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Sentara Health Plans

BEHAVIORAL HEALTH GUIDELINE

CHILD AND ADOLESCENT DEPRESSION MEDICATION MANAGEMENT

Guideline History

Date Approved	7/06
Date Revised	7/08; 7/10; 7/12; 10/18
Date Reviewed	7/14; 7/16, 7/18, 10/20
Next Review Date	10/24

Key Points

- Epidemiology:
  - Depression affects an estimated 2% of children and 4-8% of adolescents.

- Screening/Evaluation:
  - Age appropriate depression rating scales used with clinical assessment can help with both diagnosis and monitoring response to treatment.

- Risk Factors:
  - The single most predictive factor associated with the risk of developing MDD is high family loading for this disorder. However, the onset and recurrences of major depression may be moderated or mediated by the presence of stressors, coping style, support and genetic factors.

- Comorbidity:
  - The most frequent comorbid diagnoses are anxiety disorders, ADHD and (in adolescents) substance abuse.

- Differential Diagnosis:
  - Several psychiatric and medical conditions as well as reaction to stressors such as bereavement may co-occur with or mimic depression. Also, some medications can induce depression-like symptoms.

- Consequences:
  - Untreated MDD may affect the development of emotional, cognitive and social skills, including family relationships. Suicide attempts and completions are the most significant sequelae of MDD.

- Treatment:
  - **Should always include psychoeducation, supportive management and family and school involvement.**
  - For children and adolescents who do not respond to supportive psychotherapy or who have more complicated depressions, a trial with specific types of psychotherapy and/or antidepressants is indicated.
  - Overall, the SSRI's and other novel antidepressants have been well tolerated by both children and adolescents, with few short-term side effects.
  - Patients should be treated with adequate and tolerable doses for at least 4 weeks; frequent, early dose adjustments should be avoided.
  - Depressed youths should be assessed weekly for 4 weeks, then biweekly. If face-to-face visits are not feasible every week, evaluations may be carried out briefly by telephone.
  - To consolidate the response to acute treatment and avoid relapses, treatment should always be continued for 6-12 months. Some children and adolescents should be maintained in treatment for longer periods of time.
  - During all treatment phases, frequent follow-up contacts should be arranged that allow sufficient time to monitor the patient's clinical status, environmental conditions and, if appropriate, medication side effects.

ANTIDEPRESSANT MEDICATIONS: CHILDREN AND ADOLESCENTS

Drug	Indication	Dosage	Resources (Literature) for Off-Label Use	Side effects and Cautions	PA/ QTY limit
Selective Serotonin Reuptake Inhibitors					
Fluoxetine (Prozac)	Major depressive disorder	8 years and older Lower weight: initial 10 mg once daily; may increase to 20 mg once daily after several weeks; maximum daily dose: 20 mg/day Higher weight: initial 10-20 mg once daily; in patients starting at 10 mg daily, may increase dose to 20 mg after 1 week; maximum daily dose: 20 mg/day	N/A	**Side effects:** Diarrhea, headache, nausea, somnolence, tremor, xerostomia **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating), prolonged QT interval, torsade de pointes	QTY: 80mg/ day
	Depression associated with bipolar I disorder (combination with olanzapine)	10 years and older: initial 20 mg in the evening; adjust dose if needed Safety of doses >50 mg in combination with doses >12 mg of olanzapine has not been studied	N/A		
	Obsessive-compulsive disorder	7 years and older: Lower weight: initial 10 mg once daily; may increase dose after several weeks if inadequate response; recommended dose range, 20 to 30 mg daily Higher weight: initial 10 mg once daily; may increase to 20 mg once daily after 2 weeks; recommended dose range: 20 to 60 mg daily	N/A		
	OFF-LABEL USE (Not FDA Approved)				
	Obsessive-compulsive disorder	younger than 7 years old, 5 mg once daily	Gleason 2007		
	Anxiety associated with phobias and panic attacks	2-6 years, 5 mg dose or 0.25 mg.kg/dose once daily	Gleason 2007		
	Bulimia nervosa	12 years and older, initial 20 mg once daily for 3 days, then 60 mg once daily	Gable 2005 Kotler 2003 Rosen 2010		
	Repetitive behavior associated with autism spectrum disorders	5 years and older, initial 2.5 mg once daily for 7 days, then may titrate at weekly intervals using 0.3 mg/kg/day during week 2, 0.5 mg/kg/day during week 3, max of 0.8 mg/kg/day	Hollander 2005		
	Selective mutism	5 years and older, initial 5 mg once daily for 7 days, increase to 10 mg daily for 7 days, increase to 20 mg daily; max daily dose of 60 mg/day	Black 1994 Dummitt 1996 Kaakeh 2008		

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Citalopram (Celexa)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** Constipation, dizziness, headache, insomnia, nausea, sedation, xerostomia **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating), prolonged QT interval, torsade de pointes, agranulocytosis Slower titration of dose every 2 to 4 weeks may minimize risk of SSRI associated behavioral activation, which has been shown to increase risk of suicidal behavior. Doses >40 mg are not recommended due to risk of QT prolongation	QTY: 40mg/ day
	Major depressive disorder	7-11 years: initial 10 mg once daily; increase dose slowly by 5 mg/day every 2 weeks as needed; recommended dose range: 20-40 mg/day 12 years and older: initial 20 mg once daily; increase dose slowly by 10 mg/day every 2 weeks as needed; recommended dose range: 20-40 mg/day	Wagner 2004 Dopheide 2006 <u>Did not show benefit:</u> Sharp 2006 Von Knorring 2006 Wagner 2005		
	Obsessive-compulsive disorder	7-11 years: initial 5-10 mg once daily; increase dose slowly by 5 mg/day every 2 weeks as needed; recommended dose range: 10-40 mg/day 12 years and older: initial 10-20 mg once daily; increase dose slowly by 10 mg/day every 2 weeks as needed; recommended dose range: 10-40 mg/day	Mukaddes 2003 Thomsen 1997 Thomsen 2001		
Escitalopram (Lexapro)	Major depressive disorder	≥12 years: Initial: 10 mg/day given once daily; may be increased to 20 mg/day after a minimum of 3 weeks	N/A	**Side effects:** Headache, nausea, sedation **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating), prolonged QT interval, torsade de pointes	QTY: 20mg/ day
	OFF-LABEL USE (Not FDA Approved)				
	Autism and pervasive developmental disorders (PDD)	6-17 years old: initial 2.5mg once daily; may increase if needed by 5 mg/day after 1 week; maximum dose 20 mg/day	Owley 2005		
	Social anxiety disorder	10-17 years: Initial: 5 mg once daily for 7 days, then 10 mg/day for 7 days; may then increase at weekly intervals by 5 mg/day if needed, based on clinical response and tolerability; maximum dose: 20 mg/day	Isolan 2007		
Fluvoxamine (Luvox)	Obsessive compulsive disorder	Children 8-17 years: Immediate release- Initial: 25 mg once daily at bedtime; adjust in 25 mg increments at 7 to 14 day intervals, as tolerated; Recommended dose range: 50-200 mg/day; daily doses >50 mg should be divided into 2 doses; administer larger portion at bedtime; lower doses may be effective in female versus male patients 8-11 years: maximum dose of 200 mg/day 12-17 years: maximum dose of 300 mg/day	N/A	**Side effects:** Headache, nausea, sedation **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating), prolonged QT interval, torsade de pointes	QTY: ER/IR: 300mg/ day

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Paroxetine (Paxil)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** Abnormal ejaculation, asthenia, constipation, diarrhea, headache, insomnia, nausea, somnolence **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating)	QTY: IR 60mg/ day ER 62.5mg/ day
	Obsessive compulsive disorder	7-17 years old: initial 10 mg once daily; titrate every 7-14 days in 10 mg/day increments; maximum daily dose 60 mg/day	Geller 2004 Rosenberg 1999		
	Social anxiety disorder	8-17 years old: initial 10 mg once daily; titrate at intervals of at least 7 days in 10 mg/day increments; maximum daily dose 50 mg/day	Wagner 2004		
Sertraline (Zoloft)	Obsessive-compulsive disorder	6-12 years old: initial 25 mg once daily; may increase by 25-50 mg/day increments at intervals of at least 1 week; recommended dose range: 25-200 mg/day; maximum daily dose: 200 mg/day 13-17 years old: initial 50 mg once daily; may increase by 50 mg/day increments at intervals of at least 1 week; recommended dose range: 25-200 mg/day; maximum daily dose: 200 mg/day	N/A	**Side effects:** Diarrhea, fatigue, headache, insomnia, nausea **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating)	QTY: 200mg/ day
	OFF-LABEL USE (Not FDA Approved)				
	Depression	6-12 years old: initial: 12.5-25 mg once daily; titrate dose upwards if clinically needed; may increase by 25-50 mg/day increments at intervals of at least 1 week; recommended dose range: 25-200 mg/day; maximum dose: 200 mg/day 13 to 17 years old: initial 25-50 mg once daily; titrate dose upwards if clinically needed; may increase by 50 mg/day increments at intervals of at least 1 week; recommended dose range: 25-200 mg/day; maximum dose: 200 mg/day	Dopheide 2006 Tierney 1995 McConville 1996 Ambrosini 1999 Dopheide 2006		
Vortioxetine (Trintellix)	**OFF-LABEL USE (Not FDA Approved)** Not indicated under the age of 18, no off-label resources			N/A	√ PA 20mg/ day
Levomilnacipran (Fetzima)	**OFF-LABEL USE (Not FDA Approved)** Not indicated under the age of 18, no off-label resources			N/A	√ PA 120mg/ day
Vilazodone (Viibryd)	**OFF-LABEL USE (Not FDA Approved)** Not indicated under the age of 18, no off-label resources			N/A	√ PA 40mg/ day

ANTIDEPRESSANT MEDICATIONS: CHILDREN AND ADOLESCENTS

Atypical Antidepressants					
Venlafaxine (Effexor)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** Dizziness, headache, insomnia, nausea, somnolence, xerostomia **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating), GI hemorrhage, hepatotoxicity	QTY: ER/IR: 450mg/ day
	Depression	Due to the lack of demonstrated efficacy and concerns about an increased risk for suicidal behavior, venlafaxine should be reserved for pediatric patients with major depression who do not respond to fluoxetine or sertraline			
		7-12 years old: Immediate release: initial 12.5 mg once daily for 3 days, increased to 12.5 mg twice daily for 3 days, increased to 12.5 mg three times a day 13-17 years old: initial 25 mg once daily for 3 days, increased to 25 mg twice daily for 3 days, increased 25 mg three times a day	Mandoki 1997		
		7-17 years old: Extended release: initial 37.5 mg once daily for 1 week, increase to 75 mg once daily for weeks 2-8	Weller 2000 Walter 1998		
	ADHD	8-17 years old: Immediate release: initial 12.5 mg then titrate <40 kg increase by 12.5 mg/week to maximum daily dose 50 mg/day divided into 2 doses ≥40 kg increase by 25 mg/week to maximum daily dose 75 mg/day divided into 3 doses	Olvera 1996 Pleak 1995		
	Autism spectrum disorders	3 years or older: Immediate release: initial 12.5 mg once daily at breakfast; titrated on clinical response and side effects; dose range: 6.25-50 mg/day	Hollander 2000		
Desvenlafaxine (Pristiq)	**OFF-LABEL USE (Not FDA Approved)** Not indicated under the age of 18, no off-label resources			N/A	√ PA QTY: 100mg/ day
Duloxetine (Cymbalta)	Generalized anxiety disorder	7-17 years: initial 30 mg once daily; after 2 weeks, may increase based on response and tolerability to 60 mg once daily Titrate doses >60 mg in increments of 30 mg once daily; maximum dose 120 mg/day	N/A	**Side effects:** Headache, nausea **Cautions:** Suicidal thinking/behavior, Serotonin syndrome, hepatotoxicity	QTY: 120mg/ day
Mirtazapine (Remeron)	**OFF-LABEL USE (Not FDA Approved)** Not indicated under the age of 18, no off-label resources			N/A	QTY: 60mg/ day

ANTIDEPRESSANT MEDICATIONS: CHILDREN AND ADOLESCENTS

Bupropion (Wellbutrin/ Forfivo XL/ Aplenzin)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** Agitation, constipation, dizziness, headache, insomnia, nausea, tachyarrhythmia, tremor, xerostomia **Cautions:** Cardiac dysrhythmia, mania, seizure, suicidal thoughts, wide QRS complex	QTY: ER/IR 450mg/ day
	ADHD	6 years and older: Immediate release: initial 3 mg/kg/day in 203 divided doses; maximum initial dose 150 mg/day; titrate dose as needed to a maximum dose of 6 mg/kg/day or 300 mg/day	Dopheide 2009 Pliszka 2007		
	Depression (refractory to SSRIs)	8-11 years old: Immediate release: initial 37.5 mg twice daily; titrate to response; recommended dose range: 100-400 mg/day	Dopheide 2006		
		12 years and older: 12-hour sustained release: initial 2 mg/kg up to 100 mg administered in the morning; titrate every 2-3 weeks: step 2- increase up to 3 mg/kg every morning, step 3- increased up to 3 mg/kg every morning and 2 mg/kg at 5pm, step 4- increase up to 3 mg/kg twice daily; maximum dose 150 mg	Daviss 2001		
		12 years and older: 24-hour extended release: initial 150 mg once daily; titrate after 2 weeks to 300 mg once daily if adequate response not achieved, maximum dose 400 mg/day	Daviss 2006 Dopheide 2006		
	Smoking Cessation	14 years and older AND ≥40.5 kg: 12-hour sustained release: initial 150 mg once daily for 3 days; increase to 150 mg twice daily; maximum dose: 300 mg/day (treatment should start while patient is still smoking)	Muramoto 2007		
Trazodone (Desyrel)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** drowsiness, dizziness, hypertension, nervousness, xerostomia, blurred vision **Cautions:** suicidal thinking, bleeding risk, cardiac arrhythmias, CNS depression, priapism, serotonin syndrome	QTY: 600mg/ day
	Insomnia	18 months to <3 years: Initial: 25 mg at bedtime; may increase dose based on response and tolerability at 2-week intervals in 25 mg increments up to 100 mg 3 to 5 years: Initial 50 mg at bedtime; may increase dose based on response and tolerability at 2-week intervals in 25 mg increments up to 150 mg >5 years and Adolescents: Initial: 0.75 to 1 mg/kg or 25 to 50 mg at bedtime; reported range: 0.5 to 2 mg/kg/day (do not exceed 200 mg/day)	Pranzatelli 2005 Hollway 2011 Kratochvil 2005		
Nefazodone (Serzone)	**OFF-LABEL USE (Not FDA Approved)** Not indicated under the age of 18, no off-label resources			N/A	

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Tricyclic Antidepressants					
Imipramine (Tofranil)	Enuresis	6 years and older: initial 10-25 mg 1 hour before bedtime; if inadequate response still seen after 1 week of therapy, increase by 25 mg daily; 6-12 years old: maximum dose 2.5 mg/kg/day or 50 mg at bedtime 13 years and older: maximum dose: 75 mg at bedtime	N/A	*Clinical trials have not shown TCAs to be superior to placebo for depression in children, may be beneficial for patient with comorbid conditions (ADHD, enuresis) Birmaher 2007 Dopheide 2006 Wagner 2005	
	Major depressive disorder	Adolescents: initial 30-40 mg/day; increase gradually; maximum 100 mg/day in single or divided doses	N/A		
	OFF-LABEL USE (Not FDA Approved)				
	ADHD	6 years and older: initial 1 mg/kg/day in 1-3 divided doses; titrate as needed; maximum daily dose: 4 mg/kg/day or 200 mg/day Doses >2 mg/kg/day: monitor serum concentrations	Himpel 2005 Pliszka 2007		
Amitriptyline (Elavil)	Depressive disorder	12 years and older: 10 mg three times daily and 20 mg at bedtime; maximum daily dose 200 mg/day Usual range: 30-100 mg at bedtime or in divided doses twice daily	N/A	**Side effects:** weight gain, constipation, xerostomia, dizziness, headache **Cautions:** Hepatotoxicity, arrhythmias	
	OFF-LABEL USE (Not FDA Approved)				
	Depressive disorder	9-12 years old: initial 1 mg/kg/day in 3 divided doses; after 3 days, dose may be increased to 1.5 mg/kg/day in 3 divided doses	Kashani 1984 Kliegman 2007		
	Chronic pain management	Initial 0.1 mg/kg at bedtime, may advance as tolerated over 2-3 weeks to 0.5-2 mg/kg at bedtime	APS 2008 Freidrichsdorf 2007 Kliegman 2011		
	Migraine prophylaxis	Initial 0.25 mg/kg/day at bedtime; increase dose by 0.25 mg/kg/day every 2 weeks to 1 mg/kg/day; dosing range: 0.2-1.7 mg/kg/day	Hershey 2000 Lewis 2004		
Desipramine (Norpramin)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** constipation, xerostomia, dizziness, somnolence, blurred vision, fatigue **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating)	
	Depression	6-12 years old: 1-3 mg/kg/day in divided doses; maximum daily dose 5 mg/kg/day Monitor carefully with doses >3 mg/kg/day 13 years and older: initial start at lower dosage level and increase based on tolerance and response; maximum dose of 150 mg daily; usual maintenance dose 25-100 mg once daily or in divided doses	Kliegman 2007		
	ADHD	**Weight-based dosing**: 5 years and older: initial 1.5 mg/kg/day divided twice daily; titrate weekly up to target dose of 3.5 mg/kg/day in 2 divided doses by week 3 **Fixed dose:** 7-13 years old: initial 25 mg at bedtime, increase at weekly intervals in 25 mg/day increments; maximum 100 mg/day (25 mg four time day) or 3 mg/kg/day	Spencer 1993 Spencer 1996 Spencer 2002 Singer 1995		

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Nortriptyline (Pamelor)	**OFF-LABEL USE (Not FDA Approved)**			*Should not be used first-line; use should be reserved for cases where other therapies have failed or not tolerated Pliszka 2007 Dopheide 2005 Analgesic effects of TCAs are typically observed at a lower dose compare to doses for depression	
	ADHD	6 years and older: initial 0.5 mg/kg/day, may increase by 0.5 mg/kg/day increments at weekly intervals; maximum daily dose 2 mg/kg/day up to 100 mg/day	Pliszka 2007 Prince 2000 Spencer 1996 Wilens 1993		
	Enuresis	6 years and older: initial 10-20 mg/day; titrate up to maximum daily dose of 40 mg/day Administer dose 30 minutes before bedtime, treatment duration ≤3 months	Deshpande 2012 Kliegman 2007		
	Depression	6-12 years old: 1-3 mg/kg/day in 4 divided doses; maximum daily dose 150 mg/day	Kliegman 2007		
		13 years and older: 30-50 mg/day in 3-4 divided doses or as a dingle daily dose; maximum daily dose 150 mg/day			
	Neuropathic pain	Usual range 0.05-1 mg/kg/dose at bedtime; begin at the lower end of dosing range and titrate every 3 days to effect; maximum daily dose 3 mg/kg/day or 150 mg/day	APS 2016 Kliegman 2011		
Clomipramine (Anafranil)	Obsessive-compulsive disorder	10 years and older: initial 25 mg daily; gradually increase as tolerated over the first 2 weeks to 3 mg/kg/day or 100 mg daily in divided doses (may be divided with meals); maintenance maximum daily dose 3 mg/kg/day or 200 mg/day (may give as a single once daily dose at bedtime)	N/A	**Side effects:** constipation, xerostomia, nausea, dizziness, somnolence, tremor, fatigue **Cautions:** Suicidal thinking/behavior, Serotonin syndrome (agitation, confusion, overheating)	
Doxepin (Sinequan)	**OFF-LABEL USE (Not FDA Approved)**			**Side effects:** Xerostomia, constipation, nausea **Cautions:** Cardiac dysrhythmia, hepatotoxicity, suicidal thoughts	
	Depression and/or anxiety	7-11 years: 1-3 mg/kg/day in single or divided doses 12 years and older: initial 25-75 mg/day at bedtime or in 2-3 divided doses; begin at the low end of range and gradually titrate; maximum single dose 150 mg; maximum daily dose 300 mg/day	Kliegman 2007		

Lexi-Comp Online, Pediatric Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc.; 2018; July 31, 2018

Additional References/Resources:

- **Pediatrics. 2018;141(3):e20174081**

  http://pediatrics.aappublications.org/content/141/3/e20174081

  Guidelines for Adolescent Depression in Primary Care (GLAD-PC): I. Practice Preparation, Identification, Assessment, and Initial Management

  Zuckerbrot RA, Cheung AH, Jensen PS, Stein REK, Laraque D; GLAD-PC Steering Group

- **Pediatrics. 2018;141(3):e20174082**

  http://pediatrics.aappublications.org/content/141/3/e20174082

  Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and Ongoing Management

  Cheung AH, Zuckerbrot RA, Jensen PS, Laraque D, Stein REK; GLAD-PC Steering Group

- **GLAD-PC Toolkit**

  http://www.gladpc.org/

  Guidelines for Adolescent Depression in Primary Care (GLAD-PC) Toolkit