



**Clinician Summary
Second Generation
Antidepressants
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Produced by:
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Category: Second Generation Antidepressants

Data reviewed through September 2010

Drug classes:

SSRIs: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline

SNRIs: desvenlafaxine, duloxetine, venlafaxine

Others: bupropion, mirtazapine, nefazodone, trazodone

Limitations of the evidence

1. Study duration were shorter (mostly 6-12 weeks) than the usual duration of treatment (9-12 months.)
2. High dropout rates.
3. No effectiveness studies
4. Depression in children is not as well studied as in adults.

Conclusions – Efficacy, Adults:

Good evidence: no significant difference in overall efficacy among second generation antidepressants in adults with major depressive disorder.

Fair evidence: Second generation antidepressants were no better than placebo for major depressive disorder in patients with comorbid conditions including methadone maintained opioid addiction, cocaine abuse, HIV, multiple sclerosis, arthritis, diabetes, cancer or substance abuse disorder.

Insufficient evidence: to determine a comparative difference in efficacy among the studied agents for dysthymia, generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, social anxiety disorder, premenstrual dysphoric disorder and late luteal phase dysphoric disorder.

Conclusions – Efficacy, children and adolescents

Good evidence: Citalopram and fluoxetine are the only two agents studied shown to be better than placebo. Sertraline, venlafaxine, and paroxetine were shown to be no better than placebo.

Good evidence: In patients ≤ 18 years the risk of self-harm increased with SSRIs vs TCAs. There were no statistically significant differences among SSRIs.

Good evidence: A systematic review of published and unpublished data suggests that only fluoxetine has a favorable risk/benefit profile in pediatric populations.

Fair Evidence: , Second generation antidepressants were no better than placebo for comorbid alcohol use disorder in adolescents

Adverse effects:

Black box warning:

1. Nefazodone and active liver disease.
2. All included drugs carry a black box warning regarding suicidality

Good evidence: The risk of suicidality is not increased in adult patients \geq age 18.

Good evidence: Higher rate of nausea and vomiting with venlafaxine.

Good evidence: Higher rate of discontinuation with venlafaxine and duloxetine

Fair evidence: Sexual side effects:

Higher risk: paroxetine, sertraline and mirtazapine.

Lower risk: bupropion and nefazodone

Fair evidence: Greater weight gain with mirtazapine and paroxetine than with sertraline and fluoxetine.

Conclusions – Subgroups

Fair evidence: A retrospective cohort study of women ≥ 66 y.o. with breast cancer shows that use of paroxetine increased the risk of death from breast cancer among women taking tamoxifen. There is insufficient data to assess the risk for other medications in this class.

Insufficient evidence: to determine a comparative difference among agents in this class based on subpopulations of age, comorbidities, ethnicity or gender.

Good evidence: A large meta-analysis of paroxetine vs. placebo suggests that the response rate is lower in Hispanic and Asian populations compared to White and Black populations for major depressive disorders in adults, anxiety disorders, and post menstrual dysphoric disorder.

Table 1. Second-generation antidepressants approved for use in the United States

Class	Generic Name	US Trade Name ^a	Dosage Forms	Labeled Uses
Selective Serotonin Reuptake Inhibitors (SSRI)	Citalopram ^b	Celexa®	10, 20, 40mg tabs; 1, 2 mg/ml solution	MDD (adult)
	Escitalopram	Lexapro®	10, 20 mg tabs 1 mg/ml solution	MDD (adult/ <u>adolescents</u>); GAD ^e
	Fluoxetine ^b	Prozac®; Prozac Weekly®; Sarafem®	10, 20, 40mg caps; 10 mg tabs; 4 mg/ml solution; 90 mg pellets (weekly)	MDD (adult/ped); OCD; PMDD; Panic disorder
	Fluvoxamine ^b	Luvox® Luvox CR®	25, 50, 100 mg tabs	OCD Social anxiety disorder
	Paroxetine ^b	Paxil®; Paxil CR®	10, 20, 30, 40 mg tabs; 2 mg/ml solution; 12.5, 25, 37.5 mg CR tabs	MDD (adult); OCD ^c ; Panic disorder; Social anxiety disorder; GAD ^c ; PTSD ^c ; PMDD ^d
	Sertraline	Zoloft®	25, 50, 100 mg tabs; 20 mg/ml solution	MDD (adult); OCD; Panic disorder; PTSD; PMDD; Social anxiety disorder
Selective Serotonin and Norepinephrine Reuptake Inhibitor (SSNRI)	Duloxetine	Cymbalta®	20, 30, 60 mg caps	MDD (adult) DPNP GAD
Serotonin and Norepinephrine Reuptake Inhibitors (SNRI)	Desvenlafaxine	Pristiq®	50, 100 mg tabs	MDD (adult)
	Venlafaxine	Effexor®; Effexor XR®	25, 37.5, 50, 75, 100 mg tabs; 37.5, 75, 150 mg XR caps	MDD (adult); GAD ^a ; Panic disorder; Social anxiety disorder ^a
Other second-generation antidepressants	Bupropion ^b	Wellbutrin®; Wellbutrin SR®; Wellbutrin XL®;	75, 100 mg tabs; 50, 100, 150, 200 mg SR tabs 150, 300 mg XL tabs	MDD (adult) Seasonal affective disorder
	Mirtazapine ^b	Remeron®	15, 30, 45 mg tabs; 15, 30, 45 mg orally disintegrating tabs	MDD (adult)
	Nefazodone ^b	Serzone®	50, 100, 150, 200, 250 mg tabs	MDD (adult)

^a CR, SR, XL, and XR are registered trademarks referring to controlled, sustained, or extended-release dosage forms

GAD, generalized anxiety disorder; MDD, major depressive disorder; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; PMDD, premenstrual dysphoric disorder; DPNP, diabetic peripheral neuropathic pain

^b Generic available for some dosage forms.

^c Only Paxil CR® (not Paxil®) is approved for the treatment of PMDD.

^d Only Effexor XR® is approved for the treatment of GAD and Social Anxiety Disorder

^e Lexapro was denied approval for social anxiety disorder 3/30/2005