

BEHAVIORAL HEALTH GUIDELINE

BIPOLAR AND SCHIZOPHRENIA GUIDELINE

Guideline History

Date Approved	7/20
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These Guidelines are promulgated by Sentara Healthcare (SHC) as recommendations for the clinical Management of specific conditions. Clinical data in a particular case may necessitate or permit deviation from these Guidelines. The SHC Guidelines are institutionally endorsed recommendations and are not intended as a substitute for clinical judgment.

MOOD STABILIZERS

Medication	Indication	Dosage	Side Effects
Divalproex (Depakote)			
	Bipolar I disorder- Manic	DR Initial 750 mg orally daily in divided doses; increase as quickly as possible to clinical effect; usual trough plasma level 50 to 125 mcg/ml (347 to 693 mcmol/L); MAX 60 mg/kg/day ER Initial 25 mg/kg/day orally once daily increase as quicky as possible to clinical usual trough plasma level 85 to 125 mcg (589 to 867 mcmol/L); MAX 60 mg/kg/day	Pancreatitis, Thrombocytopenia (dose
Lamotrigine (Lamictal)			
	Bipolar I disorder, monotherapy Bipolar I disorder, in combination with valproic acid	Initial 25mg/day orally for 2 weeks Titration 50mg/day for 2 weeks 100mg/day for 1 week Maintenance 200mg/day Initial 25mg/day orally every other day for 2 weeks Titration 25mg/day for 2 weeks 50mg/day for 1 week Maintenance 100mg/day	Common: Rash, Abdominal pain, Diarrhea, Nausea/Vomiting, Dizziness, Headache, Somnolence, Blurred vision Serious: Stevens-Johnson syndrome/Toxic Epidermal Necrolysis, Liver failure, Aseptic meningitis, Neuroleptic malignant syndrome
	Bipolar I disorder, in combination with carbamazepine or other enzyme inducing antiepileptic	Initial 50mg/day orally for 2 weeks Titration 100mg/day for 2 weeks in divided doses 200mg/day for 1 week in divided doses 300mg/day for 1 week in divided doses Maintenance	

Carbamazepine El (Equetro)		May increase up to the usual maintenance dose of 400mg/day in divided doses Initial	Common
	Bipolar I disorder, acute manic or mixed episodes	Titration May increase in increments of 200mg/day Max dose Doses in excess of 1600mg/day have not been studied	Common: Dizziness, Drowsiness, Ataxia, Nausea, Vomiting, Pruritus, Skin Rash, Constipation, Xerostomia Serious: Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, Aplastic Anemia, Agranulocytosis
Lithium			
	Bipolar I disorder, a cute treatment of manic or mixed episodes monotherapy	Immediate Release Initial 300mg orally 3 times daily Titration Add 300mg every 3 days to acute goal Extended Release 1800mg/day orally in 2-3 divided doses Target Serum Level 0.8-1.2meq/L	Common: Hyperparathyroidism, Weight gain, Dizziness/Fatigue, Leukocytosis, Increased thirst Serious: Bradyarrythmia, Hypothyroidism, Erythema multiforme, Blurred vision, Nephrogenic diabetes insipidus
	Bipolar I disorder, maintenance monotherapy	Immediate-release tablet and capsule Initial 300mg or ally 3 times daily; titrate by 300 mg every 3 days to maintenance goal, desired serum lithium level 0.8 to 1 mEq/L usually 300 to 600 mg 2 to 3 times daily. Extended-release tablet 900 to 1200 mg/day or ally in 2 to 3 divided doses; desired serum lithium level 0.6 to 1.2 mEq/L	

FIRST GENERATION ANTIPSYCHOTICS

Medication	Indication	Dosage	Side Effects
Chlorpromazine (Thorazine)			
	Bipolar Disorder, Manic Episode (hospitalized)	Oral preparation: Initial 25 mg orally 3 times a day Titration Increase gradually until effective dose is reached (usually 400mg/day) Injectable preparation: Initial 25 mg IM for control of severe symptoms May give 25-50mg in 1 hour as needed Titration Increase subsequent IM doses gradually over several days as needed 400 mg IM every 4-6 hours until patient is controlled	Common: Orthostatic hypotension, Tachycardia, Ineffective themoregulation (heat stroke or hypothermia), Constipation, Xerostomia, Akathisia, Dizziness, Parkinsonism, Somnolence, Tardive dyskinesia Serious QT prolongation, Agranulocytosis, Aplastic Anemia, Anaphylaxis, Dystonia, Neuroleptic Malignant Syndrome
	Schizophrenia (hospitalized)	Same as a bove	
	Bipolar Disorder, Maintenance	Initial 10mg orally 3-4 times daily OR 25mg orally 2-3 times daily Titration Increase gradually until symptom control Continue optimal dosage for 2 weeks Gradually reduce to lowest effective dose Typical dose 200mg-800mg/day is typical target range	
	Schizophrenia, Maintenance	Same as a bove	

Thioridazine (Mellaril)			
	Schizophrenia, refractory	Initial 50-100mg orally 3 times a day Titration increase gradually to a max of 800mg/day in 2-4 divided doses Maintenance reduce dose to determine minimum maintenance dose (range 200- 800mg/day) Max dose 800mg/day	Common: Orthostatic hypotension, Diminished sweating, Photosensitivity, Constipation, Xerostomia, Extrapyramidal disease, Somnolence, Blurred vision, Epithelial Keratopathy, Urinary Retention Serious: QT prolongation, Paralytic Ileus, Myelosuppression, Drug induced lupus, Ineffective thermoregulation
Loxapine (Adasuve)			
	Bipolar I Disorder – psychomotor a gitation	Initial/Maintenance 10mg via oral inhalation as single dose within a 24 hour period	Common: Altered taste sense, Sedation, Pharyngitis
	Schizophrenia – psychomotor a gitation	Initial/Maintenance 10mg via oral inhalation as single dose within a 24 hour period	Serious: Bronchospasm, Cerebrovascular Accident/Transient Ischemic Attack, Death
Perphenazine (Trilafon)			
	Schizophrenia (hospitalized)	Initial/ Maintenance 8-16mg orally 2-4 times daily Max dose 64mg/day	Common Orthostatic hypotension, Diminished sweating, Constipation, Xerostomia, Extra pyramidal disease, Somnolence, Tardive Dyskinesia, Blurred Vision, Urinary Retention, Epithelial Keratopathy, Retinitis Pigmentosa, Nasal congestion Serious: QT prolongation, Drug induced Lupus

Fluphenazine Hyd (Prolixin)	drochloride		
Fluphenazine Dec	Schizophrenia	Oral preparation: Initial 2.5-10mg/day in divided doses every 6-8 hours and may increase to clinical effect and tolerance usually achieved at less than 20mg/ day; 40mg/day may be necessary in severe cases, however safety of prolonged use is not estanblished. Maintenence 1 to 5mg orally once daily after acute symptom control that is generally achieved with higher doses. Oral dose is generally 2 to 3 times the parenteral dose. Injection: (Acute agitation) 2 - 5mg IM Depending on the severity of symptoms, daily dosage may range from 2.5 to 10 mg IM given in divided doses every six to eight hours. Exceed 10mg/day with caution. Switch to oral therapy when feasible. IM dose is generally about one-third to one-half the oral dose.	Common: Hypotension, Extrapyramidal disea se, Tardive dyskinesia, Na sal Congestion Serious: Agranulocytosis, Leukopenia, Neutropenia, Thrombocytopenia, Drug induced Lupus, Dystonia, Neuroleptic ma lignant syndrome
(Long Acting Inje	Schizophrenia, chronic	Initial 12.5-25mg IM or SQ with the dose being repeated or increased as needed and tolerated; generally a single injection may control symptoms up to 4 to 6 weeks. Titration: Dosage should not exceed 100mg. If doses greater than 50mg are deemed necessary, the next dose and succeeding doses should be increased cautiously in increments of 12.5mg	Common: Hypotension, Extrapyramidal Disea se, Tardive dyskinesia Serious: QT prolongation, Paralytic ileus, Agranulocytosis, Leukopenia, Thrombocytopenia, Liver Da mage, Drug induced Lupus, Neuroleptic Ma lignant Syndrome
Haloperidol Lacta (Haldol)	ıte		
	Schizophrenia	Initial/Maintenance 0.5-5mg orally 2-3 times a day Injection (acute agitation) 2 to 5 mg IM; may repeat every 4 to 8 hours depending on patient response; increase to every 1 hour if needed; MAX 20mg/day	Common: Hypotension, Constipation, Xerostomia, Extrapyramidal Disease, Somnolence, Blurred Vision Serious: QT prolongation (particularly in IV form), Paralytic ileus, Priapism Agranulocytosis, Dystonia, Neuroleptic Malignant Syndrome

(Long Acting Inje	ŕ		
	Schizophrenia, chronic	Patients stabilized on oral doses up to 10 mg/day 10-15 times previous daily oral dose IM monthly Initial doses > 100 mg should be administered in 2 separate doses Patients stabilized on oral doses > 10 mg/day 20 times previous daily oral dose IM for the first month, then 10-15 times previous oral dose IM monthly Max dose Doses > 450 mg monthly have limited clinical experience	Common: Extra pyramidal disea se Serious: QT prolongation, Agra nulo cytosis, Leukopenia, Anaphylaxis, Neuroleptic Malignant Syndrome, Seizure, Pulmonary Embolism
Thiothixene (Navane)			
	Schizophrenia	Initial 2 mg orally 3 times daily (milder conditions) or 5 mg orally twice daily (severe conditions) with gradual titration to optimal clinical effect. Typical dosage 20-30 mg/day Max dose 60 mg/day	Common: Orthostatic hypotension, Diminished sweating, Photosensitivity, Constipation, Xerostomia, Extra pyramidal Disea se, Somnolence, Blurred vision, Epithelial keratopathy, Retinitis Pigmentosa, Urinary retention Serious: QT prolongation, Paralytic Ileus, Agra nulocytosis, Thrombocytopenia, Cholestatic jaundice, Drug induced lupus

SECOND GENERATION ANTIPSYCHOTICS

Aripiprazole			
(Abilify)			
	Bipolar I disorder- Acute treatment of manic or mixed episodes; in combination with lithium or valproate; Adjunct Acute treatment of manic or mixed episodes; monotherapy	Initial 10-15mg orally once a day; target dose 15 mg once a day; may increase to MAX 30 mg/day Initial and target dose, 15 mg orally once a day; may increase to MAX dose of 30 mg/day	Common: Weight gain, Constipation, Nausea/Vomiting, Extrapyramidal disease, Headache, Insomnia, Sedation, Blurred vision, Anxiety Serious: QT prolongation, Myocardial Infarction, DKA, Pancreatitis, Agranulocytosis, Leukopenia, CVA/TIA, Suicidal behavior, Angioedema
	Schizophrenia	Initial 10-15mg orally oncedaily Titration	
		May increase after 2 weeks at each dose strength	
Aripiprazole Laur (Abilify Maintena			
	Bipolar I disorder- ma intenance monotherapy	Initial/ Maintenance 400mg IM once monthly continue oral aripiprazole after initial injection for 14 consecutive days	Common: Weight gain, Constipation, Nausea/Vomiting, Extrapyramidal disease, Headache, Insomnia, Sedation, Blurred vision, Anxiety
	Schizophrenia	Same as a bove	Serious: QT prolongation, Myocardial Infarction, DKA, Pancreatitis, Agranulocytosis, Leukopenia, CVA/TIA, Suicidal behavior, Angioedema
Asenapine (Saphris)			
	Bipolar I disorder – adjunct	Initial 5 mg sublingually twice daily with either lithium or valproate	Common: Ora l Hypoesthesia, Myalgia s, Extra pyramidal disea se, Dizziness
		Titration May increase to 10mg twice daily Max dose Safety of doses > 10mg twice daily is not established	Serious: QT prolongation, Hyperglycemia, Hypercholesterolemia, Hypertriglyceridemia, Weight gain, Agranulocytosis, Hypersensitivity, Somnolence, Suicidal thoughts
	Bipolar I disorder monotherapy Schizophrenia	Initial/ Maintenance 5-10mg sublingually twice daily Initial/ Maintenance	

		5 mg sublingually twice daily	
		Titration a fter 1 week may increase to 10mg twice daily	
Brexpiprazole (Rexulti)			
	Schizophrenia	Initial Img orally once daily on days 1-4 Titration 2mg orally once daily on days 5-7 Typical dosage Target dosage of 4mg orally once daily beginning on day 8 based on response and tolerability Max dose 4mg	Common: Hyperglycemia, Hypertriglyceridemia, Weight gain, Extra pyramidal disease, Headache Serious: CVA/TIA, Orthostatic hypotension, Syncope, DKA, Agranulocytosis, Seizure, Increased suicidal thoughts, Neuroleptic Malignant Syndrome
Cariprazine (Vraylar)			
	Bipolar I disorder, Acute mixed or manic episodes	Initial 1.5 mg or ally once daily on day 1 Titration Increase to 3 mg once daily on day 2 Further adjust dose in 1.5 or 3 mg increments as needed Max dose 6 mg/day	Common: Indigestion, Vomiting, Extrapyramidal disease, Somnolence Serious: Ischemic stroke, Orthostatic hypotension, Diabetes Mellitus, Hyperglycemia, Dyslipidemia, Esophageal dysmotility, Leukopenia, Seizure, Increased Risk of
	Bipolar I disorder, Maintenance	Maintenance Continue 3 to 6 mg orally once daily	Suicide
	Schizophrenia	Initial 1.5mg orally once daily on day 1 Titration Increase to 3mg once daily on day 2 Further adjust dose in 1.5 or 3mg increments as needed Maintenance 1.5 to 6mg daily Max dose 6mg/day	

Clozapine (Clozaril)			
Iloperidone	Schizophrenia, Treatment Resistant or with Recurrent Suicidal Behavior	Initial 12.5mg orally 1-2 times daily Titration Increase in increments of 25 to 50mg per day as tolerated Target maintenance dose 300-450mg/day in 2-3 divided doses by the end of 2 weeks Rapid titration in hospitalized patients Day 1-50mg followed by 50-100mg as needed every 6 hours up to a max of 150 additional mg Continue with daily increases in increments of 50-100mg per day therea fter as tolerated. Max dose 900mg/day	Common: Hypotension, Syncope, Tachycardia, Sweating, Weight gain, Constipation, Excess salivation, Nausea, Fever Serious: Cardiomyopathy, QT prolongation, Diabetes Mellitus, Hepatotoxicity, Neuroleptic Malignant Syndrome Life Threatening: Agranulocytosis - prior to initiation, baseline absolute neutrophil count should be at least 1500/mcL or 1000/mcL for patients with documented ethnic neutropenia - CBC with differential and ANC weekly for the first 6 months, then once every two weeks for the next 6 months, then once a month
(Fanapt)	Schizophrenia	Initial 1 mg orally twice daily Titration Slow increase not to exceed increase of 2mg twice daily or 4mg/day Target maintenance dose 6-12mg twice daily Max dose 12mg twice daily	Common: Orthostatic hypotension, Tachycardia, Weight gain, Hyperprolactinemia, Xerostomia, Dizziness, Somnolence, Congestion Serious: Hyperglycemia, CVA/TIA, Neuroleptic malignant syndrome
Lurasidone (Latuda)	Bipolar disorder, depressed phase in combination with lithium or valproate Schizophrenia	Initial 20mg or ally once daily with food (350 cal) Max dose 120mg daily Initial 40mg or ally once daily with food (350 cal) Max dose 160mg daily	Common: Dyslipidem ia, Hyperglycemia, Weight ga in, Dia rrhea, Na usea/Vomiting, Extra pyramidal disea se, Somnolence Serious: Orthostatic hypotension, Agra nulocytosis, CVA/TIA, Suicidal thoughts, Increased creatinine, Neuroleptic Malignant Syndrome

Quetiapine (Seroquel)			
	Bipolar disorder, depressed phase Monotherapy in acute management	Initial 50mg or ally once daily on day 1 Titration 100 mg once daily on day 2;200mg once daily on day 3;300mg once daily on day 4, all doses given at bedtime Max dose 300mg/day	Common: Orthostatic hypotension, Hypercholesterolemia, Hypertriglyceridemia, Weight Gain, Abdominal pain, Constipation, Xerostomia, Increased LFTs, Weakness, Dizziness, Extrapyramidal disease, Headache, Somnolence Serious: QT prolongation, Syncope, DKA,
	Bipolar disorder, maintenance in combination with lithium or divalproex	Initial/maintenance 400 to 800mg per day orally divided twice daily, generally continuation of stabilization dose Max dose 800mg/day	Pancreatitis, Agranulocytosis, Seizure, Suicidal thoughts, Neuroleptic Malignant Syndrome
	Bipolar Mania- Adults Monotherapy or as an adjunct to lithium or divalproex	Initial day 1:100mg orally divided twice daily Titration day 2:200mg divided twice daily day 3:300mg divided twice daily day 4:400mg divided twice daily; with further dose adjustments in increments of not more than 200mg/day Max dose 800mg/day by day 6	
	Schizophrenia	Initial day 1: 25mg orally twice daily Titration increase total daily dosage by 25 to 50mg divided into 2 to 3 doses on days 2 and 3 to achieve a target dose of 300 to 400mg by day 4 further dose a djustment should generally occur in increments of 20 to 50mg twice daily at intervals of no less than 2 days Max dose 750mg/day	

Quetiapine Extend (Seroquel)	ded Release		
	Bipolar disorder, depressed phase Monotherapy in acute management	Initial 50mg or ally once daily on day 1 Titration 100 mg once daily on day 2;200mg once daily on day 3;300mg once daily on day 4, with all doses at bedtime Max dose 300mg/day	Common: Orthostatic hypotension, Hypercholesterolemia, Hypertriglyceridemia, Weight Gain, Abdominal pain, Constipation, Xerostomia, Increased LFTs, Weakness, Dizziness, Extrapyramidal disease, Headache, Somnolence Serious: QT prolongation, Syncope, DKA,
	Bipolar disorder, maintenance in combination with lithium or divalproex	Initial/maintenance 400 to 800mg per day orally divided twice daily, generally continuation of stabilization dose Max dose 800mg/day	Pancreatitis, Agranulocytosis, Seizure, Suicidal thoughts, Neuroleptic Malignant Syndrome
	Bipolar Mania- Adults Monotherapy or as an adjunct to lithium or divalproex	Initial day 1:300mg orally in the evening Titration day 2: 600mg divided twice daily day 3: further dosage a djustment to usual daily dose (400-800mg) Max dose 800mg/day	
	Schizophrenia	Initial 300mg or ally in the evening on day 1 Titration usual maintenance dose between 400 to 800mg once daily dose increases may occur at intervals of at least 1 day in increments of up to 300mg/day Max dose 800mg/day	
	Schizophrenia, Maintenance	400 to 800mg per day orally once daily in the evening	
Paliperidone (Invega)			
	Bipolar I disorder, Acute manic and mixed episodes (off label)	Initial 6mg orally oncedaily Titration	Common: Tachycardia, Hyperprolactinemia, Weight gain, Constipation, Indigestion, Extrapyramidal Disease, Somnolence, Tremor

	Schizoa ffective disorder Schizophrenia	Adjust based on efficacy and tolerance with 3 mg/day increments at intervals of more than 4 days Max dose 12 mg/day Same as a bove Initial 6 mg or ally once daily Titration Adjust based on efficacy and tolerance with 3 mg/day increments at intervals of more than 5 days Max dose 12 mg/day	Serious: QT prolongation, Agranulocytosis, Dysphagia, Tardive dyskinesia
Ziprasidone (Geodon)			
	Bipolar I disorder, Acute manic or mixed episodes, monotherapy	Initial 40mg twice daily with food on day 1 Titration 60 or 80mg twice daily with food on day 2 Adjust based on tolerance and efficacy within range of 40 to 80mg twice daily Max dose Up to 80mg twice a day	Common: Rash, Weight gain, Constipation, Nausea/Vomiting, Headache, Somnolence, Extrapyramidal disease, Dizziness Serious: Dysphagia, QT prolongation, Seizure, Neuroleptic malignant syndrome
	Bipolar I disorder, adjunct with lithium or valproate	Initial/maintenance 40 to 80mg orally twice daily with food	
	Schizophrenia	Initial 20mg or ally twice a day with food Titration May gradually increase dosage not less than every 2 days Max dose Up to 80mg twice a day Periodically reassess the need for maintenance treatment and use lowest effective dose; no a dditional benefit has been demonstrated for doses greater than 20mg twice daily	

Risperidone (Risperdal)			
	Bipolar I disorder	Initial 2-3 mg orally once a day Maintenance Dosage a djustments should be made in increments of 1 mg/day at intervals of at least 24 hours, Max dose Doses higher than 6 mg/day have not been evaluated in clinical trials	Common: Rash, Hyperprolactinemia, Weight gain, Constipation, Diarrhea, Excess salivation, Nausea/Vomiting, Xerostomia, Extrapyramidal Disease, Sedation, Tremor, Anxiety Serious: QT prolongation, Syncope, DKA, Pancreatitis, Agranulocytosis, Thrombocytopenia, Seizure, Priapism
	Schizophrenia	Initial 2mg/day orally, a dministered in either one or two doses Titration Increase as tolerated in increments of 1 to 2 mg/day at intervals not less than 24 hours Typical dosage 4 to 8mg/day Max dose Doses higher than 16mg/day have not been evaluated in clinical trials	Common: Rash, Hyperprolactinemia, Weight gain, Constipation, Diarrhea, Excess salivation, Nausea/Vomiting, Xerostomia, Extrapyramidal Disease, Sedation, Tremor, Anxiety Serious: QT prolongation, Syncope, DKA, Pancreatitis, Agranulocytosis, Thrombocytopenia, Seizure, Priapism

Risperidone Long Acting Injectable Establish tolerability to oral risperidone prior to initiation of treatment for all indications					
	Bipolar I disorder	Initial 25 mg IM every 2 weeks, oral risperidone or a nother antipsychotic medication should be given with the initial injection, continued for 3 weeks, and then discontinued	Common: Rash, Hyperprolactinemia, Weight gain, Constipation, Diarrhea, Excess salivation, Nausea/Vomiting, Xerostomia, Extrapyramidal Disease, Sedation, Tremor, Anxiety		
		Titration Dose may be increased to 37.5mg or 50mg IM with a djustments made not more frequently than every 4 weeks; clinical effects of dose adjustment should not be expected earlier than 3 weeks after any dose change	Serious: QT prolongation, Syncope, DKA, Pancreatitis, Agranulocytosis, Thrombocytopenia, Seizure, Priapism		
		Max dose 50mg IM every 2 weeks			
	Schizophrenia	IM: same as a bove SQ: 90 or 120mg SQ in a bdomen once a month, max 90 to 120mg/month; no loading dose or supplemental oral risperidone is a dvised			

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Resources

DailyMed: https://dailymed.nlm.nih.gov

Micromedex: https://www.micromedexsolutions.com

Lexicomp: https://online.lexi.com

Resources

National Institute of Mental Health (NIMH) https://nimh.nih.gov/health/index.shtml

National Alliance on Mental Illness (NAMI) https://nami.org/About-Mental-Illness

Substance Abuse and Mental Health Services Administration (SAMHSA) https://www.samhsa.gov

Depression and Bipolar Support Alliance https://dbsalliance.org

Mental Health America https://mhanational.org

SMI Adviser https://www.smiadviser.org

Additional Reference

The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia, Third Edition. Published September 2020, Copyright 2021. psychiatryonline.org/doi/epdf/10.1176/appi.books.9780890424841