.
- **Adolescents (12 to 18 years old), older persons (> 65 years old) or persons with liver diseases:** benzodiazepine doses may need to be reduced.

Box 18: Inpatient assisted alcohol detoxification

Inpatient detoxification is preferable to outpatient detoxification when there is a high risk of severe withdrawal such as in the following situations:

- Past episodes of severe withdrawal symptoms, including seizures or delirium.
- Comorbid significant medical or psychiatric issues.
- Significant withdrawal features develop within 6 hours of the person's last drink.
- Multiple failed outpatient cessation attempts in the past.
- The person is homeless or without any social support.



CHAPTER 8: OTHER DISORDERS

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A. Dementia

- General considerations
- Pharmacological treatment of associated behavioural and psychological symptoms

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B. Behavioural disorders in children with developmental disorders

- General considerations
- Pharmacological treatment of associated behavioural disorders

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C. Insomnia

- General considerations
 - Pharmacological treatment of insomnia
-

CHAPTER 8: OTHER DISORDERS

Other disorders addressed in this guide are: (A) Dementia; (B) Behavioural disorders in children with developmental disorders; and (C) Insomnia.

A. DEMENTIA

GENERAL CONSIDERATIONS

- Rule out medical conditions that can mimic dementia.
- Follow-up on medical comorbidities that are often present.
- Offer psychoeducation to the family/carer (where applicable), psychosocial interventions for cognitive symptoms, promoting independence, functioning and mobility, social network reactivation. Promote functioning in daily living and community activities and assess family/carer who may present a mental condition associated with providing care.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

PHARMACOLOGICAL TREATMENT OF ASSOCIATED BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS

Particular attention should be granted for behavioural and psychological symptoms associated with dementia and pharmacological treatment might be beneficial in certain cases:

- **Depression:** SSRIs are the drugs of choice at the same doses as in adults. Beware as older persons are more prone to develop bleeding and hyponatremia (*see box 1*) with SSRIs. Therapeutic response may be delayed. TCAs are best avoided due to risk of hypotension, falls, constipation and urinary retention.
- **Psychosis:** use a third to a half of the usual dose of antipsychotics medication. Anticipate an increased risk of drug-drug interactions.
- **⚠ Caution:** antipsychotics carry an increased risk of cerebrovascular events and **death** in older persons with dementia-related psychosis.
- **Agitation, aggression:** psychosocial interventions should always be tried first to manage these symptoms. Where there is clear and imminent risk of harm with severe and distressing symptoms, the short term use of haloperidol or risperidone may be considered (haloperidol 2.5 mg per day or risperidone syrup 0.25-2 mg per day).

B. BEHAVIOURAL DISORDERS IN CHILDREN WITH DEVELOPMENTAL DISORDERS

GENERAL CONSIDERATIONS

Children with developmental disorders (intellectual disability, autism spectrum disorder) often present with challenging behaviours like agitation, irritability, and aggressivity. In most cases, this should not implicate a prescription of medications. It is important to do the following steps:

- Rule out medical conditions (epilepsy, constipation, pain, visual or hearing impairment).
- Look out for other mental conditions like mood disorders or Attention Deficit Hyperactivity Disorder (ADHD).
- Protect the child from any form of maltreatment at home, school, and in the community.
- Offer psychoeducation and psychological interventions based on behavioural techniques to the person and family/carer (where applicable). Assess family/carer who may present a mental condition associated with providing care.
- Refer to psychotherapy as needed such as family focused therapy.
- Promote full engagement of persons in their care and recovery plan.
- Consider the use of measurement tools as supportive tools to follow-up on the improvement in functioning and/or on the decrease in symptoms.

PHARMACOLOGICAL TREATMENT OF ASSOCIATED BEHAVIOURAL DISORDERS

If severe symptoms persist after a comprehensive and intensive psychosocial intervention, especially if they put the child as a danger to self or others, medication can be tried as a last resort and for short periods of time. Discuss the advantages and disadvantages of medication with the family/carer. The best available treatment is then a small dose of antipsychotic, if possible risperidone (0.25-2 mg per day).

Children going through adverse situations tend to have behavioural problems that could be linked to different reasons. Caution against labelling these behavioural problems as mental conditions before thorough assessment of the child, the family and the context. However, some behavioural problems can be linked to mental conditions such as depression, anxiety, adjustment, etc. For behavioural problems that are a manifestation of such disorders, the underlying condition should be addressed as per WHO guidelines. In some cases, the behavioural conditions are linked to an ADHD. Proper pharmacological treatment of ADHD after thorough assessment and diagnosis of the condition can be very useful if psychosocial interventions did not succeed in improving the situation. For children with ADHD, the use of antipsychotics medication to control behavioural problems is not recommended.

C. INSOMNIA

GENERAL CONSIDERATIONS

Insomnia is a common symptom that can present isolated or as part of a disorder like depression. General guidance is provided below:

- Rule out:
 - » Mental comorbidities and treat them appropriately if present.
 - » Medical comorbidities, especially sleep apnea.

In case of isolated insomnia:

- Always make sure proper psychoeducation is provided, focused on teaching and monitoring sleep hygiene techniques (*see box 19*).

Box 19: Sleep hygiene techniques

Sleep hygiene refers to appropriate sleeping habits. Some techniques are:

- Bedtime routine:
 - » Having a fixed schedule and specific bedtime habits such as going to bed when the person is tired and using the bed for sleeping only (and not for watching television, reading, or eating).
 - » Always getting up at the same time in the morning.
- Noise reduction:
 - » Ensuring that the bedroom is quiet, relaxing, dark, and of comfortable temperature.
 - » Removing electronic devices (e.g. televisions, computers, tablets, smartphones, etc.) from the bedroom.
- Avoiding large heavy meals, spicy food, drinking alcohol, coffee, or tea and other stimulants as well as nicotine before bedtime.
- Regular exercise: being more physically active during the day.

PHARMACOLOGICAL TREATMENT OF INSOMNIA

- In case of failure of psychoeducation and if insomnia is severe and incapacitating, hydroxyzine and promethazine can be tried on a PRN basis.
- Benzodiazepines should be considered as a second line treatment for insomnia because of their addictive potential (need for increased doses with time for the same hypnotic effect and emergence of withdrawal symptoms and rebound insomnia when stopped). They are not recommended for periods longer than 2-4 weeks and are better given on a PRN basis.

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APPENDIX A: NATIONAL LIST OF PSYCHOTROPIC AND NEUROLOGICAL MEDICATIONS FOR HUMANITARIAN RESPONSE – V2.0

Latest update of the list is available at: www.moph.gov.lb

Class	Medication (molecular name)	Form and dosage
Antidepressants	Amitriptyline*	Tablet 25 mg
	Fluoxetine*	Tablet 20 mg
	Sertraline*	Tablet 50 mg
	Clomipramine	Tablet 75 mg
Antipsychotics	Chlorpromazine*	Tablet 100 mg
	Haloperidol*	Tablet 5 mg
	Risperidone	Tablet 2 mg
	Risperidone	Syrup 1 mg/ml
	Zuclopenthixol decanoate ¹	Injectable solution 200 mg/ml
Anxiolytics	Clozapine ¹	Tablet 100 mg
	Diazepam ²	Tablet 5 mg
Antiepileptics	Clonazepam ²	Tablet 2 mg
	Phenytoin*	Tablet 100 mg
Antiepileptics / Mood stabilizers	Levetiracetam ¹	Tablet 500 mg
	Levetiracetam ¹	Syrup 100 mg/ml
	Carbamazepine*	Tablet 200 mg
Antiepileptics / Mood stabilizers	Carbamazepine *	Tablet 400 mg
	Carbamazepine	Syrup 100 mg/5 ml
	Sodium valproate*	Tablet 500 mg
	Sodium valproate*	Tablet 500 mg CHRONO
	Sodium valproate*	Syrup 200 mg/5 ml
	Lamotrigine ¹	Tablet 100 mg
Mood stabilizers	Lithium ¹	Tablet 400 mg
Antiparkinson/ Treatment of antipsychotic medications side effects	Carbidopa/ Levodopa*	Tablet 25 mg/250 mg
	Trihexyphenidyl*	Tablet 5 mg
	Biperiden	Tablet 4 mg

* Ministry of Public Health of Lebanon. 2014. Chronic Disease Medications Provided by MOPH in Collaboration with YMCA, available at: <http://www.moph.gov.lb/userfiles/files/HealthCareSystem/PHC/YMCADrugs.pdf>

¹ This medication is recommended for use only under supervision of a specialist.

² Diazepam and clonazepam are strictly controlled by the Lebanese drug law # 673/1998 and their dispensing requires the maintenance of specific registries available at the level of pharmacies, and usually not available at the level of primary healthcare centers.

APPENDIX B: RECOMMENDED MEDICAL TESTS TO MONITOR THE SIDE EFFECTS OF PSYCHOTROPIC AND NEUROLOGICAL MEDICATIONS*

Class	Medication	Medical tests	Frequency	
Antidepressants	Amitriptyline	If clinically indicated such as: <ul style="list-style-type: none"> • Sodium levels if symptoms of hyponatremia. • ECG if TCAs used in a person at risk of cardiac diseases. • Weight in an overweight person etc. 	Before starting or for monitoring purposes.	
	Fluoxetine			
	Sertraline			
	Clomipramine			
Antipsychotics	Chlorpromazine	Weight, pulse and blood pressure	Before starting, and then once monthly during the first 3 months, at 1 year and then annually thereafter.	
	Haloperidol	Blood lipids and fasting glucose (especially when risk factors are present and second generation antipsychotics used).	After 6 months of starting, then at 1 year and yearly thereafter.	
	Risperidone			
	Zuclopenthixol decanoate			
	Clozapine	Full blood count (if these regular checks are not feasible, clozapine should not be prescribed, due to the risk of life-threatening agranulocytosis).	Weekly for 18 weeks, then every 2 weeks until a year, and monthly thereafter.	
			Weight, pulse and blood pressure.	Before starting, and then once monthly during the first 3 months, at 1 year and then annually thereafter.
			Blood lipids and fasting glucose (especially when risk factors are present).	After 6 months of starting, then at 1 year and yearly thereafter.
			ECG if clinically indicated (high blood pressure or personal history of cardiac disease).	Before starting, after 3 months, at 1 year then annually thereafter.
	Anxiolytics	Diazepam	No need for baseline or monitoring tests.	
		Clonazepam		
Antiepileptics	Phenytoin	Weight, urea, electrolytes, SGPT, SGOT, gammaGT, FBC.	Before starting. Repeat annually or if clinically indicated.	
	Levetiracetam			
Antiepileptics / mood stabilizers	Carbamazepine	Weight, urea, electrolytes, SGPT, SGOT, gammaGT, FBC.	Before starting. Repeat annually or if clinically indicated.	
	Sodium valproate	Sodium valproate level (not required in epilepsy compared to bipolar affective disorder unless there is suspicion of non adherence, toxicity, or in case of persistence of seizures).	Until dose stabilization in the first weeks of treatment. No need for continuous monitoring unless evidence of ineffectiveness, non adherence, or toxicity.	
		Weight, SGPT, SGOT, gammaGT, FBC	Before starting, then at 6 months, 1 year and then annually.	
		Pregnancy test	Before starting (where applicable).	
		Blood ammonia level	If signs of hyperammonemia (confusion, lethargy, vomiting, seizures).	
	Lamotrigine	No need for baseline or monitoring tests.		
Mood stabilizers	Lithium (do not start lithium if the tests are not feasible)	Lithium level (before the morning dose and 12 hours after the evening dose)	For every dose change in the first weeks, then every 3 months for first year then every 6 months.	
		Weight, FBC, urea, creatinine, TSH	Before starting, then every 6 months.	
		ECG	Before starting, if clinically indicated.	
		Pregnancy test	Before starting (where applicable).	

*Based on the "National list of psychotropic and neurological medications for humanitarian response".

APPENDIX C: PSYCHOSOCIAL INTERVENTIONS

A. Psychoeducation

- Provide information about the mental, neurological, and substance use disorder to the person, including:
 - » What the disorder is and its expected course and outcome.
 - » Available treatments for the disorder and their expected benefits.
 - » Duration of treatment.
 - » Importance of adhering to treatment, including what the person can do (e.g. taking medication practicing relevant psychological interventions such as relaxation exercises) and what family/carer can do to help the person adhere to treatment.
 - » Potential side effects (short and long term) of any prescribed medication that the person (and family/carer) need to monitor.
 - » Potential involvement of social workers, community health workers or other trusted members in the community.

B. Reduce stress and strengthen social support

- Address current psychosocial stressors:
 - » Identify and discuss relevant psychosocial issues that place stress on the person and/or impact their life including, but not limited to, family and relationship problems, employment/occupation/livelihood issues, housing, finances, access to basic security and services, stigma, discrimination, etc.
 - » Assist the person to manage stress by discussing methods such as problem solving techniques.
 - » Assess and manage any situation of maltreatment, abuse (e.g. domestic violence) and neglect (e.g. of children or the older persons).
 - » Discuss with the person possible referrals to a trusted protection agency or informal protection network. Contact legal and community resources, as appropriate.
 - » Identify supportive family members and involve them as much as possible and appropriate.
 - » Strengthen social support and try to reactivate the person's social network.
 - » Identify prior social activities that, if reinitiated, would have the potential for providing direct or indirect psychosocial support (e.g. family gatherings, visiting neighbours, community activities, religious activities, etc.).
 - » Teach stress management such as relaxation techniques.

C. Promote functioning in daily activities

- Provide the person support to continue regular social, educational, and occupational activities as much as possible.
- Facilitate inclusion in economic activities.
- Offer life skills training and/or social skills training if needed.

D. Psychological treatment

Psychological treatments are interventions that typically require substantial dedicated time and tend to be provided by specialists trained in providing them. Nonetheless, they can be effectively delivered by trained and supervised non-specialized workers and through guided self-help (e.g. with use of e-mental health programmes or self-help books).

APPENDIX D: GLOSSARY OF TERMS

Behavioural activation

Psychological treatment that focuses on improving mood by engaging again in activities that are task-oriented and used to be enjoyable, in spite of current low mood. It may be used as a stand-alone treatment, and it is also a component of cognitive behavioural therapy.

Cognitive behavioural therapy

Psychological treatment that combines cognitive components (aimed at thinking differently, for example through identifying and challenging unrealistic negative thoughts) and behavioural components (aimed at doing things differently, for example by helping the person to do more rewarding activities).

Cognitive remediation therapy

A type of rehabilitative treatment that offers exercises aiming at improving attention, memory, language and/or executive functions. It aims at improving functioning in everyday life.

Eye Movement Desensitization and Reprocessing (EMDR)

A psychotherapy treatment designed to alleviate the distress associated with traumatic memories. It facilitates the accessing and processing of traumatic memories and other adverse life experience to bring these to an adaptive resolution.

Family focused therapy

The therapy includes all family members and consists of several stages, beginning with psychoeducation about the symptoms and etiology, and importance of adherence to treatment. Families are talked to respond early to emergent symptoms, and provided with training about the best coping responses. Families also learn communication and problem solving skills to reduce conflicts and resolve family problems.

Interpersonal Psychotherapy

Psychological treatment that focuses on the link between depressive symptoms and interpersonal problems, especially those involving grief, disputes, life changes and social isolation.

Motivational interview

It is a technique that helps persons resolve the ambivalence that prevents them from realizing personal goals.

Problem solving techniques

Defining specific problems, generating and evaluating solutions, and implementing solutions to problems in the individual's or family's life

Relaxation training

Involves training in techniques such as breathing exercises to elicit the relaxation response.

