

Second Generation Antidepressants

Key Questions and Inclusion Criteria

Update # 4

Key Questions

1. For outpatients with depressive, anxiety, and/or premenstrual dysphoric disorders, do second-generation antidepressants differ in efficacy or effectiveness?
2. For outpatients with depressive, anxiety, and/or premenstrual dysphoric disorders, do second-generation antidepressants differ in safety or adverse events?
3. Are there subgroups of patients based on demographics (age, racial groups, and sex), other medications, or comorbidities for which one second-generation antidepressant is more effective or associated with fewer adverse events than another?

Inclusion Criteria

Populations

1. Adult outpatient populations with one of the following indications (as diagnosed by validated DSM-III-R or DSM-IV screening instruments):
 - Depressive Disorders (Major Depressive Disorder, Dysthymia, other depressive disorders such as minor depression, recurrent brief depressive disorder, and seasonal affective disorder)
 - Anxiety Disorders
 - Generalized Anxiety Disorder (GAD)
 - Obsessive Compulsive Disorder (OCD)
 - Panic Disorder
 - Post-Traumatic Stress Disorder (PTSD)
 - Social Anxiety Disorder
 - Premenstrual Dysphoric Disorder (PMDD) (DSM-IV) or Late Luteal Phase Dysphoric Disorder (LLPDD) (DSM-III-R)
2. Pediatric (age < 18) outpatient populations with Major Depressive Disorder (MDD) (*see *Study Designs* section below)

Interventions

Classification	Generic Name	Trade Name
Selective serotonin reuptake inhibitor (SSRI)	Fluoxetine	Prozac (various generics) Prozac Weekly (not available in Canada) Sarafem (not available in Canada)
	Sertraline	Zoloft (various generics)
	Paroxetine	Paxil (various generics) Paxil CR
	Citalopram	Celexa (various generics)
	Escitalopram	Lexapro, CipraleX (Canadian trade name)
	Fluvoxamine	Luvox (various generics)
Serotonin norepinephrine reuptake inhibitor (SNRI)	Venlafaxine	Effexor Effexor XR
Noradrenergic and specific serotonergic reuptake inhibitor (NaSSA)	Mirtazapine	Remeron (various generics), Remeron RD (orally disintegrating tablet available in Canada)
Selective serotonin and norepinephrine reuptake inhibitor (SSNRI)	Duloxetine	Cymbalta (not available in Canada)
Norepinephrine and dopamine reuptake inhibitor (NDRI)	Bupropion	Wellbutrin (no longer available in Canada) Wellbutrin SR (one generic SR available) Wellbutrin XL
5-HT ₂ receptor antagonist (5-HT ₂)	Nefazodone	Serzone (not available in Canada)

Efficacy/ Effectiveness outcomes

- Response
- Remission
- Speed and duration of response/remission
- Relapse (on and off treatment)
- Recurrence
- Functional capacity (quality of life, work productivity)
- Hospitalization

Safety outcomes

- Overall adverse effect reports
- Withdrawals due to adverse effects
- Serious adverse events reported
- Danger to self (suicide attempts and completions)
- Specific adverse effects or withdrawals due to specific adverse events (e.g., hyponatremia, activation of mania/hypomania, seizures, suicide, hepatotoxicity, weight gain, GI symptoms, loss of libido, etc.)
- Mortality

Study designs

1. For effectiveness, controlled clinical trials.
2. For safety, in addition to controlled clinical trials, observational studies will be included.
3. For effectiveness and safety in the pediatric population, good-quality systematic reviews