MAJOR DEPRESSION
CLINICAL PRACTICE GUIDELINE

Reviewed and Updated by the Behvioral Health Subcommittee 7/20/2017

Topic	Recommendations
Purpose	SummaCare Health Plan bases its Clinical Practice Guideline for Major Depressive Disorder in Adults on clinical guidelines established by the American Psychiatric Association and a review of current scientific literature. The purpose for the guideline is to ensure consistent and appropriate diagnosis, treatment, and referral for members with a Major Depressive Disorder (MDD), irrespective of the practice setting in which they access care.
Access	▪ Members may seek initial treatment for depression from their Primary Care Physician (PCP) and/or directly from a behavioral health specialist. SummaCare members may access care directly from behavioral health practitioners without a referral from their Primary Care Physician. ▪ Members will have access to behavioral health care according to the following standards: ▪ A member with life-threatening emergency needs is seen immediately ▪ A member with non-life threatening emergency needs has access to care within 6 hours ▪ A member with urgent needs has access to care within 48 hours ▪ A member has access to a routine office visit within 10 working days ▪ A member discharged from the hospital for a mental health diagnosis will have a follow-up appointment within 7 days of discharge
Assessment	▪ The diagnosis of Major Depressive Disorder (MDD) is determined following a face-to-face clinical evaluation that is conducted by a Primary Care Physician (PCP) or behavioral health specialist. ▪ The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up. (B recommendation) ▪ The practitioner conducting the assessment will carefully rule out medical disorders or use of medications that can mimic, mask, or potentiate symptoms associated with MDD. ▪ A thorough assessment for substance abuse and/or dependence are necessary to rule out a substance induced mood disorder. ▪ Personal history (e.g. psychological development, response to life transitions, major life events)

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Screening Tools	▪ Social, occupational and family histories ▪ Assess the patient's suicide risk. Hospitalization should be considered if the risk is significant. ▪ Assess the patient's homicidal risk. Hospitalization should be considered if the patient is at risk to harm someone else. ▪ Screening adults for depression is recommended in clinical practices that have systems in place to ensure accurate diagnosis, effective treatment, and follow-up. ▪ The PHQ-2 is accurate for depression screening in adolescents, adults, and older adults. This is a short screening tool utilized as a patient health questionnaire, consisting of two simple questions about mood and anhedonia. Evidence rating B recommended. ▪ Depression screening in older adults can be accomplished with multiple instruments, including the PHQ-2, PHQ-9, and various Geriatric Depression Scales. Evidence rating B recommended. ▪ Use of the testing tool, PHQ-9 or PHQ-A, may be completed at any time based upon patient presentation or risk and symptomology (e.g. emotional problems as the chief complaint). The PHQ-9 is one of the most common instruments used for depression screening, and only takes two to five minutes to complete. A total score of 10 points or greater on the PHQ-9 or PHQ-A indicates the need for clinical evaluation and documentation of a follow-up plan. *See Appendix 1, Depression Treatment in Adults Algorithm for: Acute Phase (6-12 weeks), Continuation Phase (4-9 months), and Maintenance Phase (1 year to lifetime).

Diagnosis	▪ DSM--5 OR DSM-5-PC criteria should be used to support the diagnosis of MDD. Accurate diagnosis is essential, as selection of effective treatment options is increasingly driven by a differential diagnosis for specific types of depression, such as Dysthymia, Seasonal Affective Disorder, and Substance Induced Mood Disorder. See Appendix 2* for the DSM-5 criteria.
	▪ Family history and/or prior patient history for depression can further support the diagnosis.
	▪ The diagnosis should be comprehensive and include all five axes for DSM-V.
	  ▪ Type and severity of depression should be specified using 5-digit coding
	  ▪ Axis IV describes psychosocial stressors that may require psychotherapy and/or social intervention
	  ▪ Axis III identifies co-existing medical conditions that necessitate coordination of care with the patient's PCP
	  ▪ Use of Global Assessment of Function (GAF) score on Axis V clarifies the degree of current functional impairment in contrast to the highest function level in the past year

Treatment and Referral	▪ Discuss the diagnosis of Major Depression with the member and, as consented to, with his or her support system when appropriate. This discussion should include therapeutic goals and objectives and the treatment options available for achieving those goals and objectives. ▪ The patient should be apprised of treatment options, associated benefits and risks at the time treatment is initiated, and again when the patient is stable. ▪ Appropriate treatment considerations include:

Topic	Recommendations
	▪ Provision of safety and appropriate level of care ▪ Provision of treatment in the least intensive, clinically appropriate setting ▪ Regular monitoring for crises, decline in function, or other indications that may warrant a change in the level of care ▪ Initiation of psychotherapy and/or medication based on an accurate diagnosis, severity of condition, and co-occurring factors (e.g. pregnancy, psychosocial stressors, personality factors) ▪ Referral to the member's PCP as clinically warranted to rule-out potential medical disorders that may be mimicking, masking, or affecting symptoms ▪ When the diagnosis is made by a PCP, referral to a behavioral health specialist for psychotherapy when there are the following situations is encouraged: ▪ As an primary form of treatment in patients with mild to moderate depression ▪ In the presence of psychosocial issues, interpersonal problems, intrapsychic conflict, or co-occurring Axis II disorder ▪ Uncertainty about the diagnosis, especially if Bipolar Disorder or Severe Depression is considered ▪ Possibility of organic brain disease or dementia ▪ Failure to respond to treatment ▪ Comorbidity with drugs or alcohol ▪ Comorbidity with other psychiatric conditions ▪ Trauma History ▪ Children or adolescents ▪ Risk of suicide, homicide or other violence ▪ Severe or complex presentations ▪ The need for psychotherapy as adjunctive treatment to medications ▪ Non-adherence to recommended advice or treatment ▪ Clinical judgment warrants a need for greater resources ▪ Patients with a diagnosis of Depression with Psychotic Features (fifth digit of 4) and MDD, Severe (fifth digit of 3) must be referred for an evaluation with a psychiatrist. ▪ Coordination of care between behavioral health practitioners when more than one specialist is involved in the care. (A therapist and a psychiatrist). ▪ Coordination of care between the member's behavioral health practitioner(s) and PCP.' ▪ Provide education to patient and family about the illness as appropriate
	▪ Suggested follow-up for persons whose treatment includes initiation of anti-depressant medication is recommended as follows: ▪ <u>Acute Phase of Treatment (6-12 weeks): percentage of members who remained on an antidepressant medication for at least 84 days (12 weeks). Members are allowed 30 gap days in treatment, so actually looking for 84 days of medication treatment over the course of 114 days from the Index Prescription Start Date. (HEDIS Measure).</u> ▪ Due to comparable efficacy, the specific antidepressant choice is primarily determined by anticipated side effects, safety, tolerability,

Topic	Recommendations
Medication Management	pharmacologic properties (half-life, effect on cytochrome P450, and other drug interactions) ▪ Treatment with anti-depressant medication should be continuous during this time ▪ Monitor the patient closely for response to the medication and assess that he or she is taking the medication as prescribed ▪ Appropriate follow-up when an antidepressant medication is prescribed for a new episode of depression is at least three outpatient visits during the 12-week acute phase of treatment. One of the visits should be with the prescribing practitioner. ▪ Make certain the dose of medication is adequate. Many antidepressants can be started at a therapeutic dose. ▪ Titrate the dose upward, according to manufacturer and FDA recommendations and patient tolerance, when response is ineffective. ▪ If there is no improvement within 4-6 weeks non-behavioral health practitioners should consider consultation with a psychiatrist to verify the diagnosis and consider a substitute or augmentation strategy. ▪ If there is partial improvement within 4-6 weeks of antidepressant treatment, the dosage should be increased. ▪ Psychiatrists should consider verifying the diagnosis and substitution or augmentation strategies if there is no improvement in 4-6 weeks. ▪ Recognize during acute phase, depressed patients may be poorly motivated, pessimistic and may suffer from memory deficits ▪ Antipsychotic medications should be used when there is evidence of severe depression with psychotic symptoms. <u>Continuation Phase of Treatment (6 months)-percentage of members who remained on an antidepressant medication for at least 180 days (6 months). Members are allowed 51 gap days in treatment, so actually looking for 180 days of medication treatment over the course of 231 days from Intake Prescription Start Date (IPSD). HEDIS Measure.</u> ▪ Review the need to continue treatment with the patient. ▪ Continue medication at the full therapeutic dose for 16-20 weeks after full remission of symptoms. Appropriate dosing and continuation of antidepressant therapy through the acute and continuation phases of treatment decreases recurrence of depression. ▪ Carefully monitor for signs of relapse, especially during the first 8 weeks of remission. ▪ Member must not have filled an Rx for an antidepressant within 105 days prior to the IPSD. ▪ Ok to switch between antidepressants as long as you meet the rules of continuous use, as described above. ▪ <u>Maintenance Phase of Treatment</u> ▪ Consider the need for maintenance treatment when: ▪ There is a co-morbid medical condition that is likely to complicate recovery ▪ There is a history of multiple depressive disorders and poor inter-episode recovery

Topic	Recommendations
	▪ The current episode has lasted for 2 years or more ▪ The current episode is a severe type ▪ Discuss treatment options with the patient, including benefits and risks. ▪ Patients may undervalue the benefits of continued treatment and focus on burdens of treatment during this phase
Psychotherapy	▪ Use of a depression-focused psychotherapy alone is recommended as an initial treatment of choice for patients with mild to moderate major depressive disorder. In older adults studies have shown that depressed older adults treated with psychotherapy were more than twice as likely to go into remission as those who received no treatment at all. ▪ The strongest clinical evidence is for cognitive-behavioral therapy (CBT) and interpersonal psychotherapy. Cognitive therapy alone should only be used for people in remission and not for initial treatment. Other therapy options include: ▪ Behavioral activation ▪ Brief psychodynamic psychotherapy ▪Mindfulness therapy considered for people with less severe depressive conditions and those who are doing better. ▪problem-solving based cognitive therapies Individual, couples, family, and group therapy formats are appropriate based on clinical presentation and patient preference. Family therapy and parental involvement should be strongly considered for children and adolescents with depression. ▪ Psychotherapy suggested therapy schedule would be: ▪ Initial two visits for assessment and formulation of a treatment plan. ▪ The treatment plan should determine the optimal number of visits and frequency to obtain symptom remission (6-12 visits is typical) ▪ Additional visits may be necessary based on specified treatment goals and progress toward those goals ▪ Referral to community services, such as Al Anon, Consumer Credit Counseling, or Victim Assistance as warranted ▪ Referral for Case Management services as warranted

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PRESCRIBING GUIDELINES FOR ANTIDEPRESSANTS FOR PRIMARY CARE PHYSICIANS

This information is to be considered as a source of information for primary care physicians in their treatment of a major depressive disorder and is to be used in conjunction with the Treatment Guidelines for Major Depressive Disorder.

There are many classes of antidepressants to consider. Each of the antidepressants has individual benefits and is indicated for different types of depression. Along with the benefits, however, each medication class also has side effects to consider. Remember, not every patient responds to antidepressants in the same way. It may take a trial of a few different medications to find the most effective treatment.

Below are listed classes of antidepressants, the average starting dose, the recommended daily range and the major possible side effects of the medications as listed by the American Psychiatric Association. The provided information is only to be used as a quick reference. The information does not include all the clinical information relevant to the medication or all the side effects and safety information.

Selective serotonin reuptake inhibitors (SSRIs), selective noradrenaline reuptake inhibitors (SNRIs), combined SRI/NRIs, Mirtazapine, and Bupropion, should be the initial drugs of choice for depression. They are the "first line antidepressant agents. SSRI's and the newer agents are found to have less serious side effects than other anti-depressants. They also are safer if the patient overdoses. Newer agents are more expensive than older antidepressants (such as the tricyclic medications and many SNRIs). The SSRI's have been found effective for treatment of depression, anxiety and obsessive compulsive disorders. Cardiac monitoring should be considered when prescribing Celexa (citalopram) as it can prolong QT intervals and may put patients at increased risk of developing an abnormal heart beat.

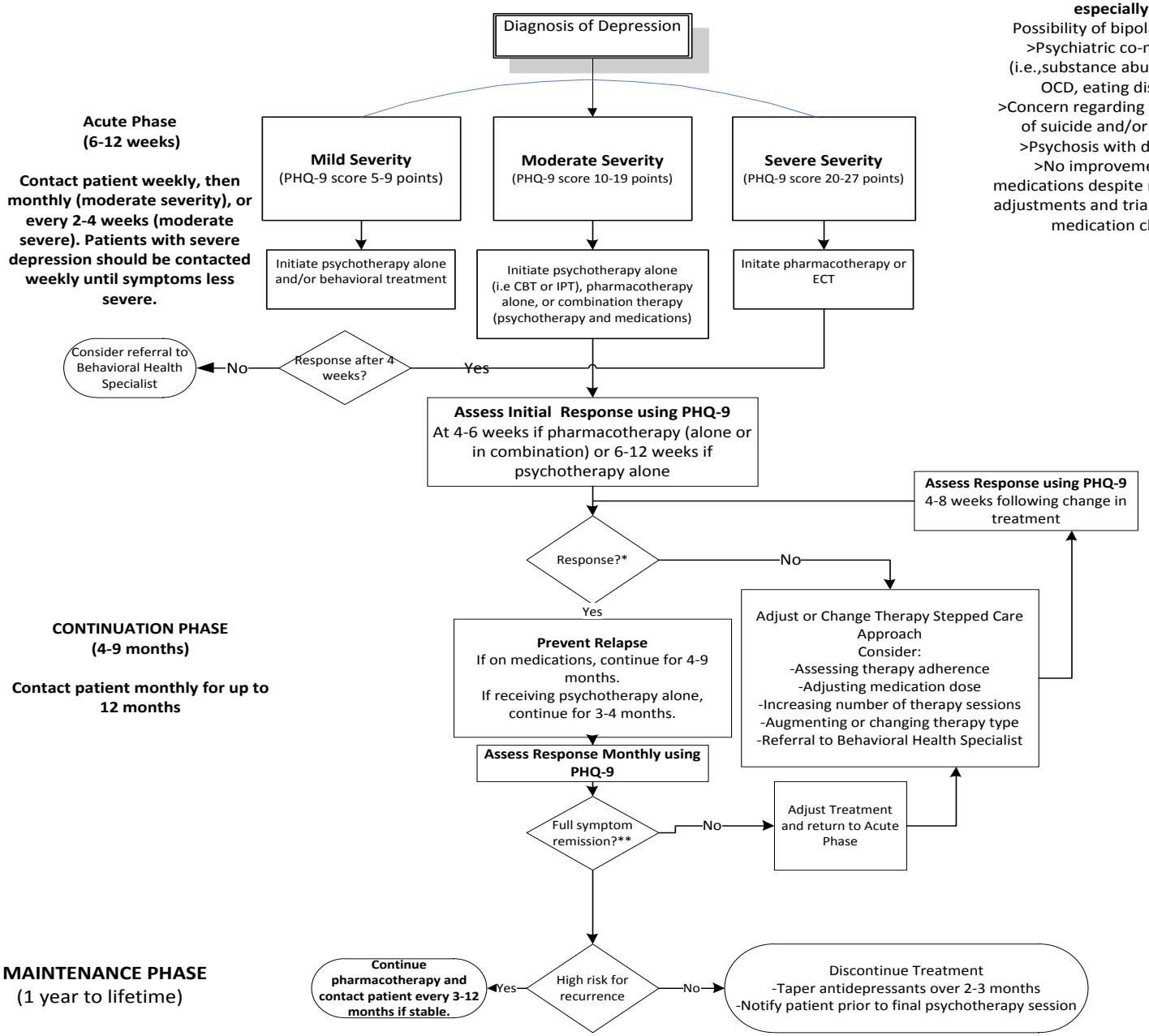
Antidepressant agents typically require minimal titration of dosages and may be effective at the starting dose. The medications do take 4-6 weeks to gain efficacy in treatment of the depressive symptoms. If one particular medication does not work to alleviate depressive symptoms after an appropriate treatment time, the physician may consider changing the prescription to a different antidepressant.

Many antidepresants are available in generic form including: Fluoxetine HCl, Venlafaxine, Mirtazapine, Paroxetine, Citalopram, and Sertraline.

Tricyclic medications or TCA's may be prescribed for depressive symptoms that do not respond to other antidepressants. The TCA's have more complicated side effects, have a higher lethality in the event of an overdose and may require specific expertise in dosing. Tricyclics are considered potentially inappropriate medications (PIM) for use in the elderly population. Consultation with a psychiatrist is recommended with their usage.

Monoamine oxidase inhibitors or MAO's are considered in refractory depression. Special considerations must be given to a patient's diet when MAO's are prescribed. Their side effects are more extensive and the MAO's also have a high lethality in the event of an overdose. Again, consultation with a psychiatrist is recommended for their use.

Decision Tree for Management of Major Depression



Consider referral to Behavioral Health Specialist at any time, especially if:
Possibility of bipolar disorder
>Psychiatric co-morbidity (i.e.,substance abuse, anxiety, OCD, eating disorder)
>Concern regarding the possibility of suicide and/or homicide
>Psychosis with depression
>No improvement with medications despite multiple dose adjustments and trials of different medication classes

*__Response:__ a 50% or greater reduction in symptoms (as measured by the PHQ-9.

**__Remission__: the absence of depressive symptoms, or the presence of minimal depressive symptoms (PHQ-9 score of < 5 points).

Source: APA Guidelines for Major Depressive Disorder; PHQ-9 Scoring

APPENDIX 2

DSM-5 Criteria for Major Depressive Disorder *

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g. feels sad, empty, hopeless) or observation made by others (e.g., appears tearful).
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day, (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g. a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
4. Insomnia or hypersomnia nearly every day.
5. Psycho motor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt, nearly every day.
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either from subjective feelings or observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The symptoms are not attributable to the physiological effects of a substance (e.g. a drug of abuse, a medication) or a general medical condition.

*Source: DSM-5 Diagnostic Criteria, 5th Ed. Washington, DC, APA.

Selective Serotonin Re-Uptake Inhibitors

Med D Tier	Comm Tier	MP Tier	Antidepressant Drug	Starting Dose	Effective Range	GI Distrubance	Sedation	Agitation	Weight Gain	Sexual Dysfunction	Drug Interactions	Receptor Site
1*	1*	1*	*Fluoxetine HCl*	20 mg qd	20-80 mg/day	++	-	+	-	++	++	5-HT reuptake inhibitors
NF	3	NF	**Prozac**									
NF	3	5	**Sarafem**									
1*	1*	1	*Paroxetine HCl*	20 mg qd	20-50 mg/day	++	++	-	+	+	+	5-HT reuptake inhibitors
NF	3	5	**Paxil**									
NF	3	5	**Pexeva**									
NF	3	NF	**Brisdelle**	7.5 mg qhs	7.5 mg qhs							
2	2	3	*Paroxetine*	25 mg qd	25-62.5 mg/day	++	++	-	+	+	+	5-HT reuptake inhibitors
NF	3	NF	**Paxil CR**									
1*	1*	2	Sertraline HCl	50 mg qd	50-200 mg/day	++	-	-	-	+	+	5-HT reuptake inhibitors
NF	3	NF	**Zoloft**									
1*	1	2	*Escitalopram*	10 mg qd	10-20 mg/day	+	0/+	-	-	+	-	5-HT reuptake inhibitors
NF	3	NF	**Lexapro**									
1	1	1*	*Citalopram*	20 mg qd	20-40 mg/day	+	+	-	-	+	-	5-HT reuptake inhibitors
NF	3	NF	**Celexa**									
NA	NA	NA	*Vilazodone*	10 mg qd	20-40 mg/day	+	-	+	-	+	-	Serotonin reuptake inhibitor and 5-HT_{1A} partial agonist
4	3	5	**Viibryd**									
NA	NA	NA	*Vortioxetine*	10 mg qd	5-20mg/day	+	-	-	-	+	-	Inhibits 5-HT_3, 5-HT_{1d}, 5-HT_7, agonized 5-HT_{1a}, and partial agonist 5-HT_{1b}
4	3	5	**Trintellix**									

Other Antidepressant Agents

Med D Tier	Comm Tier	MP Tier	Antidepressant Drug	Starting Dose	Effective Range	GI Distrubance	Sedation	Agitation	Weight Gain	Sexual Dysfunction	Drug Interactions	Receptor Site
2	1	2	*Bupropion*	100 mg bid	300-450 mg/day	-	-	+	-	-	+	NE and Da reuptake inhibitor
NF	3	NF	**Wellbutrin**									
NF	1	2	**Budeprion**									
2	1	NF	**Buproban**									
NF	3	NF	**Forfivo**									
2	1	2	*Bupropion ER*	150 mg qam								
NF	3	NF	**Wellbutrin SR**									
2	1	2	*Bupropion XL*									
NF	3	5	**Forfivo XL**									
NF	3	NF	**Wellbutrin XL**									
NF	3	5	**Aplenzin**	174 mg/day	348mg/day							
NA	NA	NA	*Isocarboxazid*	10 mg bid	20 mg bid	+	+	+	-	+	++	
4	3	5	**Marplan**									
2	1	2	*Maprotiline*	25-37.5 mg bid-tid	75-150 mg qd	+	++	+	++	+	+	NE Reuptake inhibitor
2	1	2	*Mirtazapine*	15 mg qpm	15-45 mg/day	+	++	-	++	-	+	Antagonizes alpha-2 autoreceptors and antagonizes 5-HT_{2A} and 5-HT_3
NF	3	NF	**Remeron**									

2	2	2	*Nefazodone*	100 mg bid	300 mg bid	++	++	+	++	+	++	5-HT and NE uptake inhibitor
2	1	2	*Phenelzine*	15 mg tid	30 mg tid	+	+	+	++	++	++	MAO inhibitor
NF	3	NF	**Nardil**									
NA	NA	NA	*Selegiline*	6 mg/24 hr qd	6-12 mg/24 hr qd	+	+	+	-	+	+++	MAO-A and MAO-B inhibitor
5	3	5	**Emsam**									
2	1	2	*Tranylcypromine*	10 mg qd	10-20 mg tid	+	+	+	+	+	+++	MAO inhibitor
NF	3	NF	**Parnate**									
2	1	2	*Venlafaxine*	37.5-75 mg qd	75-225 mg/day	++	-	+	-	+	+	5-HT and NE Reuptake Inhibitor
2	1	2	*Venlafaxine ER*									
NF	3	NF	**Effexor XR**									
2	2	3	*Duloxetine*	40-60 mg qd	60-120 mg/day	+	+	-	-	-	+	5-HT and NE Reuptake Inhibitor
NF	3	NF	**Cymbalta**									
NF	3	NF	**Irenka**									
1	1*	1*	*Trazodone*	150 mg qd	150-600 mg/day	++	+++	-	-	+	+	5-HT Reuptake inhibitor and 5-HT_{2a} blocker
NF	3	NF	**Oleptro**									
NF	2*	3*	*Desvenlafaxine*	50mg qd	50 mg qd	+	-	-	-	-	+	5-HT and NE Reuptake Inhibitor
NF	3	NF	**Khedezla**									
4	3	5	**Pristiq**									
NA	NA	NA	*Levomilnacipran*	20 mg qd	40-120 mg/day	++	-/+	++	-/+	++	+	5-HT and NE Reuptake Inhibitor
4	3	5	**Fetzima**									

Tricyclic Agents

Med D Tier	Comm Tier	MP Tier	Antidepressant Drug	Starting Dose	Effective Range	GI Distrubance	Sedation	Agitation	Weight Gain	Sexual Dysfunction	Drug Interactions	Receptor Site
2	1*	2	*Amitriptyline*	25-50 mg qhs	100-300 mg/day	+	+++	++	+++	+++	++	5-HT and NE Reuptake inhibitors
2	1	2	*Amoxapine*	50 MG bid-tid	200-300 mg/day	+	+	+	+	+++	++	5-HT and NE Reuptake inhibitors
2	1	2	*Desipramine*	25-50 mg qd	100-300 mg/day	+	+	+	++	+++	++	5-HT and NE Reuptake inhibitors
NF	3	NF	**Norpramin**									
2	1*	2	*Doxepin*	25-50mg qd	100-300mg qd	+	++	+	++	+++	++	5-HT and NE Reuptake inhibitors
3	3	5	**Silenor**	3-6mg qhs	6mg qhs							
2	1*	2	*Nortriptyline*	25-50 mg qd	100-150 mg/day	-	++	-	+	+++	++	5-HT and NE Reuptake inhibitors
NF	3	NF	**Pamelor**									
2	2*	3	*Imipramine*	75 mg qd	Outpatients 75-200 mg/day Inpatients: 100-300 mg/day	++	+	++	++	+++	++	5-HT and NE Reuptake inhibitors
NF	3	NF	**Tofranil**									
2	1	2	*Protriptyline*	10-20 mg q6-8	60mg/day	-	++	-	+	+++	++	5-HT and NE Reuptake inhibitors
NF	3	NF	**Vivactil**									
2	1	2	Trimipramine	25-50 mg hs	75 -300 mg/day	-	+++	-	++	+++	++	5-HT and NE Reuptake inhibitors
4	3	5	**Surmontil**									

* Please note that different dosage forms/strengths may have different tiers *

NF = Non-Formulary

NA - Generic not available